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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/205,400	03/18/2021	Michael Ragusa	130670-80104	4686

86738 7590 01/07/2025

MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

EXAMINER	
DEAK, LESLIE R	

ART UNIT	PAPER NUMBER
3799	

NOTIFICATION DATE	DELIVERY MODE
01/07/2025	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@mccarter.com

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0001

APPLICATION NO.	ISSUE DATE	PATENT NO.
17/205,400	07-Jan-2025	12186474

MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

EGRANT NOTIFICATION

Your electronic patent grant (eGrant) is now available, which can be accessed via Patent Center at https://patentcenter.uspto.gov

The electronic patent grant is the official patent grant under 35 U.S.C. 153. For more information, please visit https://www.uspto.gov/electronicgrants

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0002

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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/205,400	01/07/2025	12186474	130670-80104	4686

86738 7590 12/18/2024

MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at https://patentcenter.uspto.gov/. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

The USPTO is implementing electronic patent issuance with a transition period, during which period the USPTO will mail a ceremonial paper copy of the electronic patent grant to the correspondence address of record. Additional copies of the patent (i.e., certified and presentation copies) may be ordered for a fee from the USPTO's Certified Copy Center at https://certifiedcopycenter.uspto.gov/index.html. The Certified Copy Center may be reached at (800)972-6382.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 966 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Center (https://patentcenter.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0003

INVENTOR(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional inventors):

Michael Ragusa, Hingham, MA;

APPLICANT(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional applicants):

Haemonetics Corporation, Boston, MA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0004

UNITED STATES
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P.O. Box 1450
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ISSUE FEE TRANSMITTAL FORM

APPLICATION #	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET #
17205400	**03/18/2021**	**Michael Ragusa**	**130670-80104**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

Application Information

APPLICATION TYPE	Nonprovisional Application under 35 USC 111(a)	**DATE DUE**	12/05/2024
CONFIRMATION #	4686	**ISSUE FEE DUE**	$ 1200
EXAMINER	LESLIE DEAK	**PUBLICATION DUE**	$ 0
GROUP ART UNIT	3799	**TOTAL FEES DUE**	$1200
CLASS - SUBCLASS	604/006040	**PREV. PAID FEE**	$ 0
ENTITY STATUS	Regular Undiscounted		

1. CHANGE OF CORRESPONDENCE ADDRESS AND/OR INDICATION OF FEE ADDRESS (37 CFR 1.33 & 1.363)

Correspondence Address

CURRENT ADDRESS

Maintenance Fee Address

CURRENT ADDRESS

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0005

☐ Change of correspondence address requested,system generated AIA/122-PC form attached

☐ Fee address indication requested, system generatedSB/47-PC form attached

2. ENTITY STATUS

Change in Entity Status

NEW STATUS

3. THE FOLLOWING FEES ARE SUBMITTED

☑ Issue Fee

☑ Publication Fee

4. FEE AUTHORIZATION

☐ I authorize USPTO to apply my previously paid issue fee to the current fees due

☐ The Director is herby authorized to apply my previously paid issue fee to the current fee due and to charge deficient fees to Deposit Account Number:

☑ If in addition to the payment of the issue fee amount submitted with this form, there are any discrepencies in any amount(s) due, the Director is authorized to charge any deficiency, or credit any overpayment, to Deposit Account Number: 504876

5. FIRM AND/OR ATTORNEY NAMES TO BE PRINTED

NOTE: If no name is listed, no name will be printed
For printing on the patent front page, list to be displayed as entered

McCarter & English, LLP
Jonathan C. Lovely

6. ASSIGNEE NAME(S) AND RESIDENCE DATA TO BE PRINTED

NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a susbstitute for filing an assignment.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0006

Haemonetics Corporation	Boston, MA UNITED STATES	Corporation

Signature

I certify, in accordance with 37 CFR 1.4(d)(4) that I am an attorney or agent registered to practice before the Patent and Trademark Office who has filed and has been granted power of attorney in this application. I also certify that this Fee(s) Transmittal form is being transmitted to the USPTO via Patent Center on the date indicated below.

Signature	Name	Registration #	Date
/Jonathan Lovely/	Jonathan Lovely	60821	12/03/2024

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0007

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www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/205,400	**12/03/2024 01:23:38 PM Z ET**	**130670-80104**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	4686	FILED BY	Jonathan Lovely
PATENT CENTER #	68184466	FILING DATE	03/18/2021
CUSTOMER #	86738	FIRST NAMED INVENTOR	Michael Ragusa
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
web85b.pdf	3	Issue Fee Payment (PTO-85B)	58 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
web85b.pdf	8FD7783DCC3968952F078E3A7FE4378A973AF8BDF456E3626 1FD03D3E76849218E7D7437F14A9D8501556DCD97679C8B78 6D820E57904E647FF2E2AC73243086

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/205,400	**12/03/2024 01:23:38 PM Z ET**	**130670-80104**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	4686	FILED BY	Jonathan Lovely
PATENT CENTER #	68184466	AUTHORIZED BY	-
CUSTOMER #	86738	FILING DATE	03/18/2021
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Michael Ragusa

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 504876	**E2024B3D24105219**	**Jonathan Lovely**

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
1501	UTILITY ISSUE FEE	1200.00	1	1200.00
			TOTAL AMOUNT:	**$1,200.00**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

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If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0010

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Haemonetics Corporation

Application No.: 17/205,400 Confirmation No.: 4686

Filed: March 18, 2021 Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING PLASMA Examiner: L. R. Deak

COMMENTS ON STATEMENT OF REASONS

FOR ALLOWANCE

MS Issue Fee
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Madam:

In response to the Examiner's statement of reasons for allowance contained in the Notice of Allowance mailed on September 5, 2024, please enter the following Comments. In accordance with MPEP 1302.14, these comments are submitted with the Issue Fee Transmittal.

Applicant believes that the claims of the present application are in condition for allowance. The Examiner's Statement of Reasons for Allowance, however, states that "…the prior art fails to disclose a method of collecting blood plasma wherein a volume of anticoagulant in the collected plasma component is calculated in real time, as the plasma is being collected (such as by counting anticoagulant pump revolutions)…" While the prior art fails to teach or suggest this limitation, the present claims do not include such a limitation and do not require real time calculation of the volume of anticoagulant in the collected plasma component.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 50-4876, under Order No. 130670-80104.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0012

Dated: December 3, 2024

Respectfully submitted,

Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6500
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0013

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/205,400	**12/03/2024 01:18:57 PM Z ET**	**130670-80104**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	4686	FILED BY	Tricia Troup
PATENT CENTER #	68187451	FILING DATE	03/18/2021
CUSTOMER #	86738	FIRST NAMED INVENTOR	Michael Ragusa
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Jonathan Lovely

Documents

TOTAL DOCUMENTS: 1

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
Comments on Statement of Reasons for Allowance_130670-80104.pdf	2	Post Allowance Communication - Incoming	20 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
Comments on Statement of Reasons for Allowance_130670-80104.pdf	87739CC98EA65D5B3AE73116A711EC7244EA0560B7EFADDF7178427690A028959269BDB57846CC8A8AAD7D4CF8B98756CE7768864D309069C2757242ADF93A3D

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as

described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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NOTICE OF ALLOWANCE AND FEE(S) DUE

86738 7590 09/05/2024
MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

EXAMINER	
DEAK, LESLIE R	
ART UNIT	PAPER NUMBER
3799	

DATE MAILED: 09/05/2024

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/205,400	03/18/2021	Michael Ragusa	130670-80104	4686

TITLE OF INVENTION: SYSTEM AND METHOD FOR COLLECTING PLASMA

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	12/05/2024

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0016

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

86738 7590 09/05/2024

MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/205,400	03/18/2021	Michael Ragusa	130670-80104	4686

TITLE OF INVENTION: SYSTEM AND METHOD FOR COLLECTING PLASMA

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	12/05/2024

EXAMINER	ART UNIT	CLASS-SUBCLASS
DEAK, LESLIE R	3799	604-006040

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. Fees submitted: ❑ Issue Fee ❑ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via the USPTO patent electronic filing system ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

❑ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

❑ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0017

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/205,400	03/18/2021	Michael Ragusa	130670-80104	4686

86738 7590 09/05/2024

MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

EXAMINER	
DEAK, LESLIE R	
ART UNIT	PAPER NUMBER
3799	

DATE MAILED: 09/05/2024

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0018

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/ owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).
https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf

Routine uses of the information in this record may include disclosure to:

1) law enforcement, in the event that the system of records indicates a violation or potential violation of law;
2) a federal, state, local, or international agency, in response to its request;
3) a contractor of the USPTO having need for the information in order to perform a contract;
4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record;
5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;
6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;
7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;
8) another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c));
9) the Office of Personnel Management (OPM) for personnel research purposes; and
10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Notice of Allowability	Application No. 17/205,400	Applicant(s) Ragusa, Michael	
	Examiner LESLIE R DEAK	Art Unit 3799	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to TD and amendments filed 6 August 2024.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 1-4 and 6-27 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information , please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☐ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/LESLIE R DEAK/
Primary Examiner, Art Unit 3799

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0020

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Terminal Disclaimer

2. The terminal disclaimer filed on 6 August 2024 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of **US 10,758,652 and US 10,980,926** has been reviewed and is accepted. The terminal disclaimer has been recorded.

Allowable Subject Matter

3. Claims 1-4, 6-27 are allowed.

4. The following is an examiner's statement of reasons for allowance: The prior art fails to disclose or suggest the method and system as claimed by Applicant. In particular, the prior art fails to disclose a method of collecting blood plasma wherein a volume of anticoagulant in the collected plasma component is calculated in real time, as the plasma is being collected (such as by counting anticoagulant pump revolutions), along with the other steps and limitations of the claims. The prior art systems rely on calculations prepared in advance.

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE R DEAK whose telephone number is (571)272-4943. The examiner can normally be reached Monday-Friday, 9am to 5:30pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tom Sweet can be reached on 571-272-4761. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LESLIE R DEAK/
Primary Examiner, Art Unit 3799
27 August 2024

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/205,400	Ragusa, Michael
	Examiner	**Art Unit**
	LESLIE R DEAK	3799

CPC - Searched*		
Symbol	**Date**	**Examiner**
(A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC.	10/28/2019	LRD
A61M1/029 A61M1/3672 A61M1/3693 A61M1/38 A61M2202/0415 A61M2230/207	11/05/2020	LRD

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
inventor name search, EAST BRS search, consulted foreign search report	10/28/2019	LRD
updated prior searches, consulted primary examiners	02/27/2020	LRD
updated prior searches	05/05/2020	LRD
consulted parent case, updated searches, ODP	11/06/2020	LRD
consulted parent cases, updated searches, ODP	04/30/2024	LRD
updated prior searches	08/27/2024	LRD

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/205,400	Ragusa, Michael
	Examiner	**Art Unit**
	LESLIE R DEAK	3799

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
	"current value of the hematocrit of the donor".clm.	08/27/2024	LRD

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/205,400	Ragusa, Michael
	Examiner	**Art Unit**
	LESLIE R DEAK	3799

CPC						
Symbol					**Type**	**Version**
A61M	/	1	/	38	F	2013-01-01
A61M	/	1	/	385	I	2013-01-01
A61M	/	1	/	3644	I	2014-02-04
A61M	/	1	/	3672	A	2013-01-01
A61M	/	1	/	3693	A	2013-01-01
A61M	/	2202	/	0415	A	2013-01-01
A61M	/	1	/	3496	A	2013-01-01
A61M	/	2205	/	3379	A	2013-01-01
A61M	/	2205	/	3393	A	2013-01-01
A61M	/	2205	/	3306	A	2013-01-01
A61M	/	1	/	3626	A	2013-01-01
A61M	/	2230	/	207	A	2013-01-01

CPC Combination Sets								
Symbol					**Type**	**Set**	**Ranking**	**Version**
	/		/					

Use images from artifact folder? (•) Yes ( ) No

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 26	
/LESLIE R DEAK/ Primary Examiner, Art Unit 3799 (Primary Examiner)	27 August 2024 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 4

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0025

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/205,400	Ragusa, Michael
	Examiner	**Art Unit**
	LESLIE R DEAK	3799

INTERNATIONAL CLASSIFICATION				
CLAIMED				
A61M1/38	/	1	/	38
A61M1/36	/	1	/	36
A61M1/34	/	1	/	34

NON-CLAIMED				
	/		/	

US ORIGINAL CLASSIFICATION	
CLASS	**SUBCLASS**

CROSS REFERENCES(S)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**					

Use images from artifact folder? (•) Yes ( ) No

NONE (Assistant Examiner)	(Date)	**Total Claims Allowed:** 26	
/LESLIE R DEAK/ Primary Examiner, Art Unit 3799 (Primary Examiner)	27 August 2024 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 4

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0026

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/205,400	Ragusa, Michael
	Examiner	**Art Unit**
	LESLIE R DEAK	3799

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☑ T.D. ☐ R.1.47

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1	10	11	19	20										
2	2	11	12	20	21										
3	3	12	13	21	22										
4	4	13	14	22	23										
5	6	14	15	23	24										
6	7	15	16	24	25										
7	8	16	17	25	26										
8	9	17	18	26	27										
9	10	18	19												

Use images from artifact folder? ◉ Yes ○ No

NONE		**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	26	
/LESLIE R DEAK/ Primary Examiner, Art Unit 3799	27 August 2024	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	4

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0027

Bibliographic Data

Application No: 17/205,400

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☑ No ☐ Met After Allowance

Verified and Acknowledged: /LESLIE R DEAK/ Examiner's Signature | Initials

Title: SYSTEM AND METHOD FOR COLLECTING PLASMA

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
03/18/2021	604	3799	
RULE			

APPLICANTS

Haemonetics Corporation, Boston, MA,

INVENTORS

Michael Ragusa, Hingham, MA, UNITED STATES

CONTINUING DATA

This application is a CON of 16931333 07/16/2020 PAT 10980934

16931333 is a CON of 15793339 10/25/2017 PAT 10792416

15793339 is a CIP of 15608183 05/30/2017 PAT 10758652

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

03/29/2021

STATE OR COUNTRY

UNITED STATES

ADDRESS

FILING FEE RECEIVED

$3,000

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2019/10/28 11:36 AM
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Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0029

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Terumo v. Haemonetics - PGR2026-00063
Petitioner Terumo Exhibit 1014-0030

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Terumo v. Haemonetics - PGR2026-00060
Petitioner Terumo Exhibit 1014-0032

		| "3456875" | "3489145" | "3565330" | "3655058" | "3737096" | "3774840" | "3987961" | "4007871" | "4010894" | "4014497" | "4040965" | "4056224" | "4082217" | "4086924" | "4140268" | "4142670" | "4151844" | "4197847" | "4285464" | "4300717" | "4303193" | "4321921" | "4387848" | "4425114" | "4430072" | "4447221" | "4457747" | "4464167" | "4466888" | "4482342" | "4490135" | "4530691" | "4534863" | "4643714" | "4647279" | "4655742" | "4680025" | "4684361" | "4692136" | "4708712" | "4713176" | "4734089" | "4740202" | "4740313" | "4755300" | "4767396" | "4795419" | "4795448" | "4806247" | "4806252" | "4808307" | "4850995" | "4869812" | "4871462" | "4876013" | "4889524" | "4911833" | "4934995" | "4940543" | "4943273" | "4968295" | "4983156" | "4983158" | "4985153" | "4994188" | "5039401" | "5045048" | "5098372" | "5098373" | "5100372" | "5100564" | "5112298" | "5114396" | "5135667" | "5141486" | "5147290" | "5154716" | "5174894" | "5194145" | "5217426" | "5217427" | "5234403" | "5254248" | "5273517" | "5277701" | "5298016" | "5298171" | "5300060" | "5316540" | "5318511" | "5318512" | "5348533" | "5368542" | "5368555" | "5386734" | "5387174" | "5387187" | "5403272" | "5405308" | "5417650" | "5431814" | "5437598" | "5437624" | "5462667" | "5470483" | "5484396" | "5494592" | "5505685" | "5514070" | "5543062" | "5551941" | "5585007" | "5607579" | "5649903" | "5651766" | "5656163"				

		| "5665061" | "5712798" | "5728060" | "5733253" | "5733446" | "5733545" | "5738792" | "5762791" | "5779660" | "5783085" | "5792351" | "5849203" | "5882289" | "5906589" | "5919125" | "5964724" | "5970432" | "5980760" | "6007725" | "6059979" | "6207063" | "6234989" | "6296602" | "6464624" | "6497676" | "6558307" | "6623443" | "6743192" | "7115205" | "7186231" | "7270645" | "7704454" | "8628489" | "8702637" | "8759094" | "9283316" | "10758652" | "20010000185" | "20010027156" | "20020043492" | "20020062100" | "20020120227" | "20030055375" | "20030066807" | "20030125881" | "20030175150" | "20040186409" | "20050209522" | "20050235733" | "20060058167" | "20060155236" | "20070112289" | "20080146993" | "20120175313" | "20140039373" | "20140356851" | "20180344910" | "20180344921").pn. AND (PGPB | USPT | USOC).dbnm.					
L36	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L37	11	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415 and A61M2230/207).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L38	11	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM

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Petitioner Terumo Exhibit 1014-0034

L39	53	((A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L40	7	"20120175313"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L41	7	"20030125881"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L42	43	2009/0215602	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L43	13	"20090215602"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L44	2	L1 AND ((A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L45	12466	((A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L46	2470	L10 and hematocrit	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L47	7	"I11" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L48	6	"I10" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L49	16	"I10" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L50	59	((("RAGUSA") near3 ("Michael"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L51	11	"I15" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L52	183	("20010000185"|"20020062100"|"1025059"|"1611725"|"20010027156"|"20020043492"|"20020120227"|"20030055375	(US-PGPUB; USPAT)	OR	OFF	OFF	2024/04/30 04:36 PM

Terumo v. Haemonetics - PGR2026-00067
Petitioner Terumo Exhibit 1014-0035

		"|"20030066807"|"2003 0125881"|"2003017515 0"|"20040186409"|"200 50209522"|"200502357 33"|"20060058167"|"20 060155236"|"20070112 289"|"20080146993"|"2 0120175313"|"2014003 9373"|"20140356851"|" 20180344921"|"208777 8"|"2661150"|"2750107" |"2792172"|"3096283"|" 3145713"|"3239136"|"3 244362"|"3244363"|"34 09213"|"3456875"|"348 9145"|"3565330"|"3655 058"|"3737096"|"37748 40"|"3987961"|"400787 1"|"4010894"|"4014497" |"4040965"|"4056224"|" 4082217"|"4086924"|"4 140268"|"4142670"|"41 51844"|"4197847"|"428 5464"|"4300717"|"4303 193"|"4321921"|"43878 48"|"4425114"|"443007 2"|"4447221"|"4457747" |"4464167"|"4466888"|" 4482342"|"4490135"|"4 530691"|"4534863"|"46 43714"|"4647279"|"465 5742"|"4680025"|"4684 361"|"4692136"|"47087 12"|"4713176"|"473408 9"|"4740202"|"4740313" |"4755300"|"4767396"|" 4795419"|"4795448"|"4 806247"|"4806252"|"48 08307"|"4850995"|"486 9812"|"4871462"|"4876 013"|"4889524"|"49118 33"|"4934995"|"494054 3"|"4943273"|"4968295" |"4983156"|"4983158"|" 4985153"|"4994188"|"5 039401"|"5045048"|"50 98372"|"5098373"|"510 0372"|"5100564"|"5112 298"|"5114396"|"51356 67"|"5141486"|"514729 0"|"5154716"|"5174894" |"5194145"|"5217426"|" 5217427"|"5234403"|"5 254248"|"5273517"|"52 77701"|"5298016"|"529 8171"|"5300060"|"5316 540"|"5318511"|"53185 12"|"5348533"|"536854				

		2"|"5368555"|"5386734"|"5387174"|"5387187"|"5403272"|"5405308"|"5417650"|"5431814"|"5437598"|"5437624"|"5462667"|"5470483"|"5484396"|"5494592"|"5505685"|"5514070"|"5543062"|"5551941"|"5585007"|"5607579"|"5649903"|"5651766"|"5656163"|"5665061"|"5712798"|"5728060"|"5733253"|"5733446"|"5733545"|"5738792"|"5762791"|"5779660"|"5783085"|"5792351"|"5849203"|"5882289"|"5906589"|"5919125"|"5964724"|"5970432"|"5980760"|"6007725"|"6059979"|"6207063"|"6234989"|"6296602"|"6464624"|"6497676"|"6558307"|"6623443"|"6743192"|"7115205"|"7186231"|"7270645"|"7704454"|"8628489"|"8702637"|"8759094").PN.				
L53	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L54	11	"l15" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L55	1	("10758652").PN.	(USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L56	0	("20120175313").PN.	(USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L57	5	"20120175313"	(USPAT)	OR	OFF	OFF	2024/04/30 04:36 PM
L58	13	("4713176" | "6348156" | "6875191" | "7011761" | "7087177" | "7297272" | "7708710" | "8075468").PN. OR ("8852140").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L59	9	L23 and prim$3	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L60	0	(10/302682).APP.	(USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L61	2	"20140100507"	(USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L62	190	A61M1/024.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L63	987	G01n15/05.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM

Terumo v. Haemonetics - PGR2026-00009
Petitioner Terumo Exhibit 1014-0037

L64	220	G01n2015/055.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L65	3	((US-20030125881-A1).did. AND PGPB.dbnm.) OR ((US-10758652-B2 OR US-6348156-B1).did. AND USPT.dbnm.)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/04/30 04:36 PM
L66	0	L30 AND touchscreen	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/04/30 04:36 PM
L67	0	touchscreen WITH plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L68	4	touchscreen SAME plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L69	16	"10980926"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)	OR	ON	ON	2024/04/30 04:36 PM
L70	200	("1025059" | "1611725" | "2087778" | "2661150" | "2750107" | "2792172" | "3096283" | "3145713" | "3239136" | "3244362" | "3244363" | "3409213" | "3456875" | "3489145" | "3565330" | "3655058" | "3737096" | "3774840" | "3987961" | "4007871" | "4010894" | "4014497" | "4040965" | "4056224" | "4082217" | "4086924" | "4140268" | "4142670" | "4151844" | "4197847" | "4285464" | "4300717" | "4303193" | "4321921" | "4387848" | "4425114" | "4430072" | "4447221" | "4457747" | "4464167" | "4466888" | "4482342" | "4490135" | "4530691" | "4534863" | "4643714" | "4647279" | "4655742" | "4680025" | "4684361" | "4692136" | "4708712" | "4713176" | "4734089"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2024/04/30 04:36 PM

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0038

		| "4740202" | "4740313" | "4755300" | "4767396" | "4795419" | "4795448" | "4806247" | "4806252" | "4808307" | "4850995" | "4869812" | "4871462" | "4876013" | "4889524" | "4911833" | "4934995" | "4940543" | "4943273" | "4968295" | "4983156" | "4983158" | "4985153" | "4994188" | "5039401" | "5045048" | "5098372" | "5098373" | "5100372" | "5100564" | "5112298" | "5114396" | "5135667" | "5141486" | "5147290" | "5154716" | "5174894" | "5194145" | "5217426" | "5217427" | "5234403" | "5254248" | "5273517" | "5277701" | "5298016" | "5298171" | "5300060" | "5316540" | "5318511" | "5318512" | "5348533" | "5368542" | "5368555" | "5386734" | "5387174" | "5387187" | "5403272" | "5405308" | "5417650" | "5431814" | "5437598" | "5437624" | "5462667" | "5470483" | "5484396" | "5494592" | "5505685" | "5514070" | "5543062" | "5551941" | "5585007" | "5607579" | "5649903" | "5651766" | "5656163" | "5665061" | "5712798" | "5728060" | "5733253" | "5733446" | "5733545" | "5738792" | "5762791" | "5779660" | "5783085" | "5792351" | "5849203" | "5882289" | "5906589" | "5919125" | "5964724" | "5970432" | "5980760" | "6007725" | "6059979" | "6207063" | "6234989" | "6296602" | "6464624" | "6497676" | "6558307" | "6623443" | "6743192" | "7115205" | "7186231" | "7270645" | "7704454" | "8628489" | "8702637" | "8759094" | "9283316" | "10758652" | "20010000185" | "20010027156" |				

		"20020043492" | "20020062100" | "20020120227" | "20030055375" | "20030066807" | "20030125881" | "20030175150" | "20040186409" | "20050209522" | "20050235733" | "20060058167" | "20060155236" | "20070112289" | "20080146993" | "20120175313" | "20140039373" | "20140356851" | "20180344910" | "20180344921").pn. AND (PGPB | USPT | USOC).dbnm.					
L71	0	"current value of the hematocrit of the donor".clm.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)	OR	ON	ON	2024/08/27 02:18 PM
L72	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L73	11	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415 and A61M2230/207).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L74	11	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L75	53	((A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L76	8	"20120175313"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L77	9	"20030125881"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L78	44	2009/0215602	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L79	15	"20090215602"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0040

L80	2	L1 AND ((A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L81	12693	((A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L82	2513	L10 and hematocrit	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L83	7	"I11" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L84	6	"I10" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L85	16	"I10" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L86	60	((("RAGUSA") near3 ("Michael"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L87	11	"I15" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L88	183	("20010000185"|"20020062100"|"1025059"|"1611725"|"20010027156"|"20020043492"|"20020120227"|"20030055375"|"20030066807"|"20030125881"|"20030175150"|"20040186409"|"20050209522"|"20050235733"|"20060058167"|"20060155236"|"20070112289"|"20080146993"|"20120175313"|"20140039373"|"20140356851"|"20180344921"|"2087778"|"2661150"|"2750107"|"2792172"|"3096283"|"3145713"|"3239136"|"3244362"|"3244363"|"3409213"|"3456875"|"348	(US-PGPUB; USPAT)	OR	OFF	OFF	2024/08/27 02:19 PM

		9145"|"3565330"|"3655 058"|"3737096"|"37748 40"|"3987961"|"400787 1"|"4010894"|"4014497" |"4040965"|"4056224"|" 4082217"|"4086924"|"4 140268"|"4142670"|"41 51844"|"4197847"|"428 5464"|"4300717"|"4303 193"|"4321921"|"43878 48"|"4425114"|"443007 2"|"4447221"|"4457747" |"4464167"|"4466888"|" 4482342"|"4490135"|"4 530691"|"4534863"|"46 43714"|"4647279"|"465 5742"|"4680025"|"4684 361"|"4692136"|"47087 12"|"4713176"|"473408 9"|"4740202"|"4740313" |"4755300"|"4767396"|" 4795419"|"4795448"|"4 806247"|"4806252"|"48 08307"|"4850995"|"486 9812"|"4871462"|"4876 013"|"4889524"|"49118 33"|"4934995"|"494054 3"|"4943273"|"4968295" |"4983156"|"4983158"|" 4985153"|"4994188"|"5 039401"|"5045048"|"50 98372"|"5098373"|"510 0372"|"5100564"|"5112 298"|"5114396"|"51356 67"|"5141486"|"514729 0"|"5154716"|"5174894" |"5194145"|"5217426"|" 5217427"|"5234403"|"5 254248"|"5273517"|"52 77701"|"5298016"|"529 8171"|"5300060"|"5316 540"|"5318511"|"53185 12"|"5348533"|"536854 2"|"5368555"|"5386734" |"5387174"|"5387187"|" 5403272"|"5405308"|"5 417650"|"5431814"|"54 37598"|"5437624"|"546 2667"|"5470483"|"5484 396"|"5494592"|"55056 85"|"5514070"|"554306 2"|"5551941"|"5585007" |"5607579"|"5649903"|" 5651766"|"5656163"|"5 665061"|"5712798"|"57 28060"|"5733253"|"573 3446"|"5733545"|"5738 792"|"5762791"|"57796					

		60"|"5783085"|"5792351"|"5849203"|"5882289"|"5906589"|"5919125"|"5964724"|"5970432"|"5980760"|"6007725"|"6059979"|"6207063"|"6234989"|"6296602"|"6464624"|"6497676"|"6558307"|"6623443"|"6743192"|"7115205"|"7186231"|"7270645"|"7704454"|"8628489"|"8702637"|"8759094").PN.					
L89	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L90	11	"I15" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L91	1	("10758652").PN.	(USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L92	0	("20120175313").PN.	(USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L93	6	"20120175313"	(USPAT)	OR	OFF	OFF	2024/08/27 02:19 PM
L94	14	("4713176" | "6348156" | "6875191" | "7011761" | "7087177" | "7297272" | "7708710" | "8075468").PN. OR ("8852140").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L95	9	L23 and prim$3	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L96	0	(10/302682).APP.	(USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L97	2	"20140100507"	(USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L98	195	A61M1/024.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L99	996	G01n15/05.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L100	225	G01n2015/055.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L101	3	((US-20030125881-A1).did. AND PGPB.dbnm.) OR ((US-10758652-B2 OR US-6348156-B1).did. AND USPT.dbnm.)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/08/27 02:19 PM
L102	0	L30 AND touchscreen	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR,	OR	ON	ON	2024/08/27 02:19 PM

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			GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L103	0	touchscreen WITH plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L104	4	touchscreen SAME plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L105	16	"10980926"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)	OR	ON	ON	2024/08/27 02:19 PM
L106	200	("1025059" | "1611725" | "2087778" | "2661150" | "2750107" | "2792172" | "3096283" | "3145713" | "3239136" | "3244362" | "3244363" | "3409213" | "3456875" | "3489145" | "3565330" | "3655058" | "3737096" | "3774840" | "3987961" | "4007871" | "4010894" | "4014497" | "4040965" | "4056224" | "4082217" | "4086924" | "4140268" | "4142670" | "4151844" | "4197847" | "4285464" | "4300717" | "4303193" | "4321921" | "4387848" | "4425114" | "4430072" | "4447221" | "4457747" | "4464167" | "4466888" | "4482342" | "4490135" | "4530691" | "4534863" | "4643714" | "4647279" | "4655742" | "4680025" | "4684361" | "4692136" | "4708712" | "4713176" | "4734089" | "4740202" | "4740313" | "4755300" | "4767396" | "4795419" | "4795448" | "4806247" | "4806252" | "4808307" | "4850995" | "4869812" | "4871462" | "4876013" | "4889524" | "4911833" | "4934995" | "4940543" | "4943273" | "4968295" | "4983156" | "4983158" | "4985153" | "4994188" | "5039401" | "5045048" | "5098372" | "5098373" | "5100372"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2024/08/27 02:19 PM

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Petitioner Terumo Exhibit 1014-0044

		| "5100564" | "5112298" | "5114396" | "5135667" | "5141486" | "5147290" | "5154716" | "5174894" | "5194145" | "5217426" | "5217427" | "5234403" | "5254248" | "5273517" | "5277701" | "5298016" | "5298171" | "5300060" | "5316540" | "5318511" | "5318512" | "5348533" | "5368542" | "5368555" | "5386734" | "5387174" | "5387187" | "5403272" | "5405308" | "5417650" | "5431814" | "5437598" | "5437624" | "5462667" | "5470483" | "5484396" | "5494592" | "5505685" | "5514070" | "5543062" | "5551941" | "5585007" | "5607579" | "5649903" | "5651766" | "5656163" | "5665061" | "5712798" | "5728060" | "5733253" | "5733446" | "5733545" | "5738792" | "5762791" | "5779660" | "5783085" | "5792351" | "5849203" | "5882289" | "5906589" | "5919125" | "5964724" | "5970432" | "5980760" | "6007725" | "6059979" | "6207063" | "6234989" | "6296602" | "6464624" | "6497676" | "6558307" | "6623443" | "6743192" | "7115205" | "7186231" | "7270645" | "7704454" | "8628489" | "8702637" | "8759094" | "9283316" | "10758652" | "20010000185" | "20010027156" | "20020043492" | "20020062100" | "20020120227" | "20030055375" | "20030066807" | "20030125881" | "20030175150" | "20040186409" | "20050209522" | "20050235733" | "20060058167" | "20060155236" | "20070112289" | "20080146993" |				

		"20120175313" | "20140039373" | "20140356851" | "20180344910" | "20180344921").pn. AND (PGPB | USPT | USOC).dbnm.					
L107	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L108	11	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415 and A61M2230/207).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L109	11	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L110	53	((A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L111	8	"20120175313"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L112	9	"20030125881"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L113	44	2009/0215602	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L114	15	"20090215602"	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L115	2	L1 AND ((A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L116	12693	((A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM

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		G01N15/042 OR G01N33/86).CPC.)					
L117	2513	L10 and hematocrit	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L118	7	"I11" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L119	6	"I10" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L120	16	"I10" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L121	60	((("RAGUSA") near3 ("Michael"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L122	11	"I15" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L123	183	("20010000185"|"20020062100"|"1025059"|"1611725"|"20010027156"|"20020043492"|"20020120227"|"20030055375"|"20030066807"|"20030125881"|"20030175150"|"20040186409"|"20050209522"|"20050235733"|"20060058167"|"20060155236"|"20070112289"|"20080146993"|"20120175313"|"20140039373"|"20140356851"|"20180344921"|"2087778"|"2661150"|"2750107"|"2792172"|"3096283"|"3145713"|"3239136"|"3244362"|"3244363"|"3409213"|"3456875"|"3489145"|"3565330"|"3655058"|"3737096"|"3774840"|"3987961"|"4007871"|"4010894"|"4014497"|"4040965"|"4056224"|"4082217"|"4086924"|"4140268"|"4142670"|"4151844"|"4197847"|"4285464"|"4300717"|"4303193"|"4321921"|"4387848"|"4425114"|"4430072"|"4447221"|"4457747"|"4464167"|"4466888"|"4482342"|"4490135"|"4530691"|"4534863"|"4643714"|"4647279"|"4655742"|"4680025"|"4684361"|"4692136"|"4708712"|"4713176"|"4734089"|"4740202"|"4740313"	(US-PGPUB; USPAT)	OR	OFF	OFF	2024/08/27 02:19 PM

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Petitioner Terumo Exhibit 1014-0047

		|"4755300"|"4767396"|"4795419"|"4795448"|"4806247"|"4806252"|"4808307"|"4850995"|"4869812"|"4871462"|"4876013"|"4889524"|"4911833"|"4934995"|"4940543"|"4943273"|"4968295"|"4983156"|"4983158"|"4985153"|"4994188"|"5039401"|"5045048"|"5098372"|"5098373"|"5100372"|"5100564"|"5112298"|"5114396"|"5135667"|"5141486"|"5147290"|"5154716"|"5174894"|"5194145"|"5217426"|"5217427"|"5234403"|"5254248"|"5273517"|"5277701"|"5298016"|"5298171"|"5300060"|"5316540"|"5318511"|"5318512"|"5348533"|"5368542"|"5368555"|"5386734"|"5387174"|"5387187"|"5403272"|"5405308"|"5417650"|"5431814"|"5437598"|"5437624"|"5462667"|"5470483"|"5484396"|"5494592"|"5505685"|"5514070"|"5543062"|"5551941"|"5585007"|"5607579"|"5649903"|"5651766"|"5656163"|"5665061"|"5712798"|"5728060"|"5733253"|"5733446"|"5733545"|"5738792"|"5762791"|"5779660"|"5783085"|"5792351"|"5849203"|"5882289"|"5906589"|"5919125"|"5964724"|"5970432"|"5980760"|"6007725"|"6059979"|"6207063"|"6234989"|"6296602"|"6464624"|"6497676"|"6558307"|"6623443"|"6743192"|"7115205"|"7186231"|"7270645"|"7704454"|"8628489"|"8702637"|"8759094").PN.				
L124	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L125	11	"I15" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L126	1	("10758652").PN.	(USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0048

L127	0	("20120175313").PN.	(USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L128	6	"20120175313"	(USPAT)	OR	OFF	OFF	2024/08/27 02:19 PM
L129	14	("4713176" | "6348156" | "6875191" | "7011761" | "7087177" | "7297272" | "7708710" | "8075468").PN. OR ("8852140").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L130	9	L23 and prim$3	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L131	0	(10/302682).APP.	(USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L132	2	"20140100507"	(USPAT; USOCR)	OR	OFF	OFF	2024/08/27 02:19 PM
L133	195	A61M1/024.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L134	996	G01n15/05.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L135	225	G01n2015/055.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L136	3	((US-20030125881-A1).did. AND PGPB.dbnm.) OR ((US-10758652-B2 OR US-6348156-B1).did. AND USPT.dbnm.)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/08/27 02:19 PM
L137	0	L30 AND touchscreen	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/08/27 02:19 PM
L138	0	touchscreen WITH plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L139	4	touchscreen SAME plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/08/27 02:19 PM
L140	16	"10980926"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)	OR	ON	ON	2024/08/27 02:19 PM
L141	200	("1025059" | "1611725" | "2087778" | "2661150" | "2750107" | "2792172" | "3096283" | "3145713"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2024/08/27 02:19 PM

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Petitioner Terumo Exhibit 1014-0049

		| "3239136" | "3244362" | "3244363" | "3409213" | "3456875" | "3489145" | "3565330" | "3655058" | "3737096" | "3774840" | "3987961" | "4007871" | "4010894" | "4014497" | "4040965" | "4056224" | "4082217" | "4086924" | "4140268" | "4142670" | "4151844" | "4197847" | "4285464" | "4300717" | "4303193" | "4321921" | "4387848" | "4425114" | "4430072" | "4447221" | "4457747" | "4464167" | "4466888" | "4482342" | "4490135" | "4530691" | "4534863" | "4643714" | "4647279" | "4655742" | "4680025" | "4684361" | "4692136" | "4708712" | "4713176" | "4734089" | "4740202" | "4740313" | "4755300" | "4767396" | "4795419" | "4795448" | "4806247" | "4806252" | "4808307" | "4850995" | "4869812" | "4871462" | "4876013" | "4889524" | "4911833" | "4934995" | "4940543" | "4943273" | "4968295" | "4983156" | "4983158" | "4985153" | "4994188" | "5039401" | "5045048" | "5098372" | "5098373" | "5100372" | "5100564" | "5112298" | "5114396" | "5135667" | "5141486" | "5147290" | "5154716" | "5174894" | "5194145" | "5217426" | "5217427" | "5234403" | "5254248" | "5273517" | "5277701" | "5298016" | "5298171" | "5300060" | "5316540" | "5318511" | "5318512" | "5348533" | "5368542" | "5368555" | "5386734" | "5387174" | "5387187" | "5403272" | "5405308" | "5417650" | "5431814" | "5437598" | "5437624" | "5462667" | "5470483" | "5484396" | "5494592" | "5505685" | "5514070" | "5543062" | "5551941" | "5585007"				

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Petitioner Terumo Exhibit 1014-0050

		| "5607579" | "5649903" | "5651766" | "5656163" | "5665061" | "5712798" | "5728060" | "5733253" | "5733446" | "5733545" | "5738792" | "5762791" | "5779660" | "5783085" | "5792351" | "5849203" | "5882289" | "5906589" | "5919125" | "5964724" | "5970432" | "5980760" | "6007725" | "6059979" | "6207063" | "6234989" | "6296602" | "6464624" | "6497676" | "6558307" | "6623443" | "6743192" | "7115205" | "7186231" | "7270645" | "7704454" | "8628489" | "8702637" | "8759094" | "9283316" | "10758652" | "20010000185" | "20010027156" | "20020043492" | "20020062100" | "20020120227" | "20030055375" | "20030066807" | "20030125881" | "20030175150" | "20040186409" | "20050209522" | "20050235733" | "20060058167" | "20060155236" | "20070112289" | "20080146993" | "20120175313" | "20140039373" | "20140356851" | "20180344910" | "20180344921").pn. AND (PGPB | USPT | USOC).dbnm.					
L142	0	"current value of the hematocrit of the donor".clm.	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)	OR	ON	ON	2024/08/27 02:19 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

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Petitioner Terumo Exhibit 1014-0051

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/205,400	**08/06/2024 12:52:17 PM Z ET**	**130670-80104**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	4686	FILED BY	Tricia Troup
PATENT CENTER #	66667806	AUTHORIZED BY	Jonathan Lovely
CUSTOMER #	86738	FILING DATE	03/18/2021
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Michael Ragusa

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 504876	**E202486C52389388**	**Jonathan Lovely**

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
1814	STATUTORY DISCLAIMER, INCLUDING TERMINAL DISCLAIMER	170.00	1	170.00
			TOTAL AMOUNT:	**$170.00**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C.

Terumo v. Haemonetics - PGR2026-00006
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371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A PRIOR PATENT

APPLICATION #	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET #
17205400	**03/18/2021**	**Michael Ragusa**	**130670-80104**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

☑	Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action
☑	This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.

Owner	Percent interest
Haemonetics Corporation	100%
Total	**100%**

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on pending reference Application Number(s)

Application #	Filing Date

as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent granted on the reference application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.
In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term of any patent granted on said reference application, "as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application," in the event that any such patent granted on the pending reference application: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as shortened by any terminal disclaimer filed prior to its grant.

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent number(s)

Patent #
10758652
10980926

as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.
In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later:
- expires for failure to pay a maintenance fee;
- is held unenforceable;
- is found invalid by a court of competent jurisdiction;
- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
- is reissued; or
- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Terminal disclaimer fee under 37 CFR 1.20(d) included with Electronic Terminal Disclaimer request.

Applicant claims the following entity status:
Regular Undiscounted

I hereby declare that all statements made herein of my own knowledge are true and that all statemnts made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I certify, in accordance with 37 CFR 1.4(d)(4) that I am: An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application

Signature	Name	Registration #
/Jonathan C. Lovely/	Jonathan Lovely	60821

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* Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner). Form PTO/SB/96 may be used for making this certification. See MPEP 324.

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/205,400	**08/06/2024 12:52:17 PM Z ET**	**130670-80104**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	4686	FILED BY	Tricia Troup
PATENT CENTER #	66667806	FILING DATE	03/18/2021
CUSTOMER #	86738	FIRST NAMED INVENTOR	Michael Ragusa
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Jonathan Lovely

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
petition-request.pdf	3	Terminal Disclaimer-Filed (Electronic)	44 KB
grantLetter.pdf	1	Terminal Disclaimer-Electronic-Approved	18 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
petition-request.pdf	E5C5BCAF4F41E80596C9CBE66FACFC3A63D5BFD773BF3597CF436007A5A9C47F7466000491198C781C28EC70526CBB4FF0FF9628D16001132A384C9EE4370ACD
grantLetter.pdf	D7E53406D9D4BCDB07C33B2CA2C12495F378241CAE69BCA0

2B6634C3D3F8ABB21D215332B86D431F768B47007687E7CBF
CB371B5DB4E83D1FD939F607192074E

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES
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Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

APPROVAL LETTER

APPLICATION #	FILING DATE	APPLICANT/PATENT UNDER REEXAMINATION
17/205,400	**03/18/2021**	**Michael Ragusa**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

Electronic terminal disclaimer filed on 08/06/2024

☑ Approved

This patent is subject to a Terminal Disclaimer

Approved / Disapproved by: Electronic Terminal Disclaimer automatically approved

UNITED STATES
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P.O. Box 1450
Alexandria, VA 22313 - 1450
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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/205,400	**08/06/2024 12:48:43 PM Z ET**	**130670-80104**

Title of Invention

SYSTEM AND METHOD FOR COLLECTING PLASMA

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	4686	FILED BY	Tricia Troup
PATENT CENTER #	66668080	FILING DATE	03/18/2021
CUSTOMER #	86738	FIRST NAMED INVENTOR	Michael Ragusa
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	Jonathan Lovely

Documents

TOTAL DOCUMENTS: 4

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
Response to Non-Final Office Action.pdf		12	-	55 KB
Response to Non-Final Office Action-A....pdf	(1-1)	1	Amendment/Request for Reconsideration-After Non-Final Rejection	18 KB
Response to Non-Final Office Action-SPEC.pdf	(2-2)	1	Specification	18 KB
Response to Non-Final Office Action-CLM.pdf	(3-9)	7	Claims	39 KB
Response to Non-Final Office Action-REM.pdf	(10-12)	3	Applicant Arguments/Remarks Made in an Amendment	25 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
Response to Non-Final Office Action.pdf	D53CDD2B1D77574F5C9294DADA7F8E75E584A5596FC944B6 8BCCECFDF4B023837DA41864629D13FFE9673AE3B75AF183 021A25219965D9B071219084C0B5EDDC
Response to Non-Final Office Action-A....pdf	D5DC50E0231234142C5B296291446B55EAF0C2631E14DDAA6 26FAA18515D6203EF003EAF97F54ED497BBCF42CB8187AE19 9DF54FDD7118270DF6C71DA1C9642B
Response to Non-Final Office Action-SPEC.pdf	F6947D406FE2B78A8D3F1A8C1DA9251C890057512270CBFC9 EAD3B31F3F200E3026359DC4B775B9EBB1EF5C39CD9FE9ED ECB959B6F20CBEDA92D65A976449FDC
Response to Non-Final Office Action-CLM.pdf	1BAA9EC1934A703DACD08E2C2321A38300F9002026E7BF0B6 DE0AFD75D2C8CEAA970272BA0C5C66B032EDA587B1DECF1 524E5D221F85614EB86AA9711418FA0C
Response to Non-Final Office Action-REM.pdf	6C1F325CBCD334569921CD4ABAABC24834F3C9F3A4972860 81BD6C0976D98A1661BE06528A67EF98937CCC0BCBD319A8 31C92C43F67DCD6F5E2F59208D925D68

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Haemonetics Corporation

Application No.: 17/205,400 Confirmation No.: 4686

Filed: March 18, 2021 Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING PLASMA Examiner: L. R. Deak

AMENDMENT IN RESPONSE TO NON-FINAL OFFICE ACTION UNDER 37 C.F.R. § 1.111

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

INTRODUCTORY COMMENTS

In response to the Office Action dated May 8, 2024, please amend the above-identified U.S. patent application as follows:

Amendments to the Specification are reflected on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 3 of this paper.

Remarks/Arguments begin on page 10 of this paper.

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Petitioner Terumo Exhibit 1014-0062

AMENDMENTS TO THE SPECIFICATION

Please amend paragraph **[0002]** of the originally filed application as shown below:

[0002] U.S. Application No. 16/931,333, in turn, is a continuation of and claims priority from U.S. Application No. 15/793,339, entitled "System and Method for Collecting Plasma," filed October 25, 2017, now U.S. Patent No. 10,792,416, attorney docket number 130670-80102 (formerly 1611/C86), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0063

AMENDMENTS TO THE CLAIMS

The following **Listing of Claims** will replace all prior versions, and listing, of claims in the application.

Listing of Claims

1. (Currently Amended) A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight and hematocrit, to determine a target volume for plasma product and/or raw plasma based on the donor's total blood volume and/or the donor's plasma volume, to control the system to operate a draw and return cycle to withdraw the whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor, to establish a current value of the hematocrit of the donor and a new target volume for plasma product and/or raw plasma, and to control the system to operate a subsequent draw and return cycle, whereby the donor's changing hematocrit is taken into account in calculating the new target volume for plasma product and/or raw plasma.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0064

2. (Original) The system of claim 1, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma before a start of a first draw and return cycle.

3. (Original) The system of claim 2, wherein the controller is programmed to repeat draw and return phases until the target volume of plasma product and/or raw plasma is collected, wherein the target volume for plasma product and/or raw plasma is redetermined prior to the start of each draw phase.

4. (Original) The system of claim 3, wherein the controller is programmed to perform the draw and return phases at least three times.

5. (Canceled)

6. (Original) The system of claim 1, wherein the controller is programmed to initiate a final return of the second blood component when (1) a measured volume of plasma product in the plasma collection container reaches the target volume for plasma product and/or (2) a volume of raw plasma in the plasma collection container reaches the target volume for raw plasma.

7. (Currently Amended) A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

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Petitioner Terumo Exhibit 1014-0065

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height, sex and hematocrit, to determine a target volume for plasma product and/or raw plasma based at least in part on ~~the weight, height, sex, and hematocrit~~ the donor's total blood volume and/or the donor's plasma volume, to control the system to operate draw and return phases to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

8. (Original) The system of claim 7, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separately from the plasma product.

9. (Original) The system of claim 8, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separate from the plasma product attributable to a priming or other pre-processing step.

10. (Currently Amended) A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

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Petitioner Terumo Exhibit 1014-0066

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height and hematocrit and to determine a target volume for plasma product comprising raw plasma and anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on ~~an anticoagulant ratio, the donor's weight, height, and the donor's hematocrit~~ the donor's total blood volume and/or the donor's plasma volume, the controller programmed to then control the system to operate a plurality of draw and return cycles to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

11. (Currently Amended) The system of claim 10, wherein the controller is programmed to determine the target volume for plasma product based an anticoagulant ratio ~~on the donor's total blood volume and the donor's plasma volume~~.

12. (Currently Amended) The system of claim 10 ~~11~~, wherein the controller is programmed to determine the donor's total blood volume based on multiple parameters selected from the group consisting of the weight, height, sex, age, and morphology of the donor.

13. (Original) The system of claim 10, wherein the controller is configured to receive the donor's weight and hematocrit electronically.

14. (Original) The system of claim 10, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until the plasma product in the plasma product collection container reaches the determined target volume.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0067

15. (Original) The system of claim 10, wherein the controller is programmed to perform the draw and return cycles at least three times and the controller is programmed to determine a volume of whole blood to be drawn in a final draw phase which is different than a volume drawn in a prior draw phase.

16. (Currently Amended) A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive donor parameters electronically, to determine a target volume for plasma product and/or raw plasma based at least in part on the donor parameters and on the donor's total blood volume and/or the donor's plasma volume, the controller also configured ~~and~~ to control the system to operate draw and return phases to withdraw whole blood from a donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

17. (Original) The system of claim 16, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until a collected volume of plasma product reaches the target volume for plasma product and/or raw plasma.

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Petitioner Terumo Exhibit 1014-0068

18. (Original) The system of claim 16, further comprising a control system, wherein the control system is in electronic communication with the controller.

19. (Original) The system of claim 18, wherein the control system is programmed to calculate the target volume for plasma product and/or raw plasma and the controller is programmed to determine a target volume for plasma product and/or raw plasma by receiving the target volume for plasma product and/or raw plasma from the control system.

20. (Original) The system of claim 16, wherein the controller determines the target volume for plasma product and/or raw plasma by calculating the target volume for plasma product and/or raw plasma and wherein the controller is local to and coupled to the blood separator.

21. (Original) The system of claim 16, wherein the donor parameters received electronically comprise a donor weight, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor weight.

22. (Original) The system of claim 21, wherein the donor parameters received electronically comprise a donor hematocrit, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor hematocrit.

23. (Original) The system of claim 22, wherein the controller is programmed to determine a target volume for plasma product based on the donor's total blood volume and the donor's plasma volume.

24. (Original) The system of claim 23, wherein the controller is programmed to determine the donor's total blood volume based on the weight and height of the donor.

25. (Original) The system of claim 24, wherein the controller is programmed to determine the donor's total blood volume before whole blood is withdrawn from the donor during a donation.

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Petitioner Terumo Exhibit 1014-0069

26. (Original) The system of claim 25, wherein the controller is programmed to determine the target volume for plasma product comprising raw plasma and anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on an anticoagulant ratio, the donor's weight and the donor's hematocrit.

27. (Original) The system of claim 16, further comprising a reservoir separate from the blood separator for receiving concentrated red blood cells.

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Petitioner Terumo Exhibit 1014-0070

REMARKS

Applicants would like to thank the examiner for the review of the present application. Applicants request reconsideration of the pending claims in view of the following remarks. Applicant has amended claims 1, 7, 10, 11, 12 and 16 and canceled claim 5 herewith. Claims 1-4, 6-27 are currently pending in the application.

Amendment to the Specification

Applicant has amended paragraph [0002], as outlined above, to correct a typographical error in the serial number for the priority application number for U.S. Application No. 16/931,333, filed on July 16, 2020. The Application Data Sheet as filed on March 18, 2021, the Filing Receipt dated March 30, 2021 and the Patent Center data for the present application is correct. Applicant believes that no petition is required to correct this typographical error. Therefore, Applicant respectfully requests that the specification be updated to reflect the correct application number.

Double Patenting

The office action suggests that claims 1-27 of the present application are patentably indistinct from claim 1-22 of application no. 17/205,374 and that the patentably indistinct claims must be canceled from all but one application or a clear line of demarcation must be maintained between the applications. To expedite prosecution of the present application, Applicant has amended independent claims 1, 7, 10, and 16 to include at least some of the subject matter of claims 5, 11 and 23. In particular, Applicant has amended claims 1, 7, 10 and 16 to specify that the controller determines a target volume for plasma product and/or raw plasma based on the donor's total blood volume and/or the donor's plasma volume. Applicant fails to see where any of claims 1-22 of application no. 17/205,374 teach such a limitation. Accordingly, Applicant believes that independent claims 1, 7, 10 and 16 (and dependent claims 2-4, 6, 7-27) are patentably distinct from claim 1-22 of application no. 17/205,374.

The office action rejected claims 1-27 on the grounds of nonstatutory double patenting as being unpatentable over claim 11 of U.S. Patent No. 10,758,652 in view of U.S. Publication No.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0071

2012/0165685 to Weasler et al. (hereinafter "Weasler"). Additionally, the office action rejected claims 1-22 on the grounds of nonstatutory double patenting as being unpatentable over claims 8 and 23 of U.S. Patent No 10,980,926 in view of Weasler. To expedite prosecution, Applicant files herewith a terminal disclaimer with respect to U.S. Patent No. 10,758,652 and 10,980,926. Accordingly, Applicant believes that this rejection is now moot.

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Petitioner Terumo Exhibit 1014-0072

CONCLUSION

It is believed that the application is now in order for allowance and Applicant respectfully requests that a notice of allowance be issued. Applicant does not believe that any extension of time is required. However, if an extension of time is required, please charge the associated fee and any additional fees required by this paper or credit any overpayment to deposit account number 50-4876. Applicants also request that the examiner contact applicant's attorney, Jonathan C. Lovely, if it will assist in processing this application through issuance.

Dated: August 6, 2024

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
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(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0073

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 17/205,400	Filing Date 03/18/2021	☐ To be Mailed

ENTITY: ☑ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $100 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $480 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT	08/06/2024	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 26	Minus	** 27	= 0		x $100 =	0
	Independent (37 CFR 1.16(h))	* 4	Minus	*** 4	= 0		x $480 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/DAWN BREWER/
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".	
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This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

TO: docket@mccarter.com
FROM: noreply@uspto.gov
CC: patentcenter_eofficeaction@uspto.gov
SUBJECT: USPTO: Patent Electronic System - e-Postcard Notification for Customer Number 86738

Wed May 15 05:05:03 EDT 2024

Dear Patent Center Customer:

Correspondence Address:

MCCARTER &ENGLISH, LLP BOSTON
265 Franklin Street
Boston,MASSACHUSETTS,02110
UNITED STATES

An email notification regarding the correspondence was sent to the following email address(es) associated with customer number 86738:

docket@mccarter.com

This is a courtesy reminder that new correspondence is available for the application. If you have not done so already, please review the correspondence listed below. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

Application	Document	Mailroom Date	Attorney Docket No.
17205400	CTNF	05/08/2024	130670-80104
17205400	892	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104
17205400	1449	05/08/2024	130670-80104

To view your correspondence online, please sign in to Patent Center and then select Workbench/View correspondence. Or to update your email addresses, select Manage/Manage customer numbers.

If you have any questions, please contact the Patent Electronic Business Center (EBC) at ebc@uspto.gov or 866-217-9197 Monday – Friday, 6 a.m. to midnight ET.

Please do not reply to this email as it was sent from an unmonitored mailbox.

Sincerely,

The Patent Center Team

United States Patent and Trademark Office

Office of the Commissioner for Patents

Dear Applicant,

You recently received an Office action from your examiner. Review of your patent application is under way! You can continue to advertise or mark any products covered by your application for your invention as "Patent Pending" for as long as this application is pending. This letter provides information about how to continue through the patent application process and the help available to you on your journey.

Where are you in the patent application process? Your patent application is now in step 3, Application Prosecution (www.uspto.gov/UtilityPatentGuide.) Though the Office action includes a "rejection," that does not mean that you don't have a good idea you can patent. It means your examiner believes your application is not yet ready for allowance.

Ready to respond? Responding to the Office action is your opportunity to address the issues raised by your examiner. Responses must be timely, complete, and in writing. In your response, you may want to consider amending your application (www.uspto.gov/patents/maintain/responding-office-actions).

We provide Pro Se Assistance, support specifically geared for independent inventors without an agent or attorney. Visit www.uspto.gov/ProSePatents for a consolidated list of resources, including a sample amendment format. Full description of amendment formatting can be found at www.uspto.gov/web/offices/pac/mpep/s714.html. Call us at 866-767-3848, or email proseassistancecenter@uspto.gov.

Have questions about the Office action? Contact your examiner! A conversation with your examiner (called an "interview") may help clarify and resolve any issues and possibly identify what you can patent. While an interview does not stop the clock for your official response or substitute for a response, there is no fee for an interview. To schedule a call or video, you can:

1. use the USPTO's Automated Interview Request (AIR) form (www.uspto.gov/patents/uspto-automated-interview-request-air-form);
2. file the Applicant Initiated Interview Request form (PTOL-413A) (www.uspto.gov/sites/default/files/documents/PTOL413A.pdf); or
3. contact your examiner directly via telephone (contact information is provided at the end of your Office action).

Need help near you? We have regional offices across the country (www.uspto.gov/locations), as well as Patent and Trademark Resource Centers in libraries in nearly every state (www.uspto.gov/ptrc), with specialists standing by to help you at no cost.

Become a *registered* electronic filer (registered eFiler). As a registered eFiler, you can electronically view your submission, track progress of your application, and respond to USPTO correspondence. (www.uspto.gov/NewPatentFilers)

Contact us

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Want to learn more?

- Hear about resources for startups, inventors, and entrepreneurs, as well as our initiatives engaging women, the military community, and others. These programs offer helpful tips and tricks on identifying and managing your IP, finding options for funding, and expanding your network to support your business.
  - www.uspto.gov/startups
  - www.uspto.gov/inventors
  - www.uspto.gov/initiatives
- Access our free services all in one spot. Find all of our contact centers, nationwide services, events, education and training. (www.uspto.gov/FreeServices)
- Connect with us on Instagram, LinkedIn, Twitter, Facebook, and YouTube.
- Hear about the great things we are doing by subscribing at www.uspto.gov/subscribe.

Best,

Vaishali Udupa
Commissioner for Patents
United States Patent and Trademark Office

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0076

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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P.O. Box 1450
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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/205,400	03/18/2021	Michael Ragusa	130670-80104	4686

86738 7590 05/08/2024
MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

EXAMINER	
DEAK, LESLIE R	

ART UNIT	PAPER NUMBER
3799	

NOTIFICATION DATE	DELIVERY MODE
05/08/2024	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@mccarter.com

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0077

Office Action Summary	Application No. 17/205,400	Applicant(s) Ragusa, Michael	
	Examiner LESLIE R DEAK	Art Unit 3799	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 18 March 2021.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL.** 2b) ☑ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 1-27 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-27 is/are rejected.

8) ☐ Claim(s) _____ is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☑ The drawing(s) filed on 18 March 2021 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0078

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See

MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

3. Claims 1-27 of this application is patentably indistinct from claims 1-22 of Application No. 17/205,374. Pursuant to 37 CFR 1.78(f), when two or more applications filed by the same applicant or assignee contain patentably indistinct claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the patentably indistinct claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

4. Claims 1-27 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 11 of U.S. Patent No. 10,758,652 in view of US 2012/0165685

to Weasler et al. Although the claims at issue are not identical, they are not patentably distinct from each other.

With regard to instant claims 1, 7, 10, 16, patented claim 11 recites a venipuncture needle as an access device, a blood component separation device that separates plasma and sends it to a container, along with a container for red blood cells, a donor line with a pump, an anticoagulant line "configured to introduce anticoagulant" wherein the configuration comprises a pump, and a controller programmed to operate the device with various control schemes. Patented claim 11 does not recite a user interface or a touchscreen. However, Weasler discloses a plasmapheresis apparatus with venous access, containers, and pumps, coupled with a touchscreen user interface to enter patient parameters, enter control schemes, and relay information (see Weasler ¶0020-0023).

Where a claimed improvement on a device or apparatus is no more than "the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement," the claim is unpatentable under 35 U.S.C. 103(a). Ex Parte Smith, 83 USPQ.2d 1509, 1518-19 (BPAI, 2007) (citing KSR v. Teleflex, 127 S.Ct. 1727, 1740, 82 USPQ2d 1385, 1396 (2007)). Applicant claims a combination that only unites old elements with no change in the respective functions of those old elements, and the combination of those elements yields predictable results; absent evidence that the modifications necessary to effect the combination of elements is uniquely challenging or difficult for one of ordinary skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a). Ex Parte Smith, 83 USPQ.2d at 1518-19 (BPAI, 2007) (citing KSR, 127 S.Ct. at 1740, 82 USPQ2d at1396.

Accordingly, since the applicant[s] have submitted no persuasive evidence that the combination of the above elements is uniquely challenging or difficult for one of ordinary skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a) because it is no more than the predictable use of prior art elements according to their established functions resulting in the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement. In the instant case, it is within the skill of a worker in the art to provide a plasmapheresis apparatus with a user interface in the form of a touchscreen in order to program desired control schemes since such elements are known in the art.

With regard to claims 2-6, 8, 9, 11-15, 17-26, Applicant is reciting different control schemes that the controller uses to operate the plasmapheresis machine. It is within the skill of a worker in the art to program a controller to generate the desired outcome. Accordingly, the instantly presented claims are unpatentable over the prior art of record.

With regard to claim 27, Applicant is claiming an additional container. It has been held that the mere duplication of the parts of an apparatus found in the prior art is not patentably significant unless a new and unexpected result is produced. See MPEP § 2144.04 (VI)(B).

5. Claims 1-22 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 8 and 23 of U.S. Patent No. 10,980,926 in view of US 2012/0165685 to Weasler et al. Although the claims at issue are not identical, they are not patentably distinct from each other.

With regard to instant claims 1, 7, 10, 16, patented claims 8 and 23 recite a venipuncture needle as an access device, a blood component separation device that separates plasma and sends it to a container, along with a container for red blood cells, a donor line with a pump, an anticoagulant line "configured to introduce anticoagulant" wherein the configuration comprises a pump, and a controller programmed to operate the device with various control schemes. Patented claim 11 does not recite a user interface or a touchscreen. However, Weasler discloses a plasmapheresis apparatus with venous access, containers, and pumps, coupled with a touchscreen user interface to enter patient parameters, enter control schemes, and relay information (see Weasler ¶0020-0023).

Where a claimed improvement on a device or apparatus is no more than "the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement," the claim is unpatentable under 35 U.S.C. 103(a). Ex Parte Smith, 83 USPQ.2d 1509, 1518-19 (BPAI, 2007) (citing KSR v. Teleflex, 127 S.Ct. 1727, 1740, 82 USPQ2d 1385, 1396 (2007)). Applicant claims a combination that only unites old elements with no change in the respective functions of those old elements, and the combination of those elements yields predictable results; absent evidence that the modifications necessary to effect the combination of elements is uniquely challenging or difficult for one of ordinary skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a). Ex Parte Smith, 83 USPQ.2d at 1518-19 (BPAI, 2007) (citing KSR, 127 S.Ct. at 1740, 82 USPQ2d at1396. Accordingly, since the applicant[s] have submitted no persuasive evidence that the combination of the above elements is uniquely challenging or difficult for one of ordinary

skill in the art, the claim is unpatentable as obvious under 35 U.S.C. 103(a) because it is no more than the predictable use of prior art elements according to their established functions resulting in the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for improvement. In the instant case, it is within the skill of a worker in the art to provide a plasmapheresis apparatus with a user interface in the form of a touchscreen in order to program desired control schemes since such elements are known in the art.

With regard to claims 2-6, 8, 9, 11-15, 17-26, Applicant is reciting different control schemes that the controller uses to operate the plasmapheresis machine. It is within the skill of a worker in the art to program a controller to generate the desired outcome. Accordingly, the instantly presented claims are unpatentable over the prior art of record.

With regard to claim 27, Applicant is claiming an additional container. It has been held that the mere duplication of the parts of an apparatus found in the prior art is not patentably significant unless a new and unexpected result is produced. See MPEP § 2144.04 (VI)(B).

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE R DEAK whose telephone number is (571)272-4943. The examiner can normally be reached on Monday-Friday, 9am to 5:30pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an

interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tom Sweet can be reached on 571-272-4761. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see https://ppair-my.uspto.gov/pair/PrivatePair. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LESLIE R DEAK/
Primary Examiner, Art Unit 3799
3 May 2024

Notice of References Cited	Application/Control No. 17/205,400	Applicant(s)/Patent Under Reexamination Ragusa, Michael	
	Examiner LESLIE R DEAK	Art Unit 3799	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date YYYY-MM-DD	Name	CPC Classification	US Classification
*	A	US-10758652-B2	2020-09-01	Ragusa; Michael	A61M1/024	1/1
*	B	US-10980926-B2	2021-04-20	Ragusa; Michael	A61M1/029	1/1
*	C	US-20120165685-A1	2012-06-28	Weasler; Marc N.	A61B5/02042	600/595
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*		Document Number Country Code-Number-Kind Code	Date YYYY-MM-DD	Country	Name	CPC Classification
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NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
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	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in YYYY-MM-DD format are publication dates. Classifications may be US or foreign.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0086

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/205,400	Ragusa, Michael
	Examiner	**Art Unit**
	LESLIE R DEAK	3799

CPC - Searched*		
Symbol	**Date**	**Examiner**
(A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC.	10/28/2019	LRD
A61M1/029 A61M1/3672 A61M1/3693 A61M1/38 A61M2202/0415 A61M2230/207	11/05/2020	LRD

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
inventor name search, EAST BRS search, consulted foreign search report	10/28/2019	LRD
updated prior searches, consulted primary examiners	02/27/2020	LRD
updated prior searches	05/05/2020	LRD
consulted parent case, updated searches, ODP	11/06/2020	LRD
consulted parent cases, updated searches, ODP	04/30/2024	LRD

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0087

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/205,400	Ragusa, Michael
	Examiner	Art Unit
	LESLIE R DEAK	3799

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
	N/A	05/05/2020	LRD

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0088

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

U.S.PATENTS

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FOREIGN PATENT DOCUMENTS

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2002-282352	JP	A	2002-10-02	Terumo Corp		X

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NON-PATENT LITERATURE DOCUMENTS

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0089

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH ... R 1.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

	1		

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EXAMINER SIGNATURE

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0090

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2022-04-04
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0091

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.C.L./

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0092

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /A.R./

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 18, 2021
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 Confirmation No.: 4686

Filed: March 18, 2021 Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING PLASMA Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents. Applicant submits herewith copies of foreign patents in accordance with 37 C.F.R. § 1.98(a)(2).

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0093

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH /JCL/

Application No.: 17/205,400 Docket No.: 130670-80104

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	10,980,926	Issued	130670-08005
17/205,374	March 18, 2021	2021-0205509	Published	130670-08006
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	10,980,934	Issued	130670-80103

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: November 18, 2021

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0094

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 4, 2022
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 Confirmation No.: 4686

Filed: March 18, 2021 Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING PLASMA Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional document. A PTO Form SB/08 and a full copy of the document required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

Applicant submits herewith a copy of the cited foreign patent in accordance with 37 C.F.R. § 1.98(a)(2).

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0095

Application No.: 17/205,400 Docket No.: 130670-80104

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	10,980,926	Issued	130670-08005
17/205,374	March 18, 2021	2021-0205509	Published	130670-08006
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	10,980,934	Issued	130670-80103

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed reference.

Applicant believes no fee is due with this response.

Dated: April 4, 2022

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0096

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6200287	B1	2001-03-13	Keller et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20050131334	A1	2005-06-16	Langley et al.	
	2	20140100507	A1	2014-04-10	Flexman, Greg	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	103354755	CN	A	2013-10-16	Haemonetics Corp		☒
	2	69434848	DE		2007-04-12	Gambro Inc		☒

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /A.R./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0097

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17205400
	Filing Date	2021-03-18
	First Named Inventor	Michael Ragusa
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	130670-80104

	3	2003-516175	JP	A	2003-05-13	Baxter International, Inc.		☒
	4	2012/091720	WO	A1	2012-07-05	Haemonetics Corp		☐
	5	2019/084278	WO	A1	2019-05-02	Haemonetics Corp		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0098

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2022-12-08
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0099

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.C.L./

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0100

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	8075468	B2	2011-12-13	Min et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20090215602	A1	2009-08-27	Min et al.	
	2	20230001059	A1	2023-01-05	Ragusa, Michael	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.R./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0101

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0102

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2023-01-17
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0103

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /JCL/

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0104

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

U.S.PATENTS

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5681273		1997-10-28	Brown	
	2	8454548	B2	2013-06-04	Ohashi et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2252788	RU	C1	2005-05-27	Mepotex		☒
	2	2601449	RU	C2	2016-11-10	Fenval Ink		☒

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0105

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH ... 1

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

If you wish to add additional Foreign Patent Document citation information please click the Add button [Add]

NON-PATENT LITERATURE DOCUMENTS [Remove]

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

If you wish to add additional non-patent literature document citation information please click the Add button [Add]

EXAMINER SIGNATURE

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0106

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2021-11-18
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0107

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Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0108

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH

Used in Lieu of PTO/SB/08A/B
(Based on PTO 10-07 version)

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 6

Complete if Known	
Application Number	Not Yet Assigned
Filing Date	Concurrently Herewith
First Named Inventor	Michael Ragusa
Art Unit	3781
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	AA	US-1,025,059	04-30-1912	Hatton et al.	
	AB	US-1,611,725	12-21-1926	Degerth et al.	
	AC	US-2,087,778	07-20-1937	Nelin	
	AD	US-2,661,150	12-01-1953	Abbott, Jr.	
	AE	US-2,750,107	06-12-1956	More	
	AF	US-2,792,172	05-14-1957	Tait	
	AG	US-3,096,283	07-02-1963	Hein	
	AH	US-3,145,713	08-25-1964	Latham, Jr.	
	AI	US-3,239,136	03-08-1966	Hein	
	AJ	US-3,244,362	04-05-1966	Hein	
	AK	US-3,244,363	04-05-1966	Hein	
	AL	US-3,409,213	11-05-1968	Latham, Jr.	
	AM	US-3,456,875	07-22-1969	Hein	
	AN	US-3,489,145	01-13-1970	Judson et al.	
	AO	US-3,565,330	02-23-1971	Latham, Jr.	
	AP	US-3,655,058	04-11-1972	Novak	
	AQ	US-3,737,096	06-05-1973	Jones et al.	
	AR	US-3,774,840	11-27-1973	Boatright	
	AS	US-3,987,961	10-26-1976	Sinn et al.	
	AT	US-4,007,871	02-15-1977	Jones et al.	
	AU	US-4,010,894	03-08-1977	Kellogg et al.	
	AV	US-4,014,497	03-29-1977	Spiewok et al.	
	AW	US-4,040,965	08-09-1977	Kohlheb	
	AX	US-4,056,224	11-01-1977	Lolachi	
	AY	US-4,082,217	04-04-1978	Westberg	
	AZ	US-4,086,924	05-02-1978	Latham, Jr.	
	AA1	US-4,140,268	02-20-1979	Lacour	
	AB1	US-4,142,670	03-06-1979	Ishimaru et al.	
	AC1	US-4,151,844	05-01-1979	Cullis et al.	
	AD1	US-4,197,847	04-15-1980	Djerassi	
	AE1	US-4,285,464	08-25-1981	Latham, Jr.	
	AF1	US-4,300,717	11-17-1981	Latham, Jr.	
	AG1	US-4,303,193	12-01-1981	Latham, Jr.	
	AH1	US-4,321,921	03-30-1982	Laszczower	
	AI1	US-4,387,848	06-14-1983	Kellogg et al.	
	AJ1	US-4,425,114	01-10-1984	Schoendorfer et al.	
	AK1	US-4,430,072	02-07-1984	Kellogg et al.	
	AL1	US-4,447,221	05-08-1984	Mulzet	
	AM1	US-4,457,747	07-03-1984	Tu	
	AN1	US-4,464,167	08-07-1984	Schoendorfer et al.	
	AO1	US-4,466,888	08-21-1984	Verkaart	
	AP1	US-4,482,342	11-13-1984	Lueptow et al.	
	AQ1	US-4,490,135	12-25-1984	Troutner	
	AR1	US-4,530,691	07-23-1985	Brown	
	AS1	US-4,534,863	08-13-1985	Bacon et al.	

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

ME1 36057896v.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0109

Used in Lieu of PTO/SB/08A/B
(Based on PTO 10-07 version)

Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	Not Yet Assigned
				Filing Date	Concurrently Herewith
				First Named Inventor	Michael Ragusa
				Art Unit	3781
(Use as many sheets as necessary)				Examiner Name	Not Yet Assigned
Sheet	2	of	6	Attorney Docket Number	130670-80104

	AT1	US-4,643,714	02-17-1987	Brose	
	AU1	US-4,647,279	03-03-1987	Mulzet et al.	
	AV1	US-4,655,742	04-07-1987	Vantard	
	AW1	US-4,680,025	07-14-1987	Kruger et al.	
	AX1	US-4,684,361	08-04-1987	Feldman et al.	
	AY1	US-4,692,136	09-08-1987	Feldman et al.	
	AZ1	US-4,708,712	11-24-1987	Mulzet	
	AA2	US-4,713,176	12-15-1987	Schoendorfer et al.	
	AB2	US-4,734,089	03-29-1988	Cullis	
	AC2	US-4,740,202	04-26-1988	Stacey et al.	
	AD2	US-4,740,313	04-26-1988	Schoendorfer et al.	
	AE2	US-4,755,300	07-05-1988	Fischel et al.	
	AF2	US-4,767,396	08-30-1988	Powers	
	AG2	US-4,795,419	01-03-1989	Yawn et al.	
	AH2	US-4,795,448	01-03-1989	Stacey et al.	
	AI2	US-4,806,247	02-21-1989	Schoendorfer et al.	
	AJ2	US-4,806,252	02-21-1989	Brown et al.	
	AK2	US-4,808,307	02-28-1989	Fischel et al.	
	AL2	US-4,850,995	07-25-1989	Tie et al.	
	AM2	US-4,869,812	09-26-1989	Schoendorfer et al.	
	AN2	US-4,871,462	10-03-1989	Fischel et al.	
	AO2	US-4,876,013	10-24-1989	Shmidt et al.	
	AP2	US-4,889,524	12-26-1989	Fell et al.	
	AQ2	US-4,911,833	03-27-1990	Schoendorfer et al.	
	AR2	US-4,934,995	06-19-1990	Cullis	
	AS2	US-4,940,543	07-10-1990	Brown et al.	
	AT2	US-4,943,273	07-24-1990	Pages	
	AU2	US-4,968,295	11-06-1990	Neumann	
	AV2	US-4,983,156	01-08-1991	Knelson	
	AW2	US-4,983,158	01-08-1991	Headley	
	AX2	US-4,985,153	01-15-1991	Kuroda et al.	
	AY2	US-4,994,188	02-19-1991	Prince	
	AZ2	US-5,039,401	08-13-1991	Columbus et al.	
	AA3	US-5,045,048	09-03-1991	Kaleskas et al.	
	AB3	US-5,098,372	03-24-1992	Jonsson	
	AC3	US-5,098,373	03-24-1992	Polaschegg	
	AD3	US-5,100,372	03-31-1992	Headley	
	AE3	US-5,100,564	03-31-1992	Pall et al.	
	AF3	US-5,112,298	05-12-1992	Prince et al.	
	AG3	US-5,114,396	05-19-1992	Unger et al.	
	AH3	US-5,135,667	08-04-1992	Schoendorfer	
	AI3	US-5,141,486	08-25-1992	Antwiler	
	AJ3	US-5,147,290	09-15-1992	Jonsson	
	AK3	US-5,154,716	10-13-1992	Bauman et al.	
	AL3	US-5,174,894	12-29-1992	Ohsawa et al.	
	AM3	US-5,194,145	03-16-1993	Schoendorfer	
	AN3	US-5,217,426	06-08-1993	Bacehowski et al.	
	AO3	US-5,217,427	06-08-1993	Cullis	
	AP3	US-5,234,403	08-10-1993	Yoda et al.	

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

ME1 36057896v.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0110

Used in Lieu of PTO/SB/08A/B
(Based on PTO 10-07 version)

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 3 of 6

Complete if Known	
Application Number	Not Yet Assigned
Filing Date	Concurrently Herewith
First Named Inventor	Michael Ragusa
Art Unit	3781
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

	AQ3	US-5,254,248	10-19-1993	Nakamura	
	AR3	US-5,273,517	12-28-1993	Barone et al.	
	AS3	US-5,277,701	01-11-1994	Christie et al.	
	AT3	US-5,298,016	03-29-1994	Gordon	
	AU3	US-5,298,171	03-29-1994	Biesel	
	AV3	US-5,300,060	04-05-1994	Nelson	
	AW3	US-5,316,540	05-31-1994	McMannis et al.	
	AX3	US-5,318,511	06-07-1994	Riquier et al.	
	AY3	US-5,318,512	06-07-1994	Neumann	
	AZ3	US-5,348,533	09-20-1994	Papillon et al.	
	AA4	US-5,368,542	11-29-1994	McMannis et al.	
	AB4	US-5,368,555	11-29-1994	Sussman et al.	
	AC4	US-5,386,734	02-07-1995	Pusinelli	
	AD4	US-5,387,174	02-07-1995	Rochat	
	AE4	US-5,387,187	02-07-1995	Fell et al.	
	AF4	US-5,403,272	04-04-1995	Deniega et al.	
	AG4	US-5,405,308	04-11-1995	Headley et al.	
	AH4	US-5,417,650	05-23-1995	Gordon	
	AI4	US-5,431,814	07-11-1995	Jorgensen	
	AJ4	US-5,437,598	08-01-1995	Antwiler	
	AK4	US-5,437,624	08-01-1995	Langley	
	AL4	US-5,462,667	10-31-1995	Wollinsky et al.	
	AM4	US-5,470,483	11-28-1995	Bene et al.	
	AN4	US-5,484,396	01-16-1996	Naficy	
	AO4	US-5,494,592	02-27-1996	Latham, Jr. et al.	
	AP4	US-5,505,685	04-09-1996	Antwiler	
	AQ4	US-5,514,070	05-07-1996	Pages	
	AR4	US-5,543,062	08-06-1996	Nishimura	
	AS4	US-5,551,941	09-03-1996	Howell	
	AT4	US-5,585,007	12-17-1996	Antanavich et al.	
	AU4	US-5,607,579	03-04-1997	Latham, Jr. et al.	
	AV4	US-5,649,903	07-22-1997	Deniega et al.	
	AW4	US-5,651,766	07-29-1997	Kingsley et al.	
	AX4	US-5,656,163	08-12-1997	Brown	
	AY4	US-5,665,061	09-09-1997	Antwiler	
	AZ4	US-5,712,798	01-27-1998	Langley et al.	
	AA5	US-5,728,060	03-17-1998	Kingsley et al.	
	AB5	US-5,733,253	03-31-1998	Headley et al.	
	AC5	US-5,733,446	03-31-1998	Holm	
	AD5	US-5,733,545	03-31-1998	Hood, III	
	AE5	US-5,738,792	04-14-1998	Schoendorfer	
	AF5	US-5,762,791	06-09-1998	Deniega et al.	
	AG5	US-5,779,660	07-14-1998	Kingsley et al.	
	AH5	US-5,783,085	07-21-1998	Fischel	
	AI5	US-5,792,351	08-11-1998	Wehrle et al.	
	AJ5	US-5,849,203	12-15-1998	Brown et al.	
	AK5	US-5,882,289	03-16-1999	Sakota et al.	
	AL5	US-5,906,589	05-25-1999	Gordon et al.	
	AM5	US-5,919,125	07-06-1999	Berch	

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

ME1 36057896v.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0111

Used in Lieu of PTO/SB/08A/B
(Based on PTO 10-07 version)

Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	Not Yet Assigned
				Filing Date	Concurrently Herewith
				First Named Inventor	Michael Ragusa
(Use as many sheets as necessary)				Art Unit	3781
				Examiner Name	Not Yet Assigned
Sheet	4	of	6	Attorney Docket Number	130670-80104

	AN5	US-5,964,724	10-12-1999	Rivera et al.	
	AO5	US-5,970,432	10-19-1999	Ishimoto et al.	
	AP5	US-5,980,760	11-09-1999	Min et al.	
	AQ5	US-6,007,725	12-28-1999	Brown	
	AR5	US-6,059,979	05-09-2000	Brown	
	AS5	US-6,207,063-B1	03-27-2001	Brown	
	AT5	US-6,234,989-B1	05-22-2001	Brierton et al.	
	AU5	US-6,296,602-B1	10-02-2001	Headley	
	AV5	US-6,464,624-B2	10-15-2002	Pages	
	AW5	US-6,497,676-B1	12-24-2002	Childers et al.	
	AX5	US-6,558,307-B2	05-06-2003	Headley	
	AY5	US-6,623,443-B1	09-23-2003	Polaschegg	
	AZ5	US-6,743,192-B1	06-01-2004	Sakota et al.	
	AA6	US-7,115,205-B2	10-03-2006	Robinson et al.	
	AB6	US-7,186,231-B2	03-06-2007	Takagi et al.	
	AC6	US-7,270,645-B2	09-18-2007	Langley et al.	
	AD6	US-7,704,454-B1	04-27-2010	Langley et al.	
	AE6	US-8,628,489-B2	01-14-2014	Pages et al.	
	AF6	US-8,702,637-B2	04-22-2014	Pages et al.	
	AG6	US-8,759,094-B2	06-24-2014	Ranby	
	AH6	US-9,283,316-B2	03-15-2016	Flexman	
	AI6	US-10,758,652-B2	09-01-2020	Ragusa	
	AJ6	US-10,792,416-B2	10-06-2020	Ragusa	
	AK6	US-20010000185-A1	04-05-2001	Keller et al.	
	AL6	US-20010027156-A1	10-04-2001	Egozy et al.	
	AM6	US-20020043492-A1	04-18-2002	Bischof	
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	AP6	US-20030055375-A1	03-20-2003	Holst et al.	
	AQ6	US-20030066807-A1	04-10-2003	Suzuki	
	AR6	US-20030125881-A1	07-03-2003	Ryan	
	AS6	US-20030175150-A1	09-18-2003	Grimm	
	AT6	US-20040186409-A1	09-23-2004	Cavalcanti et al.	
	AU6	US-20050209522-A1	09-22-2005	Tadokoro et al.	
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	AW6	US-20060058167-A1	03-16-2006	Ragusa et al.	
	AX6	US-20060155236-A1	07-13-2006	Gara et al.	
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	AA7	US-20120175313-A1	07-12-2012	Barry, JR. et al.	
	AB7	US-20140039373-A1	02-06-2014	Ragusa et al.	
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	AE7	US-20200345924-A1	11-05-2020	Ragusa	
	AF7	US-20200261630-A1	08-20-2020	Ragusa	

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

ME1 36057896v.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Used in Lieu of PTO/SB/08A/B
(Based on PTO 10-07 version)

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 5 of 6

Complete if Known	
Application Number	Not Yet Assigned
Filing Date	Concurrently Herewith
First Named Inventor	Michael Ragusa
Art Unit	3781
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3]-Number[4]-Kind Code[5] *(if known)*	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T[6]
	BA**	CN-2735985-Y	10-26-2005	Shanghai Dahua Medical Apparatus Co., Ltd		√
	BB**	EP-0128683-A2	12-19-1984	Baxter Travenol Laboratories, Inc		
	BC**	EP-0171749-A1	02-19-1986	Terumo Corp		
	BD**	EP-0208061-A1	01-14-1987	Biotest Pharma GmbH		
	BE**	EP-257755-A1	03-02-1988	Haemonetics Corp		
	BF**	EP-0578086-A1	01-12-1994	Terumo Corp		
	BG**	EP-619145-A2	10-12-1994	Electromedics, Inc		
	BH**	EP-0654277-A1	05-24-1995	Cobe Laboratories, Inc		
	BI**	EP-664159-A1	07-26-1995	Haemonetics Corp		
	BJ**	EP-799645-A1	10-08-1997	Haemonetics Corp		
	BK**	EP-0885619-A1	12-23-1998	Terumo Corp		
	BL**	EP-1057534-A1	12-06-2000	Haemonetics Corp		
	BM**	EP-1295619-A2	03-26-2003	Terumo Corp		
	BN**	EP-1374927-A1	01-02-2004	Terumo Corp		
	BO**	FR-2258898-A1	08-22-1975	Heraeus Christ Gmbh,dt		
	BP**	GB-2047110-A	11-26-1980	Hogman, C F		
	BQ**	JP-S59-006952	01-14-1984	Hitachi Koki KK		√
	BR**	JP-S59-069166	04-19-1984	Nikkiso Co Ltd.		√
	BS**	JP-H02-052665	02-22-1990	Nissho KK		√
	BT**	JP-H03-131268	06-04-1991	Fresenius AG		√
	BU**	JP-H07-075746	03-20-1995	Electromedics Inc.		√
	BV**	JP-H08-131539	05-28-1996	Terumo Corp.		√
	BW**	JP-H09-192215	07-29-1997	Nakane Takaharu		√
	BX**	JP-2002-291872-A	10-08-2002	Terumo Corp		√
	BY**	JP-2008-506424-A	03-06-2008			√
	BZ**	SU-660718-A1	05-05-1979	Sp K B Biofizicheskoj Apparatu		
	BA1**	SU-762982-A1	09-15-1980	Sp K B Biofizicheskoj Apparatu		
	BB1**	SU-1146098-A1	03-23-1985	Sp K B Biofiz App		
	BC1**	WO-1985/02561-A1	06-20-1985	Baxter Travenol Laboratories, Inc		
	BD1**	WO-1990/00059-A1	01-11-1990	Sirchia, Girolamo		
	BE1**	WO-1990/07383-A1	07-12-1990	Haemonetics Corp		
	BF1**	WO-1994/06535-A1	03-31-1994	Fischel, Halbert		
	BG1**	WO-1996/11747-A2	04-25-1996	Transfusion, Technologies Corporation		
	BH1**	WO-1996/33023-A1	10-24-1996	Cobe Laboratories, Inc		
	BI1**	WO-2002/05059-A2	01-17-2002	Baxter Int		

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

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Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0113

Used in Lieu of PTO/SB/08A/B
(Based on PTO 10-07 version)

Substitute for form 1449/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	Not Yet Assigned
				Filing Date	Concurrently Herewith
				First Named Inventor	Michael Ragusa
(Use as many sheets as necessary)				Art Unit	3781
				Examiner Name	Not Yet Assigned
Sheet	6	of	6	Attorney Docket Number	130670-80104

	BJ1**	WO-2007/041716-A1	04-12-2007	Gambro, Inc		☐

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. * CITE NO.: Those application(s) which are marked with an single asterisk (*) next to the Cite No. are not supplied (under 37 CFR 1.98(a)(2)(iii)) because that application was filed after June 30, 2003 or is available in the IFW. ** CITE NO.: Those document(s) which are marked with an double asterisk (**) next to the Cite No. are not supplied because they were previously cited by or submitted to the Office in a prior application relied upon in this application for an earlier filing date under 35 U.S.C. 120. [1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	CA**	Haemonetics Nomogram - Male, 2 pages, May 1990.	
	CB**	LEMMENS et al., Estimating blood volume in obese and morbidly obese patients. Obes Surg. 2006 Jun;16(6):773-6.	
	CC**	NADLER et al., Prediction of blood volume in normal human adults. Surgery. 1962 Feb;51(2):224-32.	
	CD**	WINTERS, Complications of donor apheresis. J Clin Apher. 2006 Jul;21(2):132-41.	
	CE**	International Search Report and Written Opinion for Application No. PCT/US2018/033826, dated August 3, 2018, 10 pages.	
	CF**	International Search Report and Written Opinion for Application No. PCT/US2018/057528, dated January 7, 2019, 17 pages.	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1]Applicant's unique citation designation number (optional). [2]Applicant is to place a check mark here if English language Translation is attached.

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

ME1 36057896v.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

PTO/SB/92 (07-16)
Approved for use through 12/31/2020. OMB 0561-0031
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   P.O. Box 1450
   Alexandria, VA 22313-1450

   on _____ .
   Date

2. ☐ Facsimile transmitted to the United States Patent and Trademark Office, or

   OR

3. ☒ EFS-Web transmitted to the USPTO.

/Jonathan C. Lovely, Reg. No. 60,821/	March 22, 2021
Signature	Date
Jonathan C. Lovely	(617) 449-6556
Typed or printed name	Telephone number

Note: Each paper must have its own certificate of mailing or transmission, or this certificate must identify each submitted paper:

IDS (Citation) by Applicant (230 References) (6 pages)

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Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0115

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: December 8, 2022
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 Confirmation No.: 4686

Filed: March 18, 2021 Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING PLASMA Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications. Applicant submits herewith copies of foreign patents and non-patent literature in accordance with 37 C.F.R. § 1.98(a)(2).

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0116

Application No.: 17/205,400 Docket No.: 130670-80104

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	10,980,926	Issued	130670-08005
17/205,374	March 18, 2021	2021-0205509	Published	130670-08006
17/943,410	September 13, 2022		Pending	130670-08007
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	10,980,934	Issued	130670-80103

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: December 8, 2022

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0117

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	3799
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

U.S.PATENTS

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20060226086	A1	2006-10-12	Robinson et al.	
	2	20210205509	A1	2021-07-08	Ragusa	

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	1	1128887	EP	A1	2001-09-05	Baxter Int		

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Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0118

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	3799
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/LESLIE R DEAK/ (05/02/2024)	Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0119

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	3799
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2021-07-14
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0120

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.C.L./

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0121

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 14, 2021
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 Confirmation No.: 4686

Filed: March 18, 2021 Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING PLASMA Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patent applications. Applicant submits herewith a copy of the cited foreign patent in accordance with 37 C.F.R. § 1.98(a)(2).

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0122

Application No.: 17/205,400 Docket No.: 130670-80104

The Examiner is advised that the following co-pending applications contain subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	10,980,926	Issued	130670-08005
17/205,374	March 18, 2021	2021-0205509	Published	130670-08006
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	10,980,934	Issued	130670-80103

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: July 14, 2021

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0123

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2019/10/28 11:36 AM
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Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0124

L11	1805	L10 and hematocrit	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2019/10/28 12:26 PM
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L13	1	"l10" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2019/10/28 12:30 PM
L14	2	"l10" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2019/10/28 12:30 PM
L15	44	((("RAGUSA") near3 ("Michael"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	OFF	OFF	2019/10/28 12:31 PM
L16	2	"l15" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2019/10/28 12:31 PM
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Terumo v. Haemonetics - PGR2026-00063
Petitioner Terumo Exhibit 1014-0125

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L20	1	("10758652").PN.	(USPAT; USOCR)	OR	OFF	OFF	2020/11/05 03:16 PM
L21	0	("20120175313").PN.	(USPAT; USOCR)	OR	OFF	OFF	2020/11/05 04:22 PM

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0126

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L24	8	L23 and prim$3	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2020/11/05 04:22 PM
L25	0	(10/302682).APP.	(USPAT; USOCR)	OR	OFF	OFF	2020/11/05 04:26 PM
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L27	120	A61M1/024.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2021/02/01 01:20 PM
L28	708	G01n15/05.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2021/02/01 01:21 PM
L29	150	G01n2015/055.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2021/02/01 01:21 PM
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L31	0	L30 AND touchscreen	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/04/30 12:21 PM
L32	0	touchscreen WITH plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 12:22 PM
L33	4	touchscreen SAME plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 12:22 PM
L34	16	"10980926"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)	OR	ON	ON	2024/04/30 03:40 PM
L35	200	("1025059" | "1611725" | "2087778" | "2661150" | "2750107" | "2792172" | "3096283" | "3145713" | "3239136" | "3244362" | "3244363" | "3409213"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2024/04/30 04:01 PM

Terumo v. Haemonetics - PGR2026-00060
Petitioner Terumo Exhibit 1014-0127

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L38	11	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM

L39	53	((A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
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L45	12466	((A61M1/024 OR A61M1/029 OR A61M1/3672 OR A61M1/3693 OR A61M1/38 OR A61M2202/0415 OR A61M2230/207 OR G01N15/05 OR G01N2015/055 OR G01N15/042 OR G01N33/86).CPC.)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L46	2470	L10 and hematocrit	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L47	7	"I11" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L48	6	"I10" and (hematocrit with anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
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L50	59	((("RAGUSA") near3 ("Michael"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
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Terumo v. Haemonetics - PGR2026-00067
Petitioner Terumo Exhibit 1014-0130

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L53	2	("20180344910").PN.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L54	11	"I15" and (hematocrit same anticoagulant)	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L55	1	("10758652").PN.	(USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L56	0	("20120175313").PN.	(USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L57	5	"20120175313"	(USPAT)	OR	OFF	OFF	2024/04/30 04:36 PM
L58	13	("4713176" | "6348156" | "6875191" | "7011761" | "7087177" | "7297272" | "7708710" | "8075468").PN. OR ("8852140").URPN.	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L59	9	L23 and prim$3	(US-PGPUB; USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L60	0	(10/302682).APP.	(USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L61	2	"20140100507"	(USPAT; USOCR)	OR	OFF	OFF	2024/04/30 04:36 PM
L62	190	A61M1/024.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L63	987	G01n15/05.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM

Terumo v. Haemonetics - PGR2026-00009
Petitioner Terumo Exhibit 1014-0132

L64	220	G01n2015/055.cpc.	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L65	3	((US-20030125881-A1).did. AND PGPB.dbnm.) OR ((US-10758652-B2 OR US-6348156-B1).did. AND USPT.dbnm.)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/04/30 04:36 PM
L66	0	L30 AND touchscreen	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2024/04/30 04:36 PM
L67	0	touchscreen WITH plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L68	4	touchscreen SAME plasmapheresis	(US-PGPUB; USPAT; USOCR; DERWENT)	OR	OFF	OFF	2024/04/30 04:36 PM
L69	16	"10980926"	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, CA, CH, CN, DD, DE, EA, EP, ES, FR, GB, JP, KR, OA, RU, SU, WO); EPO; JPO; DERWENT)	OR	ON	ON	2024/04/30 04:36 PM
L70	200	("1025059" | "1611725" | "2087778" | "2661150" | "2750107" | "2792172" | "3096283" | "3145713" | "3239136" | "3244362" | "3244363" | "3409213" | "3456875" | "3489145" | "3565330" | "3655058" | "3737096" | "3774840" | "3987961" | "4007871" | "4010894" | "4014497" | "4040965" | "4056224" | "4082217" | "4086924" | "4140268" | "4142670" | "4151844" | "4197847" | "4285464" | "4300717" | "4303193" | "4321921" | "4387848" | "4425114" | "4430072" | "4447221" | "4457747" | "4464167" | "4466888" | "4482342" | "4490135" | "4530691" | "4534863" | "4643714" | "4647279" | "4655742" | "4680025" | "4684361" | "4692136" | "4708712" | "4713176" | "4734089"	(US-PGPUB; USPAT; USOCR)	OR	ON	ON	2024/04/30 04:36 PM

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0133

		| "4740202" | "4740313" | "4755300" | "4767396" | "4795419" | "4795448" | "4806247" | "4806252" | "4808307" | "4850995" | "4869812" | "4871462" | "4876013" | "4889524" | "4911833" | "4934995" | "4940543" | "4943273" | "4968295" | "4983156" | "4983158" | "4985153" | "4994188" | "5039401" | "5045048" | "5098372" | "5098373" | "5100372" | "5100564" | "5112298" | "5114396" | "5135667" | "5141486" | "5147290" | "5154716" | "5174894" | "5194145" | "5217426" | "5217427" | "5234403" | "5254248" | "5273517" | "5277701" | "5298016" | "5298171" | "5300060" | "5316540" | "5318511" | "5318512" | "5348533" | "5368542" | "5368555" | "5386734" | "5387174" | "5387187" | "5403272" | "5405308" | "5417650" | "5431814" | "5437598" | "5437624" | "5462667" | "5470483" | "5484396" | "5494592" | "5505685" | "5514070" | "5543062" | "5551941" | "5585007" | "5607579" | "5649903" | "5651766" | "5656163" | "5665061" | "5712798" | "5728060" | "5733253" | "5733446" | "5733545" | "5738792" | "5762791" | "5779660" | "5783085" | "5792351" | "5849203" | "5882289" | "5906589" | "5919125" | "5964724" | "5970432" | "5980760" | "6007725" | "6059979" | "6207063" | "6234989" | "6296602" | "6464624" | "6497676" | "6558307" | "6623443" | "6743192" | "7115205" | "7186231" | "7270645" | "7704454" | "8628489" | "8702637" | "8759094" | "9283316" | "10758652" | "20010000185" | "20010027156" |				

		"20020043492" | "20020062100" | "20020120227" | "20030055375" | "20030066807" | "20030125881" | "20030175150" | "20040186409" | "20050209522" | "20050235733" | "20060058167" | "20060155236" | "20070112289" | "20080146993" | "20120175313" | "20140039373" | "20140356851" | "20180344910" | "20180344921").pn. AND (PGPB | USPT | USOC).dbnm.					

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0135

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: March 22, 2021
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 Confirmation No.: N/A

Filed: March 18, 2021 Art Unit: 3781

For: SYSTEM AND METHOD FOR COLLECTING PLASMA Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98, the attention of the United States Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of the above-identified application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed within three months of the U.S. filing date (37 C.F.R. § 1.97(b)(1)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications.

In accordance with 37 C.F.R. § 1.98(d)(1) and as noted by a double-asterisk next to the Cite No. on the attached PTO/SB/08, the cited references are not supplied because they were previously

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0136

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.C.L./

cited by or submitted to the Office in prior application numbers 16/931333 filed July 16, 2020, 15/793339 filed October 25, 2017, and 15/608183 filed May 30, 2017 and relied on in the above-identified application for an earlier effective filing date under 35 U.S.C. § 120.

The Examiner is advised that the following co-pending application contains subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	2020-0261630	Allowed	130670-08005
17/205,374	March 18, 2021		Pending	130670-08006
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	2020-0345924	Allowed	130670-80103

/LESLIE R DEAK/ (05/02/2024)

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0137

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /L.R.D./

Applicant believes no fee is due with this response.

Dated: March 22, 2021

Respectfully submitted,

Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/

Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0138

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.C.L./

PTO/SB/08a (01-22)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	8075468	B2	2011-12-13	Min et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20090215602	A1	2009-08-27	Min et al.	
	2	20230001059	A1	2023-01-05	Ragusa, Michael	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0139

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0140

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17205400
	Filing Date	2021-03-18
	First Named Inventor	Michael Ragusa
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2023-01-17
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0141

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0142

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: January 17, 2023
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 | Confirmation No.: 4686

Filed: March 18, 2021 | Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING PLASMA | Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08a and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications.

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0143

an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: January 17, 2023

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0144

Electronic Acknowledgement Receipt

EFS ID:	47377086
Application Number:	17205400
International Application Number:	
Confirmation Number:	4686
Title of Invention:	SYSTEM AND METHOD FOR COLLECTING PLASMA
First Named Inventor/Applicant Name:	Michael Ragusa
Customer Number:	86738
Filer:	Jonathan Lovely
Filer Authorized By:	
Attorney Docket Number:	130670-80104
Receipt Date:	17-JAN-2023
Filing Date:	18-MAR-2021
Time Stamp:	11:58:41
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	130670-80104_-_Information_Disclosure_Statement_Fillable_PDF.pdf	1263200 aea70d91cbb87a642b34504556290d30e6b5f8b7	no	4

Warnings:

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0145

Information:					
2	Transmittal Letter	Information_Disclosure_Statement.pdf	22280 4f17cd35fe971e424691bfd83301d2d1ac2d552b	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	1285480	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/08a (01-22)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6200287	B1	2001-03-13	Keller et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20050131334	A1	2005-06-16	Langley et al.	
	2	20140100507	A1	2014-04-10	Flexman, Greg	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	103354755	CN	A	2013-10-16	Haemonetics Corp		☓
	2	69434848	DE		2007-04-12	Gambro Inc		☒

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0147

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17205400
	Filing Date	2021-03-18
	First Named Inventor	Michael Ragusa
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	130670-80104

	3	2003-516175	JP	A	2003-05-13	Baxter International, Inc.		☒
	4	2012/091720	WO	A1	2012-07-05	Haemonetics Corp		☐
	5	2019/084278	WO	A1	2019-05-02	Haemonetics Corp		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0148

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2022-12-08
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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Petitioner Terumo Exhibit 1014-0150

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: December 8, 2022
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 | Confirmation No.: 4686

Filed: March 18, 2021 | Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING PLASMA | Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications. Applicant submits herewith copies of foreign patents and non-patent literature in accordance with 37 C.F.R. § 1.98(a)(2).

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	10,980,926	Issued	130670-08005
17/205,374	March 18, 2021	2021-0205509	Published	130670-08006
17/943,410	September 13, 2022		Pending	130670-08007
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	10,980,934	Issued	130670-80103

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: December 8, 2022

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

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Petitioner Terumo Exhibit 1014-0152

Electronic Acknowledgement Receipt

EFS ID:	47168838
Application Number:	17205400
International Application Number:	
Confirmation Number:	4686
Title of Invention:	SYSTEM AND METHOD FOR COLLECTING PLASMA
First Named Inventor/Applicant Name:	Michael Ragusa
Customer Number:	86738
Filer:	Jonathan Lovely
Filer Authorized By:	
Attorney Docket Number:	130670-80104
Receipt Date:	08-DEC-2022
Filing Date:	18-MAR-2021
Time Stamp:	13:28:35
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	130670-08006_-_CN103354755A.pdf	1453318 3995ee6a4b89044fc76ea622e6a55a53bb2c0dc2	no	20

Warnings:

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Petitioner Terumo Exhibit 1014-0153

Information:					
2	Foreign Reference	130670-08006_-_DE69434848D1.pdf	521594 7fe209b3e980efe69c16b64182b4a2b8fdecdae4	no	31
Warnings:					
Information:					
3	Foreign Reference	JP2003-516175.PDF	537737 17a8a4260f1a039ab70a14c8f45692f877aa96f7	no	55
Warnings:					
Information:					
4	Foreign Reference	130670-08006_-_WO2012091720A1.pdf	1668381 5e3a5f0b086c3624c2de927fd5c0cb9e2285da6e	no	36
Warnings:					
Information:					
5	Foreign Reference	130670-80104_-_WO2019084278A1.pdf	1958593 167d000d21fca87cd0fa49b9a10d076e1b503e61	no	38
Warnings:					
Information:					
6	Information Disclosure Statement (IDS) Form (SB08)	130670-80104_-_Information_Disclosure_Statement_Fillable_PDF.pdf	1263517 ce372a64594fb04bf72ceb314c39b1bdacca5912	no	4
Warnings:					
Information:					
7	Transmittal Letter	Information_Disclosure_Statement.pdf	25366 3c6848e84187133cba01b41eee28e479284dad74	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	7428506	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Espacenet

Bibliographic data: CN103354755 (A) — 2013-10-16

System and method for collecting platelets and anticipating plasma return

Inventor(s): PAGES ETIENNE ± (PAGES ETIENNE)

Applicant(s): HAEMONETICS CORP ± (HAEMONETICS CORPORATION)

Classification: - international: ***A61M37/00***
- cooperative: **A61M1/0272 (EP)**; **A61M1/3603 (EP)**; **A61M1/3696 (EP)**; **A61M1/38 (EP)**; A61M2202/0415 (EP); A61M2202/0427 (EP)

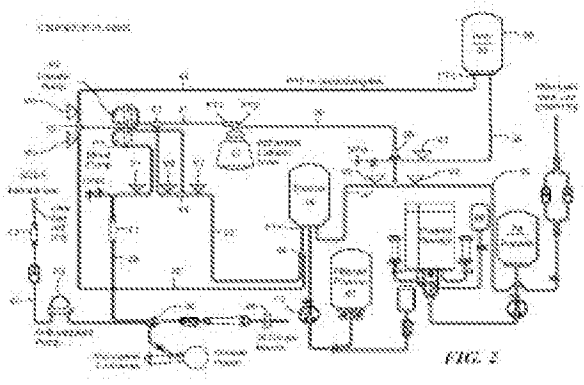
Application number: CN20108071156 20101230 Global Dossier

Priority number (s): WO2010US62540 20101230

Also published as: CN103354755 (B) EP2658596 (A1) EP2658596 (A4) EP2658596 (B1) HK1190103 (A1) more

Abstract of CN103354755 (A)

A blood processing system for collecting plasma reduced platelets and anticipating plasma return includes a venous access device, a blood component separation device, a first return line, a recirculation line, and a second return line. The venous access device draws whole blood from a subject and returns blood components to the subject using a first pump. The blood component separation device separates the drawn blood into a first blood component and a second blood component, and sends the first blood component to a first blood component bag. The first return line fluidly connects the venous-access device and the blood component separation device. The recirculation line connects the first blood component container and the separation device. The second return line fluidly connects the first blood component container and the first return line and is configured to return the first blood component within the first blood container to the subject.



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Petitioner Terumo Exhibit 1014-0156

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Petitioner Terumo Exhibit 1014-0157

(19)中华人民共和国国家知识产权局

(12)发明专利申请

(10)申请公布号 CN 103354755 A
(43)申请公布日 2013.10.16

(21)申请号 201080071156.9
(22)申请日 2010.12.30
(85)PCT申请进入国家阶段日
2013.08.01
(86)PCT申请的申请数据
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(87)PCT申请的公布数据
WO2012/091720 EN 2012.07.05
(71)申请人 美国血液技术公司
地址 美国马萨诸塞
(72)发明人 E·帕热斯
(74)专利代理机构 中国国际贸易促进委员会专利商标事务所 11038
代理人 焦丽雅
(51)Int.Cl.
A61M 37/00(2006.01)

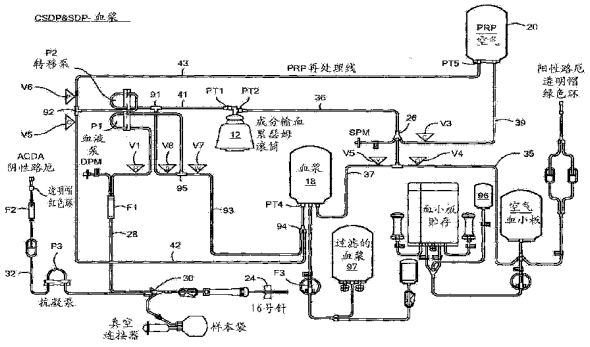
权利要求书4页 说明书9页 附图4页

(54)发明名称

用于收集血小板和预期血浆返回的系统和方法

(57)摘要

用于收集血浆减少的血小板并预期血浆返回的血液处理系统包括静脉接入装置、血液成分分离装置、第一返回线、再循环线和第二返回线。使用第一泵，静脉接入装置从受试者抽取全血并将血液成分返回至受试者。血液成分分离装置将抽取的血液分离成第一血液成分和第二血液成分，并且将第一血液成分传送至第一血液成分袋。第一返回线流体连接静脉接入装置和血液成分分离装置。再循环线连接第一血液成分容器和分离装置。第二返回线流体连接第一血液成分容器和第一返回线，并且构造成将第一血液容器内的第一血液成分返回至受试者。



CN 103354755 A

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Petitioner Terumo Exhibit 1014-0158

1. 一种用于收集血浆减少的血小板和预期血浆返回的方法，其包括：

a）从供体抽取全血；

b）将抗凝剂引入从供体抽取的全血中；

c）将抗凝全血引入分离室中，分离室将抗凝全血分离成多种血液成分。

d）将从抗凝全血分离出的血浆转移至血浆容器中；

e）将来自血浆容器的第一体积的血浆返回至供体；

f）重复步骤 a 至 d；

g）从分离室中将富含血小板的血浆提取至富含血小板的血浆容器中；和

h）将分离室内剩余的血液成分返回至供体。

2. 根据权利要求 1 的方法，进一步包括：

i）重复步骤 a 至 c，以将分离装置部分填充抗凝全血；

j）将来自富含血小板的血浆容器的富含血小板的血浆重新引入分离室中；

k）将来自分离室的血浆转移至血浆容器中；和

l）将重新引入的富含血小板的血浆再处理，以在分离装置内形成扩大的血小板层。

3. 根据权利要求 2 的方法，进一步包括：

m）将来自血浆容器的血浆返回至供体，同时再处理富含血小板的血浆。

4. 根据权利要求 2 的方法，进一步包括：

m）将来自血浆容器的血浆返回至供体，同时将富含血小板的血浆重新引入分离室中。

5. 根据权利要求 2 的方法，进一步包括：

m）使用浪涌淘洗方法取出分离装置内的扩大的血小板层，使得将血小板转移至血小板容器中；和

n）将分离室内剩余的血液成分返回至供体。

6. 根据权利要求 5 的方法，进一步包括在停歇时间过程中将来自血浆容器的血浆返回至供体。

7. 根据权利要求 1 的方法，进一步包括：

计算额外身体体积和血管内不足中的至少一个，并且步骤（e）过程中返回的血浆体积至少部分基于计算的额外身体体积或血管内不足。

8. 根据权利要求 1 的方法，其中从分离室提取富含血小板的血浆包括通过浪涌淘洗提取富含血小板的血浆。

9. 根据权利要求 8 的方法，其中通过浪涌淘洗从分离室提取富含血小板的血浆包括用血浆浪涌。

10. 一种用于收集血浆减少的血小板和预期血浆返回的系统，其包括：

使用第一泵从患者抽取第一体积的全血和将血液成分返回至患者的静脉接入装置；

用于将抽取的血液分离成第一血液成分和第二血液成分的血液成分分离装置，血液成分分离装置构造成将第一血液成分传送至第一血液成分袋和将第二血液成分传送至第二血液成分袋；

流体连接静脉接入装置和血液成分分离装置的第一返回线，用于将分离装置中剩余的血液成分返回至患者；

连接第一血液成分容器和分离装置的再循环线，其中通过再循环线和再循环泵将第一

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血液成分容器内的第一血液成分重新引入分离室中；和

流体连接第一血液成分容器和第一返回线的第二返回线，并构造成将第一血液容器内的第一血液成分返回至患者。

11. 根据权利要求 10 的系统，其中第一泵将第一血液成分容器内的第一血液成分返回至患者。

12. 根据权利要求 10 的系统，其中第一泵将分离装置中剩余的血液成分返回至患者。

13. 根据权利要求 10 的系统，其中分离装置是离心滚筒。

14. 根据权利要求 10 的系统，其中第一血液成分是血浆，而第二血液成分是血小板。

15. 根据权利要求 10 的系统，其中除了第一和第二血液成分外，分离装置将全血分离成第三种血液成分。

16. 根据权利要求 15 的系统，其中分离装置内剩余的血液成分包括第三种血液成分。

17. 根据权利要求 15 的系统，其中第三种血液成分是红细胞。

18. 根据权利要求 10 的系统，其中使用浪涌淘洗方法从分离装置中取出第二血液成分。

19. 根据权利要求 18 的系统，其中浪涌淘洗方法包括以递增的速率通过再循环线将第一血液成分重新引入血液成分分离装置中，直至从血液成分分离装置中取出第二血液成分。

20. 根据权利要求 10 的系统，进一步包括连接抗凝剂来源的抗凝剂线，抗凝剂线将抗凝剂引入抽取的血液中。

21. 根据权利要求 10 的系统，其中第二血液成分是血小板，并且在第二血液成分容器内收集预定量的血小板后，重新引入血液成分分离装置中，使得从分离装置提取血浆减少的血小板产品。

22. 根据权利要求 10 的系统，进一步包括流体连接第二血液成分袋和血液成分分离装置的重新引入线，其中从患者抽取第二体积的全血时，将第二血液成分袋内的第二血液成分重新引入血液成分分离装置中，由此在血液成分分离装置内形成扩大的第二血液成分层，使用浪涌淘洗方法从血液成分分离装置中取出扩大的第二血液成分层。

23. 根据权利要求 22 的系统，其中随着将第二血液成分重新引入血液成分分离装置中，将第一血液成分容器内的第一血液成分返回至患者。

24. 根据权利要求 10 的系统，其中在停歇时间过程中将第一血液成分容器内的第一血液成分返回至患者。

25. 根据权利要求 10 的系统，进一步包括控制器，控制器计算额外身体体积和血管内不足中的至少一个，至少部分基于计算的额外身体体积或血管内不足，系统通过第二返回线返回一定体积的第一血液成分。

26. 一种用于收集血浆减少的血小板和预期血浆返回的系统，其包括：

用于从患者抽取第一体积的全血并将血液成分返回至患者的装置，

用于将抽取的血液分离成第一血液成分和第二血液成分的血液成分分离装置，血液成分分离装置构造成将第一血液成分传送至第一血液成分袋和将第二血液成分袋传送至第二血液成分袋；

流体连接用于抽取第一体积全血的装置和血液成分分离装置的第一返回装置，第一返

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回装置构造成将分离装置内剩余的血液成分返回至患者，

连接第二血液成分容器和分离装置的再循环装置，其中再循环装置将第二血液成分容器内的第二血液成分重新引入分离装置中；和

流体连接第一血液成分容器和第一返回装置的第二返回装置，并且构造成将第一血液成分容器内的第一血液成分返回至患者。

27. 根据权利要求 26 的系统，其中用于抽取全血的装置包括第一泵，第一泵构造成将第一血液成分容器内的第一血液成分返回至受试者。

28. 根据权利要求 27 的系统，其中第一泵还构造成将分离装置中剩余的血液成分返回至受试者。

29. 根据权利要求 26 的系统，进一步包括用于控制流体通过系统的流动的控制器，控制器重复地将供体的全血抽取至分离装置中，从分离装置提取第一和第二血液成分，使用第二返回装置将第一血液成分容器内的第一血液成分返回至受试者，并且使用第一返回装置将分离装置内剩余的成分返回至受试者，其中在第二血液成分容器中获得预定体积的第二血液成分后，将来自第二血液成分容器的第二血液成分重新引入分离装置中。

30. 根据权利要求 29 的方法，其中控制器计算额外身体体积和血管内不足中的至少一个，使用第二返回装置返回的第一血液成分的量至少部分基于额外身体体积和血管内不足中的至少一个。

31. 根据权利要求 26 的系统，其中第一血液成分是血浆，而第二血液成分是血小板。

32. 根据权利要求 26 的系统，其中除了第一和第二血液成分外，分离装置将全血分离成第三种血液成分。

33. 根据权利要求 32 的系统，其中分离装置内剩余的血液成分包括第三种血液成分。

34. 根据权利要求 32 的系统，其中第三种血液成分是红细胞。

35. 根据权利要求 26 的系统，其中使用浪涌淘洗方法从分离装置中取出第二血液成分。

36. 根据权利要求 35 的系统，其中浪涌淘洗方法包括以递增的速率通过再循环装置将第一血液成分重新引入血液成分分离装置中，直至从血液成分分离装置中取出第二血液成分。

37. 根据权利要求 26 的系统，进一步包括用于将抗凝剂引入抽取的全血中的装置。

38. 根据权利要求 26 的系统，其中第二血液成分是血小板，并且在第二血液成分容器内收集预定量的血小板后，重新被引入血液成分分离装置中，使得从分离装置提取血浆减少的血小板产品。

39. 根据权利要求 26 的系统，进一步包括流体连接第二血液成分袋和血液成分分离装置的重新引入装置，其中从受试者抽取第二体积的全血时，将第二血液成分袋内的第二血液成分重新引入血液成分分离装置中，由此在血液成分分离装置内形成扩大的第二血液成分层，使用浪涌淘洗方法从血液成分分离装置中取出扩大的第二血液成分层。

40. 一种用于收集血浆减少的血小板和预期血浆返回的方法，其包括：

a）从来源抽取全血；

b）将抗凝剂引入从来源抽取的全血中；

c）将抗凝全血引入分离室中，分离室将抗凝全血分离成多种血液成分。

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d）将从抗凝全血分离出的血浆转移至血浆容器中；

e）将来自血浆容器的第一体积的血浆返回至来源；

f）重复步骤 a 至 d；

g）从分离室将富含血小板的血浆提取至富含血小板的血浆容器中；和

h）将分离室内剩余的血液成分返回至来源。

41. 根据权利要求 40 的方法，进一步包括：

i）重复步骤 a 至 c，以将分离装置部分填充抗凝全血；

j）将来自富含血小板的血浆容器的富含血小板的血浆重新引入分离室中；

k）将来自分离室的血浆转移至血浆容器中；和

l）将重新引入的富含血小板的血浆再处理，以在分离装置内形成扩大的血小板层。

42. 根据权利要求 41 的方法，进一步包括：

m）将来自血浆容器的血浆返回至来源，同时再处理富含血小板的血浆。

43. 根据权利要求 41 的方法，进一步包括：

m）将来自血浆容器的血浆返回至来源，同时将富含血小板的血浆重新引入分离室中。

44. 根据权利要求 41 的方法，进一步包括：

m）使用浪涌淘洗方法取出分离装置内的扩大的血小板层，使得将血小板转移至血小板容器中；和

n）将分离室内剩余的血液成分返回至来源。

45. 根据权利要求 44 的方法，进一步包括在停歇时间过程中将来自血浆容器的血浆返回至来源。

46. 根据权利要求 40 的方法，进一步包括：

计算额外身体体积和血管内不足中的至少一个，并且步骤（e）过程中返回的血浆体积至少部分基于计算的额外身体体积或血管内不足。

47. 根据权利要求 40 的方法，其中从分离室提取富含血小板的血浆包括通过浪涌淘洗提取富含血小板的血浆。

48. 根据权利要求 47 的方法，其中通过浪涌淘洗从分离室提取富含血小板的血浆包括用血浆浪涌。

49. 一种用于收集血浆减少的血小板的方法，其包括：

a）从来源抽取全血；

b）将抗凝剂引入从来源抽取的全血中；

c）将抗凝全血引入分离室中，分离室将抗凝全血分离成多种血液成分。

d）将从抗凝全血分离出的血浆转移至血浆容器中；

e）将来自血浆容器的第一体积的血浆返回至来源；

f）重复步骤 a 至 d；

g）从分离室将富含血小板的血浆提取至富含血小板的血浆容器中；和

h）取出分离室内剩余的血液成分。

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用于收集血小板和预期血浆返回的系统和方法

技术领域

[0001] 本发明涉及用于血液处理和血液成分收集的系统和方法，并且特别涉及用于收集血小板和预期血浆返回的系统和方法。

背景技术

[0002] 成分输血是其中自临时从患者中取出的全血中分离和收集单独的血液成分的程序。通常，通过插入患者手臂静脉的针取出全血并放入细胞分离器中，如离心滚筒。一旦将全血分成其各种成分，可以从离心滚筒中取出一种或多种成分。将剩余的成分与任选的用来补足取出成分体积的代偿流体一起返回患者。取出和返回的过程持续至收集到一定量的所需成分，在这一点停止该过程。成分输血系统的重要特征是将处理过的但不需要的成分返回至供体。分离的血液成分可以包括，例如，高密度成分，如红细胞，中密度成分，如血小板或白细胞，和较低密度的成分，如血浆。

[0003] 在通过成分输血可观察到的各种血液成分产物中，对血浆减少的血小板的需求正快速增长。这特别是因为，随着癌症治疗的提高，需要将越来越多的血小板给药于造血功能降低的患者，但所述患者可能不需要输入用于悬浮血小板的血浆。血小板是位于骨髓中的称为巨核细胞的大细胞的碎片，并且主要通过执行凝集功能来促进止血。血小板在组织愈合中也起着作用。成人体内的正常血小板计数为 150,000-400,000 个 /mm^3。低于 20,000 个 /mm^3 的血小板计数会引起各种问题，如自发性出血。

[0004] 血小板具有 4-6 天的短半衰期，并且供体的数量有限。因此，在生产血浆减少的血小板（plasma reduced platelet）产物中，重要的是以最大产量和所需的含量从供体提供的全血中收集血小板。此外，已知血浆减少的血小板产物受到白细胞的污染可能导致严重的中间并发症，如 GVH 反应。因此，将白细胞污染的水平保持尽可能的低，同时有效收集血小板也是非常重要的。为此，已经研发了各种技术。例如，使用“浪涌（surge）”技术，在收集全血并在离心机内离心分离成较高密度、中密度和较低密度成分并收集血浆（称为“抽取”步骤）后，通过离心以浪涌流速（例如，随着时间增加的流速）来提供血浆。通过进行浪涌，可以优先从中密度成分（其作为主要包含血小板和白细胞的混合物的血沉棕黄层存在）中转移出血小板，并以提高的产量生产血浆减少的血小板产物。

[0005] 替代使用浪涌技术，也可以通过层“推动（push）”从离心机提取出血小板层，其中将抗凝的全血引入滚筒中直至推出血小板层，或通过使用浪涌和推动方法的组合。收集所需的一种或多种成分后，将主要包含红细胞和柠檬酸盐化血浆的残余血液成分返回至供体（称为“返回”步骤）。

[0006] 如上所述，在许多血液成分输血程序和应用中，将不需要的成分（例如，未收集的成分）返回至供体。除了污染问题（例如，待返回至供体的污染、微粒等），必须考虑患者的舒适性。例如，将柠檬酸盐化血浆返回患者太快或一次返回太多柠檬酸盐化血浆给患者可能引起患者明显的不舒适性。此外，必须注意限制体外的流体体积（例如，额外身体体积）和 / 或体内流体的减少（例如，血管内不足）。

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[0007] 发明概述

[0008] 根据本发明一个实施方案，提供了一种用于收集血浆减少的血小板和预期血浆返回的方法。首先从供体抽取全血，抗凝，并引入分离室中。分离室将抗凝的全血分离成各种血液成分。该方法然后将从抗凝全血分离的血浆转移至血浆容器中，并且将来自血浆容器的第一体积的血浆返回至供体。该方法然后重复抽取、抗凝、引入和转移步骤，以将分离装置填充其他抗凝全血。

[0009] 一旦将抗凝全血引入分离室中(例如，填充该室)，该方法从分离室提取富含血小板的血浆(“PRP”)(例如，使用浪涌淘洗方法和 / 或用血浆浪涌)并放入 PRP 室中。该方法然后将分离室内剩余的血液成分返回至供体，并重复抽取、抗凝和引入步骤，直至分离室再次部分填充抗凝全血。一旦分离室部分填充，该方法然后将来自 PRP 容器的 PRP 再次引入分离室中，将来自分离室的血浆转移至血浆容器中，并且将重新引入的 PRP 再处理，以在分离装置内形成扩大的血小板层。

[0010] 根据一些实施方案，该方法可以预期血浆返回，并且将血浆容器内的血浆返回至供体，同时将 PRP 重新引入分离室和 / 或再处理 PRP。该方法然后再一次重复抽取、抗凝和引入步骤，以填充分离室，使用浪涌淘洗方法取出分离室内扩大的血小板层，使得将血小板转移至血小板容器中。该方法然后将分离室内剩余的血液成分返回至供体。

[0011] 根据相关的实施方案，该方法还可以在停歇时间(dead time)(目前的成分输血程序既没有抽取也没有将血液或血液成分返回至供体过程中的时间)过程中将血浆容器的血浆返回至供体。此外，该方法可以计算额外身体体积和 / 或血管内不足，并且返回至供体的血浆的第一体积可以基于，或至少部分基于计算的额外身体体积或血管内不足。

[0012] 根据本发明的另一个实施方案，用于收集血浆减少的血小板和预期血浆返回的系统包括静脉接入装置、血液成分分离装置、第一返回线、再循环线和第二返回线。静脉接入装置构造成使用第一泵从患者抽取第一体积的全血并将血液成分返回至患者。血液成分分离装置(例如，离心滚筒)将抽取的血液分离成第一血液成分(例如，血浆)和第二血液成分(例如，血小板)，并且构造成将第一血液成分传送至第一血液成分袋以及将第二血液成分传送至第二血液成分袋。

[0013] 第一返回线流体连接静脉接入装置和血液成分分离装置，并且构造成将分离装置中剩余的血液成分返回至患者。再循环线连接第一血液成分容器和分离装置。第二返回线流体连接第一血液成分容器和第一返回线，并且构造成将第一血液容器内的第一血液成分返回至患者。还可以将第一血液成分容器内的第一血液成分通过再循环线和再循环泵重新引入分离室内。

[0014] 第一泵可以用于将第一血液成分容器内的第一血液成分和分离装置内剩余的血液成分返回至患者。除了第一和第二血液成分外，分离装置还可以将全血分离成第三种血液成分(例如，红细胞)，并且分离装置中剩余的血液成分可以包括第三种血液成分。

[0015] 在一些实施方案中，可以使用浪涌淘洗方法从分离装置中取出第二血液成分。浪涌淘洗方法包括通过再循环线将第一血液成分以递增的速率重新引入血液成分分离装置中，直至第二血液成分从血液成分分离装置中取出。第二血液成分可以是血小板并且可以在第二血液成分容器内收集了预定量的血小板后重新引入血液成分分离装置中，使得从分离装置提取血浆减少的血小板产物。

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[0016] 系统还可以包括抗凝剂线和重新引入线。抗凝剂线可以连接抗凝剂来源，并且可以将抗凝剂引入吸出的血液中。重新引入线可以流体连接第二血液成分袋和血液成分分离装置。当从患者抽出第二体积的全血在血液成分分离装置内形成扩大的第二血液成分层时，可以将第二血液成分袋内的第二血液成分重新引入血液成分分离装置中。

[0017] 随着将第二血液成分重新引入血液成分分离装置中和/或在停歇时间过程中，系统可以将第一血液成分返回至患者。系统还可以包括计算额外身体体积和血管内不足中的至少一种的控制器。系统然后可以通过第二返回线返回一定体积的第一血液成分，所述体积至少部分基于计算的额外身体体积或血管内不足。

[0018] 根据本发明再进一步的实施方案，用于收集血浆减少的血小板的系统可以包括(1)用于从患者抽取第一体积的全血并将血液成分返回至患者的装置，(2)用于将抽取的血液分离成第一血液成分和第二血液成分的血液成分分离装置，(3)流体连接用于抽取第一体积全血的装置和血液成分分离装置并用于将分离装置内剩余的血液成分返回至患者的第一返回装置，(4)连接第二血液成分容器和分离装置的再循环装置，和(5)流体连接第一血液成分容器和第一返回装置的第二返回装置。血液成分分离装置可以构造成将第一血液成分传送至第一血液成分袋以及将第二血液成分传送至第二血液成分袋。再循环装置可以将第二血液成分容器内的第二血液成分重新引入分离装置中。第二返回装置可以构造成将第一血液容器内的第一血液成分返回至患者。

[0019] 用于抽取全血的装置可以包括构造成将第一血液成分容器内的第一血液成分返回至患者的第一泵。第一泵还可以将分离装置中剩余的血液成分返回至患者。

[0020] 根据其他实施方案，系统还可以包括用于控制流体通过系统流动的控制器。控制器可以重复地将来自供体的全血抽取至分离装置中，从分离装置提取第一和第二血液成分，使用第二返回装置将第一血液成分返回至患者，并使用第一返回装置将分离装置中的剩余成分返回至患者。此外，在第二血液成分容器中获得预定体积的第二血液成分后，可以将来自第二血液成分容器的第二血液成分重新引入分离装置中。控制器还可以计算额外身体体积和/或血管内不足，并且使用第二返回装置返回的血浆含量可以(至少部分)基于额外身体体积和/或血管内不足。

[0021] 此外，系统还可以包括用于将抗凝剂引入抽取的全血中的装置，和流体连接第二血液成分袋和血液成分分离装置的再循环装置。当从患者抽出第二体积的全血以在血液成分分离装置内形成扩大的第二血液成分层时，可以将第二血液成分袋内的第二血液成分重新引入血液成分分离装置中。可以使用浪涌淘洗方法从血液成分分离装置中取出扩大的第二血液成分层。另外地或替换地，第二血液成分可以是血小板，并且在第二血液成分容器内收集预定量的血小板后，可以重新引入血液成分分离装置中，使得从分离装置提取血浆减少的血小板产物。

[0022] 根据其他实施方案，提供了用于收集血浆减少的血小板和预期血浆返回的方法。首先从来源抽取全血，抗凝，并引入分离室中。分离室将抗凝的全血分离成多种血液成分。然后该方法将从抗凝全血分离的血浆转移至血浆容器中，并且将第一体积的来自血浆容器的血浆返回至来源。该方法然后重复抽取、抗凝、引入和转移步骤，以将分离装置填充其他抗凝全血。

[0023] 一旦将抗凝全血引入分离室中(例如，填充该室)，该方法从分离室提取富含血小

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板的血浆(“PRP”)(例如,使用浪涌淘洗方法和/或用血浆浪涌)并放入 PRP 室中。该方法然后将分离室内剩余的血液成分返回至来源,并重复抽取、抗凝和引入步骤,直至分离室再次部分填充抗凝全血。一旦分离室部分填充,该方法然后将来自 PRP 容器的 PRP 再次引入分离室中,将来自分离室的血浆转移至血浆容器中,并且将重新引入的 PRP 再处理,以在分离装置内形成扩大的血小板层。

[0024] 根据一些实施方案,该方法可以预期血浆返回,并且将血浆容器内的血浆返回至来源,同时将 PRP 重新引入分离室和/或再处理 PRP。该方法然后再一次重复抽取、抗凝和引入步骤,以填充分离室,使用浪涌淘洗方法取出分离装置内扩大的血小板层,使得将血小板转移至血小板容器中。该方法然后将分离室内剩余的血液成分返回至来源。

[0025] 根据相关的实施方案,该方法还可以在停歇时间过程中将血浆容器内的血浆返回至来源。此外,该方法可以计算额外身体体积和/或血管内不足,并且返回至来源的血浆的第一体积可以至少部分基于计算的额外身体体积或血管内不足。

[0026] 在再进一步的实施方案中,用于收集血浆减少的血小板的方法包括从来源抽取全血,并将抗凝剂引入从来源抽取的全血中,并且将抗凝的全血引入分离室中。分离室又可以将抗凝的全血分离成多种血液成分。该方法然后将从抗凝全血分离出的血浆转移至血浆容器中,将来自血浆容器的第一体积的血浆返回至来源,并且重复以上步骤。另外,该方法还可以从分离室提取富含血小板的血浆,并放入富含血小板的血浆容器中,并且从分离室取出剩余的血液成分。

[0027] 附图简述

[0028] 通过参考以下详述以及参考附图将更容易地理解本发明之前的特征,其中:

[0029] 图 1 是根据本发明一个实施方案的成分输血仪的示意图。

[0030] 图 2 是根据本发明一个实施方案,可以与图 1 的仪器一起使用的一次性系统的示意图。

[0031] 图 3 是根据本发明一个实施方案,可以与图 1 的仪器一起使用的离心滚筒的侧视图。

[0032] 图 4 是根据本发明一个实施方案,描绘了用于从供体收集血浆减少的血小板并预期血浆返回的方法的流程图。

[0033] 特定实施方案的详述

[0034] 参考图 1 和 2,成分输血设备 10 使用血液成分分离装置,如用于将抗凝的全血分离成其组成成分的标准 Latham 型离心机 11,如 US 专利 No. 3,145,713 中所述的,按引用并入并文中。可以使用其他类型的分离室和装置,如,但不限于,整体吹塑离心滚筒,如 U.S. 专利 No. 4,983,156 和 4,943,273 中所述的,按引用并入本文中。离心机 11 包括转筒 12 以及通常通过旋转封口 74 紧密结合滚筒内部的固定输入和输出口 PT1 和 PT2(参见图 3)。当阀 11 打开时,离心机 11 的输入口 PT1 通过血液微聚集体滤器 F1、管 28 和 Y- 接头 30 与静脉接入装置 24(例如,放血针)流体连通。在首先集合然后供应全血的情况中,静脉接入装置 24 可以由全血袋(未显示)替代。管 28 与血液具有相容性,设备 10 中的所有管道也是这样。离心机 11 的出口 PT2 通过管 36、阀 V2 和管 37 与悬挂在台秤 33 上的标记为血浆的第一容器 18 选择性地连接。标记为血小板的第二容器 20 通过管 36、阀 V3 和管 39 与出口 PT2 选择性地连接。此外,标记为血小板存储的第三个容器 22 通过管 36、阀 V4 和管 35 与

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出口 PT2 选择性地连接。第二容器 20 和第三个容器 22 也可以分别通过台秤 67 和 77 来悬挂。如以下更详细的讨论，一些实施方案还可以包括管 93，一端与血浆容器 18 流体连接（通过接头 94），而另一端与管 41 流体连接（例如，通过接头 95）。管 93 可以用于将血浆容器 18 内的柠檬酸盐化血浆在停歇时间过程中返回至供体和 / 或同时处理离心机 11 内的全血。

[0035] 用于存储抗凝剂的袋或容器 16 通过细菌滤器 F2、管 32 和 Y- 接头 30 与静脉接入装置 / 放血针 24 流体连通。细菌滤器 F2 防止抗凝剂（ACD）容器 16 中的任何细菌进入系统中。容器 16、18、20 和 22 优选是由血液相容材料制得的塑料袋。蠕动泵 P1、P2 和 P3，与阀 V1、V2、V3 和 V4 一起，响应由线路传感器 14、供体压力监控器（DPM）M1、系统压力监控器（SPM）M2 和空气检测器 D1、D2 和 D3 产生的信号而控制通过设备 10 流动的方向和持续时间。空气检测器 D1、D2 和 D3 检测流体的不存在或存在。压力监控器 M1 和 M2 监控设备 10 内的压力水平。线路传感器 14 是光学传感器并且检测从出口 PT2 通过线路传感器 14 的血液成分的存在。

[0036] 在最初的运行中，给泵 P1 和 P3 通电，给设备 10 的管 28 灌注来自容器 16 的抗凝剂。在到达空气检测器 D1 前，抗凝剂通过滤器 F2 和 Y- 接头 30。空气检测器 D1 感受到在 D1 存在抗凝剂并终止抗凝剂灌注运行。在灌注运行过程中，阀 V2 打开并且抗凝剂置换的滚筒中的无菌空气进入血浆容器 18 的顶部开口 PT3。然后将静脉接入装置 24 插入供体中并且准备开始进行抽取步骤。

[0037] 图 4 是根据本发明一个实施方案，描绘了用于从患者收集血液成分（例如，血小板）并预期将柠檬酸盐化血浆返回至患者的方法的流程图。在抽取步骤 401 过程中，从患者抽取全血，通常是以约 80ml/min 的速率，并且使用泵 P1 和 P3 与抗凝剂混合（步骤 402）（往回参考图 1-2）。泵 P3 将来自容器 16 的抗凝剂与从患者或集合袋抽取的全血混合。阀 V1 打开，在通过进口 PT1 泵入分离装置 12 中之前，使抗凝的全血通过管 28 和血液滤器 F1。

[0038] 将全血通过进料管（未显示）引入分离装置 12 的底部，图 4 的步骤 403。抗凝剂与全血的比例通常为约 1:10。可以在控制器（未显示）（其可以是，例如，微处理器）的控制下，根据所需的实验方案来进行成分输血设备 10 中的每个泵和阀的运行。

[0039] 参考图 3，离心机 11 具有固定的进口 PT1 和固定的出口 PT2。旋转封口 74 将固定的进口 PT1 流体连接滚筒 12 较低的内部部分，将出口 PT2 流体连接滚筒内部的较上部分，用于收集分离的级分。核心 72 占据与滚筒 12 内部同轴的体积并且在核心 72 的壁和外滚筒壁 70 之间提供分离区。

[0040] 随着滚筒 12 旋转，离心力将滚筒底部容纳的抗凝全血分离成红细胞（RBC）、白细胞（WBC）、血小板和血浆。滚筒 12 的转速可以选择，例如，在 4,000 至 6,000rpm 范围内，并且通常是 4,800rpm。根据成分密度，将血液分成不同的级分。将较高密度成分，即 RBC60，推动至滚筒 12 的外壁 70，而较低密度的血浆 66 位于核心 72 附近。在血浆 66 和 RBC60 之间形成血沉棕黄层 61。血沉棕黄层 61 由血小板内层 64、血小板和 WBC 的过渡层 68 和 WBC 外层 62 构成。血浆 66 是从分离区离出口最近的成分，并且随着其他抗凝全血通过进口 PT1 进入滚筒 12，血浆 66 是通过出口 PT2 从滚筒 12 转移出的第一流体成分。随着血浆 66 从滚筒 12 中转移出来，将其通过线 36 和 37 转移至血浆容器 18（图 4 的步骤 404）。

[0041] 返回至图 1，转移出的血浆通过线传感器 14、管 36、3- 通 T- 接头 26 和阀 V2（在打开状态），并进入第一容器 18。通过泵 P2 将进入第一容器 18 中的血浆经由管 42、阀 V5（打

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开状态)、Y- 接头 92 和管 40 自较低的开口 PT4 从容器 18 中抽取，并且经由 Y- 接头 91 和线 41 通过进口 PT1 再循环至滚筒 12 中。再循环的血浆稀释了进入滚筒 12 中的抗凝全血并且使血液成分更快分离。将光学传感器 21 应用于滚筒 12 的肩部，用于监控从滚筒 12 的外壁 70 逐渐且同轴地朝向核心 72 前进时的每层血液成分。光学传感器可以安置在能够检测到血沉棕黄层到达特定半径的位置，并且响应检测可以终止从供体 401 抽取全血并将全血引入滚筒 402 的步骤。

[0042] 如 1999 年 9 月 9 日提交的共同未决的发明名称为“用于生产血液制品的成分输血装置和方法”的 U. S. 专利申请 09/392,880 中所述的，可以响应至少一个与全血相关的特征，如全血的血细胞比容值、血小板数量、血液总量等，来改变滚筒 12 处理的全血量，按引用将该篇文献并入本文中。如之前所述的，这种变量控制可以在微计算机的控制下进行。或者，可以人工执行每一步。

[0043] 如上所述，本发明的一些实施方案将血浆容器内的血浆(例如，柠檬酸盐化血浆)在成分输血过程中以不同间隔返回，以预期血浆返回和避免在成分输血过程结束时返回大的体积(例如，为了提高患者舒适性)。为此，系统 10 可以暂停抽取步骤(步骤 401)，并将血浆容器内含有的一些或全部血浆返回至供体。特别地，一旦暂停抽取步骤(步骤 401)，成分输血系统 10 可以逆转抽取 / 返回泵 P1 的方向，打开阀 V6，通过出口 PT4 从血浆容器 18 抽取血浆，并通过线 93 和 28 将血浆返回至患者 / 供体。

[0044] 在该步骤过程中返回至患者 / 供体的血浆的体积可以取决于多个因素，包括，但不限于，额外身体体积(“ECV”)和 / 或血管内不足(“IVD”)。例如，控制器可以基于来自之前循环(例如，给定的成分输血程序中之前的循环或来自现有技术程序的循环)的数据计算 ECV 或 IVD，并且确定 ECV/IVD 是否超过了估算的总血液体积(“TBV”)(例如，从供体特征估算的，如性别、大小和重量)的预定百分比。如果系统 10 (例如，控制器 / 微处理器)确定 ECV/IVD 超出了 TBV 的预定百分比，那么系统 10 可以如上所述暂停抽取(例如，步骤 401)并且返回血浆。另外地或替换地，如果从目前的循环分离出的血浆体积等于为完成滚筒填充仍然要抽取的全血的体积，系统 10 可以启动血浆返回(步骤 405)。为了保持和 / 或提高血浆返回步骤(步骤 405)过程中的血液分离，离心机 11 可以继续旋转，并且通过滚筒 12 将血浆循环(例如，使用泵 P2 和线 42)。

[0045] 通过暂停抽取步骤(步骤 401)和启动预期的血浆返回步骤(步骤 405)，系统 10 能够在很大程度上降低 ECV 和 IVD。此外，预期的血浆返回过程可以确保在多个步骤中以明显的时间间隔(例如，几分钟)来进行柠檬酸盐化血浆返回至患者 / 供体。如以上所讨论的，这有助于提高患者舒适性和降低将柠檬酸盐化血浆返回至患者 / 供体相关的风险。

[0046] 一旦完成血浆返回步骤，系统可以继续从患者 / 供体抽取全血(例如，为了完成滚筒填充)(步骤 406)并且从分离室 11/ 滚筒 12 提取血小板。从滚筒 12 提取血小板至容器中，图 4 的步骤 407。从滚筒 12 提取血小板时，可以使用各种方法，包括，但不限于，静止(dwell)、浪涌和 / 或推动方法。为了说明的目的，现在将详细描述基于静止和浪涌技术的血小板提取。

[0047] 将全血引入离心机 11 中后，图 4 的步骤 406，将阀 V1 关闭，并且将泵 P1 停止，使得不再从供体抽取血液，并且开始静止。在静止过程中，泵 P2 将血浆 66 以适当的速率(例如，约 100ml/min，在图 4 中)通过滚筒 12 再循环约 20 至 30 秒钟。在该流速下，通过血浆稀释

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血沉棕黄层 61 并扩展，但血小板没有离开滚筒 12。血沉棕黄层的稀释使较重的白细胞沉淀至血沉棕黄层的外侧，导致较轻的血小板层 64 和较重的白细胞层 62 之间更好的分离。结果，减少了过渡层 68。静止阶段还可以稳定滚筒 12 中的流动模式，并且使得微泡有更多时间离开滚筒 12 并且被清除。

[0048] 静止后，开始浪涌步骤。在浪涌中，以 5-10ml/min 的增量提高泵 P2 的速度，以再循环血浆直至达到约 200-250ml/min 的血小板浪涌速度。血小板浪涌速度是血小板可以离开滚筒 12 但红细胞或白细胞没有离开的速度。离开滚筒的血浆变成含有血小板的浑浊物，并且线传感器 14 检测到这种浑浊。线传感器 14 由 LED 和光检测器组成，LED 发射通过正离开滚筒 12 的血液成分的光，而光检测器接受通过成分后的光。光检测器接受的光量与通过线的流体密度相关。

[0049] 当血小板首先开始离开滚筒 12 时，线传感器输出开始降低。打开阀 V3，并关闭阀 V2，将血小板收集在容器 20 中。一旦从滚筒中取出大部分的血小板，离开滚筒的流体变得不太浑浊。线传感器 14 检测到这种浑浊的降低，于是关闭阀 V3。

[0050] 重要的是注意到在任何“停歇”时间过程中（例如，没有从患者 / 供体抽取全血过程中的时间，离心机 11 停止过程中的任何时间等），系统 10 可以将血浆袋 18 内所含的血浆返回至患者 / 供体。例如，当系统 10 从离心滚筒 12 中取出 / 提取出血小板时和 / 或在上述的静止过程中，系统 10 也可以以上述的相似方式将容器 18 内所含的血浆返回至患者 / 供体（例如，通过逆转泵 P1 并通过线 93 抽取血浆）。

[0051] 如果在浪涌过程中发生了血浆返回（例如，血浆通过滚筒 12 的再循环），抽取 / 返回泵 P1 和再循环泵 P2 都可以从血浆容器 18 抽取血浆，并且阀 V5 和 V7 都打开。抽取 / 返回泵 P1 可以通过管 93 抽取血浆，而再循环泵 P2 可以通过管 42 抽取血浆。为了防止分开的血浆流混合以及彼此干扰，位于接头 91 和 95 之间的阀 V8（图 2）可以关闭。

[0052] 收集血小板后，启动返回步骤 409（参见图 4）。在返回步骤 409 过程中，停止滚筒 12 的旋转，并且通过逆转泵 P1 的旋转，阀 V1 打开，经由静脉接入装置 24 将滚筒 12 中的剩余血液成分返回至供体。还将阀 V2 打开，使空气在返回过程中进入离心滚筒中。来自容器 18 的血浆稀释了滚筒 12 中剩余的血液成分。即，随着阀 V2 打开，泵 P2 将血浆与滚筒 12 中剩余的成分混合，用血浆稀释正返回的红细胞成分加快了返回时间。当滚筒中剩余的血液成分返回至供体时，停止返回步骤 409。

[0053] 参照图 4，重复从供体抽取全血（步骤 401）、将抗凝剂引入全血（步骤 402）、将全血引入分离室（步骤 403）、将血浆转移至血浆容器 18（步骤 404）、将血浆返回患者 / 供体（步骤 405）、继续全血抽取（步骤 406）、从分离室提取血小板（步骤 407）、返回血浆（步骤 408）和将剩余成分返回供体（步骤 409）的步骤，直至在容器 20 中获得所需体积的血小板，步骤 410。通常，将步骤 401-409 重复两次至四次，每个循环处理约 450-500ml 全血。所获得的血小板浓度通常为约 $1.5\times10^{6}/\mu L$。

[0054] 然后通过将容器 20 中的血小板（富含血小板的血浆）重新引入滚筒 12 中，图 4 的步骤 412，系统可以再处理容器 20 中的血小板。重新引入血小板形成了比只处理一个循环的抗凝全血获得的大几倍的血小板层。例如，在一些实施方案中，血小板层体积大致等于乘以循环加一获得的血小板数的一个循环的平均体积。通过泵 P2，经由管 43、阀 V6（打开位置）、Y- 接头 92 和管 40 从容器 20 的开口 PT5 抽取血小板，并通过进口 PT1 经由 Y- 接头

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91 和线 41 输入滚筒 12 中。为了最小化血小板和滚筒 12 之间的接触，在重新引入血小板之前，滚筒 12 可以部分地填充从通体 401 抽取的抗凝全血，图 4 的步骤 411。全血在滚筒 12 外围形成细胞床，作为滚筒外围与血小板之间的缓冲剂，降低血小板凝集。另外地或替换地，可以在血小板重新引入过程中将抗凝全血加入分离室中，使得血小板层朝向淘洗半径，或在血小板重新引入后，用于完成血小板分离和标准化启动血小板提取的条件。

[0055] 值得注意的是，如果重新引入滚筒 12 中并且再处理的血小板是富含血小板的血浆（“PRP”）形式（血小板悬浮于血浆内），那么滚筒 12 内的离心力将导致 PRP 丢弃悬浮的血小板，由此除去血浆。这种游离的血浆将从滚筒 12 排出，并传送至血浆容器 18，作为附加的流体（例如，附加的 PRP、血浆、抗凝全血等）进入滚筒 12。

[0056] 随着血小板再处理形成血浆减少的血小板产品（以下将更详细讨论），系统 10 可以再一次地将容器 18 内的血浆返回至患者 / 供体（步骤 413）。例如，随着将容器 20 的血小板重新引入滚筒 12 中，系统 10 可以打开阀 V7，并使用抽取 / 返回泵 P1，通过线 93 从容器 18 的开口 PT4 抽取血浆，并通过线 28 和静脉接入装置 24 将血浆返回至患者 / 供体。系统 10 然后可以从患者 / 供体抽取全血，并将滚筒 12 填充抗凝全血，步骤 414。

[0057] 例如，使用浪涌或推动方法，然后从目前停留在滚筒 12 中的血小板层提取出血浆减少的血小板浓缩物，图 4 的步骤 415。通过线传感器 14、管 36、3- 通 Y- 接头 26 和阀 V4（打开状态），将血浆减少的血小板产品传送至容器 22 中。血小板产品浓度通常为 $2.6\times10^6/\mu L$ 至 $5.2\times10^6/\mu L$，其是只进行一个抗凝全血循环时获得的血小板的 2-3 倍。一旦从滚筒 12 中提取出血浆减少的血小板浓缩物并收集在容器 22 中，系统 10 然后可以返回滚筒 12 内剩余的任何血液成分和血浆容器 18 内的任何仍然剩余的血浆，参见图 4 的步骤 416。

[0058] 应当注意浪涌淘洗技术可以使用血浆以外的各种流体，从分离室提取血小板和 / 或减少血浆的血小板产品（例如，可以使用盐溶液）。此外，重新引入分离室的血小板可以重新抗凝来防止血小板凝固和 / 或凝集。例如，血小板收集袋 20 或减少血浆的血小板产品袋 22 可以预先装载一定量的抗凝剂，使得从分离室抽取出来时，血小板和 / 或减少血浆的血小板产品与抗凝剂混合。另外地或替换地，可以在从患者抽取全血时，加入足量的抗凝剂，使得在再处理之前，血小板中仍然存在足够的抗凝剂。在任一种情况中，必须相对于患者的安全性来称重全血和 / 或提取的血小板中添加的抗凝剂含量。特别地，应当限制抗凝剂的含量，以防止大量抗凝剂返回至患者。

[0059] 还应当注意一旦收集到血小板或减少血浆的血小板产品，可以加入血小板防腐剂溶液来帮助防腐和存储血小板，用于之后的使用。可以在收集后（例如，从分离袋或存储容器 96）将防腐剂溶液加入血小板和血小板产品中，或血小板收集袋 20 和减少血浆的血小板产品袋 22 可以预先装载添加剂溶液。

[0060] 通过预期将返回至供体的血浆总量以及在多个步骤中返回血浆，本发明的各个实施方案能够提供优于现有技术的多个优点。例如，通过不是在程序结束时返回全部血浆，本发明的各个实施方案能够很大程度上降低与返回大体积的柠檬酸盐化血浆相关的患者的不适性和风险。此外，通过在“停歇”时间过程中返回血浆，本发明的一些实施方案能够减少总的程序时间，以及程序过程中任何给定时间的 ECV/IVD。此外，因为可以在处理过程中返回血浆并且显著降低了 EVC/IVD，本发明的各个实施方案不需要将盐水（或其他代偿流体）返回至患者来降低 ECV。

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[0061] 尽管上述的实施方案讨论了将血浆返回至患者 / 供体，但不需要返回全部血浆。例如，本发明的一些实施方案可以保留一部分收集的血浆。在这样的实施方案中，可以使用 F3 过滤血浆并存储在滤过的血浆容器 97 内。

[0062] 如果需要另外的减少血浆的血小板产品，现在可以重复上述的每一个步骤，直至收集到所需量的血浆减少的血小板产品。在各个实施方案中，可以将血浆加入血浆减少的血小板产品中，以将血浆减少的产品调节至预定的体积或浓度。

[0063] 尽管按照从患者 / 供体抽取全血并将不需要的成分返回至供体来描述了以上的实施方案，但本发明的其他实施方案可以用于无供体处理。例如，如上所述，在其中首先集合全血然后提供给分离装置 11 的情况中，静脉接入装置 24 可以由全血袋（未显示）替代。在这样的实施方案中，来自血浆容器 18 的血浆和分离装置 11 中剩余的血液成分可以返回至一个或多个存储袋 / 容器（例如，全部返回至一个容器中或返回至分开的容器中）或返回至全血袋中。这样的实施方案将仍然具有优于现有技术系统的优点，因为很大程度上减少了处理时间（例如，因为在停歇时间过程中将血浆传送至容器，等）。

[0064] 所述的本发明的实施方案仅仅是示例性的并且各种改变和变化将是本领域技术人员显而易见的。确定所有这样的改变和变化在本发明的范围内。

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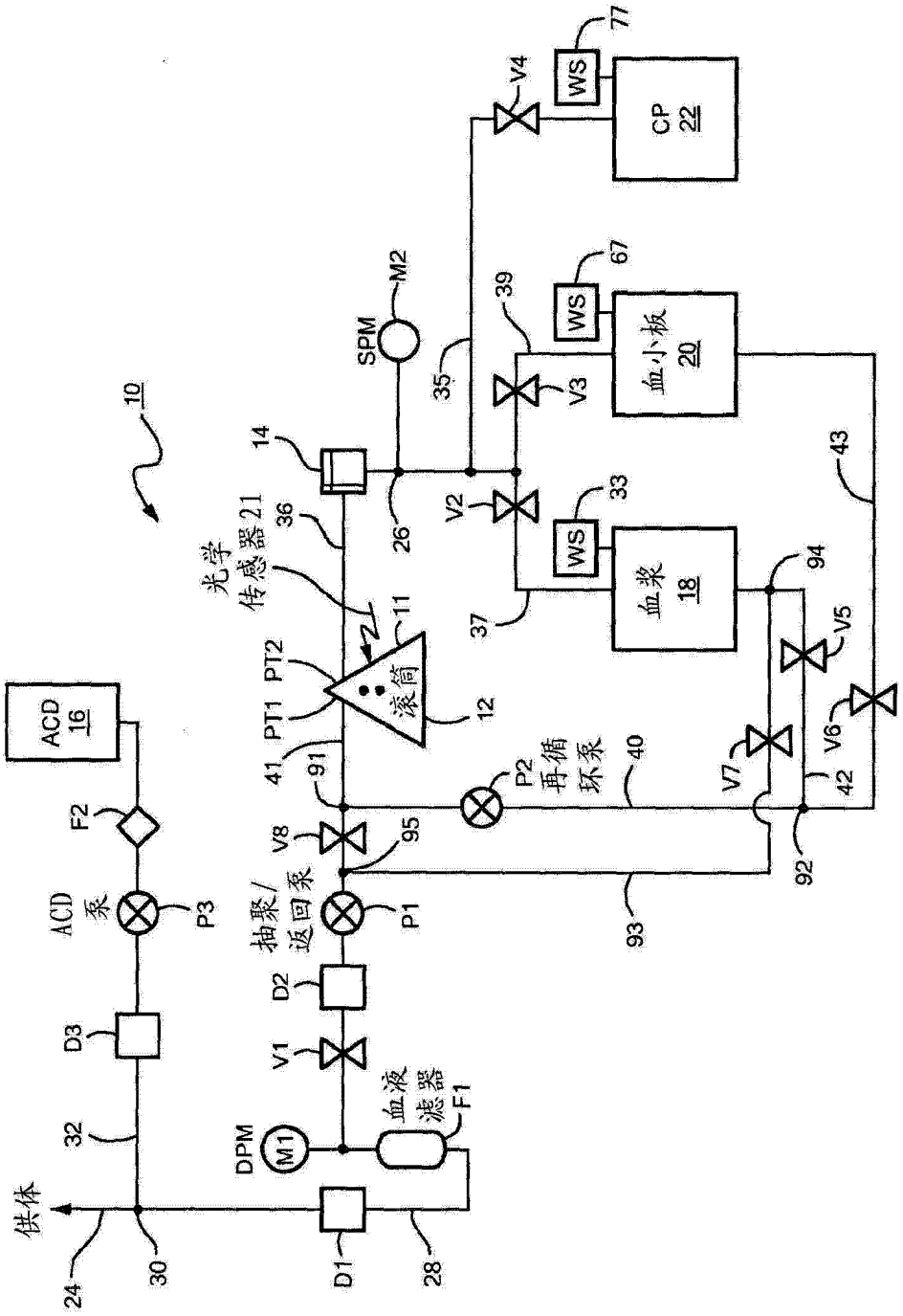

图 1

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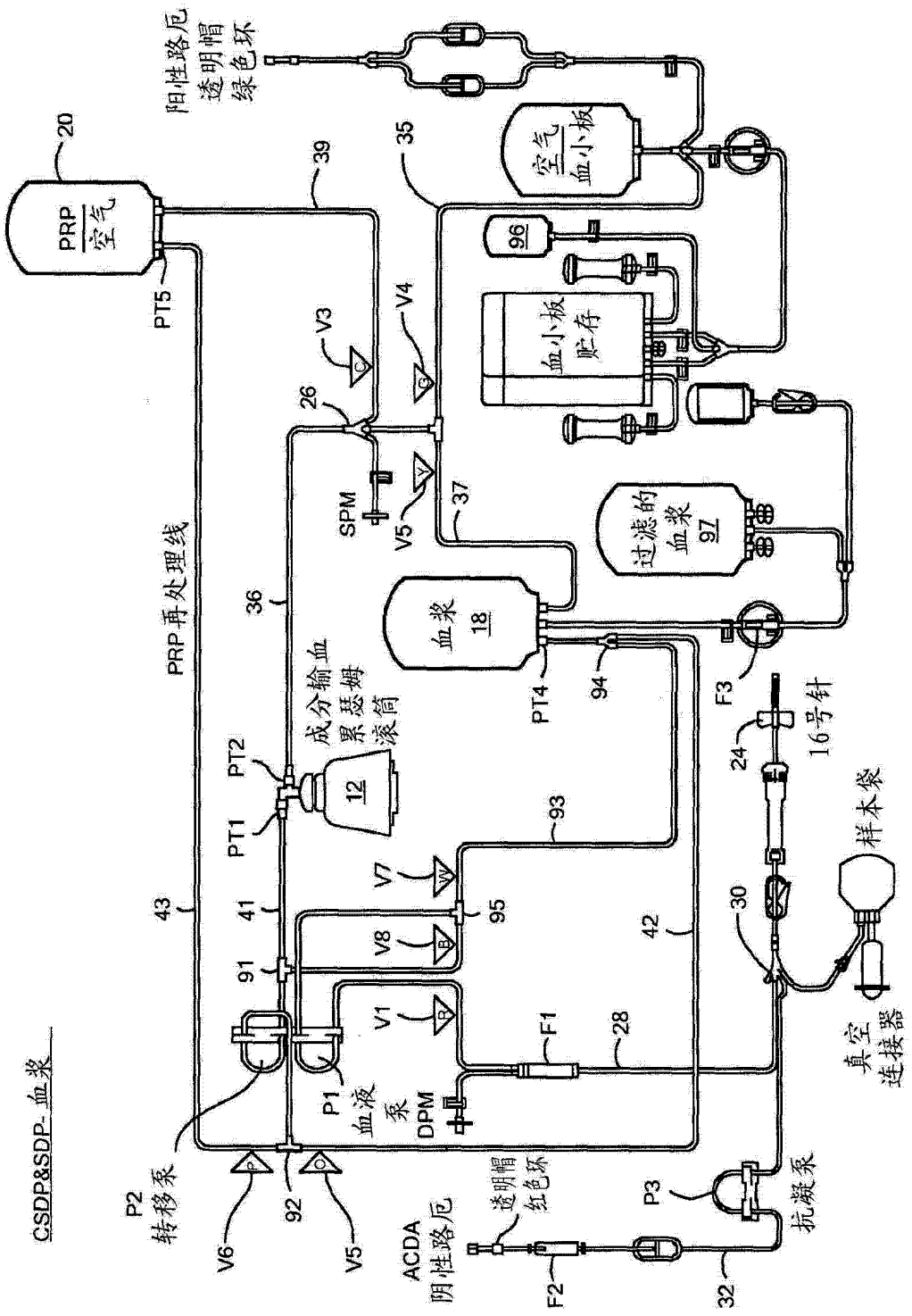

图 2

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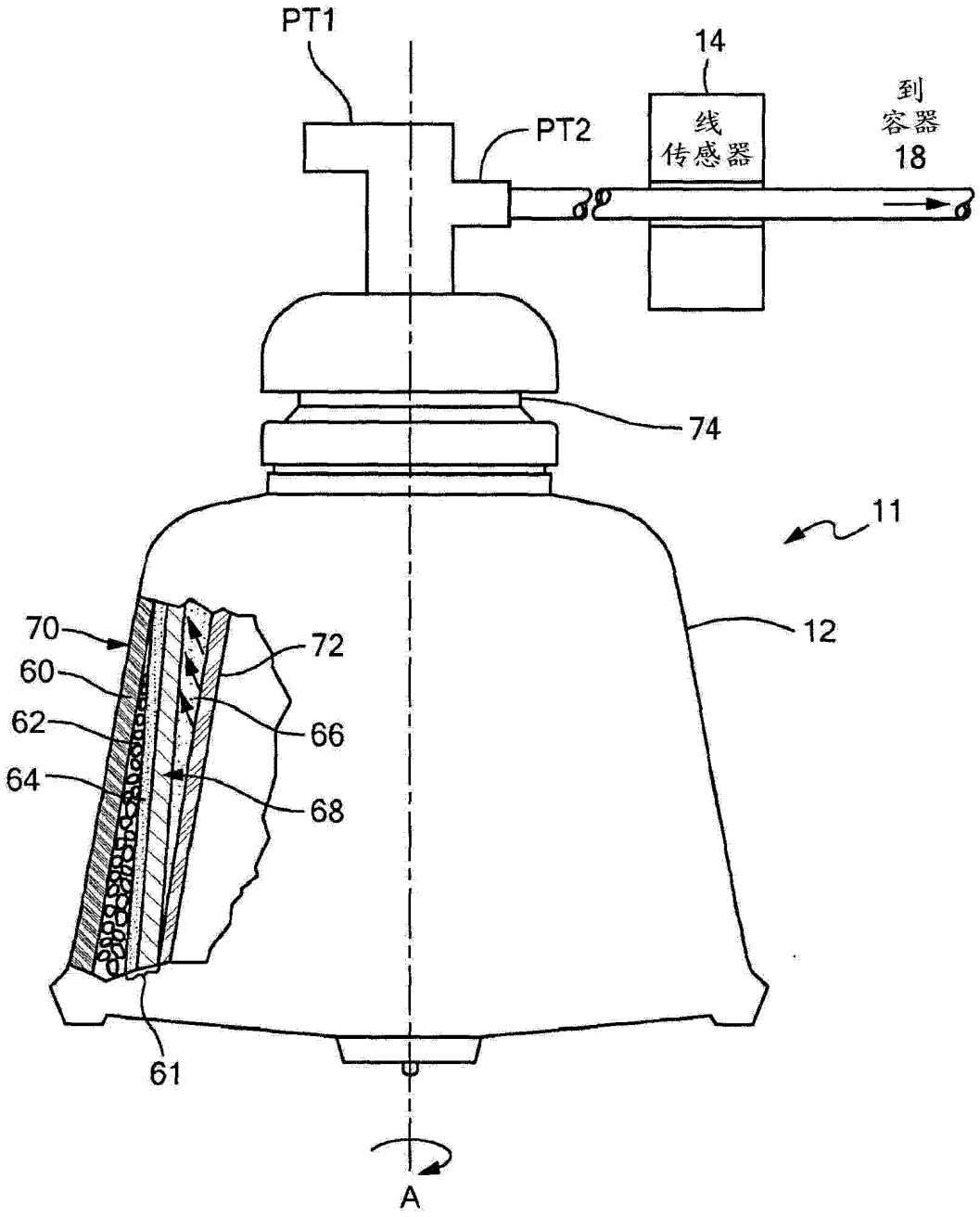

图 3

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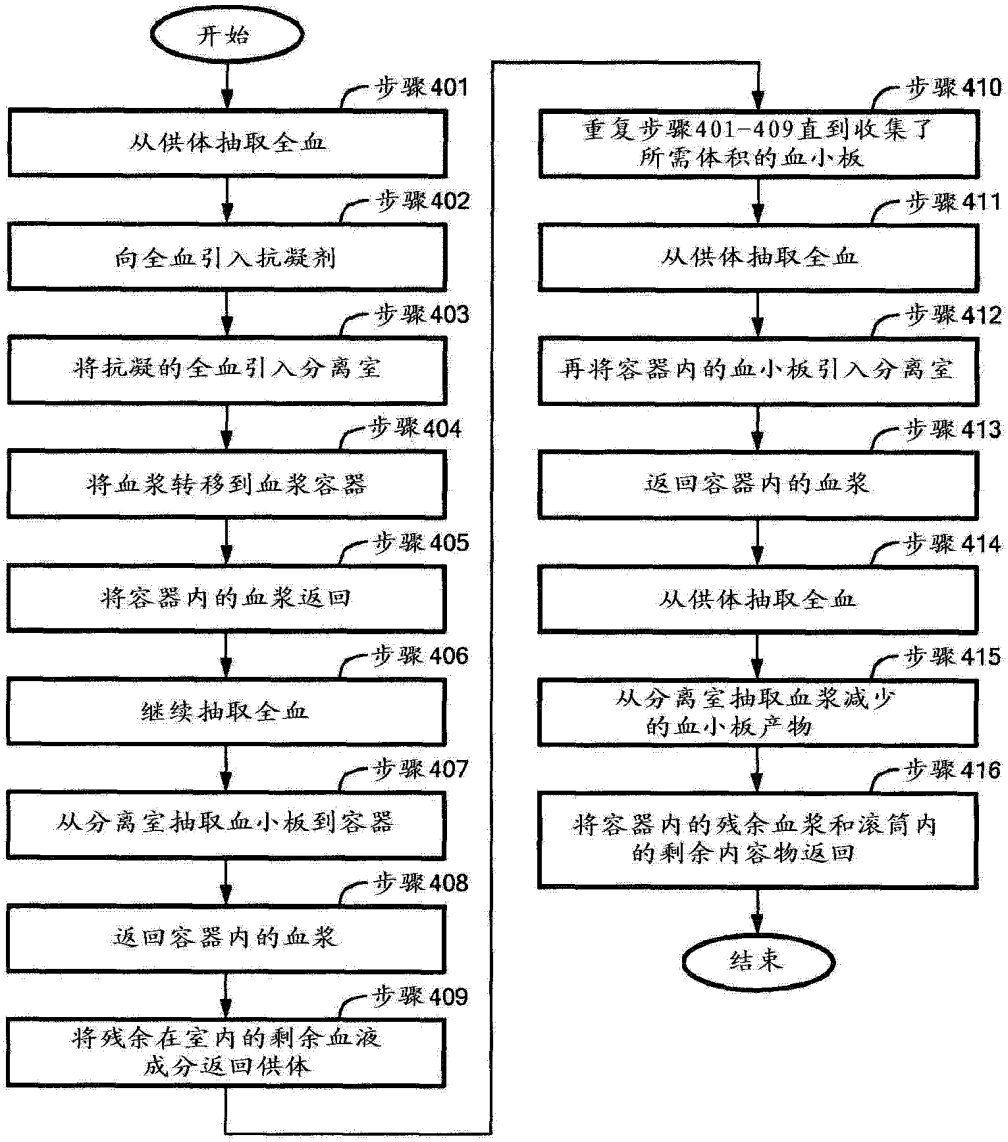

图 4

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Espacenet

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Optimized blood component collection system

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Abstract not available for DE69434848 (T2)
Abstract of corresponding document: EP0654277 (A1)

A blood component collection system with optimization capabilities. In one embodiment, process parameters are derived from an input/configured predetermined blood component yield and which is based upon the maximization of at least one process parameter. Thereafter, the blood component collection procedure is performed with these derived process control parameters. In another embodiment, process parameters are derived from an input total procedure time from a maximized value for at least one of the other process control parameters so as to maximize blood component yield in this fixed time. Thereafter, the blood component collection procedure is performed with these derived parameters.

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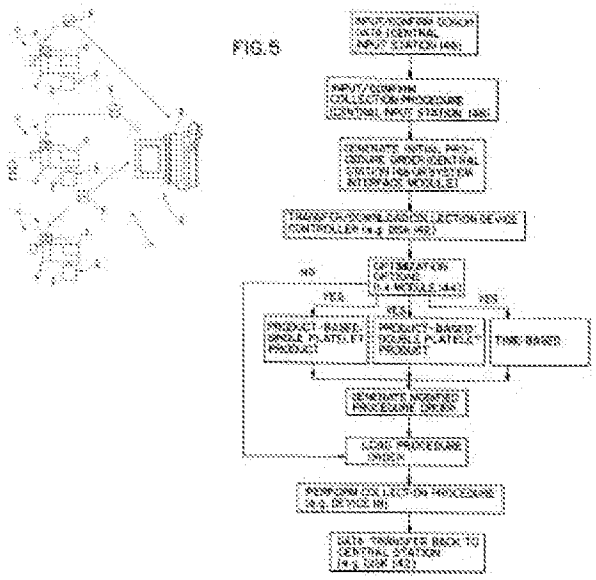

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(54) Bezeichnung: **Optimiertes System zur Sammlung von Blutkomponenten mit Optimierer**

Anmerkung: Innerhalb von neun Monaten nach der Bekanntmachung des Hinweises auf die Erteilung des europäischen Patents kann jedermann beim Europäischen Patentamt gegen das erteilte europäische Patent Einspruch einlegen. Der Einspruch ist schriftlich einzureichen und zu begründen. Er gilt erst als eingelegt, wenn die Einspruchsgebühr entrichtet worden ist (Art. 99 (1) Europäisches Patentübereinkommen).

Die Übersetzung ist gemäß Artikel II § 3 Abs. 1 IntPatÜG 1991 vom Patentinhaber eingereicht worden. Sie wurde vom Deutschen Patent- und Markenamt inhaltlich nicht geprüft.

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Beschreibung

Gebiet der Erfindung

[0001] Die vorliegende Erfindung betrifft allgemein das Gebiet der Blutkomponenten-Sammelsysteme und insbesondere das Bereitstellen von Organisationsmöglichkeiten durch das Aufnehmen von Optimierungsprinzipien in derartige Systeme.

Hintergrund der Erfindung

[0002] Die Verwendung von Blut, das Spendern abgenommen und Empfängern infundiert wird, ist für den Zweck der Behandlung von medizinischen Notfällen und unter anderen Umständen wohlbekannt. In letzter Zeit wurden ausgewählte Blutkomponenten für die spätere Infusion bei Empfängern, die eine Blutkomponententherapie benötigen, aus Blut getrennt und gesammelt. Die primären Blutkomponenten enthalten Blutplättchen, rote Blutkörperchen, weiße Blutkörperchen und Plasma.

[0003] Um Blutkomponenten zu sammeln, wird einem Spender durch eine Nadelbaueinheit oder durch eine andere Blutzugangsvorrichtung Blut abgenommen, das anschließend unter Verwendung von Zentrifugieren oder anderen geeigneten Trennungstechniken verarbeitet wird, um die gewünschten Komponenten zu isolieren und zu sammeln. Diese Prozedur wird am wirkungsvollsten in einem Online-Prozess ausgeführt, bei dem einem Spender Blut abgenommen, über einen extrakorporalen Einwegkreis verarbeitet, um die gewünschten Komponenten zu erhalten, und anschließend an den Spender zurückgegeben wird. Ein Blutkomponenten-Sammelsystem, das für diesen Typ der Blutkomponenten-Sammelprozedur vorgesehen ist, ist COBE Spectra™, das von dem Anmelder der vorliegenden Anmeldung kommerziell zur Verfügung steht.

[0004] Der Ausstoß einer bestimmten Sammlung von Blutkomponenten ist ein wesentlicher Faktor. In den Vereinigten Staaten muss z. B. gegenwärtig ein Ausstoß einer Sammlung von Blutkomponenten zugeordnet sein, damit es sich um ein nutzbares Blutkomponenten-Produkt handelt. Wie in EP-A-0 580 299 offenbart ist, erfüllt COBE Spectra™ gegenwärtig diese Forderung, indem bestimmte biologische Daten des Spenders, wie etwa Größe, Gewicht, Geschlecht und Hämatokritwert, im Voraus konfigurierte, von der Bedienperson eingegebene Daten, wie etwa die Gesamtprozedurdauer, und systembezogene Daten, wie etwa der Typ der Sammelprozedur (z. B. Einnadel- oder Zweinadelprozedur) und die Sammeleffizienz, verarbeitet werden, um bestimmte Prozessparameter, wie etwa die Einlassströmung in das COBE Spectra™ (eine kombinierte Strömung des Vollbluts vom Spender, üblicherweise zuzüglich einer Strömung von Antikoagulans) sowie einen vorhergesagten Blutkomponenten Ausstoß, zu erzeugen.

[0005] Eine zusätzliche Betrachtung, die den Blutkomponenten-Ausstoß in den Vereinigten Staaten gegenwärtig betrifft, ist, dass er die Produktklassifizierung bestimmt. In Bezug auf Blutplättchen wird gegenwärtig ein Einfach-Blutplättchen-Produkt als eine Sammlung von $3 \cdot 10^{11}$ Blutplättchen betrachtet und ein Doppel-Blutplättchen-Produkt als eine Sammlung von $6 \cdot 10^{11}$ Blutplättchen betrachtet. Wenn die Sammlung im Bereich zwischen $3 \cdot 10^{11}$ und $6 \cdot 10^{11}$ Blutplättchen liegt, wird sie trotzdem als ein Einfach-Blutplättchen-Produkt betrachtet. Diese Klassifizierung als ein Einfach- oder Doppel-Blutplättchen-Produkt ist für Blutkomponenten-Sammeleinrichtungen (z. B. Blutbanken/Blutzentren) relevant, da ein Doppel-Blutplättchen-Produkt einen höheren Verkaufspreis hat als ein Einfach-Blutplättchen-Produkt und außerdem üblicherweise einer größeren Anzahl von Patienten nützt. Der Ausstoß einer bestimmten Sammlung von Blutkomponenten kann außerdem eine relevante Betrachtung für bestimmte therapeutische Behandlungen sein.

[0006] Weitere wichtige Betrachtungen in Bezug auf Blutkomponenten-Sammelsysteme betreffen den Spender. Blutkomponenten-Sammeleinrichtungen erfahren z. B. nicht nur einen Anstieg der Gesamtforderung nach Blutkomponenten, sondern die Forderung schwankt nun üblicherweise ebenso zwischen den Blutkomponententypen. Darüber hinaus ist nicht nur der Zustrom von Spendern in vielen Fällen leider unzureichend, sondern Spender-Zeitbeschränkungen werden immer vorherrschender. Ferner kann der von einem Spender erreichbare Ausstoß zwischen den Blutkomponenten variieren (d. h. ein Spender kann eine bessere Quelle für Blutplättchen als eine Quelle für rote Blutkörperchen sein).

[0007] Auf der Grundlage des Vorhergehenden wird die Organisation der verschiedenen Aspekte von Blutkomponenten-Sammelsystemen immer wichtiger.

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Zusammenfassung der Erfindung

[0008] Die vorliegende Erfindung ist in den unabhängigen Ansprüchen definiert und betrifft in einer Anwendung ein Blutkomponenten-Sammelsystem, das Organisationsmöglichkeiten bereitstellt, indem Optimierungsprinzipien aufgenommen werden.

[0009] Im Allgemeinen und in diesem Fall verwendet die vorliegende Erfindung Prinzipien zur Optimierung in Bezug auf den Spender, das Blutkomponenten-Sammelsystem und/oder das gewünschte Blutkomponentenprodukt. Die vorliegende Erfindung kann z. B. so angepasst werden, dass sie für die Sammlung einer vorgegebenen Menge wenigstens einer vorgegebenen Blutkomponente (oder typischer für die Sammlung derartiger Blutkomponenten in einem bestimmten Bereich) in einer "minimalen" Zeitdauer und/oder für die Sammlung einer "maximalen" Menge wenigstens einer vorgegebenen Blutkomponente in einer festen Zeitdauer jeweils auf der Grundlage bestimmter Prozessbedingungen dient. Die vorliegende Erfindung kann darüber hinaus in der Weise angepasst werden, dass sie der Blutkomponenten-Bestandssteuerung dient, indem sie anhand der Blutkomponentenforderung und/oder anhand des vorhandenen Bestandes auf der Spenderauswahl und/oder auf der Sammlungsprozedurauswahl in Bezug auf den zu sammelnden Blutkomponententyp basiert. Außerdem kann die vorliegende Erfindung in der Weise angepasst werden, dass sie eine weitere Spenderorganisation schafft, indem der Blutkomponententyp bzw. die Blutkomponententypen von dem Spender gesammelt werden, der einen maximalen Ausstoß erzielt.

[0010] Die vorliegende Erfindung kann in einem Aspekt als ein Blutkomponenten-Sammelsystem charakterisiert werden, das optimierungsartige Möglichkeiten auf der Grundlage von Blutkomponentenprodukten besitzt. Eine Ausführungsform umfasst ein Verfahren zum Sammeln von wenigstens einer vorgegebenen Blutkomponente (z. B. zur Sammlung von Blutplättchen, roten Blutkörperchen) aus einer Quelle des Vollbluts unter Verwendung eines Blutkomponenten-Sammelsystems, das eine Blutkomponenten-Sammelvorrichtung enthält und eine Sammelprozedur verwendet. Im Einzelnen wird ein gewünschter Ausstoß der vorgegebenen Blutkomponente bzw. der vorgegebenen Blutkomponenten festgelegt (wobei ein derartiger Ausstoß einen einzelnen Ausstoß oder einen Bereich von Ausstößen enthält), wobei für das Blutkomponenten-Sammelsystem biologische Daten bezüglich der Quelle bereitgestellt werden. Darüber hinaus wird jedem der verschiedenen Prozessparameter, die in der Sammelprozedur verwendet werden, ein Wert oder eine Größe zugeordnet. Die Größe von wenigstens einem dieser Prozessparameter wird aus den biologischen Daten und aus dem gewünschten Ausstoß abgeleitet. Diese Größen, die alle Größen von Prozessparametern enthalten, die aus dem gewünschten Ausstoß abgeleitet sind, werden in das Blutkomponenten-Sammelsystem eingegeben. Anschließend wird die Sammelprozedur mit der Blutkomponenten-Sammelvorrichtung und mit den eingegebenen Prozessparametern ausgeführt, um den gewünschten Ausstoß der wenigstens einen vorgegebenen Blutkomponente bzw. Blutkomponenten aus der Vollblutquelle zu sammeln.

[0011] Die vorliegende Erfindung kann in einem weiteren Aspekt als ein Blutkomponenten-Sammelsystem mit zeitbasierten optimierungsähnlichen Möglichkeiten charakterisiert werden. Eine Ausführungsform davon ist ein Verfahren zum Sammeln von wenigstens einer vorgegebenen Blutkomponente von einer Quelle des Vollbluts unter Verwendung eines Blutkomponenten-Sammelsystems, das eine Blutkomponenten-Sammelvorrichtung enthält und eine Sammelprozedur verwendet. Eine Strömung des Vollbluts von der Quelle sowie eine Strömung von Antikoagulans werden an das Blutkomponenten-Sammelsystem geliefert und bilden gemeinsam eine Einlassströmung. In dem Verfahren wird (z. B. anhand der zeitlichen Verfügbarkeit des Spenders) eine Gesamtprozedurdauer für die Sammelprozedur festgelegt. Von dieser festgelegten Gesamtprozedurdauer wird wenigstens eine mögliche Einlassströmung für das System abgeleitet. Es wird eine weitere mögliche Einlassströmung für das System abgeleitet, die eine "optimale" Sammeleffzienz schafft und effektiv der Spitzenwert einer glockenförmigen Ausstoß-/Einlassströmungskurve (d. h. die Einlassströmung, die den maximalen Blutkomponentenausstoß erzeugt) ist. Demzufolge wird dann, wenn die Einlassströmung auf der Grundlage der Gesamtprozedurzeit größer als die Einlassströmung auf der Grundlage des maximalen Ausstoßes ist und somit eine Einlassströmung auf dem Abschnitt der Ausstoß-/Einlassströmungskurve mit abfallenden Anstieg ist, die Einlassströmungsgröße auf der Grundlage des maximalen Ausstoßes bei dem Verhalten der Sammelprozedur verwendet. Wenn dagegen die Einlassströmung auf der Grundlage der Gesamtprozedurzeit kleiner als die Einlassströmung auf der Grundlage des maximalen Ausstoßes ist und somit eine Einlassströmung auf dem Abschnitt der Ausstoß-/Einlassströmungskurve mit ansteigendem Anstieg ist, wird die Einlassströmung auf der Grundlage der Gesamtprozedurzeit bei dem Verhalten der Sammelprozedur verwendet.

[0012] Die vorliegende Erfindung schafft eine größere Effizienz bei der Blutkomponentensammlung und -organisation. Die vorliegende Erfindung kann z. B. verwendet werden, um Komponentenbestände von Blutbanken/Blutzentren mit geplanten Bedarfsangaben zu vergleichen und die Sammelprozeduren so einzustellen,

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dass sie diese Bedarfsangaben erfüllen. Die vorliegende Erfindung schafft des Weiteren Vorteile für Spender. Im Einzelnen können bestimmte Informationen bezüglich der physischen und medizinischen Charakteristiken des Spenders in dem System gespeichert werden und bei späteren Besuchen durch den Spender verwendet werden, um Größen für die verschiedenen Prozesssteuerungsparameter abzuleiten. Für einen Spender mit einer Antikoagulans-Unverträglichkeit kann z. B. die Größe der Antikoagulans-Infusionsrate in der Weise eingestellt werden, dass sie die Verträglichkeitsgrenze des Spenders nicht übersteigt.

Kurzbeschreibung der Zeichnung

[0013] Fig. 1 ist eine schematische Darstellung eines Blutkomponenten-Sammelsystems gemäß den Prinzipien der vorliegenden Erfindung;

[0014] Fig. 2 ist eine schematische Darstellung einer Ausführungsform einer Blutkomponenten-Trennbaueinheit, die eine Zweinadelkonfiguration verwendet und in dem Blutkomponenten-Sammelsystems von Fig. 1 enthalten sein kann;

[0015] Fig. 3 ist eine schematische Darstellung einer Ausführungsform einer Blutkomponenten-Trennbaueinheit, die eine Einnadelkonfiguration verwendet und in dem Blutkomponenten-Sammelsystems von Fig. 1 enthalten sein kann;

[0016] Fig. 4a und 4b sind eine perspektivische Ansicht bzw. eine Draufsicht eines Typs eines Einwegverarbeitungskanals, der in der Blutkomponenten-Sammelvorrichtung der Fig. 2 und Fig. 3 verwendet wird;

[0017] Fig. 5 ist ein Ablaufplan einer Blutkomponenten-Sammelprozedur, bei der Prinzipien der vorliegenden Erfindung genutzt werden;

[0018] Fig. 6 ist ein Ablaufplan eines Optimierungsmodells zum Ableiten von wenigstens einem optimalen Prozessparameter aus einem gewünschten Blutkomponentenausstoß oder aus einer Gesamtprozedurdauer gemäß den Prinzipien der vorliegenden Erfindung;

[0019] Fig. 7 ist ein Ablaufplan eines Optimierungsmodells zum Ableiten von wenigstens einem optimalen Prozessparameter aus einem gewünschten Blutkomponentenausstoß oder aus einer Gesamtprozedurdauer gemäß den Prinzipien der vorliegenden Erfindung; und

[0020] Fig. 8 ist eine Ausstoß-/Einlassströmungskurve.

Ausführliche Beschreibung

[0021] Die vorliegende Erfindung wird unter Bezugnahme auf die beigefügte Zeichnung beschrieben, die bei der Veranschaulichung ihrer vorhandenen Merkmale unterstützt. Eine Anwendung der vorliegenden Erfindung ist in einem Blutkomponenten-Sammelsystem realisiert, das wenigstens einen Blutkomponententyp (z. B. Blutplättchen, rote Blutkörperchen, weiße Blutkörperchen, Plasma) aus einer Quelle des Vollbluts (z. B. von einem Spender) unter Nutzung einer Sammelprozedur, die aus einer üblicherweise in der Einrichtung konfigurierten/von der Bedienperson eingegebenen Aufgabe (Aufgaben) und der "Maximierung" wenigstens eines Prozesssteuerungsparameters abgeleitet wird, trennt, entfernt und sammelt. Dieser Typ der Ableitung wird in dieser Beschreibung als ein "Optimierungsprozess" bezeichnet und die abgeleiteten Prozesssteuerungsparameter werden in dieser Beschreibung als "optimale Werte" bezeichnet.

[0022] In Fig. 1 ist die vorliegende Erfindung in dem Blutkomponenten-Sammelsystem **2** ausgeführt, das üblicherweise in einer Blutbank/einem Blutzentrum (nicht gezeigt) realisiert ist. Das System **2** enthält eine Optimierungsbaueinheit **140** (z. B. einen/mehrere geeignete Mikroprozessoren, wie etwa einen IBM-kompatiblen PC und Software) und wenigstens eine Blutkomponenten-Sammelbaueinheit **10** (wobei drei gezeigt sind), die jeweils eine Blutkomponenten-Sammelvorrichtung **18** als einen integralen Bestandteil hiervon enthält. Wie im Folgenden erläutert wird, sind die Optimierungsbaueinheit **140** (oder wenigstens ein Abschnitt hiervon) und zugeordnete Blutkomponenten-Sammelbaueinheiten **10** vorzugsweise in geeigneter Weise miteinander verbunden, können jedoch ebenso vollständig getrennt sein. Das heißt, die Optimierungsprozeduren gemäß den Prinzipien der vorliegenden Erfindung sind nicht darauf beschränkt, dass sie an einer bestimmten Stelle ausgeführt werden.

[0023] Die Optimierungsbaueinheit **140** enthält im Allgemeinen eine zentrale Eingabestation **148** (z. B. einen

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geeigneten Mikroprozessor, wie etwa einen IBM-kompatiblen PC und zugeordnete Software) zum Eingeben und Halten von spenderbezogenen Daten und üblicherweise außerdem zum Vorbereiten eines Anfangsprozedurauftrags (der Prozesssteuerungsparameter, die aus den spenderbezogenen Daten und anderen Betrachtungen abgeleitet werden) für einen bestimmten Spender. Diese Prozeduren können außerdem in dem geeigneten Bedienperson-Schnittstellenmodul **16** ausgeführt werden, so dass keine zentrale Eingabestation **148** erforderlich ist. Wenn jedoch eine zentrale Eingabestation **148** verwendet wird, werden diese spenderbezogenen Daten und/oder der Anfangsprozedurauftrag an eines der Bedienperson-Schnittstellenmodule **16** übertragen (z. B. an einen geeigneten Mikroprozessor, wie etwa an einen IBM-kompatiblen Mikroprozessor, der über eine RS232- oder über eine andere spezielle Laborschnittstelle mit der Vorrichtung **18** verbunden ist, einschließlich einer Vorrichtung PCP **30** der Digital Equipment Corp., die auch als der DEC-PC 325SL bekannt ist und einen 386-er Prozessor verwendet), die sich bei jeder Blutkomponenten-Sammelvorrichtung **18** befinden und die vorzugsweise, wie angegeben wurde, mit einem Optimierungsmodul **144** (einem Teil der Optimierungsbaueinheit **140**) verbunden sind, um die Bedienperson mit einer oder mehreren Optimierungsmöglichkeiten zu vorsorgen. Diese Optimierungsmöglichkeiten liefern anhand einer oder mehrerer festgelegter Bedingungen/Aufgaben (z. B. des eingegebenen Blutkomponentenausstoßes, der eingegebenen Prozedurdauer) und einer bestimmten Abweichung für die Prozesssteuerungsparameter eine andere Gruppe von Prozesssteuerungsparametern als der Anfangsprozedurauftrag. Wenn eine Optimierungsmöglichkeit ausgewählt wird, wird der Prozedurauftrag in der Weise modifiziert, dass er die Ergebnisse der Optimierung widerspiegelt, wird die Sammelprozedur mit den Ergebnissen der Optimierung initialisiert/neu initialisiert (d. h. wird die Sammelprozedur im Fall einer Optimierung, die ausgeführt wird, nachdem die Sammelprozedur initialisiert wurde, neu initialisiert, weshalb sie als eine nachgeschaltete Optimierung bezeichnet wird) und wird anschließend die Sammelprozedur mit der Blutkomponenten-Sammelvorrichtung **18** ausgeführt.

[0024] Verschiedene Ausführungsformen der Blutkomponenten-Sammelbaueinheiten können die Prinzipien der vorliegenden Erfindung enthalten. Wie oben erwähnt wurde, ist jedoch festgestellt worden, dass Online-Techniken verhältnismäßig wirkungsvoll sind, so dass die vorliegende Erfindung unter Bezugnahme auf derartige Techniken beschrieben wird. Eine Ausführungsform einer Online-Technik und der zugeordneten Vorrichtungen, die in dem Blutkomponenten-Sammelsystem **2** von Fig. 1 enthalten sein können, ist in Fig. 2 dargestellt. Die Blutkomponenten-Sammelbaueinheit **10'** verwendet eine Online-Technik dahingehend, dass ein Spender **14** (z. B. die Vollblutquelle) durch eine Fluidverbindung mit der Blutkomponenten-Sammelvorrichtung **18** direkt in das System **10'** eingebunden ist. Diese spezielle Online-Technik wird genauer als eine Zweinadelkonfiguration bezeichnet, da zwei Fluidverbindungen zwischen dem Spender **14** und der Blutkomponenten-Sammelvorrichtung **18** vorhanden sind.

[0025] Der Spender **14** steht mit der Blutkomponenten-Sammelvorrichtung **18** durch eine Einlassleitung **22** und eine (nicht gezeigte) geeignete Nadelbaueinheit in einer Fluidverbindung. Somit wird der Blutkomponenten-Sammelvorrichtung **18** unter Verwendung einer Einlasspumpe **26** (z. B. einer Peristaltikpumpe), um diese Strömung auf Wunsch/bei Bedarf aufrechtzuerhalten, über die Einlassleitung **22** ununterbrochen Vollblut von dem Spender **14** für eine Trennung der gewünschten Blutkomponenten) hiervon zugeführt. Bevor das Blut des Spenders **14** in die Blutkomponenten-Sammelvorrichtung **18** eintritt, kann dem Vollblut unter Verwendung einer AC-Pumpe **32** (z. B. einer Peristaltikpumpe) ein Antikoagulans aus einem Antikoagulans-Behälter ("AC") hinzugefügt werden, um diese spezielle Strömung auf Wunsch/bei Bedarf aufrechtzuerhalten. Demzufolge enthält die Einlassströmung in die Blutkomponenten-Sammelvorrichtung **18** üblicherweise sowohl eine Strömung des Vollbluts vom Spender **14** als auch eine Strömung des Antikoagulans von dem AC-Behälter **30**.

[0026] Die Blutkomponenten-Sammelvorrichtung **18** trennt das Vollblut, das online durch den Spender **14** geliefert wird, in drei Hauptbestandteile, und zwar Blutplättchen, eine Kombination aus roten und weißen Blutkörperchen ("RBC/WBC") und Plasma. Die von der Blutkomponenten-Vorrichtung **18** gesammelten Blutplättchen werden über eine bzw. mehrere Blutplättchen-Sammelleitungen **34** über eine Sammelpumpe **36** zu einem oder mehreren Blutplättchen-Sammelbeuteln **38** geleitet. Das Plasma und die RBC/WBC werden über eine Plasmaleitung **42** bzw. eine RBC/WBC-Leitung **46**, die beide mit einer (nicht gezeigten) zweiten Nadelbaueinheit an dem Spender **14** verbunden sind, über eine Spenderrückleitung **50** wieder an den Spender **14** zurückgegeben. Die Plasmaleitung **42** enthält eine Plasmapumpe **40** (z. B. eine Peristaltikpumpe), um die Strömung des Plasmas auf Wunsch/bei Bedarf aufrechtzuerhalten. Obgleich das Plasma in der oben beschriebenen Weise wieder an den Spender **14** zurückgegeben werden kann, kann es in einigen Fällen erwünscht sein, das getrennte Plasma zu sammeln. Dabei kann ein Plasmasammelbeutel **54** vorgesehen und mit der Plasmaleitung **42** verbunden sein (wobei die Verbindung in Strichlinien gezeigt ist). In diesem Fall kann ein geeignetes Ventil **56** in der Plasmaleitung **42** vorhanden sein.

[0027] Die Blutkomponenten-Trennbaueinheit **10"** von Fig. 3 ist abgesehen davon, dass eine (nicht gezeigte)

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Einnadelbaueinheit den Spender **14** in die Blutkomponenten-Trennbaueinheit **10"** einbindet, ähnlich der Zweinadelkonfiguration von Fig. 2. Demzufolge sind ähnliche Komponenten soweit geeignet in ähnlicher Weise bezeichnet. Bei der Einnadelkonfiguration von Fig. 3 fließt das Vollblut des Spenders **14** anfangs durch eine Spenderzugangsleitung **62** und in eine Einlassleitung **66**, die mit der Blutkomponenten-Sammelvorrichtung **18** in Fluidverbindung steht, so dass die Blutplättchen in der oben beschriebenen Weise getrennt und gesammelt werden. Das Plasma und RBC aus der Blutkomponenten-Sammelvorrichtung **18** fließen durch die Plasma- bzw. RBC/WBC-Leitungen **42**, **46**, die beide mit einer Rückfluss-Steuereinheit **74** in Fluidverbindung stehen. Wie oben angegeben kann das Plasma jedoch alternativ zu einem Plasmasammelbeutel **54** geleitet werden. Wenn das Plasma nicht gesammelt wird, werden RBC/WBC und Plasma durch die Rückfluss-Steuereinheit **74** über eine Spenderrückleitung **70**, die mit der Spenderzugangsleitung **62** verbunden ist, an den Spender **14** zurückgegeben. Da, wie erkannt wird, lediglich eine einzige Leitung, und zwar die Spenderzugangsleitung **62**, mit dem Spender **14** direkt verbunden ist, wird Blut entweder vom Spender **14** entnommen oder an diesen zurückgegeben, so dass die Prozedur in Bezug auf den Spender **14** gegenüber einer kontinuierlichen eine zweistufige Prozedur ist.

[0028] Die Blutkomponenten-Sammelvorrichtung **18**, die in der Blutkomponenten-Sammelbaueinheit **10** verwendet wird, ist in den Fig. 4A-B genauer dargestellt. Diese Vorrichtung **18** ist Gegenstand des US-Patents Nr. 4.387.848 an Kellog u. a. mit dem Titel "CENTRIFUGE ASSEMBLY", das am 14. Juni 1983 erteilt wurde und dessen Offenbarung in ihrer Gesamtheit in dieser Beschreibung durch Literaturhinweis eingeschlossen ist. Diese Vorrichtung **18** steht außerdem vom Anmelder der vorliegenden Anmeldung kommerziell zur Verfügung und ist somit im System COBE Spectra™ enthalten.

[0029] In den Fig. 4A-B verwendet die Blutkomponenten-Sammelvorrichtung **18** einen Verarbeitungskanal **80**, um den gewünschten extrakorporalen Einwegkreis zu schaffen. Der Kanal **80** ist in einer Nut angeordnet, die direkt oder indirekt in einem (nicht gezeigten) Zentrifugenrotor ausgebildet ist (z. B. kann eine getrennte Fülleinrichtung den Kanal **80** aufnehmen und an dem Zentrifugenrotor befestigt sein) und ist in der Form dargestellt, die er während der Verarbeitung annimmt (z. B. während Blut durch ihn hindurchfließt). Alle folgenden Bezugnahmen in dieser Beschreibung auf die strukturellen und funktionellen Charakteristiken der Blutkomponenten-Sammelvorrichtung **18** beziehen sich auf den Verarbeitungskanal **80** in dem dargestellten Zustand.

[0030] Der Verarbeitungskanal **80** enthält im Allgemeinen eine erste Stufe 84, um rote Blutkörperchen ("RBC") und weiße Blutkörperchen ("WBC") aus an Blutplättchen reichem Plasma gemeinsam zu trennen, eine zweite Stufe **92**, um anschließend Blutplättchen aus dem an Blutplättchen reichen Plasma zu trennen, einen Übergangsabschnitt **88**, der eine Trennung zwischen der ersten Stufe **84** und der zweiten Stufe **92** definiert, und eine Kontrollkammer **124**, um eine geeignete Grenzfläche zwischen der ersten Stufe **84** und der zweiten Stufe **92**, und zwar die Position der Grenzfläche zwischen RBC/WBC und an Blutplättchen reichem Plasma in dem Übergangsabschnitt **88**, aufrechtzuerhalten.

[0031] Die erste Stufe **84** erstreckt sich von einem Ende der Kontrollkammer **124** längs eines bogenförmigen Wegs im Allgemeinen einwärts zu der Achse **132**, um die sich der Verarbeitungskanal **80** über den Zentrifugenrotor dreht, bis sie am Übergangsabschnitt **88** endet. Das Ende der ersten Stufe **84**, das an die Kontrollkammer **124** angrenzt, ist im Einzelnen in einem größeren radialen Abstand von der Achse **132** positioniert als das Ende der ersten Stufe **84**, das an den Übergangsabschnitt **88** angrenzt. Ein Einlassrohr **96** steht mit der ersten Stufe **84** zwischen deren beiden Enden in Fluidverbindung, um Vollblut in den Verarbeitungskanal **80** einzuleiten, und ein RBC/WBC-Rohr **100** ist in der Kontrollkammer **124** vorgesehen, um die getrennten RBC/WBC aus dem Kanal **80** zu entnehmen. Sowohl das Einlassrohr **96** als auch das RBC/WBC-Rohr **100** verlaufen außerhalb der drehbaren Vorrichtung **18** für eine Verbindung mit dem Spender **14** und/oder mit den Sammelbeuteln **38**, **54**.

[0032] Wenn sich während der Drehung des Zentrifugenrotors RBC/WBC an der Außenwand in der ersten Stufe **84** absetzen, werden sie infolge der erhöhten Zentrifugalkräfte an dem RBC/WBC-Rohr **100** im Vergleich zu dem Übergangsabschnitt **88** geleitet und bilden eine Gegenströmung zu dem RBC/WBC-Rohr **100** zur Entnahme aus dem Kanal **80**. Das heißt, da sich die erste Stufe **84** ausgehend von dem Übergangsabschnitt **88** längs eines bogenförmigen Wegs im Allgemeinen auswärts weg von der Achse **132** zu der Kontrollkammer **124** erstreckt, bildet der Zentrifugalkraftunterschied längs der ersten Stufe **84** die beschriebene Gegenströmung der getrennten RBC/WBC. Darüber hinaus unterstützt der Übergangsabschnitt **88** ebenfalls die Bildung dieser Gegenströmung, da er sich ausgehend von der ersten Stufe **84** zu der zweiten Stufe **92** längs eines bogenförmigen Wegs im Allgemeinen einwärts zu der Achse **132** erstreckt.

[0033] Das an Blutplättchen reiche Plasma, das eine niedrigere Dichte als die RBC und WBC aufweist, strömt

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zur Weiterverarbeitung über den Übergangsabschnitt **88** von der ersten Stufe **84** hinaus in die zweite Stufe **92**, während die RBC/WBC in der oben beschriebenen Weise zurück zum RBC/WBC-Rohr **100** geleitet werden. Die zweite Stufe **92** beginnt am radial innersten Teil des Übergangsabschnitts **88** und erstreckt sich längs eines bogenförmigen Wegs im Allgemeinen auswärts von der Achse **132** weg zu einer Blutplättchen-Sammelkammer **104**. Die Blutplättchen werden an der Blutplättchen-Sammelkammer **104** durch ein Blutplättchenrohr **108**, das bei der Blutplättchen-Sammelkammer **104** mit einer Außenwand des Verarbeitungskanals **80** verbindet, aus dem Verarbeitungskanal **80** entnommen. Anschließend erstreckt sich die zweite Stufe **92** längs eines bogenförmigen Wegs im Allgemeinen einwärts zu der Achse **132**, bis sie an dem Plasmarohr **112** endet. Sowohl das Blutplättchenrohr **108** als auch das Plasmarohr **112** verlaufen außerhalb der drehbaren Vorrichtung **18** zur Verbindung mit dem Blutplättchen-Sammelbeutel bzw. mit den Blutplättchen-Sammelbeuteln **38** bzw. mit dem Spender **14**/dem Plasmasammelbeutel bzw. den Plasmasammelbeuteln **54**.

[0034] Blutplättchen, die sich in dem Anfangsabschnitt der zweiten Stufe **92** zwischen dem Übergangsabschnitt **88** und der Blutplättchen-Sammelkammer **104** nicht von dem Plasma trennen, werden in dem Abschnitt der zweiten Stufe **92** zwischen der Blutplättchen-Sammelkammer **104** und dem Plasmarohr **112** getrennt. Diese Blutplättchen strömen infolge der Konfiguration dieses Abschnitts der zweiten Stufe **92** in der entgegengesetzten Richtung der Strömung des an Blutplättchen reichen Plasmas/des an Blutplättchen armen Plasmas durch die zweite Stufe **92** zurück zu der Blutplättchen-Sammelkammer **104**. Das heißt, die Blutplättchen-Sammelkammer **104** nimmt die radial äußerste Position in der zweiten Stufe **92** ein, so dass alle Blutplättchen, unabhängig davon, wo die Trennung in der zweiten Stufe **92** erfolgt, zur Entnahme aus dem Kanal **80** zu der Blutplättchen-Sammelkammer **104** strömen.

[0035] An Blutplättchen armes Plasma tritt aus der zweiten Stufe **92** aus und strömt durch das Plasmarohr **112**, das mit der Innenwand des Verarbeitungskanals **80** verbindet, aus und/oder weiter durch den restlichen Abschnitt des Verarbeitungskanals **80** zu der Kontrollkammer **124**. Plasma, das zu der Kontrollkammer **124** strömt, tritt aus dem Kanal durch das Kontrollrohr **114** aus, das mit dem RBC/WBC-Rohr 100 in ein einziges Auslassrohr **120** mündet. Die Positionierungen und die Durchmesser des RBC/WBC-Rohrs **100** und des Kontrollrohrs **114** und deren Verbindung in dem gemeinsamen Auslassrohr **120** regulieren unter Verwendung von Massenerhaltungsprinzipien die Position der Grenzfläche von RBC/WBC und an Blutplättchen reichem Plasmas in dem Übergangsabschnitt **88**.

[0036] Die Blutkomponenten-Sammelvorrichtung **18** enthält ein Vorhersagemodell **20** (das wie oben angemerkt, wie in Fig. 1 gezeigt ist, vorteilhaft mit dem Bedienperson-Eingabemodul **16** verbunden ist und verwendet werden kann, um das Vorhersagemodul **20** zu konfigurieren und/oder eine Bedienpersoneingabe von verschiedenen Parametern zulässt, die durch das Vorhersagemodell **20** zu verwenden sind) zum Vorhersagen eines Blutplättchenausstoßes unter Verwendung einer Zusammenstellung von Algorithmen, bevor eine Sammelprozedur begonnen wird. Das Vorhersagemodell **20** kann von der Optimierungsbaueinheit **140** verwendet werden, die den Prinzipien der vorliegenden Erfindung zugeordnet ist und somit an dieser Stelle kurz beschrieben wird. Trotz der folgenden Erläuterung der Spezifiken des Vorhersagemodells **20** wird ein Fachmann erkennen, dass das Vorhersagemodell **20** den funktionellen und Betriebscharakteristiken der hier beschriebenen Blutkomponenten-Sammelvorrichtung **18** zugeordnet ist. Daher können und werden wahrscheinlich die in dem Vorhersagemodell **20** verwendeten Algorithmen bei anderen Blutkomponenten-Sammelvorrichtungen, die von der vorliegenden Erfindung verwendet werden können, variieren. Darüber hinaus können natürlich sogar für das Vorhersagemodell **20** unterschiedliche Algorithmen verwendet werden. Die Algorithmen sind ferner speziell für die Blutplättchensammlung geeignet und können sich und werden sich wahrscheinlich somit ändern, wenn sie in Verbindung mit anderen Blutkomponententypen, wie etwa mit roten Blutkörperchen, verwendet werden.

[0037] Das Vorhersagemodell **20** wird üblicherweise durch die Einrichtung (z. B. Blutbank/Blutzentrum) für eine bestimmte (z. B. Einnadel- oder Zweinadel-)Blutkomponenten-Sammelprozedur, die von der Einrichtung verwendet wird, konfiguriert und ist in Fig. 2 in Bezug auf die Zweinadelprozedur und eine Blutplättchen-Sammelprozedur dargestellt. Dabei müssen eine AC-Infusionsrate (d. h. die Rate, mit der ein Antikoagulans pro Blutvolumen des Spenders **14** an den Spender **14** abgegeben wird) und das AC-Verhältnis (d. h. die gemeinsame Strömung von AC und Blut durch die Einlassleitung **22** in Bezug auf die Strömung von AC durch die Leitung **22**) (durch Konfiguration oder modifizierte Eingabe, wie im Folgenden erläutert wird) festgelegt werden. Darüber hinaus muss dann, wenn in der Sammelprozedur Plasma in dem Plasmasammelbeutel **54** gesammelt werden soll, außerdem unter Berücksichtigung der medizinischen und physischen Charakteristiken des Spenders **14** die maximale Menge des Plasmas festgelegt werden, die gesammelt werden soll.

[0038] Es gibt zwei alternative Möglichkeiten zur Festlegung der Plasma-Volumengrenze. Die erste Alterna-

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tive in Bezug auf die Plasma-Volumengrenze besteht darin, eine Gewichtsgrenze bereitzustellen (z. B. 0-500 Pfund), die mit dem Gewicht des Spenders **14** zusammenhängt und in der im Folgenden beschriebenen Weise eingegeben wird. Dabei kann eine Plasmavolumen-Obergrenze (z. B. 10-1500 ml) für ein Gewicht eines Spenders **14** festgelegt werden, das diese Grenze überschreitet, und eine Plasmavolumen-Untergrenze (z. B. 10-1500 ml) für ein Gewicht eines Spenders **14** festgelegt werden, das kleiner als diese Grenze ist. Wenn die Gewichtsgrenze z. B. 175 Pfund beträgt, kann die Plasmavolumen-Obergrenze für ein Gewicht des Spenders **14**, das größer oder gleich 175 Pfund ist, bei 600 ml liegen und kann die Plasmavolumen-Untergrenze für ein Gewicht des Spenders **14**, das kleiner als 175 Pfund ist, bei 500 ml liegen.

[0039] Die zweite Alternative für eine Plasmavolumengrenze besteht darin, das Vorhersagemodell **20** in der Weise zu konfigurieren, dass die Plasmavolumengrenze als ein Anteil des totalen Blutvolumens des Spenders **14** ausgedrückt wird, das gemäß der unten stehenden Gleichung 10 berechnet wird. Die Plasmavolumengrenze kann z. B. als 1–15 % des totalen Blutvolumens des Spenders **14** festgelegt werden und wird vorzugsweise als etwa 12 % dieses Volumens festgelegt.

[0040] Bevor das Vorhersagemodell **20** seine Ausstoßvorhersagefunktion ausführt, benötigt es weitere Informationen. Zum Beispiel wird üblicherweise die Gesamtdauer der Prozedur von der Bedienperson eingegeben oder vom Benutzer (z. B. von der Blutbank/dem Blutzentrum) im Voraus konfiguriert. Wenn sie konfiguriert wird, beträgt die Prozedurdauer üblicherweise 100 Minuten. Darüber hinaus wird die Gesamtdauer der Prozedur dadurch beeinflusst, ob für die Blutkomponenten-Sammelvorrichtung **18** eine Untersetzungswahlmöglichkeit verwendet wird, um die Trennung der verschiedenen Blutkomponenten zu verbessern. Wenn diese Untersetzungswahlmöglichkeit ausgewählt wird, wird die Winkelgeschwindigkeit der Blutkomponenten-Sammelvorrichtung **18** während der Blutplättchen-Sammelprozedur schrittweise verringert. Die Untersetzungswahlmöglichkeit könnte z. B. Winkelgeschwindigkeiten für die Vorrichtung **18** von 2400, 2200 und 2000 minbereitstellen, die jeweils für eine festgelegte Dauer gelten.

[0041] Auf der Grundlage des Vorhergehenden standardisiert die Konfiguration des Vorhersagemodells **20** in Bezug auf die Blutkomponenten-Trennbaueinheit **10'** und das zugeordnete Protokoll das Einrichtungsprotokoll für den "normalen" Betrieb. Für einen bestimmten Spender **14** kann es jedoch erwünscht sein, die "Konfiguration" für einen Verarbeitungsdurchlauf zu ändern. Demzufolge verwendet das Vorhersagemodell **20** eine Prozedur, bei der bestimmte Parameter, die in den folgenden Gleichungen verwendet werden, einmalig verändert werden können. Diese werden als modifizierte Eingabedaten bezeichnet und die zugeordneten Parameter sind die Prozedurdauer (z. B. 10-999 Minuten), die Eingangsdurchflussmenge in die Vorrichtung **18** (z. B. 0-150 ml/min für die Baueinheit von Fig. 2 und 0 bis 50 ml/min für die Baueinheit von Fig. 3), die wie oben diskutierte AC-Verhältnis-Wahlmöglichkeit (3–50), das Soll-Blutplättchen-Sammelvolumen (z. B. 10-9999 ml), die Soll-Blutplättchen-Sammelkonzentration (z. B. 100-8000·10^6 ml^{-1}) und das Soll-Plasmavolumen der Quelle, das gesammelt werden soll (z. B. 0–9999 ml). Darüber hinaus können weitere Parameter, wie etwa die AC-Infusionsrate (0,8–1,1), die Untersetzungswahlmöglichkeit (ja oder nein), die Nadel-Wahlmöglichkeit (eine oder zwei) und die Wahlmöglichkeit der starken Strömung (ja oder nein) außerdem als modifizierte Eingabedaten durch eine Bedienperson eingegeben werden.

[0042] Nachdem das Vorhersagemodell **20** in der oben beschriebenen Weise konfiguriert wurde, werden die folgenden Zusatzinformationen bereitgestellt und in den verschiedenen Berechnungen der Gleichungen 1–22, die im Folgenden dargestellt sind, verwendet: (1) Nadel-Wahlmöglichkeit, und zwar, ob die Prozedur eine Zweinadelprozedur (Fig. 2) oder eine Einnadelprozedur (Fig. 3) ist; (2) Durchlauf-Kennzahl zur Zuordnung der Daten/Ausgabe, die durch die verschiedenen Gleichungen bei einem bestimmten Spender **14** und einem Verarbeitungsdurchlauf erzeugt werden; (3) das Geschlecht des Spenders **14**; (4) die Größe des Spenders **14**; (5) das Gewicht des Spenders **14**; (6) das Vollblutvolumen, das durch die folgende Gleichung 10 berechnet wird; (7) der Hämatokrit-Wert des Spenders **14**, entweder anhand einer Anfangsschätzung und einer anschließenden Aktualisierung auf der Grundlage der Analyse der Blutprobe des Spenders **14** (z. B. durch einen Zellenzähler) oder direkt von einer derartigen Analyse eingegeben; (8) die vorläufige Blutplättchen-Anzahl, entweder anhand einer Anfangsschätzung und einer anschließenden Aktualisierung auf der Grundlage der Analyse der Blutprobe des Spenders **14** (z. B. durch einen Zellenzähler) oder direkt von einer derartigen Analyse eingegeben; und (9) ob in Verbindung mit der Blutplättchensammlung eine Plasmasammlung erwünscht ist.

[0043] Anhand der oben genannten Anfangskonfiguration und der anschließenden Dateneingabe (mit Ausnahme bei Eingabe als modifizierte Eingabedaten) werden durch das Vorhersagemodell **20** die folgenden Ausgaben erzeugt: (1) Blutplättchenausstoß; (2) Eingangsdurchflussmenge; (3) AG-Verhältnis; (4) Prozedurdauer; (5) Blutplättchen-Sammelvolumen; (6) Blutplättchen-Sammelkonzentration; (7) Plasmavolumen der Quelle; (8) AC in den Blutplättchen- und in den Plasmasammelbeuteln **38**, **54**; (9) endgültige Blutplättchen-Anzahl; (10)

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AC-Infusionsrate; und (11) Ausgabefreigabe. Diese Informationen werden zumindest teilweise in den folgenden Gleichungen verwendet, um u. a. den Wert des vorhergesagten Blutplättchenausstoßes der gesammelten Blutplättchen für die Zweinadelprozedur von Fig. 2 und ebenfalls für die Einnadelprozedur von Fig. 3 zu erzeugen. Die Unterschiede zwischen diesen Prozeduren in Bezug auf das Vorhersagemodell **20** werden in dieser Beschreibung gekennzeichnet. Es wird erkannt, dass einige der Gleichungen bei der Berechnung des vorhergesagten Blutplättchenausstoßes verwendet werden, wohingegen andere Gleichungen verwendet werden, um Zusatzinformationen zur Ausgabe und zu Informationszwecken zu erzeugen. Die Variablen oder Parameter und die damit verbundenen Einheiten der Gleichungen sind nach den Gleichungen im Variablenindex angegeben.

Blutplättchenausstoß:

$$Y = 1 \cdot 10^6 C_{PR} V_B F_Y [1 - \exp[-E_C(f_{BP} - 0{,}12)]] \quad (1)$$

wobei:

$$f_{BP} = (Q_{IN} t_E + 50)(1 - 1/R) V_B \quad (2)$$

und wobei:

$$Q_{IN} = R Q_{AC} = 0{,}001 \; I \; V_B P R \leq 150 \quad (3)$$

ist.

[0044] Der Blutplättchenausstoß kann alternativ ausgedrückt werden als:

$$Y = 1 \cdot 10^6 C_{PR} V_B F_Y [1 - \exp[-E_C(0{,}001 \; I(R - 1) P t_E \cdot 50(1 - 1/R)/V_B - 0{,}12]] \geq 0 \quad (4)$$

Blutplättchensammeleffizienz:

$$E_C = C_1 - C_2 \exp[9{,}91(1 - 1/R)H] Q_{INA} \geq 0 \quad (5)$$

wobei die Konstante C_1 wie folgt definiert ist:
$C_1 = 0{,}803$ – Zweinadelprozedur, ohne Untersetzung
$C_1 = 0{,}840$ – Zweinadelprozedur, mit Untersetzung
wobei die Konstante C_2 wie folgt definiert ist:
$C_2 = 4{,}08 \cdot 10^{-5}$ – Zweinadelprozedur, ohne Untersetzung
– Zweinadelprozedur, mit Untersetzung
und wobei:

$$Q_{INA} = Q_{IN}(t_E/t_P) \quad (6)$$

ist.

[0045] In Gleichung 6 kann t_P als Konfigurationsdaten oder wie oben als modifizierte Daten bereitgestellt werden oder alternativ aus der Auflösung der Gleichung 4 nach t_E abgeleitet werden.

Effektive Prozedurdauer:

$$t_E = t_F, \; Q_{IN} \leq 45$$
$$= t_P - 500(1/45 - 1/Q_{IN}), \; Q_{IN} > 45 \quad (7)$$

[0046] Für $Q_{IN} > 45$ wird nur das Protokoll für starke Strömung verwendet.

Konstante der AC-Infusionsrate:

$$I = 1000 \; Q_{IN}/(PRV_B) \quad (8)$$

[0047] Alternativ zur Verwendung von Gleichung 8 für die Ableitung der Konstante I der AC-Infusionsrate kann diese als Konfigurationsdaten oder modifizierte Eingabedaten gemäß dem oben Stehenden bereitgestellt

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werden.

AC-Verhältnis

[0048] Anfangs kann das AC-Verhältnis als Konfigurationsdaten oder modifizierte Eingabedaten gemäß dem oben Stehenden bereitgestellt werden. Bei der Konfiguration ist es wie folgt definiert:

$$R = 1 + 2{,}51/H \quad \text{klein}$$

$$= 1{,}33\,(1 + 2{,}51/H) \quad \text{mittelgroß} \qquad (9)$$

$$= 1{,}67\,(1 + 2{,}51/H) \quad \text{groß}$$

Totales Blutvolumen:

$$V_B = 604 + 0{,}006012\,L^3 + 14{,}6\,W \text{ ml (männlich)}$$
$$= 183 + 0{,}005835\,L^3 + 15{,}0\,W \text{ ml (weiblich)} \qquad (10)$$

Plasmasammelfaktor:

[0049] Die Steuerung der AC-Infusionsrate hält die AC-Strömung zum Spender auf dem folgenden Wert:

$$Q_{ACD} = 0{,}001\,I\,V_B \qquad (11)$$

wobei die ihm zugeordnete Einlassströmung:

$$Q_{INO} = RQ_{ACD} = 0{,}001\,IRV_B \qquad (12)$$

ist.

[0050] Wie durch Gleichung 3 angegeben ist, die das AC enthält, das zu dem Blutplättchen-Sammelbeutel **38** und zu dem Plasmasammelbeutel **54** fließt, ist Q_{IN} zu der Gesamt-AC-Strömung proportional. P (Gleichung 13) ist der Faktor, um den Q_{IN}, in Bezug auf den Fall, wenn AC nicht gesammelt wird, durch die Sammlung von AC vergrößert wird. Das heißt

$$P = Q_{IN}/Q_{INO} = (\text{Mittelwert } Q_{AC})/Q_{ACD} \qquad (13)$$

wobei:

$$P = 1 + (f_{ACP}/Q_{ACD})[V_C/(t_P - 150/Q_{IN}) + V_{SP}/(t_P - 500/Q_{IN})] \qquad (14)$$

und wobei:

$$f_{ACP} = [(R - 1)(1 - H)]^{-1} \qquad (15)$$

ist.

Blutplättchen-Sammelvolumen:

$$V_C = 1 \cdot 10^{-6} Y/[C_B\,(1 + f_{ACP})] \qquad (16)$$

Plasmavolumen der Quelle:

[0051] Es werden folgende vier Auswahlmöglichkeiten bereitgestellt:

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$$V_{SP} \begin{cases} = 0 \\ = V_{CON} - V_C \\ = f_{SP}\, V_B - V_C \\ = \text{als modifizierte Eingabe festgelegt} \end{cases} \geq 0 \qquad (17)$$

wobei:

$$V_{CON} = V_{CONL},\ W < WC$$
$$V_{CONR},\ W \geq WC \qquad (18)$$

und wobei:

$$0{,}01 \leq f_{SP} \leq 0{,}15 \qquad (19)$$

ist.

Endgültiger Zählwert des Spenders:

$$C_{PO} = C_{PR} \exp[-E_C(0{,}001\ I(R-1)Pt_E + 50(1 - 1/R)/V_B - 0{,}12)] \leq C_{PR} \qquad (20)$$

Es erfolgt eine Warnung, falls $C_{PO} < 100$ ist.

Sammelvolumen:

$$V_{BC} = V_C\ (1 + f_{ACP}) \qquad (21)$$

$$V_{SPB} = V_{SP}\ (1 + f_{ACP}) \qquad (22)$$

[0052] Die Hauptgleichung, die für die Ausstoßvorhersage durch das Vorhersagemodell 20 zu lösen ist, ist Gleichung 4. Demzufolge sind die Gleichungen 1–3 und 5–22 Hilfsgleichungen für Gleichung 4, obgleich sie verwendet werden können, um andere Ausgabedaten und/oder Informationen, die von Gleichung 4 benötigt werden, zu berechnen. Im Hinblick auf die Art, in der die Gleichungen 1–22 gelöst werden, basieren alle Iterationsschleifen auf der Technik der schrittweisen Näherung, bei der jede Iteration eine Wiederholung der vorhergehenden, jedoch unter Verwendung aktualisierter Parameterwerte, die in der vorhergehenden Iteration berechnet wurden, ist. Dieser Prozess wird fortgesetzt, bis alle Konvergenzkriterien erfüllt sind. Die Konvergenzkriterien bestehen darin, dass die Variablendifferenz bei aufeinanderfolgenden Iterationen ≤ 1 für V_C, $\leq 0{,}2$ für t_E und ≤ 10 für C_B ist.

[0053] Wie oben angemerkt wurde, basiert das Vorhergehende auf einer Zweinadelkonfiguration, wie sie in Fig. 2 dargestellt ist. Wenn die Einnadelkonfiguration, wie etwa jene, die in Fig. 3 dargestellt ist, verwendet wird, wird anstelle von Gleichung 7 die folgende Gleichung 7' verwendet, wobei die Konstanten C_1 und C_2 für Gleichung 5 wie folgt lauten:

$$C_1 = 0{,}803$$

$$C_2 = 8{,}54 \cdot 10^{-5}$$

$$t_E = t_P,\ Q_{IN} \leq 20$$
$$= t_P - 215\ (1/20 - 1/Q_{IN}) + Q_{IN} > 20 \qquad (7')$$

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Variablenindex

Symbole für Gleichungen:

C_1, C_2 = Konstanten in den Gleichungen der Blutplättchensammeleffizienz
C_B = Blutplättchenkonzentration im Sammelbeutel, ausgedrückt als 10^3 Blutplättchen/Mikroliter
C_{PO} = endgültiger Spenderzählwert, ausgedrückt als 10^3 Blutplättchen/Mikroliter
C_{PR} = vorläufiger Spenderzählwert, ausgedrückt als 10^3 Blutplättchen/Mikroliter
E_C = Blutplättchensammeleffizienz
f_{ACP} = AC, Ausgedrückt als Anteil des Blutplasmavolumens
f_{BP} = Anteil von V_B, der in der Blutplättchensammelprozedur verarbeitet wird
f_{SP} = V_{CON}, ausgedrückt als ein Anteil von V_B
F_Y = benutzerspezifischer (z. B. für die Blutbank/das Blutzentrum spezifischer) Ausstoß-Kalibrierungsfaktor
H = Hämatokrit-Wert des Spenders oder Patienten
I = Konstante der AC-Infusionsrate
L = Größe des Spenders oder Patienten in Zoll
P = Plasmasammelfaktor
Q_{AC} = AC-Strömung in ml/min
Q_{ACD} = AC-Strömung, die in den Spender für Blutplättchensammelprozeduren infundiert wird, in ml/min
Q_{IN} = Einlassströmung in ml/min
Q_{INA} = gemittelte Einlassströmung für Blutplättchenprozeduren in ml/min
Q_{INO} = RQ_{ACD} = Einlassströmung, die Q_{ACD} zugeordnet ist, in ml/min
R = AC-Verhältnis
t_E = äquivalente Prozedurdauer in min
t_P = Prozedurdauer in min
V_B = totales Blutvolumen des Spenders oder Patienten in ml
V_C = Volumen des reinen Plasmas in dem Plasmasammelbeutel in ml
V_{CB} = Gesamtvolumen im Blutplättchensammelbeutel in ml
V_{CON} = Volumenbeschränkung für das gesamte gesammelte reine Plasma in ml
V_{CONH} = höherer Wert von V_{CON} in ml
V_{CONL} = niedrigerer Wert von V_{CON} in ml
V_{SP} = Volumen des reinen Plasmas in dem Plasmabeutel der Quelle in ml
V_{SPB} = Gesamtvolumen in dem Quellen-Plasmabeutel in ml
W = Gewicht des Spenders oder Patienten in Pfund
W_C = Gewichtsbeschränkung, die V_{CON} zugeordnet ist, in Pfund
Y = Blutplättchenausstoß, Anzahl der Blutplättchen.

[0054] Wie oben angemerkt wurde, verbindet die Optimierungsbaueinheit **140** gemäß den Prinzipien der vorliegenden Erfindung mit einer oder mehreren Blutkomponenten-Sammelbaueinheiten **10** oder stellt zumindest Informationen für diese bereit, um ein Blutplättchen-Sammelsystem **2** zu schaffen. Das heißt, obgleich definitiv Vorteile des Vorhandenseins einer Schnittstelle zwischen der Optimierungsbaueinheit **140**, insbesondere zwischen dem Optimierungsmodul **144**, und der Blutkomponenten-Sammelvorrichtung **18** vorhanden sind, kann die Optimierungsprozedur an irgendeiner Stelle ausgeführt werden und eine Eingabe in die Blutkomponenten-Sammelvorrichtung **18** auf beliebige Weise erfolgen. Da die allgemeinen Prinzipien der Blutkomponenten-Sammelbaueinheit **10** in Bezug auf die Sammelbaueinheiten **10**, **10"** beschrieben wurden, die die Blutkomponenten-Sammelvorrichtung **18** und ihre verschiedenen Merkmale enthalten, wird die Optimierungsbaueinheit **140** in Bezug auf diese Baueinheiten **10'**, **10"** beschrieben. Es wird jedoch anerkannt, dass die grundlegenden Optimierungsprinzipien der vorliegenden Erfindung nicht auf diese Sammelprozeduren und/oder Vorrichtungen beschränkt sind.

[0055] Wie angemerkt wurde (Fig. 1), enthält die Optimierungsbaueinheit **140** im Allgemeinen für jede Blutkomponenten-Sammelvorrichtung **18** eine zentrale Eingabestation **148** sowie ein Optimierungsmodul **144**. Anfangs sollte angemerkt werden, dass das Optimierungsmodul **144** von der internen Steuerung der Blutkomponenten-Sammelvorrichtung **18**, auf die durch das Bedienperson-Schnittstellenmodul **16** zugegriffen werden kann, getrennt sein kann. Allerdings ist das Optimierungsmodul **144** üblicherweise gemeinsam mit dem oben beschriebenen Vorhersagemodul **20** mit dieser internen Steuerung integriert.

[0056] In Fig. 5 wird die Optimierungsbaueinheit **140** in Bezug auf eine Standardprozedur beschrieben. Die zentrale Eingabestation **148** wird üblicherweise durch Blutbanken/Blutzentren als Haupteinrichtung für die Ein-

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gabe und Organisation von Spenderdaten verwendet. Bei der zentralen Eingabestation **148** werden Informationen bezüglich eines Spenders, wie etwa Geschlecht, Größe, Gewicht und demographische Angaben, eingegeben. Darüber hinaus können Informationen bezüglich des Hämatokrit-Wertes des Spenders und einer vorläufigen Anzahl der Blutkomponenten, die beide von einer Blutprobe des Spenders erhalten und durch bekannte Techniken, wie etwa durch Zellenzähleinrichtungen, bestimmt werden können, ebenfalls bei der zentralen Station **148** eingegeben werden. Außer spenderbezogenen Daten können bei der zentralen Eingabestation **148** der bestimmte Typ der Sammelprozedur, der für den Spender zu verwenden ist (z. B. Einnadel- oder Zweinadel-), eingegeben/bestätigt werden. Anhand dieser Informationen und bestimmter für die Einrichtung standardisierter Bedingungen (z. B. Gesamtdauer der Prozedur, Sammeleffizienz, AC-Infusionsrate) wird daraufhin ein Anfangsprozedurauftrag erzeugt, der die verschiedenen Prozesssteuerungsparameter festlegt, die der ausgewählten Sammelprozedur zugeordnet sind.

[0057] Der Anfangsprozedurauftrag kann dann bei Bedarf/auf Wunsch unter Verwendung des Bedienperson-Schnittstellenmoduls **16** durch eine Computerspeicherplatte **142** (Fig. 1) oder, wenn ein (nicht gezeigtes) Netzwerksystem realisiert ist, elektronisch in die interne Steuerung einer Blutkomponenten-Sammelvorrichtung **18** übertragen/heruntergeladen werden. Wenn dieses Bedienperson-Schnittstellenmodul **16** vorhanden ist, kann es natürlich für die Anfangseingabe von Spenderdaten und/oder für die Erzeugung des Anfangsprozedurauftrags verwendet werden, wodurch die Notwendigkeit für eine zentrale Eingabestation **148** vermieden wird. Es kann jedoch effizienter sein, die zentrale Eingabestation zu verwenden. Obgleich dieser Anfangsprozedurauftrag in dem Sammelvorgang verwendet werden kann, kann er in Übereinstimmung mit den Prinzipien der vorliegenden Erfindung optimiert werden, um einen oder mehrere optimale Werte für Prozesssteuerungsparameter zu erhalten. Wie angemerkt wurde, kann dieser Optimierungsprozess verwendet werden, bevor die Sammelprozedur tatsächlich begonnen wird, während er jedoch auch während einer gegebenen Sammelprozedur begonnen werden und daher als nachgeschaltete Optimierung bezeichnet werden kann.

[0058] In Bezug auf die verschiedenen Optimierungswahlmöglichkeiten können Prozesssteuerungsparameter für eine produktbasierte Optimierung abgeleitet werden. Im Einzelnen leitet die Optimierungsbaueinheit **140** und insbesondere das Optimierungsmodul **144**, wie im Folgenden in Bezug auf die Optimierungsmodelle **152** (Fig. 6), **172** (Fig. 7) erläutert wird, Prozesssteuerungsparameter zum Erreichen eines vorgegebenen Ausstoßes von Blutkomponenten durch eine Maximierung wenigstens eines Prozessparameters ab. Wie oben angemerkt wurde, enthält in den Vereinigten Staaten ein Einfach-Blutplättchen-Produkt (SPP) $3 \cdot 10^{11}$ Blutplättchen und ein Doppel-Blutplättchen-Produkt (DPP) $6 \cdot 10^{11}$ Blutplättchen. Demzufolge kann das Optimierungsmodul **144** in der Weise konfiguriert sein, dass es mehrere produktbasierte Optimierungen, wie etwa SPP und DPP, bereitstellt. Obgleich die genauen Werte für aktuelle US-SPP und -DPP in das Optimierungsmodul **144** konfiguriert werden können, um die Wahrscheinlichkeit zu erhöhen, dass der tatsächliche Ausstoß die Ausstoßforderungen für aktuelle US-SPP und -DPP erreicht oder übersteigt, kann die Einrichtung ein SPP auf $3{,}5 \cdot 10^{11}$ Blutplättchen und ein DPP auf $7{,}0 \cdot 10^{11}$ Blutplättchen konfigurieren (um z. B. effektiv einen Vertrauensgrad sicherzustellen, dass der festgelegte Ausstoß tatsächlich erreicht wird).

[0059] Außerdem kann das Optimierungsmodul **144** so konfiguriert sein, dass es eine zeitbasierte Optimierung schafft. Das heißt, für eine vorgegebene Zeitdauer, in der ein Spender zur Verfügung steht, leitet das Optimierungsmodul **144** diejenigen Prozessparameter ab, die in Bezug auf eine Maximierung wenigstens eines der Prozesssteuerungsparameter die Sammlung einer "maximalen" Menge von Blutplättchen in dieser Zeitperiode zulassen.

[0060] Nachdem die Optimierung abgeschlossen ist, werden die Werte für die hierdurch erzeugten verschiedenen Prozesssteuerungsparameter sowie alle Hilfswerte/vorher festgelegten Werte in die interne Steuerung der Blutsammelvorrichtung **18** heruntergeladen, so dass die Sammelprozedur begonnen oder, wie es gemäß diesen Werten der Fall sein kann, neu begonnen (nachgeschaltete Optimierung) werden kann. Nachdem die Prozedur abgeschlossen ist, können bestimmte Daten (über die Speicherplatte **142** oder elektronisch, wie angemerkt wurde) zur Weiterverwendung in Bezug auf den bestimmten Spender wieder zur zentralen Eingabestation **148** übertragen werden. Außerdem können diese Informationen sowie die Anfangseingabe verwendet werden, um verschiedene Typen von Berichten (z. B. einzelne Durchläufe, Spender/Patient, zusammenfassende Berichte) zu erzeugen, die bei der Organisation der Blutbank/des Blutzentrums weiter unterstützen können. Das heißt, diese Informationen können bei der Ableitung von nachfolgenden Prozeduraufträgen für den bestimmten Spender verwendet werden. Wenn z. B. in der Sammelprozedur eine bestimmte AC-Infusionsrate verwendet wurde, die bestimmte Auswirkungen auf den Spender hatte, kann diese in der zentralen Eingabestation **148** aufgezeichnet werden, so dass für spätere Spenden durch den Spender eine niedrigere AC-Infusionsrate vorgeschlagen/gefordert wird.

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[0061] Ein Modell, das in dem Optimierungsmodul **144** enthalten sein kann, ist in Fig. 6 gezeigt und wird in Bezug auf Blutplättchen-Sammlungen gemäß der Zweinadelkonfiguration von Fig. 2 beschrieben, obgleich das Modul **144** bei einer Vielzahl weiterer Sammelprozeduren verwendet werden kann und die Einnadelkonfiguration von Fig. 3 enthält sowie bei verschiedenen anderen Blutkomponenten verwendet werden kann. Anfangs sollte angemerkt werden, dass in Fig. 6 alle Bezugnahmen auf "Ableitungen" tatsächlich in dem oben erläuterten Vorhersagemodell **20** erfolgen, so dass entweder eine geeignete Schnittstelle zwischen dem Vorhersagemodell **20** und dem Optimierungsmodul **144** vorhanden ist oder das Optimierungsmodul **144** tatsächlich das Vorhersagemodell **20** enthält. Wie darüber hinaus angemerkt wurde, ist das Vorhersagemodell **20** speziell für die Blutkomponenten-Sammelvorrichtung **18** und für Blutplättchensammlungen. Wie angemerkt wurde, würde sich daher dann, wenn andere Vorrichtungen verwendet werden, das zugeordnete Vorhersagemodell ebenfalls ändern. Darüber hinaus kann sich das zugeordnete Vorhersagemodell auch in dem Fall ändern, wenn andere Blutkomponenten, wie etwa rote Blutkörperchen, gesammelt werden sollen.

[0062] Das Optimierungsmodell **152** von Fig. 6 kann sowohl für produktbasierte Optimierungen als auch für zeitbasierte Optimierungen verwendet werden. Anfangs wird das Optimierungsmodell **152** in Bezug auf eine produktbasierte Optimierung beschrieben. Das heißt, die Grundaufgabe der Optimierung besteht darin, einen vorgegebenen Ausstoß (oder einen Ausstoß in einem Ausstoßbereich) von Blutplättchen (oder eines anderen Blutkomponententyps), vorzugsweise innerhalb der minimalen Zeitdauer, zu erreichen.

[0063] Das Optimierungsmodell **152** von Fig. 6 enthält vier Iterationsschleifen. Die erste Schleife **156** ist im Allgemeinen eine Ableitung einer Einlassströmung (Q_{IN}), die einer festgelegten AC-Infusionsrate (I_{SPEC}) zugeordnet ist, die für die vorliegende Erfindung üblicherweise auf einen Maximalwert eingestellt und bei der Eingabestation **154** eingegeben wird. Diese Ableitung wird daraufhin durch die Verarbeitungsstation **158** ausgeführt und enthält die Auflösung der Gleichungen **4**, **8**, **14** und **16** und/oder deren Hilfsgleichungen durch das Vorhersagemodell **20**, wie oben erläutert wurde.

[0064] Natürlich gibt es ein unterschiedliches Konvergenzkriterium/verschiedene Konvergenzkriterien, die in der ersten Schleife **156** enthalten sein können. Die Konvergenz kann z. B. in der ersten Schleife **156** unter Verwendung einer binären Suchtechnik auf der Ist-Einlassströmung (Q_{IN-C}) basieren. In diesem Fall bleiben bei der Lösung der angegeben Gleichungen in der Verarbeitungsstation **158** bestimmte Parameter bei der iterativen Ableitung der Einlassströmung (Q_{IN}) feststehend, wodurch die festgelegte AC-Infusionsrate (I_{SPEC}) erreicht wird, wobei diese Parameter ebenfalls bei der Eingabestation **154** festgelegt werden. Diese enthalten das totale Blutvolumen (V_B), das unter Verwendung von Gleichung 10 berechnet werden kann, da die Größe, das Gewicht und das Geschlecht des Spenders bei der zentralen Eingabestation **148** eingegeben werden, und das AC-Verhältnis (R), das unter Verwendung von Gleichung 9 berechnet werden kann, da der Hämatokrit-Wert (H) des Spenders bestimmt worden ist oder auf einen bestimmten Wert festgelegt werden kann. Darüber hinaus bleibt die Gesamtprozedurdauer (t_P) bei jeder iterativen Ableitung der Einlassströmung (Q_{IN}), die der festgelegten AC-Infusionsrate (I_{SPEC}) in der ersten Schleife **156** zugeordnet ist, feststehend. Da jedoch die Gesamtprozedurdauer (t_P) bei einer produktbasierten Optimierung nicht bekannt ist und daher bei der Eingabestation **154** nicht festgelegt werden kann, wird anfangs eine Ist-Gesamtprozedurdauer (t_{P-C}) angenommen (diese Annahme ist z. B. in dem Optimierungsmodell **152** konfiguriert, und da in dem Vorhersagemodell **20**, wie oben angemerkt wurde, ein Bereich von Gesamtprozedurdauern bereitgestellt wird, wird in diesem Abschnitt des Optimierungsmodells **152** üblicherweise die mittlere Gesamtprozedurdauer (t_P) als die Ist-Anfangsgesamtprozedurdauer (t_{P-C}) konfiguriert). Die Bezeichnung "Ist " wird in diesem Fall für die Gesamtprozedurdauer verwendet, da das Optimierungsmodell **152** für eine Einstellung der Gesamtprozedurdauer nach jeder iterativen Bestimmung der Einlassströmung (Q_{IN}) dient, die in der zweiten Schleife **160** die festgelegte AC-Infusionsrate (I_{SPEC}) bereitstellt, um, wie im Folgenden genauer erläutert wird, bei einer produktbasierten Optimierung bei Bedarf den Soll-Ausstoß (Y) zu erreichen.

[0065] Die Konvergenz bei der binären Suchtechnik auf der Grundlage der Einlassströmung kann im Allgemeinen durch Annehmen eines Istwertes für die Einlassströmung (Q_{IN-C}), Berechnen eines Ist-Plasmasammelfaktors (P_C) unter Verwendung der Ist-Gesamtprozedurdauer (t_{P-C}), Berechnen einer Ist-AC-Infusionsrate (I_C) unter Verwendung der Ist-Einlassströmung (Q_{IN-C}) und des Ist-Plasmasammelfaktors (P_C) und Einstellen der Ist-Einlassströmung (Q_{IN-C}) (bei der Parameter-Aktualisierung in der ersten Schleife **156**) in Übereinstimmung mit der ausgewählten binären Suchtechnik, bis eine vorgegebene Konvergenz zwischen den zwei letzten Werten für die Ist-Einlassströmung (Q_{IN-C}) vorhanden ist (d. h. bis die Differenz zwischen den beiden letzten Werten von Q_{IN-C} kleiner als ein vorgegebener Betrag ist, d. h., bis das Konvergenzkriterium erfüllt ist), sichergestellt werden. Bei einer binären Suchtechnik gibt es immer Konvergenz (d. h. das Konvergenzkriterium wird immer erfüllt), so dass das Optimierungsmodell **152** die erste Schleife **156** immer verlässt und in die zweite Schleife **160** eintritt.

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[0066] Als eine Alternative zu dem angegebenen Konvergenzkriterium/zu den angegeben Konvergenzkriterien auf der Grundlage der Einlassströmung und der angegebenen binären Suchtechnik besteht eine andere Möglichkeit darin, die Konvergenz auf die festgelegte AC-Infusionsrate (I_{SPEC}) zu beziehen und eine iterative Ableitung zu verwenden, um die Soll-Einlassströmung (Q_{IN}) zu bestimmen. In diesem Fall wird die erste Schleife **156** ebenfalls verwendet, um die Einlassströmung (Q_{IN}), die die festgelegte AC-Infusionsrate (I_{SPEC}) bei der Verarbeitungsstation **158** bereitstellt, aus bestimmten festgelegten Parametern iterativ noch einmal abzuleiten. Das heißt, die erste Schleife **156** dient weiterhin der Maximierung der Einlassströmung (Q_{IN}) anhand der festgelegten AC-Infusionsrate (I_{SPEC}), die dem Spender **14** zugeordnet werden sollte. Dies erfolgt wiederum hauptsächlich durch die Lösung der Gleichungen 4, 8, 14 und 16 und/oder deren Hilfsgleichungen durch das oben erläuterte Vorhersagemodell **20**.

[0067] Für die Lösung der oben angegebenen Gleichungen in Bezug auf das Konvergenzkriterium auf der Grundlage der Infusionsrate bleiben bestimmte Parameter bei der iterativen Ableitung der Einlassströmung (Q_{IN}) feststehend, wodurch in der ersten Schleife **156** die festgelegte AC-Infusionsrate (I_{SPEC}) erreicht wird und diese Parameter außerdem bei der Eingabestation **154** festgelegt werden. Diese enthalten die festgelegte AC-Infusionsrate (I_{SPEC}), die bekannt ist und üblicherweise ein Maximalwert für den Spender **14** ist, das totale Blutvolumen (V_B), das unter Verwendung von Gleichung 10 berechnet werden kann, da Größe, Gewicht und Geschlecht des Spenders **14** in die zentrale Eingabestation **148** eingegeben werden, und das AC-Verhältnis (R), das unter Verwendung von Gleichung 9 berechnet werden kann, da der Hämatokrit-Wert (H) des Spenders **14** in Übereinstimmung mit dem oben Stehenden (z. B. über eine Direktanalyse mit einem Zellenzähler) bestimmt und anschließend in die zentrale Eingabestation **148** eingegeben worden ist oder als modifizierte Eingabedaten eingegeben werden kann. Darüber hinaus bleibt (t_P) bei jeder iterativen Ableitung der Einlassströmung (Q_{IN}), die der festgelegten AC-Infusionsrate (I_{SPEC}) zugeordnet ist, feststehend. Allerdings ist die Gesamtprozedurdauer (t_P) im Fall einer produktbasierten Optimierung wieder nicht bekannt und kann daher nicht bei der Eingabestation **154** festgelegt werden. Daher wird anfangs eine Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$) angenommen (wobei diese Annahme z. B. in dem Optimierungsmodell **152** konfiguriert wird und in die erste Schleife **156** des Optimierungsmodells üblicherweise die mittlere Gesamtprozedurdauer (t_P) **152** konfiguriert wird, da in dem Vorhersagemodell **20**, wie oben angegeben wurde, ein Bereich der Gesamtprozedurdauern bereitgestellt wird). Die Bezeichnung "Ist-" für die Gesamtprozedurdauer wird aus den oben angegebenen Gründen in Bezug auf die Einstellung der Gesamtprozedurdauer in der zweiten Schleife **160** verwendet, falls diese den Soll-Ausstoß (Y) erreichen muss.

[0068] Die Lösung der Gleichungen 4, 8, 14 und 16 erfordert außerdem, dass bestimmte Werte für einige der restlichen Parameter angenommen werden, während nochmals weitere Parameter aus dieser Annahme abgeleitet werden. In diesem Fall wird eine iterative Prozedur verwendet, wobei in den nächsten iterativen Berechnungen aktualisierte Werte/Ist-Werte verwendet werden. Alle Parameter, die sich bei jeder Iteration der ersten Schleife **156** ändern, sind hier mit einem Index "c" bezeichnet, um anzugeben, dass der neueste Ist-Wert zu verwenden ist. Obgleich die Ableitung dieser Einlassströmung (Q_{IN}), die die festgelegte AC-Infusionsrate (I_{SPEC}) erzeugt, über die Gleichungen 4, 8, 14 und 16 auf eine Vielzahl von Arten ausgeführt werden kann, besteht eine Möglichkeit darin, einen Ist-Wert für den Plasmasammelfaktor (P_C) anzunehmen, anschließend unter Verwendung der festgelegten AC-Infusionsrate (I_{SPEC}) die Ist-Einlassströmung ($Q_{IN\text{-}C}$) zu berechnen, dann den Ist-Ausstoß (Y_C) zu berechnen, daraufhin unter Verwendung des Ist-Ausstoßes (Y_C) den Ist-Plasmasammelfaktor (P_C) zu berechnen und diese Prozedur mit den Ist-Werten zu wiederholen, bis eine annehmbare Konvergenz bei der Ist-Einlassströmung ($Q_{IN\text{-}C}$) in Bezug auf die festgelegte AC-Infusionsrate (I_{SPEC}) vorhanden ist (z. B. dann, wenn das besondere Konvergenzkriterium/die besonderen Konvergenzkriterien erfüllt/eingehalten werden). Wenn auf der Grundlage der Infusionsrate eine annehmbare Konvergenz vorhanden ist, verlässt das Optimierungsmodell **152** die erste Schleife **156** und tritt in die zweite Schleife **160** ein. Als Schutz für Fälle, in denen es keine Konvergenz gibt, kann eine maximale Anzahl von Iterationen für die erste Schleife **156** festgelegt sein (nicht gezeigt).

[0069] Die zweite Schleife **160** des Optimierungsmodells **152** ist eine Iteration der Gesamtprozedurdauer (t_P). Das heißt, die zweite Schleife **160** ist eine iterative Einstellung der Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$). In der zweiten Schleife **160** und bei einer produktbasierten Optimierung wird das Modell **152** ursprünglich niemals bei dem ersten Komparator **162** aussteigen, da die Gesamtprozedurdauer (t_P) bei der Eingabestation **154** nicht festgelegt worden ist. Demzufolge geht das Optimierungsmodell **152** zum zweiten Komparator **166** über, wo die Konvergenzkriterien (d. h. mehr als eine Prüfung) aufgestellt werden. Ein Konvergenzkriterium, das bei dem zweiten Komparator **166** geprüft wird, besteht darin, ob der Ist-Ausstoß (Y_C) größer oder gleich dem Soll- und festgelegten Ausstoß (Y) ist. In diesem Fall kann der Ist-Ausstoß (Y_C) für den Vergleich mit dem Soll- und festgelegten Ausstoß (Y) anhand der bei der Eingabestation **154** festgelegten Werte, der bei der Verarbeitungsstation **158** abgeleiteten Werte und der Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$) berechnet werden (in einigen Fällen kann die-

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se Berechnung des Ist-Ausstoßes (Y_C) in der ersten Schleife **156** ausgeführt worden sein und braucht in der zweiten Schleife **160** nicht wiederholt zu werden). Wie im Folgenden erläutert wird, verlässt das Modell **152** die zweite Schleife **160** und verlässt tatsächlich den gesamten Durchlauf zum Ausstieg **151**, wenn das Ausstoß-Konvergenzkriterium erfüllt ist. In diesem Fall sind die festgelegten/abgeleiteten Werte "optimal" und die Sammelprozedur könnte in der Vorrichtung **18** unter Verwendung der festgestellten Werte für die verschiedenen Steuerungsparameter ausgeführt werden.

[0070] Wenn das Kriterium auf der Grundlage des Ausstoßes bei dem zweiten Komparator **166** nicht erfüllt ist, sucht der zweite Komparator **166** nach einem Konvergenzkriterium auf der Grundlage der Gesamtprozedurdauer, das dem oben in Bezug auf das Kriterium auf der Grundlage der Einlassströmung erläuterten ähnlich sein kann (z. B. unter Verwendung einer binären Suchtechnik, wobei das Konvergenzkriterium dann eine vorgegebene Differenz zwischen den beiden neuesten Ist-Werten der Gesamtprozedurdauer ($t_{P\text{-}C}$) ist). Nachdem nach dem ersten Durchlauf der zweiten Schleife **160** das angegebene Kriterium auf der Grundlage des Ausstoßes nicht erfüllt ist und das Konvergenzkriterium der Gesamtprozedurdauer nicht erfüllt ist, wird die Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$) eingestellt und das Modell **152** kehrt zur ersten Schleife **156** zurück. Das heißt, jedes Mal, wenn die Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$) in der zweiten Schleife **160** eingestellt wird, wird die vollständige erste Schleife **152** wiederholt (d. h. unter Verwendung der Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$), die durch die Einstellung in der zweiten Schleife **160** bereitgestellt wird, eine neue Einlassströmung (Q_{IN}), die der festgelegten AC-Infusionsrate (I_{SPEC}) zugeordnet ist, abgeleitet). In der zweiten Schleife **160** könnte ein anderes Konvergenzkriterium/könnten andere Konvergenzkriterien verwendet werden, wie etwa das Festlegen einer maximalen Anzahl von Iterationen, die von der zweiten Schleife **160** ausgeführt werden sollen.

[0071] Wenn das Kriterium auf der Grundlage des Ausstoßes in der zweiten Schleife **160** nicht erfüllt ist und das Konvergenzkriterium auf der Grundlage der Gesamtprozedurdauer bei dem zweiten Komparator **166** in der zweiten Schleife **160** erfüllt ist, verlässt das Optimierungsmodell **152** die zweite Schleife **160** und tritt in die dritte Schleife **164** ein. Die dritten Schleife **164** ist eine iterative Einstellung des AG-Verhältnisses (R). Allerdings greift das Modell **152** anfangs auf den dritten Komparafor **169** zu, wenn Konvergenzkriterien (d. h. mehr als ein Kriterium) geprüft werden. Ein Konvergenzkriterium ist wieder das oben angegebene Kriterium auf der Grundlage des Ausstoßes. Wenn dieses Kriterium auf der Grundlage des Ausstoßes wiederum nicht erfüllt ist, wird im dritten Komparator **169** ein Konvergenzkriterium auf der Grundlage des AC-Verhältnisses geprüft. Dieses kann dem oben erläuterten Kriterium auf der Grundlage der Einlassströmung ähnlich sein (z. B. unter Verwendung einer binären Suchtechnik, wobei sich das Konvergenzkriterium auf die beiden neuesten Ist-Werte des AC-Verhältnisses bezieht). Nachdem beim ersten Durchlauf der dritten Schleife **164** das Kriterium auf der Grundlage des Ausstoßes nicht erfüllt ist und das Konvergenzkriterium auf der Grundlage des AC-Verhältnisses nicht erfüllt ist, wird das AC-Verhältnis eingestellt und kehrt das Optimierungsmodell **152** zur ersten Schleife **152** zurück. Das heißt, jedes Mal, wenn das AC-Verhältnis (R) in der dritten Schleife **164** eingestellt wird, werden die erste und die zweite Schleife **156**, **160** jeweils vollständig wiederholt. In der dritten Schleife **164** könnten ein anderes Konvergenzkriterium/andere Konvergenzkriterien wie etwa die Festlegung einer maximalen Anzahl von Iterationen der dritten Schleife **164** verwendet werden.

[0072] Falls das Konvergenzkriterium auf der Grundlage des Ausstoßes in der zweiten bzw. in der dritten Schleife **160**, **164** und in dem zweiten bzw. in dem dritten Komparator **166**, **169** nicht erfüllt ist und das Konvergenzkriterium auf der Grundlage des AC-Verhältnisses bei dem dritten Komparator **169** in der dritten Schleife **164** erfüllt ist, verlässt das Optimierungsmodell **152** die dritte Schleife **164** und tritt in die vierte Schleife **168** ein. Die vierte Schleife **168** ist eine iterative Einstellung der festgelegten AC-Infusionsrate (I_{SPEC}). Allerdings tritt das Optimierungsmodell **152** anfangs in den vierten Komparator **170** ein, wo die Konvergenzkriterien (d. h. mehr als ein Konvergenzkriterium) geprüft werden. Ein Konvergenzkriterium ist das erwähnte Konvergenzkriterium auf der Grundlage des Ausstoßes. Falls das erwähnte Konvergenzkriterium auf der Grundlage des Ausstoßes bei dem vierten Komparator **170** nicht erfüllt ist, wird bei dem vierten Komparator **170** ein Kriterium auf der Grundlage der AC-Infusionsrate geprüft. Dies kann ähnlich dem oben diskutierten Kriterium auf der Grundlage der Einlassströmung (z. B. unter Verwendung einer binären Suchtechnik, wobei das Konvergenzkriterium die zwei neuesten Ist-Werte der AC-Infusionsrate sind) sein. Nachdem nach dem ersten Durchlauf der vierten Schleife **168** das Kriterium auf der Grundlage des Ausstoßes nicht erfüllt war und das Konvergenzkriterium auf der Grundlage der AC-Infusionsrate nicht erfüllt war, wird die AC-Infusionsrate eingestellt und kehrt das Modell **152** zu der ersten Schleife **152** zurück. Das heißt, jedes Mal, wenn die festgelegte AC-Infusionsrate (I_{SPEC}) eingestellt wird, wird die Gesamtheit der ersten, zweiten und dritten Schleife **156**, **160**, **164** in dieser Reihenfolge wiederholt (wobei das AC-Verhältnis bei jeder Iteration der vierten Schleife **168** auf seinen Anfangswert zurückgesetzt wird, wie er in die Eingabestation **154** eingegeben worden ist). In der vierten Schleife **168** kann ein anderes Konvergenzkriterium/können andere Konvergenzkriterien wie etwa die Festlegung einer Maximalzahl von Iterationen der vierten Schleife **168** verwendet werden. In Fällen, in dienen die festgelegte AC-Infusions-

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rate (I_{SPEC}) tatsächlich die maximale AC-Infusionsrate ist, wird die vierte Schleife **168** üblicherweise nur ein einziges Mal mit einer einmaligen Erhöhung der AC-Infusionsrate von z. B. 20 % (kann z. B. durch die Einrichtung konfiguriert werden) ausgeführt.

[0073] Wenn in den vorstehenden Schleifen die Konvergenzkriterien auf der Grundlage des Ausstoßes erfüllt sind, verlässt sie das Optimierungsmodell **152**, wenn die Kriterien erfüllt sind, zum Ausstieg **151**, wobei die festgelegten/abgeleiteten Werte (d. h. Ist-Werte) für die verschiedenen Prozesssteuerungsparameter zur Ausführung der Sammelprozedur für die Vorrichtung **18** bereitgestellt werden können. Allerdings kann es wie etwa dann, wenn sie das Optimierungsmodell **152** anhand dessen, dass das Konvergenzkriterium auf der Grundlage der AC-Infusionsrate erfüllt ist, zum Austritt **151** verlässt, Fälle geben, wo keine Optimierung stattfindet.

[0074] Das Optimierungsmodell **152** kann ebenfalls für eine Zeitoptimierung verwendet werden. Das heißt, das Optimierungsmodell leitet durch Maximierung wenigstens eines der Prozessparameter optimale Prozessparameter für eine vorgegebene Gesamtprozedurzeit (t_P) ab, um die Blutplättchensammlung (oder für andere Blutkomponententypen) zu maximieren. In diesem Fall führt das Optimierungsmodell **152** nur die erste Schleife **156** aus, um unter Verwendung der Eingabegesamtprozedurdauer (t_P) in dieser iterativen Ableitung anstelle der oben erwähnten angenommenen Gesamtprozedurdauer (t_P) die Einlassströmung (Q_{IN}) abzuleiten, die einer festgelegten AC-Infusionsrate (I_{SPEC}) (üblicherweise ein Maximalwert) zugeordnet ist. Wenn es wie oben in der produktbasierten Optimierung definiert eine akzeptable Konvergenz gibt, so dass das Modell **152** die erste Schleife **156** verlässt, kann in der ersten Schleife **156** der Ist-Ausstoß (Y_C) berechnet werden (wobei er aber bereits wieder in der ersten Schleife **156** bei der Verarbeitungsstation **158** berechnet worden sein kann, so dass keine weitere Berechnung erforderlich ist), wobei das Konvergenzkriterium bei dem ersten Komparator **162** erfüllt ist, wenn in die zweite Schleife **160** eingetreten wird (d. h., wenn in einer zeitbasierten Optimierung bei der Eingabestation **154** eine Gesamtprozedurdauer festgelegt wird, tritt das Modell **152**, wenn es in die zweite Schleife **158** eintritt, aus). Im Ergebnis sind die Einlassströmung (Q_{IN}) und die AC-Infusionsrate (I) optimal, wobei die Sammelprozedur mit diesen Werten ausgeführt werden kann.

[0075] In Fig. 7 ist ein weiteres Optimierungsmodell dargestellt, das sowohl für produktbasierte als auch für zeitbasierte Optimierungen verwendet werden kann. Wie im Fall des Optimierungsmodells **152** kann das Optimierungsmodell **172** mit dem Vorhersagemodell **20** verbunden sein oder das Vorhersagemodell **20** tatsächlich integral enthalten, so dass im Folgenden auf die Gleichungen 1–22 Bezug genommen wird. Im Allgemeinen beruht das Optimierungsmodell **172** auf dem Prinzip, dass eine Optimierung stattfindet, wenn in der Ableitung verschiedener Prozesssteuerungsparameter eine optimale Einlassströmung (Q_L) verwendet wird, die einer optimalen Systemsammlung effizient zugeordnet ist. Anhand von Fig. 8 ist eine repräsentative Einlassströmungs-(Q_{IN}-)/Ausstoß-(Y-)Kurve dargestellt, die die optimale Einlassströmung (Q_L) zeigt, die dem maximalen Ausstoß (Y_{MAX}) zugeordnet ist. Diese optimale Einlassströmung (Q_L) ist mathematisch durch die unten dargestellte Gleichung 23 ausgedrückt, die sich aus Differenzieren von Gleichung 4 des Vorhersagemodells **20** nach der Einlassströmung (Q_{IN}) ergibt. Wie gewürdigt werden sollte, kann die optimale Einlassströmung mathematisch auf folgende Weise ausgedrückt werden, wo in dem zugeordneten Vorhersagemodell verschiedene Algorithmen (ob auf der Grundlage der Sammlung von anderen Blutkomponenten als Blutplättchen, verschiedener Sammelvorrichtungen oder alternativer Ableitungen der verschiedenen Parameter mit derselben Sammelprozedur und -vorrichtung) verwendet werden.

$$Q_L = \left(\frac{C_1}{2C_2}\right) e^{-9{,}91(1-1/R)H} - C_3 \qquad (23)$$

$$C_3 = \frac{1}{2(t_P/K_7 - 1/K_9)}, \quad \begin{matrix} Q_0 \geq 45 \text{ für zwei Nadeln (\"DN\")} \\ \geq 20 \text{ für eine Nadel (\"SN\")} \end{matrix} \qquad (24)$$

$$= 0, \quad \begin{matrix} Q_0 < 45 \text{ für DN} \\ < 20 \text{ für SN} \end{matrix} \qquad (25)$$

$$\begin{matrix} K_7 = 500 \text{ (DN)} & K_9 = 45 \text{ (DN)} \\ = 215 \text{ (SN)} & = 20 \text{ (SN)} \end{matrix} \qquad (26)$$

C_1 = 0,803 (SN, DN ohne Untersetzung)
= 0,840 (DN mit Untersetzung) (27)

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$C_2 = 4{,}08 \cdot 10^{-5}$(DN)
$= 8{,}54 \cdot 10^{-5}$ (SN) (28)

[0076] Anhand des Vorstehenden ist die optimale Einlassströmung (Q_L) hinsichtlich der Sammelvorrichtung tatsächlich "optimal".

[0077] Wieder anhand von Fig. 7 wird das Optimierungsmodell **172** anfangs hinsichtlich einer produktbasierten Optimierung beschrieben, bei der bei der Eingabestation **184** der Soll Ausstoß (Y) festgelegt wird. Im Allgemeinen wird die Einlassströmung (Q_{IN}), die einer festgelegten AC-Infusionsrate (I_{SPEC}) (üblicherweise die maximale AC-Infusionsrate und ebenfalls bei der Eingabestation **184** festgelegt) zugeordnet ist, aus bestimmten anderen festgelegten Parametern iterativ abgeleitet. Insbesondere dann, wenn die maximale AC-Infusionsrate (I_{MAX}) und das maximale AC-Verhältnis (R_{MAX}) festgelegt werden, ist die Einlassströmung (Q_{IN}) in dieser Einlassströmungsberechnung anhand der physiologischen Betrachtungen des Spenders **14** optimal. Dies erfolgt hauptsächlich durch die Lösung der Gleichungen 4, 8, 14 und 16 und/oder deren Hilfsgleichungen durch das oben diskutierte Vorhersagemodell **20**. Zur Lösung dieser Gleichungen bleiben bestimmte Parameter in der iterativen Ableitung der Einlassströmung (Q_{IN}) feststehend, was die festgelegte AC-Infusionsrate (I_{SPEC}) erzielt, wobei diese Parameter ebenfalls bei der Eingabestation **184** festgelegt werden. Diese enthalten das totale Blutvolumen (V_B), das unter Verwendung von Gleichung 10 berechnet werden kann, da die Größe, das Gewicht und das Geschlecht des Spenders in die zentrale Eingabestation **148** eingegeben werden, und das AC-Verhältnis (R), das unter Verwendung von Gleichung 9 berechnet werden kann, da der Hämatokrit-Wert (H) des Spenders bestimmt worden ist oder auf einen Maximalwert festgelegt werden kann. Darüber hinaus bleibt die Gesamtprozedurdauer (t_P) in jeder iterativen Ableitung der Einlassströmung (Q_{IN}), die der festgelegten AC-Infusionsrate (I_{SPEC}) zugeordnet ist, feststehend. Da die Gesamtprozedurdauer (t_P) im Fall einer produktbasierten Optimierung nicht bekannt ist und somit nicht bei der Eingabestation **184** festgelegt werden kann, wird aber anfangs eine Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$) angenommen (wobei diese Annahme z. B. in das Optimierungsmodell **172** konfiguriert wird und in diesem Abschnitt des Optimierungsmodells **172** üblicherweise die mittlere Gesamtprozedurdauer (t_P) als die Anfangs-Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$) konfiguriert wird, da in dem Vorhersagemodell **20** wie oben angemerkt ein Bereich von Gesamtprozedurdauern vorgesehen ist). Die Bezeichnung "Ist " wird in diesem Fall für die Gesamtprozedurdauer verwendet, da das Optimierungsmodell **172** für eine Einstellung der Gesamtprozedurdauer nach jeder iterativen Bestimmung der Einlassströmung (Q_{IN}) dient, die die festgelegte AC-Infusionsrate (I_{SPEC}) bereitstellt, um, wie im Folgenden genauer erläutert wird, bei einer produktbasierten Optimierung bei Bedarf den Soll-Ausstoß (Y) zu erreichen.

[0078] Die Lösung der Gleichungen 4, 8, 14 und 16 erfordert außerdem, dass für bestimmte verbleibende Parameter anfangs bestimmte Werte angenommen werden. In diesem Fall wird bei der Lösung der Ausstoßgleichung (Gleichung 4) (und einschließlich deren Hilfsgleichungen wie oben angemerkt) eine iterative Prozedur verwendet, wobei in der nächsten iterativen Berechnung bzw. in den nächsten iterativen Berechnungen bei der Verarbeitungsstation **188** aktualisierte Werte verwendet werden. Obgleich die Ableitung dieser Einlassströmung (Q_{IN}), die die festgelegte (üblicherweise maximale) AC-Infusionsrate (I_{SPEC}) erzeugt, über die Gleichungen 4, 8, 14 und 16 auf eine Vielzahl von Arten ausgeführt werden kann, besteht eine Möglichkeit darin, einen Ist-Wert für den Plasmasammelfaktor (P) anzunehmen, anschließend unter Verwendung der festgelegten AC-Infusionsrate (I_{SPEC}) die Ist-Einlassströmung ($Q_{IN\text{-}C}$) zu berechnen, daraufhin den Ist-Ausstoß (Y_C) zu berechnen, daraufhin unter Verwendung des Ist-Ausstoßes (Y_C) den Ist-Plasmasammelfaktor (P_C) zu berechnen und diese Prozedur mit den aktualisierten Parametern zu wiederholen, alles innerhalb der Bearbeitungsstation **188**, bis bei der Ist-Einlassströmung ($Q_{IN\text{-}C}$) in Bezug auf die festgelegte AC-Infusionsrate (I_{SPEC}) eine annehmbare Konvergenz vorhanden ist.

[0079] Außer der Berechnung der Ist-Einlassströmung ($Q_{IN\text{-}C}$), die der festgelegten AC-Infusionsrate (I_{SPEC}) zugeordnet ist, wird bei der Verarbeitungsstation **192** die oben diskutierte optimale Einlassströmung (Q_L) berechnet. Folglich kann bei dem ersten Komparator **176** ein Vergleich zwischen der Ist-Einlassströmung ($Q_{IN\text{-}C}$), die in der oben beschriebenen Weise abgeleitet wurde, und der optimalen Einlassströmung (Q_L) vorgenommen werden. Wenn die Ist-Einlassströmung ($Q_{IN\text{-}C}$) bei dem ersten Komparator **176** kleiner als die optimale Einlassströmung (Q_L) ist, sind die festgelegten Werte für die verschiedenen Parameter, die der Einlassströmung (Q_{IN}) zugeordnet sind, "optimal", d. h. das AC-Verhältnis (R) und die AC-Infusionsrate (I), die bei der Eingabestation **184** festgelegt worden sind. Anschließend wird der Ist-Ausstoß (Y_C) (der bei der Verarbeitungsstation **188** bei der Ableitung der Ist-Einlassströmung ($Q_{IN\text{-}C}$) berechnet wurde, die der festgelegten AC-Infusionsrate (I_{SPEC}) zugeordnet ist) bei dem zweiten Komparator **180** mit dem Einlassausstoß (Y) verglichen. Falls es zwischen diesen Ausstoßwerten eine akzeptable Konvergenz gegeben hat, ist die Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$) ebenfalls "optimal". Dagegen wird dann, wenn es zwischen diesen Ausstoßwerten keine akzeptable Konvergenz gegeben hat, die Ist-Gesamtprozedurdauer ($t_{P\text{-}C}$) bei der Einstellstation **196** eingestellt und die vorstehende iterative

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Ableitung der Ist-Einlassströmung (Q_{IN-C}), die der festgelegten AC-Infusionsrate (I_{SPEC}) zugeordnet ist, wiederholt (d. h. unter Verwendung der anfangs festgelegten AC-Infusionsrate (I_{SPEC}) und der neu eingestellten Ist-Gesamtprozedurdauer (t_{P-C}) iterativ in der oben beschriebenen Weise eine neue Ist-Einlassströmung (Q_{IN-C}) abgeleitet), bis diese Konvergenz erreicht ist.

[0080] Falls wieder anhand des ersten Komparators **176** die Ist-Einlassströmung (Q_{IN-C}), die der festgelegten AC-Infusionsrate (I_{SPEC}) zugeordnet ist, die bei der Verarbeitungsstation **188** abgeleitet wird, größer als die optimale Einlassströmung (Q_L) ist, wird bei der Verarbeitungsstation **188** allgemein in der oben beschriebenen Weise (d. h., die anfangs festgelegte AC-Infusionsrate (I_{SPEC}) wird in dieser Ableitung ignoriert und iterativ eine Ist-AC-Infusionsrate (I_C) abgeleitet, die mit der Einlassströmung (Q_L) übereinstimmt) iterativ eine Ist-AC-Infusionsrate (I_C) abgeleitet, die dieser besonderen Einlassströmung (Q_L) zugeordnet ist. In diesem Fall ist die Ist-Einlassströmung (Q_{IN-C}) immer gleich der optimalen Einlassströmung (Q_L) bei dem ersten Komparator **176**, wobei dieses Optimierungsmodell **172** anschließend für den Ausstoßvergleich gemäß der oben beschriebenen Prozedur zu dem zweiten Komparator **180** übergeht.

[0081] Das Optimierungsmodell **172** kann ebenfalls für eine zeitbasierte Optimierung verwendet werden. In diesem Fall wird bei der Eingabestation **184** die Gesamtprozedurdauer (t_P) als eine festgelegte Gesamtprozedurdauer (t_{P-SPEC}) festgelegt und somit nicht als eine produktbasierte Optimierung angenommen. Daraufhin geht das Optimierungsmodell **172** mit Ausnahme bei dem zweiten Komparator **180** in der gleichen Weise wie oben hinsichtlich der produktbasierten Optimierung diskutiert vor. Da kein Ausstoß eingegeben wurde, wird bei dem zweiten Komparator **180** kein Ausstoßvergleich vorgenommen. Stattdessen wird bei dem zweiten Komparator **180** ein Gesamtprozedurdauervergleich vorgenommen. Da die Ist-Gesamtprozedurdauer (t_{P-C}) in dieser zeitbasierten Optimierung gleich der festgelegten Gesamtprozedurdauer (t_{P-SPEC}) eingestellt wurde, bevor das Modell **172** zu der Verarbeitungsstation **188** überging, steigt das Modell **172** für eine zeitbasierte Optimierung jedes Mal bei dem zweiten Komparator aus.

[0082] Außer auf die oben beschriebene produktbasierte und zeitbasierte Optimierung können die Prinzipien der vorliegenden Erfindung auf andere Anwendungen erweitert werden, die sich auf die Verbesserung der Blutkomponentensystemorganisation beziehen. Zum Beispiel kann eine Optimierung in Übereinstimmung mit Prinzipien der vorliegenden Erfindung so erweitert werden, dass sie Spenderorganisationsfragen umfasst. In einem solchen Fall wäre eine weitere "Optimierung", die dem Blutkomponenten-Sammelprozess zugeordnet ist, das Sammeln von Blutkomponenten, wie es durch den vorhandenen Bestand vorgeschrieben wird (d. h. die Verwendung einer Optimierung, wie sie durch den vorhandenen Bestand vorgeschrieben wird (d. h. die Verwendung einer Optimierung als Bestandssteuerung)). Das heißt, Informationen, die sich auf den Bestand der verschiedenen Typen von Blutkomponenten in der Blutbank/in dem Blutzentrum und/oder auf den Bedarf an einer oder an mehreren Blutkomponententypen beziehen, könnten so unterhalten werden, dass spezifische Sammelprozeduren ausgewählt werden können, um an eine niedrige Versorgung mit einem gegebenen Blutkomponententyp und/oder an einen hohen Bedarf an einem solchen Blutkomponententyp anzupassen. Genauer können dann, wenn die Versorgung mit roten Blutkörperchen niedrig und/oder der Bedarf an roten Blutkörperchen hoch ist oder angenommen wird, dass er dies in naher Zukunft sein wird, an die Bedienpersonen Aufforderungen ausgegeben werden, dass während einer gegebenen Zeitdauer nach Möglichkeit von Spendern rote Blutkörperchen zur Sammlung ausgewählt werden sollen. Verwandt damit sind die Optimierungsprinzipien der vorliegenden Erfindung auf die Unterhaltung von Daten über Blutkomponentensammlungen von einem gegebenen Spender anwendbar, so dass eine Bestimmung vorgenommen werden kann, welcher Typ oder welche Typen von Blutkomponenten von einem bestimmten Spender in der Sammelprozedur den maximalen Ausstoß lieferten. Das heißt, von früheren Blutkomponentenspenden können Informationen gesammelt und unterhalten werden, so dass für einen bestimmten Spender eine Bestimmung vorgenommen werden kann, bei welchem Typ oder bei welchen Typen von Blutkomponenten der Spender die Neigung hat, maximale Ausstöße dafür zu erzeugen.

[0083] Abgesehen von der vorstehenden Beschreibung der vorliegenden Erfindung in Bezug auf einen Online-Blutkomponenten-Sammelprozess schätzt der Fachmann auf dem Gebiet, dass die Quelle von Blut der Blutkomponenten-Sammelvorrichtung gegenüber deren Empfang direkt von dem Spender von einem (nicht gezeigten) geeigneten Blutbehälter geliefert werden kann, der mit der Blutkomponenten-Sammelvorrichtung **18** verbunden ist,. Darüber hinaus kann das Blut natürlich von alternativen Quellen wie etwa von Tieren geliefert werden. Wie in Fig. 3 veranschaulicht ist, kann die beschriebene Blutplättchen-Ernteprozedur darüber hinaus unter Verwendung einer Einnadelkonfiguration ausgeführt werden. Außerdem ist die vorliegende Erfindung auf die Sammlung anderer Typen von Blutkomponenten wie etwa roten Blutkörperchen, weißen Blutkörperchen und/oder Plasma anwendbar und ist weiter auf die gleichzeitige Sammlung mehr als eines Blutkomponententyps anwendbar. Im Fall der Sammlung roter Blutkörperchen und der Optimierung gemäß den Prin-

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zipien der vorliegenden Erfindung sollte die Blutgruppe des Spenders bekannt sein und in verschiedenen Algorithmen verwendet werden. Darüber hinaus ist die vorliegende Erfindung nicht darauf beschränkt, dass die Quelle Vollblut ist. Das heißt, die Prinzipien der vorliegenden Erfindung können auf die Entfernung einer Komponente aus irgendeiner Flüssigkeit anwendbar sein.

[0084] Die vorstehende Beschreibung der vorliegenden Erfindung ist für Veranschaulichungs- und Beschreibungszwecke dargestellt worden. Darüber hinaus soll die Beschreibung die Erfindung nicht auf die hier offenbarte Form beschränken. Dementsprechend liegen Änderungen und Abwandlungen, die den obigen Lehren und der Sachkenntnis und dem Wissenstand des relevanten Gebiets entsprechen, im Umfang der vorliegenden Erfindung. Ferner sollen die hier beschriebenen Ausführungsformen die besten bekannten Ausführungsarten der Verwirklichung der Erfindung erläutern und ermöglichen, dass ein anderer Fachmann auf dem Gebiet die Erfindung und diese weiteren Ausführungsformen auch mit verschiedenen, durch die besonderen Anwendungen oder Verwendungen der vorliegenden Erfindung erforderlichen, Abwandlungen nutzen kann. Die beigefügten Ansprüche sollen so verstanden werden, dass sie alternative Ausführungsformen in dem durch den Stand der Technik möglichen Umfang enthalten.

Patentansprüche

1. Verfahren zum Programmieren eines Blutkomponenten-Sammelsystems (**2**), das anschließend eine Blutkomponente von einem Spender unter Verwendung einer Blutkomponenten-Sammelprozedur sammelt, wobei die Sammelprozedur mehrere Steuerparameter umfasst, **dadurch gekennzeichnet**, dass das Verfahren die folgenden Schritte umfasst:
Bereitstellen biologischer Daten, die sich auf den Spender beziehen; Zuordnen einer Größe zu jedem Steuerparameter wenigstens anhand des Bereitstellungsschrittes;
Optimieren der Größe wenigstens eines der Steuerparameter in Bezug sowohl auf Spenderbeschränkungen als auch auf Systembeschränkungen, wobei der Optimierungsschritt zulässt, eine erste und/oder eine zweite Bedingung zu erfüllen, wobei die erste Bedingung das Sammeln einer vorgegebenen Menge der Blutkomponenten innerhalb einer minimalen Zeitdauer ist und die zweite Bedingung das Sammeln einer maximalen Menge der Blutkomponenten innerhalb einer vorgegebenen Zeitdauer ist;
Eingeben der Größen der Steuerparameter in die Blutkomponenten-Sammelvorrichtung nach dem Optimierungsschritt.

2. Verfahren nach Anspruch 1, das ferner den folgenden Schritt umfasst:
Auswählen eines vorgegebenen Blutkomponententyps anhand eines Bestandes des vorgegebenen Blutkomponententyps und/oder einer Anforderung für den vorgegebenen Blutkomponententyp.

3. Verfahren nach Anspruch 1 oder 2, das ferner den folgenden Schritt umfasst:
Auswählen eines Blutkomponententyps, der von dem Spender gesammelt wird, anhand von Daten, die über den Spender für mehrere Sammelprozeduren, die früher an dem Spender ausgeführt wurden, gehalten werden.

4. Verfahren nach Anspruch 3, bei dem:
die Daten eine Angabe darüber bereitstellen, dass der Spender die Neigung hat, für einen Blutkomponententyp aus dem Auswahlschritt einen höheren Ausstoß als für andere Blutkomponententypen zu erzeugen.

5. Verfahren nach einem der vorhergehenden Ansprüche, das ferner den folgenden Schritt umfasst:
Erhalten von Daten bezüglich der Sammelprozedur für die Verwendung in nachfolgenden Sammelprozeduren, die unter Verwendung des Spenders ausgeführt werden.

6. Blutkomponenten-Sammelsystem (**2**), das umfasst:
eine Zentrifugen-Blutkomponenten-Sammelvorrichtung (**18**), um eine Sammelprozedur auszuführen, die mehrere Steuerparameter umfasst;
Mittel, um biologische Daten bezüglich eines Spenders zu empfangen;
Mittel (**144**), um jedem der Steuerparameter wenigstens anhand der Bereitstellungsmittel eine Größe zuzuordnen;
Mittel (**144**), um die Größe wenigstens eines der Steuerparameter in Bezug sowohl auf Spenderbeschränkungen als auch auf Systembeschränkungen zu optimieren, wobei die Optimierungsmittel ermöglichen, eine erste und/oder eine zweite Bedingung zu erfüllen, wobei die erste Bedingung das Sammeln einer vorgegebenen Menge der Blutkomponenten innerhalb einer minimalen Zeitdauer ist und die zweite Bedingung das Sammeln einer maximalen Menge der Blutkomponenten innerhalb einer vorgegebenen Zeitdauer ist;

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Mittel (**148**), um die optimierten Größen der Parameter in die Blutkomponenten-Sammelvorrichtung einzugeben; und
Mittel, um die Sammelprozedur an der Blutkomponenten-Sammelvorrichtung unter Verwendung der Parameter auszuführen, um die Blutkomponenten von dem Spender zu sammeln, um die erste und/oder die zweite Bedingung zu erfüllen.

7. System nach Anspruch 6, das ferner umfasst:
Mittel (**148**), um einen vorgegebenen Blutkomponententyp anhand eines Bestandes des vorgegebenen Blutkomponententyps und/oder einer Anforderung für den vorgegebenen Blutkomponententyp auszuwählen.

8. System nach Anspruch 6 oder 7, das ferner umfasst:
Mittel (**148**), um einen von dem Spender zu sammelnden Blutkomponententyp anhand von Daten auszuwählen, die über den Spender für mehrere Sammelprozeduren, die früher unter Verwendung des Spenders ausgeführt wurden, zu halten.

9. System nach Anspruch 8, bei dem:
die Daten eine Angabe darüber bereitstellen, dass der Spender die Neigung hat, für einen Blutkomponententyp von dem Auswahlschritt einen höheren Ausstoß als für andere Blutkomponententypen zu erzeugen.

10. System nach einem der Ansprüche 6 bis 9, das ferner umfasst:
Mittel, um Daten über die Sammelprozedur für die Verwendung in späteren Sammelprozeduren, die unter Verwendung des Spenders ausgeführt werden, zu halten.

Es folgen 8 Blatt Zeichnungen

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Anhängende Zeichnungen

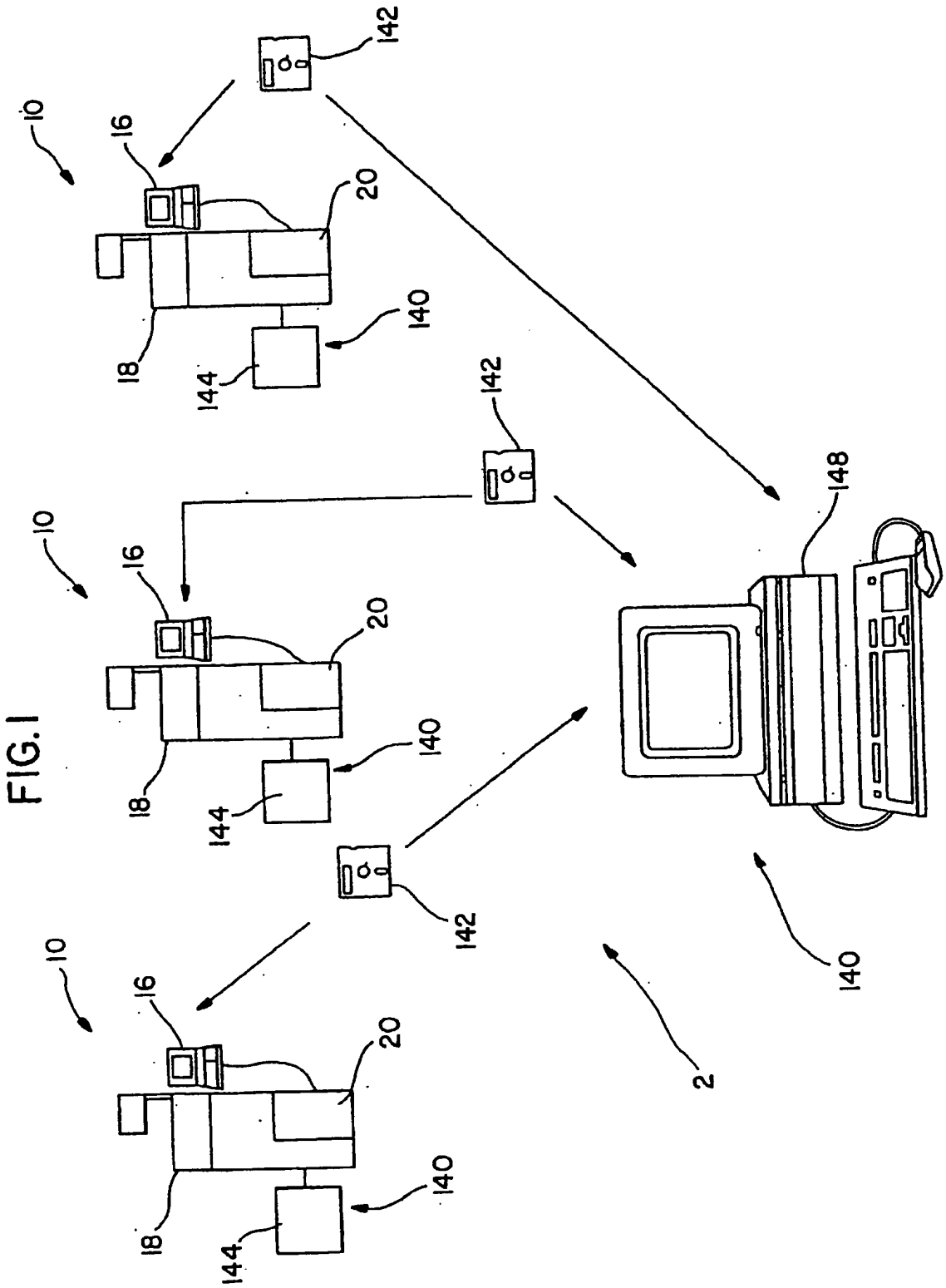

FIG. 1

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FIG.2

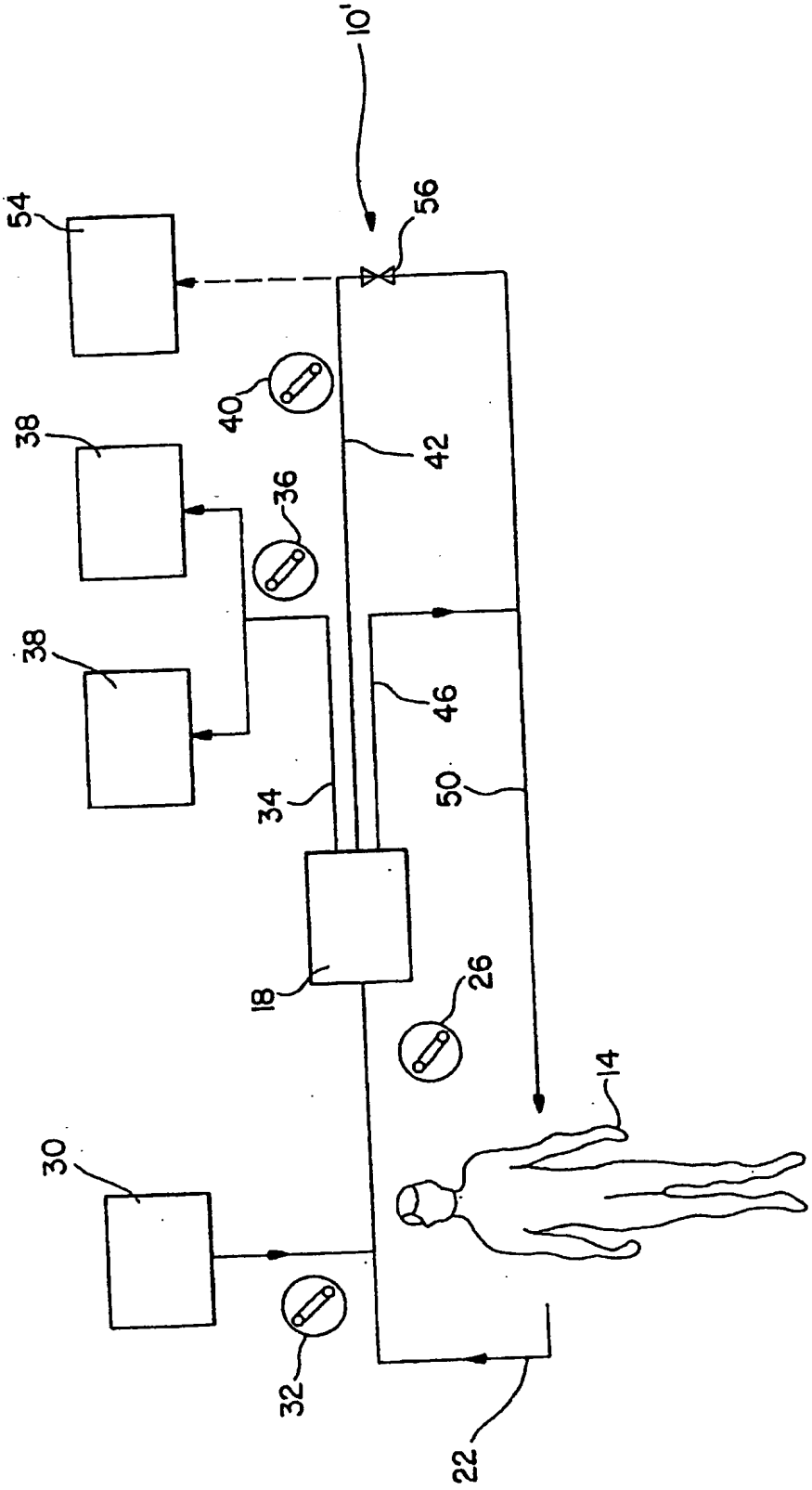

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FIG.3

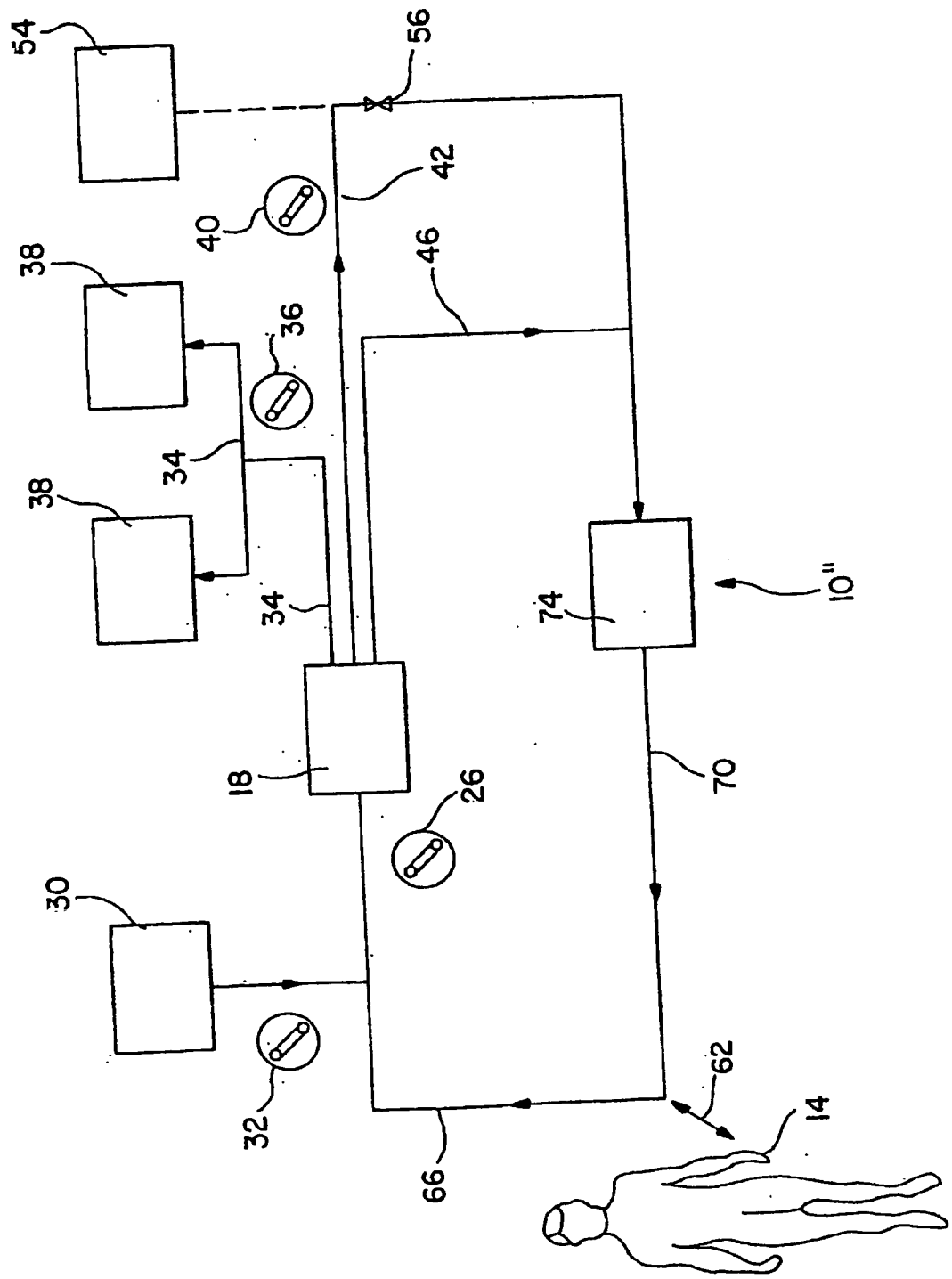

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FIG. 4A

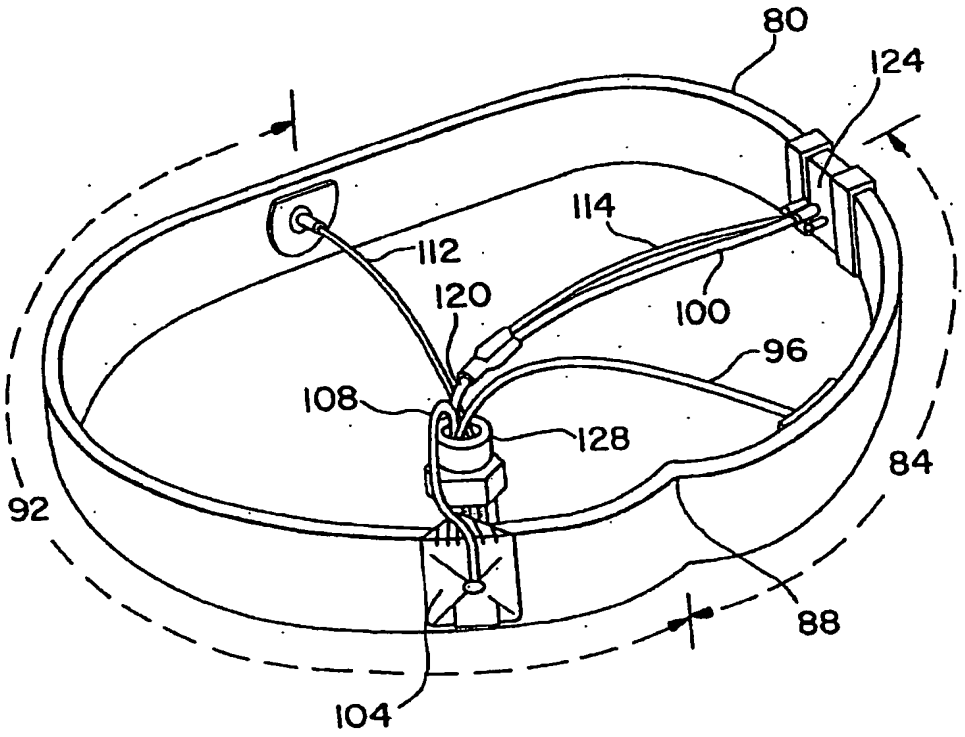

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Fig. 5

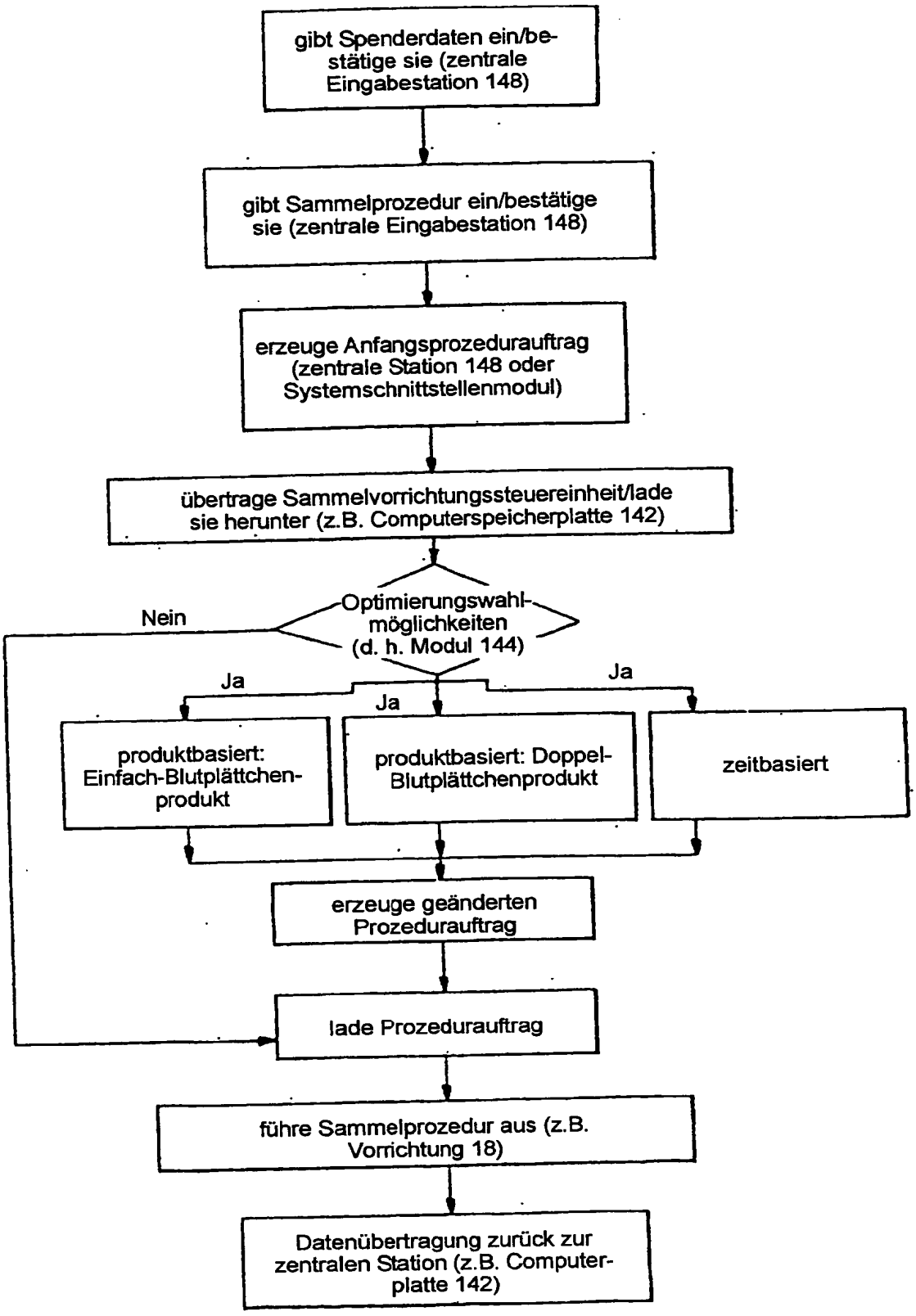

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Fig. 6

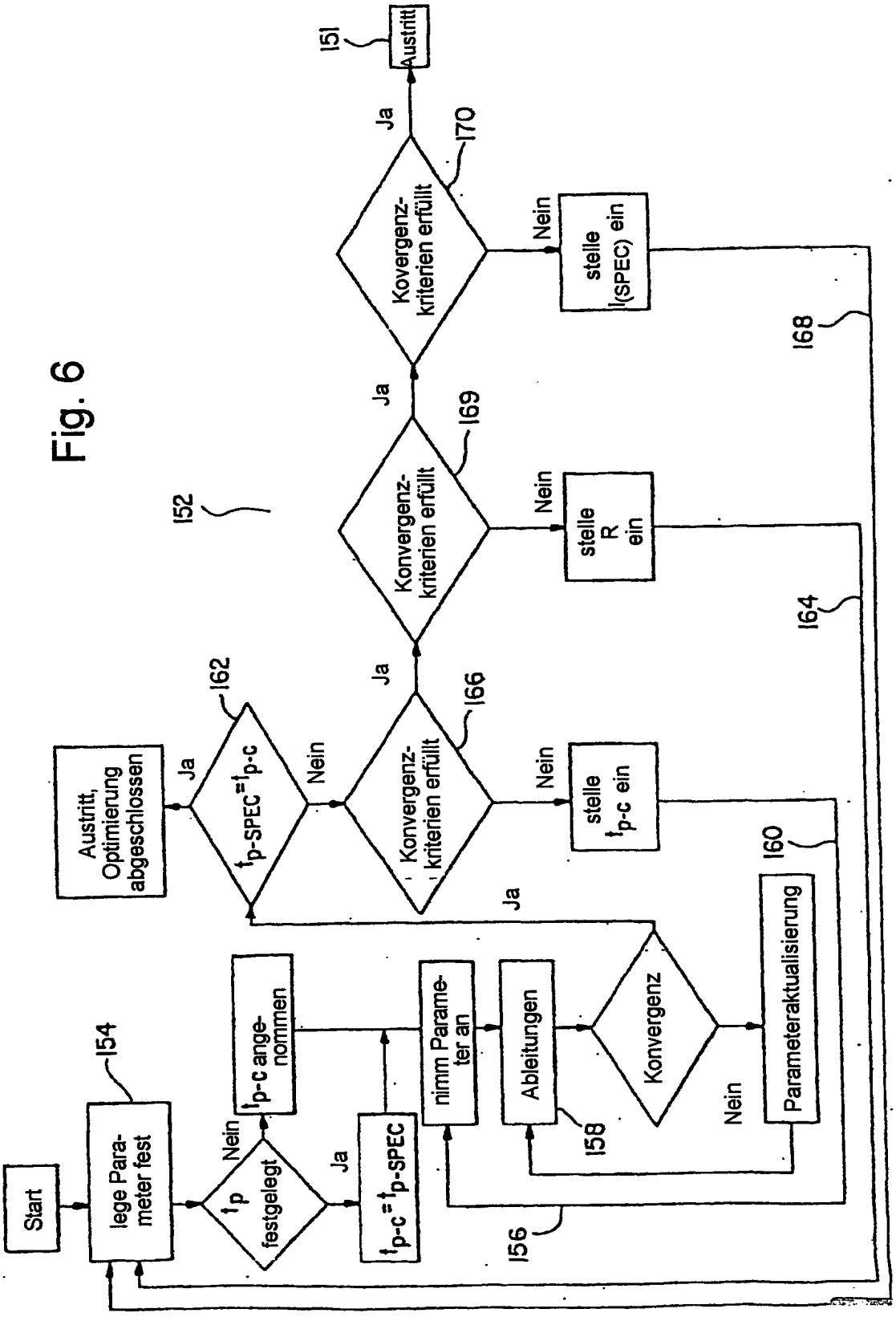

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Fig. 7

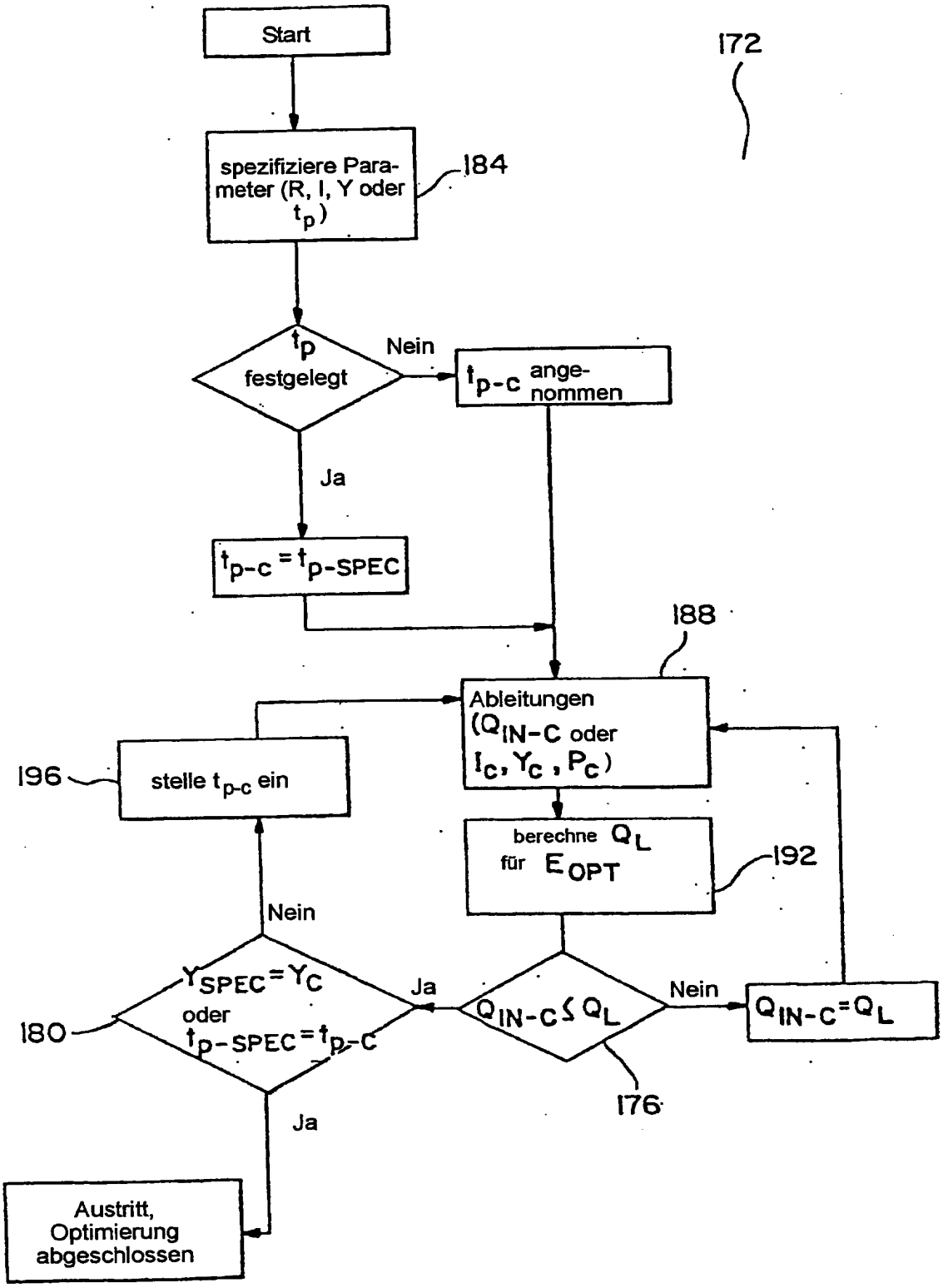

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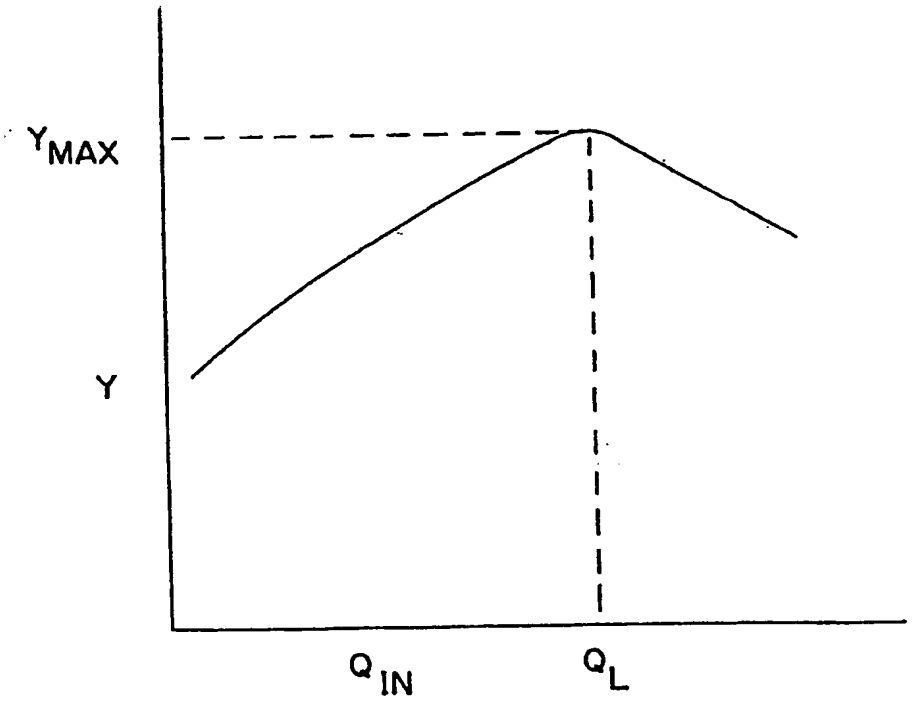
FIG. 8



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Espacenet

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AUTOMATED COLLECTION SYSTEMS AND METHODS FOR OBTAINING RED BLOOD CELLS, PLATELETS, AND PLASMA FROM WHOLE BLOOD

Inventor(s):

Applicant(s):

Classification:
- **international:** ***A61M1/02; A61M1/36; G01N33/48;*** *A61M1/30;* (IPC1-7): A61M1/02; G01N33/48
- **cooperative:** **A61M1/0222 (EP, US)**; **A61M1/0231 (EP, US)**; **A61M1/30 (EP)**; **A61M1/302 (EP, US)**; **A61M1/303 (EP, US)**; **A61M1/308 (EP, US)**; **A61M1/3603 (EP, US)**; **A61M1/3633 (EP)**; **A61M1/3693 (EP, US)**; **A61M1/3696 (EP, US)**; A61M2202/0427 (EP); A61M2202/0429 (EP); A61M2205/3393 (EP); A61M2205/60 (EP); A61M2230/207 (EP) more

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Also published as: AU1198401 (A) BR0014802 (A) CA2386040 (A1) CN100478038 (C) CN1407907 (A) more

Abstract not available for JP2003516175 (A)
Abstract of corresponding document: WO0128621 (A1)

Blood processing systems and methods separate blood drawn from a donor into red blood cells and platelets. The systems and methods operate in a first mode to collect platelets while returning red blood cells to the donor. The systems and methods operate in a second mode to concurrently collect both platelets and red blood cells without returning platelets or red blood cells to the donor.

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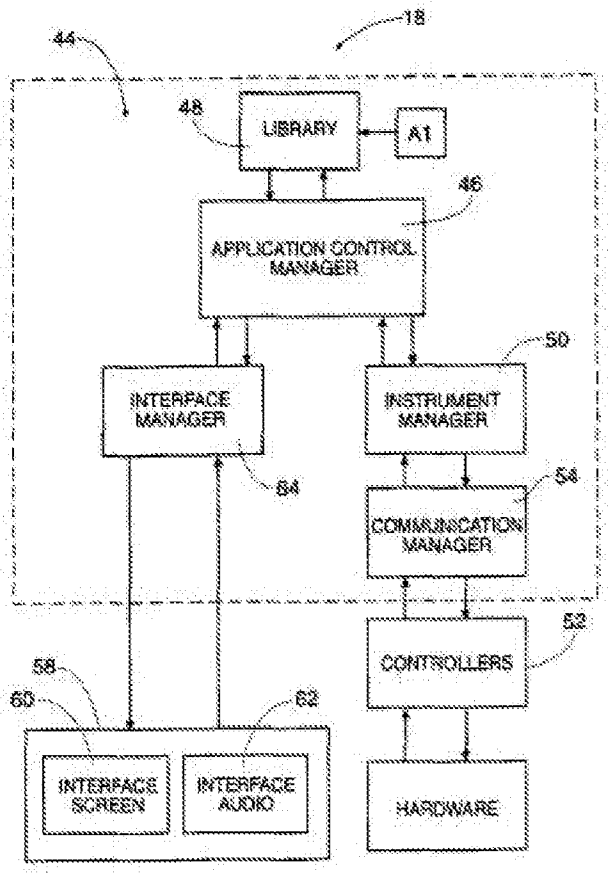

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Petitioner Terumo Exhibit 1014-0208

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	５４０		５４０	
	５７５		５７５	
// Ｇ０１Ｎ　33/48		Ｇ０１Ｎ　33/48	Ｃ	

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(81)指定国　ＥＰ(ＡＴ，ＢＥ，ＣＨ，ＣＹ，ＤＥ，ＤＫ，ＥＳ，ＦＩ，ＦＲ，ＧＢ，ＧＲ，ＩＥ，ＩＴ，ＬＵ，ＭＣ，ＮＬ，ＰＴ，ＳＥ)，ＡＵ，ＢＲ，ＣＡ，ＣＮ，ＩＮ，ＪＰ

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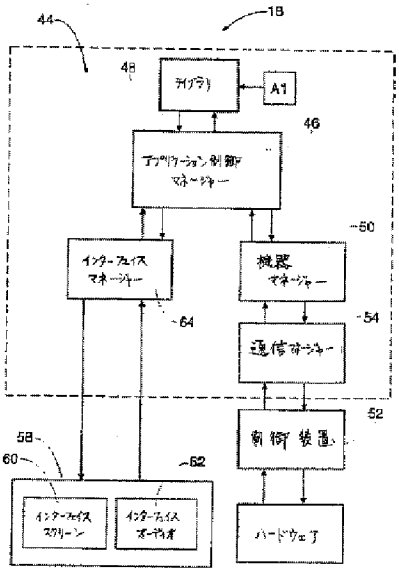
最終頁に続く

(54)【発明の名称】　全血から赤血球、血小板および血漿を得るための自動収集システムおよび方法

(57)【要約】
血液処理システムおよび方法は、ドナーから引き出した血液を赤血球と血小板に分離する。これらのシステムおよび方法は、第一モードでは、赤血球をドナーに戻しつつ、血小板を収集するように作動する。これらのシステムおよび方法は、第二モードでは、血小板または赤血球をドナーに戻すことなく、血小板および赤血球の両方を同時に収集するように作動する。１つの実施形態において、本発明は、血液処理システムであって、該システムは、分離チャンバおよび制御装置を含み、該分離チャンバは、ドナーから引き出した血液を赤血球と血小板に分離するように作動し、そして該制御装置は、第一モードにおいて、赤血球を該ドナーに戻しつつ、血小板を収集するように作動し、そして第二モードにおいて、血小板も赤血球も該ドナーに戻すことなく、血小板および赤血球を収集するように作動する、システムである。



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【特許請求の範囲】

【請求項１】　血液処理システムであって、該システムは、分離チャンバおよび制御装置を含み、

該分離チャンバは、ドナーから引き出した血液を赤血球と血小板に分離するように作動し、そして

該制御装置は、第一モードにおいて、赤血球を該ドナーに戻しつつ、血小板を収集するように作動し、そして第二モードにおいて、血小板も赤血球も該ドナーに戻すことなく、血小板および赤血球を収集するように作動する、
システム。

【請求項２】　請求項１に記載の血液処理システムであって、

ここで、前記分離チャンバが、前記血液から、血小板を実質的に含まない血漿を分離するように作動し、そして

ここで、前記第一モードにおいて、血小板を実質的に含まない該血漿の少なくとも一部が、前記ドナーに戻され、そして前記第二モードにおいて、血小板を実質的に含まない該血漿の全部が、収集されそして該ドナーに戻されない、
システム。

【請求項３】　血液を引き出してそして該血液を前記ドナーに戻すための単一の針をさらに備える、請求項１に記載の血液処理システム。

【請求項４】　血小板から白血球を除去するための要素をさらに備える、請求項１に記載の血液処理システム。

【請求項５】　赤血球から白血球を除去するための要素をさらに備える、請求項１に記載の血液処理システム。

【請求項６】　赤血球と混合するための血液添加剤溶液の供給源をさらに備える、請求項１に記載の血液処理システム。

【請求項７】　前記第一モードおよび第二モードについて血小板の所望の収量を設定するためのインプットをさらに備える、請求項１に記載の血液処理システム。

【請求項８】　前記第二モードについて赤血球の所望の収量を設定するためのインプットをさらに備える、請求項１に記載の血液処理システム。

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【請求項９】　前記制御装置が、前記第二モード中に収集した前記赤血球の一部を前記ドナーに戻して赤血球の所望の収量を達成する、第三モードで作動可能である、請求項１に記載の血液処理システム。

【請求項１０】　血液処理方法であって、該方法は、以下の工程：

ドナーから引き出した血液を赤血球と血小板に分離する工程；および

第一モードにおいて、赤血球を該ドナーに戻しつつ、血小板を収集するように作動する工程；および

第二モードにおいて、血小板濃縮物も赤血球も該ドナーに戻すことなく、血小板および赤血球の両方を同時に収集するように作動する工程、

を包含する、方法。

【請求項１１】　請求項１０に記載の血液処理方法であって、該方法は、前記血液から、血小板を実質的に含まない血漿を分離する工程をさらに包含し、

ここで、前記第一モードにおいて、血小板を実質的に含まない該血漿の少なくとも一部が、前記ドナーに戻され、そして前記第二モードにおいて、血小板を実質的に含まない該血漿の全部が、収集されそして該ドナーに戻される、

血液処理方法。

【請求項１２】　前記第一モードおよび第二モード中に収集した前記血小板を、収集した血小板を実質的に含まない前記血漿の少なくとも一部で再懸濁する工程をさらに包含する、請求項１１に記載の血液処理方法。

【請求項１３】　単一の針を使用して血液を引き出してそして該血液を前記ドナーに戻す工程をさらに包含する、請求項１０に記載の血液処理方法。

【請求項１４】　前記第一モードおよび第二モード中に収集した血小板から白血球を除去する工程をさらに包含する、請求項１０に記載の血液処理方法。

【請求項１５】　前記第二モード中に収集した赤血球から白血球を除去する工程をさらに包含する、請求項１０に記載の血液処理方法。

【請求項１６】　前記第二モード中に収集した赤血球と、血液添加剤溶液とを混合する工程をさらに包含する、請求項１０に記載の血液処理方法。

【請求項１７】　前記第一モードおよび第二モードについて血小板の所望の収量を設定する工程をさらに包含する、請求項１０に記載の血液処理方法。

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【請求項１８】　前記第二モードについて赤血球の所望の収量を設定する工程をさらに包含する、請求項１０に記載の血液処理方法。

【請求項１９】　前記第二モード中に収集した前記赤血球の一部を前記ドナーに戻して赤血球の所望の収量を達成する、第三モードで作動する工程をさらに包含する、請求項１０に記載の血液処理方法。

【請求項２０】　血液処理アセンブリであって、該アセンブリは、以下：

血液源に装着されている、主要経路；

該主要経路に連結された第一分枝経路であって、血液添加剤溶液を保持する収集容器を備える、第一分枝経路；

該第一分枝経路の下流で該主要経路に連結された第二分枝経路であって、第二の収集容器を備える、第二分枝経路；および

該第二の分枝経路中にある、白血球除去フィルター、

を備える、アセンブリ。

【請求項２１】　通気経路をさらに含み、該通気経路が、前記第二の収集容器および前記主要経路に連結されて、前記白血球除去フィルターをバイパスする経路において該第二の収集容器から空気を逃すためにある、請求項２０に記載の血液処理アセンブリ。

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【発明の詳細な説明】

【０００１】

（発明の分野）

本発明は、遠心血液処理システムおよび装置に関する。

【０００２】

（発明の背景）

特定の治療法では、大量の血液成分を輸血する。例えば、化学療法を受けている患者には、日常的に、多数の血小板を輸血する必要がある人もいる。手動血液バッグシステムは、単に、個々のドナーからこれらの多数の血小板を収集する効率的な方法ではない。

【０００３】

今日では、この要求を満たすために、多数の血小板を収集するのに、オンライン血液分離システムが使用されている。オンラインシステムは、ドナーと共に、連続プロセスで、全血から血小板濃縮物を分離するのに必要な分離工程を実行する。オンラインシステムは、ドナーからの全血の流れを確立し、この流れから所望の血小板を分離し、そして残留している赤血球および血漿をドナーに戻し、全ては、連続的な流れループで行われる。

【０００４】

オンラインシステムを使用すると、大量の全血（例えば、２．０リットル）が処理できる。その大きな処理容量に起因して、高い収量の濃縮血小板（例えば、流体２００ｍｌに懸濁した４×１０^{11}個の血小板）が収集できる。それにもかかわらず、依然として、高い容量のオンライン血液収集環境（血小板および赤血球のような、必要性が大きい細胞血液成分の高い収量が実現できる）での使用に適する様式で、血液成分から赤血球のような細胞リッチな濃縮物を収集するシステムおよび方法をさらに改良する必要がある。

【０００５】

（発明の要旨）

本発明は、ドナーから引き出した血液を赤血球と血小板に分離する血液処理システムおよび方法を提供する。該システムおよび方法は、第一および第二モード

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で作動する。

【０００６】

第一作動モードでは、該システムおよび方法は、全血を処理して、そして血小板を収集する。第一モードでは、赤血球は、同時には収集されずに、該ドナーに戻される。

【０００７】

第二作動モードでは、該システムおよび方法は、全血を処理し、そして対応するさらなる容量の血小板と共に赤血球を同時に収集する。第二モード中にて、血液成分は、該ドナーに戻されない。

【０００８】

１実施態様では、該システムおよび方法はまた、第三モードで作動する。第三作動モードでは、該システムおよび方法は、最終血液容量トリミング（ｔｒｉｍｍｉｎｇ）機能を実行する。該容量トリミング機能中にて、収集した赤血球容量の一部は、該ドナーに戻すことができる。該容量トリミング機能は、実際に収集した成分容量が目標収集容量を超えないことを保証する。

【０００９】

本発明は、その精神または本質的な特徴から逸脱することなく、いくつかの形態で具体化され得る。本発明の範囲は、後述の詳細な説明ではなく、添付の請求の範囲で規定される。これらの請求の範囲と等価の意味および範囲内に入る全ての実施態様は、従って、請求の範囲に包含されると解釈される。本発明は、以下の詳細な説明で述べたかまたは図面で示した部分の構成および配置の詳細には限定されない。本発明は、他の実施態様および種々の他の様式で、実施できる。これらの専門用語および語句は、説明に使用されており、限定と見なすべきではない。

【００１０】

（好ましい実施態様の説明）

図１は、概略形態で、自動血液収集手順を実行するためのオンライン血液処理システム１０を示す。

【００１１】

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図示しているように、システム１０は、単一針血液収集ネットワークを備えるが、二重針ネットワークもまた、使用できる。

【００１２】

Ｉ．システムの概要

システム１０は、耐久性ハードウェア要素の配置を備え、その作動は、処理制御装置１８で管理されている。これらのハードウェア要素は、遠心機１２を備え、ここで、ドナーからの全血（ＷＢ）は、血小板、血漿および赤血球に分離される。使用できる代表的な遠心機は、Ｂｒｏｗｎらの米国特許第５，６９０，６０２号で示されており、その内容は、本明細書中で参考として援用されている。

【００１３】

これらのハードウェア要素はまた、種々のポンプ（これらは、典型的には、蠕動性である）（Ｐ１～Ｐ７と命名する）ならびに種々のインラインクランプおよびバルブ（Ｖ１～Ｖ７と命名する）を備える。もちろん、他の型のハードウェア要素（ソレノイド、圧力モニターなどのようなもの）は、典型的には存在し得るが、図１では図示していない。

【００１４】

システム１０はまた、典型的には、ある形態のディスポーサブル流体処理アセンブリ１４を備え、これは、これらのハードウェア要素と共同で使用される。図示した実施態様では、アセンブリ１４は、処理チャンバ１６を備え、これらは、２個のステージ２４および３２を有する。使用中、遠心機１２は、処理チャンバ１６を回転して、血液成分を遠心分離する。

【００１５】

この二段階処理チャンバ１６の構成は、変更し得る。例えば、それは、Ｃｕｌｌｉｎｓらの米国特許第４，１４６，１７２号（その内容は、本明細書中で参考として援用されている）で示されそして記載された処理チャンバのような、二重バッグの形態をとることができる。あるいは、この処理チャンバ１６は、Ｂｒｏｗｎの米国特許第５，６３２，８９３号（その内容は、本明細書中で参考として援用されている）で示され記載したような、細長い二段階一体型バッグの形態をとることができる。

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【００１６】

図示した血液処理システム１０では、処理アセンブリ１４はまた、流体回路を形成する可撓性チューブのアレイを備える。この流体回路は、処理チャンバ１６からおよび処理チャンバ１６に流体を運搬する。ポンプＰ１～Ｐ７およびバルブＶ１～Ｖ７は、このチュービングと係合して、この流体の流れを所定様式で管理する。この流体回路は、さらに、処理中に液体を分配しそして受容する多数の容器（Ｃ１～Ｃ５と命名されている）を備える。

【００１７】

制御装置１８は、アセンブリ１４を使用する１つまたはそれ以上の処理作業を実行するために、種々のハードウェア要素の操作を管理する。制御装置１８はまた、血液成分の分離および収集を最大化においてオペレーターを補助する、処理条件および出力情報のリアルタイム評価を実行する。

【００１８】

システム１０は、多様な種類の血液分離プロセスを達成するように、構成され得る。図１は、単一のドナーから、以下の（ｉ）、（ｉｉ）および（ｉｉｉ）を収集するために、単一針２２を使用して自動手順を実行するように構成されたシステム１０を示す：（ｉ）（例えば、２治療単位より多い）血漿（ＰＣ）に懸濁した所望の収量の濃縮された血小板（これは、（所望の場合に）白血球を実質的に含まないように提供され得る）；（ｉｉ）（例えば、約１００％の血球容量で約２００ｍｌまたは約８５％の血球容量で約２３０ｍｌより多くの）所望の容量の濃縮された赤血球（ＲＢＣ）（これもまた、（所望の場合）白血球を実質的に含まないように提供され得る）；および（ｉｉｉ）（所望の場合）所望の容量の低血小板（ｐｌａｔｅｌｅｔ－ｐｏｏｒ）血漿（ＰＰＰ）。

【００１９】

システム１０は、許容可能な血液容量に対する適用可能な調節により管理されるので、種々の容量のＰＣ、ＰＰＰおよびＲＢＣ産物を収集できる。例えば、米国では、システム１０が現在提供し得る成分容量反復は、例えば、以下を含む：（ｉ）各々１治療単位のＰＣ、ＰＰＰおよびＲＢＣ；または（ｉｉ）各々１治療単位のＰＣおよびＲＢＣ；または（ｉｉｉ）２治療単位のＰＣおよび１単位のＲ

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ＢＣ。

【００２０】

これらの血液処理目的を達成するためのシステム１０の操作のさらなる詳細は、以下で記述する。

【００２１】

ＩＩ．システム制御装置

制御装置１８は、先に記載したようなシステム１０の全体的なプロセス制御およびモニタリング機能を実行する。

【００２２】

図示した好ましい実施態様（図２を参照）では、この制御装置は、主要処理ユニット（ＭＰＵ）４４を含む。好ましい実施態様では、ＭＰＵ４４は、Ｍｏｔｏｒｏｌａ　Ｃｏｒｐｏｒａｔｉｏｎ製の６８０３０型マイクロプロセッサを含むが、他の型の通常のマイクロプロセッサが、使用できる。

【００２３】

好ましい実施態様では、ＭＰＵ４４は、従来のリアルタイムなマルチタスキング（ｍｕｌｔｉ－ｔａｓｋｉｎｇ）を使用して、ＭＰＵサイクルを処理タスクに割り付ける。周期的なタイマーインターラプト（例えば、５ミリ秒毎）は、実行中のタスクを強制排除（ｐｒｅｅｍｐｔ）し、実行準備完了状態にある他のタスクをスケジュールする。もし、再スケジュールが要求されるなら、この準備完了状態において、最も優先順位が高いタスクがスケジュールされる。さもなければ、準備完了状態にあるリスト上の次のタスクが、スケジュールされる。

【００２４】

（Ａ．ハードウェア制御）

ＭＰＵ４４は、アプリケーション制御マネージャー４６を備える。アプリケーション制御マネージャー４６は、制御アプリケーションのライブラリ４８の起動を管理する。各制御アプリケーションは、所定の様式でこのシステムハードウェア（例えば、遠心機１２、ポンプＰ１～Ｐ７およびバルブＶ１～Ｖ７）を使用して、所定の機能的タスクを実行する手順を命令する。図示した好ましい実施態様では、これらのアプリケーションは、ＭＰＵ４４において、ＥＰＲＯＭで、処理

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ソフトウェアとして常駐している。

【００２５】

機器マネージャー５０もまた、ＭＰＵ４４において、ＥＰＲＯＭで、処理ソフトウェアとして常駐している。機器マネージャー５０は、アプリケーション制御マネージャー４６と通信している。機器マネージャー５０はまた、このシステムのポンプ、ソレノイド、バルブおよび他の機能的ハードウェア用の、ローレベル周辺制御装置５２と通信している。

【００２６】

図２で示すように、アプリケーション制御マネージャー４６は、起動したアプリケーションでコールアップとき、機器マネージャー５０に特定の機能コマンドを送る。機器マネージャー５０は、この機能を実行するための周辺制御装置（単数または複数）５２を識別し、そしてハードウェア仕様コマンドをコンパイルする。周辺制御装置５２は、このハードウェアと直接通信して、このハードウェア仕様コマンドを実行し、これが、このハードウェアを特定の様式で作動させる。通信マネージャー５４は、ローレベルプロトコルを管理し、そして機器マネージャー５０と周辺制御装置５２との間を通信する。

【００２７】

また、図２で示すように、機器マネージャー５０はまた、この処理手順の操作条件および機能条件についての状態データを、アプリケーション制御マネージャー４６に戻し伝える。この状態データは、例えば、流体の流速、感知した圧力、および測定された流体容量によって表わされる。

【００２８】

アプリケーション制御マネージャー４６は、ディスプレイ用の選択した状態データをオペレータに伝達する。アプリケーション制御マネージャー４６は、操作条件および機能条件を、手順アプリケーションＡ１および性能モニタリングアプリケーションＡ２に伝達する。

【００２９】

（Ｂ．オペレータインターフェイス）

図示した実施形態では、ＭＰＵ４４はまた、対話式ユーザーインターフェイス

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５８を含む。インターフェイス５８により、オペレータは、システム１０の操作に関する情報を見て理解できるようになる。インターフェイス５８により、また、オペレータは、アプリケーション制御マネージャー４６に備わっているアプリケーションを選択するだけでなく、システム１０の一定の機能および性能規準を変えることができるようになる。

【００３０】

インターフェイス５８は、インターフェイススクリーン６０、および好ましくは、オーディオ装置６２を含む。インターフェイススクリーン６０は、アルファベット－数字のフォーマットで、かつ、図式画像として、オペレータが見るための情報を表示する。オーディオ装置６２は、オペレータの注意を引くためにか、またはオペレータの行為を認知するためかのいずれかのために、音響プロンプトを供給する。

【００３１】

図示した好ましい実施形態では、インターフェイススクリーン６０はまた、入力装置として役立つ。それは、通常のタッチ起動により、オペレータからの入力を受信する。あるいは、またはタッチ起動と組み合わせて、入力装置とし、マウスまたはキーボードが使用され得る。

【００３２】

インターフェイスマネージャー６４は、インターフェイススクリーン６０およびオーディオ装置６２と連絡している。インターフェイスマネージャー６４は、順に、アプリケーション制御マネージャー４６と連絡している。インターフェイスマネージャー６４は、ＭＰＵ４４において、ＥＰＲＯＭで、処理ソフトウェアとして備わっている。

【００３３】

ＭＰＵ４４およびインターフェイス５８のさらなる詳細は、Ｌｙｌｅらの米国特許第５，５８１，６８７号で開示されており、その内容は、本明細書中で参考として援用されている。

【００３４】

（Ｃ．システム制御機能）

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（図２で示すように）図示した実施形態では、ライブラリ４８は、少なくとも１個のシステム制御アプリケーションＡ１を含む。システム制御アプリケーションＡ１は、いくつかの特定の（しかし、相関した）ユーティリティー機能を含む。もちろん、ユーティリティー機能の数および種類は、変えることができる。

【００３５】

図示した実施形態では、ユーティリティー機能Ｆ１は、システム１０の血小板収量（Ｙｌｄ）を誘導する。ユーティリティー機能Ｆ１は、その分離効率によるシステム１０の瞬間的な物理的状態と収集に利用できる循環血小板数によるドナーの瞬間的な生理学的状態の両方を確認する。これらにより、ユーティリティー機能Ｆ１は、処理期間にわたって、連続的に、血小板の瞬間的な収量を誘導する。

【００３６】

別のユーティリティー機能Ｆ２は、選択した情報ステータス値およびパラメータを生じさせるために、計算した血小板少量（Ｙｌｄ）および他の処理状態に依存している。これらの値およびパラメータは、インターフェイス５８に表示されて、オペレータが最適な性能条件を確立し維持するのを助ける。ユーティリティー機能Ｆ２により誘導されたステータス値およびパラメータは、変えることができる。例えば、図示した実施形態では、ユーティリティー機能Ｆ２は、処理されるべき残留容量、残りの処理時間、および成分収集容量および速度を報告する。

【００３７】

他のユーティリティー機能は、最適な処理状態を確立し維持するために、アプリケーション制御マネージャー４６により使用する進行中の処理状態に基づいて、制御変数を生じる。例えば、１ユーティリティー機能Ｆ３は、第一ステージ２４で、血小板分離条件を最適化するために、制御変数を生じさせる。別のユーティリティー機能Ｆ４は、クエン酸塩抗凝血剤がＰＰＰと共にドナーに戻って潜在的なクエン酸毒性反応を回避する速度を制御するために、制御変数を生じる。

【００３８】

これらのユーティリティー機能および他のユーティリティー機能のさらなる詳細は、Ｂｒｏｗｎの米国特許第５，６７６，８４１号で見出され、その内容は、

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本明細書中で参考として援用されている。依存している種々のユーティリティー機能の要旨は、本明細書の最後に見られる。

【００３９】

（ＩＩＩ．システム操作）

図示した実施形態では、システム１０は、少なくとも３つの処理目的を達成するように調整される。第一目的は、所望収量の濃縮血小板（ＰＣ）を収集することにある。第二目的は、収集したＰＣの保存媒体として供するために、所望容量のＰＰＰを収集することにある。第三目的は、所望容量の赤血球（ＲＢＣ）を収集することにある。他の目的は、例えば、保存用の追加容量のＰＰＰを収集するために、確立され得る。

【００４０】

これらの目的を達成するために、ユーティリティー機能Ｆ１は、システム１０を調整して、少なくとも３つの異なる作動モードで、血液を収集し処理する。

【００４１】

第一作動モードでは、システム１０は、全血を処理し、そしてＰＣおよびＰＰＰを収集するように調整される。第一モードでは、ＲＢＣは、同時には収集されず、ドナーに戻される。所望容量よりも過剰のＰＰＰもまた、ドナーに戻され得る。

【００４２】

第二作動モードでは、システム１０は、全血を処理し、そして付随した追加容量のＰＣおよびＰＰＰと共にＲＢＣを同時に収集するように調整される。第二モード中にて、血液成分は、ドナーには戻されない。

【００４３】

第三作動モードでは、システム１０は、最終血液容量トリミング機能を実行するように調整される。この容量トリミング機能中にて、収集したＲＢＣ容量の一部、または収集したＰＰＰ容量の一部または全部、またはそれらの両方は、ドナーに戻すことができる。この容量トリミング機能は、実際に収集された成分容量が収集用の目標容量を超えないことを保証する。

【００４４】

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この処理手順の着手時点で、オペレータは、インターフェイス５８を使用して、収集する所望のＰＣ収量（Ｙｌｄ$_{Goal}$）、収集する所望のＲＢＣ容量（ＲＢＣ$_{Goal}$）および収集する所望のＰＰＰ容量（ＰＰＰ$_{Goal}$）を入力する。

制御装置１８は、システム１０を調整して、第一作動モードで、血液処理を続行する。制御装置１８は、第一作動モードから第二作動モードへの変化および第二作動モードから第三作動モードへの変化を命令する際の２つの処理変数を考慮している。第一処理変数は、所望の血小板収量を得るのに必要な残留全血容量（すなわち、Ｖｂ$_{rem}$（ｍｌ））である。第二処理変数は、所望容量の赤血球（ＲＢＣ$_{Goal}$）（すなわち、Ｖｂ$_{RBC}$）を得るために処理する必要がある全血の容量である。

【００４５】

Ｖｂ$_{rem}$＝Ｖｂ$_{RBC}$のとき、制御装置１８は、第一作動モードから第二作動モードへと切り替わる。Ｖｂ$_{rem}$がゼロになるとき、この制御装置は、第二作動モードから第三作動モードへと切り替わる。

【００４６】

（ｉ）Ｖｂ$_{rem}$の計算

ユーティリティー機能Ｆ２は、Ｙｌｄ$_{Goal}$を得るために処理する必要がある全血容量を誘導する第一ユーティリティー機能Ｆ１によるＹｌｄの計算に依存している。血液処理中にて、ユーティリティー機能Ｆ２は、現在の作動効率η_{Plt}を反映するように補正しつつ、この手順の残りにわたって、収集する残留収量を予想平均血小板数で割ることにより、所望血小板収量Ｖｂ$_{rem}$（ｍｌ）を得るのに必要な追加処理容量を連続的に誘導する。

【００４７】

図示した実施形態では、ユーティリティー機能Ｆ２は、以下の式を使用して、この値を誘導する：

【００４８】

【数１】

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$$Vb_{rem}=\frac{200,000\times(Yld_{Goal}-Yld_{Current})}{\eta_{Plt}\times ACDil\times(Plt_{Current}+Plt_{Post})}$$

ここで：

Ｙｌｄ$_{Goal}$は、所望血小板収量（ｋ／μｌ）である；

Ｖｂ$_{rem}$は、Ｙｌｄ$_{Goal}$を得るのに必要な追加処理容量（ｍｌ）である。

【００４９】

Ｙｌｄ$_{current}$は、（以下の「要旨」で述べる）現在処理値に基づいてユーティリティー機能Ｆ１により計算した現在血小板収量（ｋ／μｌ）である。

【００５０】

η_{Plt}は、現在の（瞬間的な）血小板収集効率であり、これは、（以下の「要旨」で述べる）現在処理値に基づいて、計算できる。

【００５１】

ＡＣＤｉｌは、（以下の「要旨」で述べる）抗凝血剤希釈因子である。

【００５２】

Ｐｌｔ$_{current}$は、現在の（瞬間的な）循環ドナー血小板数であり、これは、（以下の「要旨」で述べる）現在処理値に基づいて、計算される。

【００５３】

Ｐｌｔ$_{post}$は、処理後の予想ドナー血小板数であり、これもまた、（以下の「要旨」で述べる）全処理値に基づいて、計算される。

【００５４】

（ｉｉ）Ｖ$_{RBC}$の計算

ユーティリティー機能Ｆ２は、ＲＢＣ$_{Goal}$に基づいて、そして、ドナーの全血ヘマトクリット容量（Ｈｃｔ）を考慮することにより、ＶｂＲＢＣを誘導する。ドナーの全血ヘマトクリット容量Ｈｃｔは、この手順の着手時に測定した値、または手順の過程でオンライン感知した値を含み得る。

【００５５】

図示した実施形態では、Ｈｃｔは、直接的には測定または感知されない。その

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代わりに、制御装置１８は、この分離チャンバに入る全血の見かけ血球容量値Ｈｂに依存している。Ｈｂは、感知された流動状態および理論的な要件に基づいて、制御装置１８により誘導される。Ｈｂの誘導は、以下の「要旨」で、さらに詳細に説明する。

【００５６】

Ｈｂに基づいて、ユーティリティー機能Ｆ２は、以下の式を使って、ＶｂＲＢＣを誘導できる：

【００５７】

【数２】

$$Vb_{RBC} = \frac{RBC_{Goal} + Buf}{H_b}$$

ここで：

Ｂｕｆは、所定緩衝液容量（例えば、２０ｍｌ）である。

【００５８】

図示した実施形態では、ユーティリティー機能Ｆ２は、ＶｂＲＢＣの計算容量を、例えば、１０で割り切れる次に最も高い整数に切り上げることにより、さらなる容量緩衝液を供給する。

【００５９】

図示した実施形態では、ユーティリティー機能Ｆ２はまた、ＶｂＲＢＣの計算値と所定最大容量（例えば、６００ｍＬ）とを比較する。もし、ＶｂＲＢＣが所定最大値に等しいかそれを超えるなら、ユーティリティー機能Ｆ２は、その値を、規定より少ない容量（例えば、５９５ｍＬ）まで切り下げる。

【００６０】

（ｉｉｉ）第一作動モード

第一または非同時作動モードでは、システム１０は、全血を処理し、そして保存用のＰＣおよびＰＰＰを収集する。第一モード中にて、ＲＢＣおよび未収集容量のＰＰＰは、ドナーに戻される。

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【００６１】

図１で示したシステム１０は、単一の管腔静脈切開針２２を使用する。この非同時モード中にて、制御装置１８は、一連のドローサイクルおよびリターンサイクルで、システム１０を作動する。ドローサイクル（図３）中にて、制御装置１８は、針２２を通って、ドナーのＷＢを処理用チャンバ１６に供給する。リターンサイクル（図４）中にて、制御装置１８は、同じ針２２を通って、ＲＢＣおよびＰＰＰ血液成分をドナーに戻す。

【００６２】

図示した実施形態では、システム１０は、一連のドローサイクルおよびリターンサイクル中にて、中断することなく、チャンバ１６で分離を起こすことができるように設計されている。さらに特定すると、システム１０は、ドローレザバ６６を含む。ドローサイクル（図３）中にて、一定量のドナーのＷＢは、レザバ６６にプールされ、その容量の過剰量は、処理用チャンバ１６に送られる。システム１０はまた、リターンレザバ６８を含む。リターンサイクル（図４を参照）中にてドナーに定期的に戻すために、ドローサイクル中にて、リターンレザバ６８では、一定量のＲＢＣが集まる。このリターンサイクル中では、ＷＢは、ドローレザバ６６からチャンバ１６へと運搬されて、分離を中断せずに行う。

【００６３】

非同時モード（図３）のドローサイクルでは、全血ポンプＰ１は、ＷＢを、針２２から、第一配管分枝２０を通って、ドローレザバ６６に入れる。その間、補助配管分枝２６は、容器Ｃ２から抗凝血剤ポンプＰ３を通ってＷＢ流れに入る抗凝血剤を計量する。抗凝血剤の種類は、変えることができるものの、図示した実施形態は、ＡＣＤＡを使用し、これは、フェレーシスで一般的に使用される抗凝血剤である。

【００６４】

容器Ｃ２は、生理食塩水溶液を収容している。別の補助配管分枝２８は、この生理食塩水を、処理を開始する前にアセンブリ１４から空気を感作し一掃する際に使用するために、インラインバルブＶ１を経由して、第一配管分枝２０へと運搬する。生理食塩水溶液はまた、再度、処理後に導入されて、ドナーに戻すため

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に、アセンブリ１４からの残留成分をフラッシュする。

【００６５】

処理制御装置１８は、重量スケール７０から、処理情報を受信する。重量スケール７０は、ドローレザバ６６で収集したＷＢの容量をモニターする。一旦、重量スケール７０が、所望容量のＷＢがドローレザバ６６内に存在していることを指示すると、制御装置１８は、全血処理ポンプＰ２に対して、ドローレザバ６６から入口分枝３６を通って処置チャンバ１６の第一ステージ２４へとＷＢを連続的に運搬するように作動する命令を出す。制御装置１８は、全血処理ポンプＰ２（これは、（例えば、５０ｍｌ／分で）連続的に作動して、一定量の抗凝血血液をレザバ６６に収集する）よりも高い流速（例えば、１００ｍｌ／分）で、全血ポンプＰ１を作動する。重量スケール７０を使用して重量をモニターすることにより、この制御装置は、断続的に、全血入口ポンプＰ１を作動して、ドローレザバ６６において、所望容量のＷＢを維持する。

【００６６】

抗凝血ＷＢは、処理チャンバ１６の第一ステージ２４に入ってそれを満たす。そこで、遠心機１２の回転中に発生した遠心力により、ＷＢは、赤血球（ＲＢＣ）と血小板リッチな（ｐｌａｔｅｌｅｔ－ｒｉｃｈ）血漿（ＰＲＰ）に分離される。

【００６７】

ＰＲＰポンプＰ４は、処理チャンバ１６の第一ステージ２４から、処理チャンバ１６の第二ステージ３２へと輸送するための第二配管分枝３０へと、ＰＲＰを引き出すように作動する。そこで、ＰＲＰは、血小板濃縮物（ＰＣ）と低血小板血漿（ＰＰＰ）に分離される。

【００６８】

制御装置１８は、処理チャンバ１６の第一ステージ２４内のＲＢＣとＰＲＰの間のインターフェイスの位置を光学的にモニターする。制御装置１８は、ＰＲＰポンプＰ４を作動して、このインターフェイスを、処理チャンバ２４の第一ステージ２４内の所望位置で保持する。これにより、このインターフェイスを占めている白血球の相当部分がＰＲＰ流れに入ることを回避する。

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【００６９】

必要に応じて、このＰＲＰはまた、白血球を除去するために、第二ステージ３２での分離前に、フィルターＦを通って運搬され得る。フィルターＦは、Ｎｉｓｈｉｍｕｒａらの米国特許第４，９３６，９９８号（その内容は、本明細書中で参考として援用されている）で開示された種類の繊維を含む濾過材を使用できる。これらの繊維を含む濾過材は、ＳＥＰＡＣＥＬＬの商品名のフィルターで、Ａｓａｈｉ　Ｍｅｄｉｃａｌ　Ｃｏｍｐａｎｙから市販されている。

【００７０】

システム１０は、再循環配管分枝３４および付属再循環ポンプＰ５を含む。処理制御装置１８は、ポンプＰ５を作動して、処理チャンバ１６の第一ステージ２４に入るＷＢと再混合するために、処理チャンバ１６の第一ステージ２４を出ていくＰＲＰの一部を反らす。ＰＲＰの再循環により、第一ステージ２４の入口領域において、ＲＢＣおよびＰＲＰの最大分離を生じる所望の状態が確立される。

【００７１】

ＲＢＣ分枝３８は、このＲＢＣを、処理チャンバ１６の第一ステージ２４から、リターンレザバ６８（これは、バルブＶ３で制御される）へと運搬する。重量スケール７２は、容器Ｃ４に収集されたＰＰＰの容量をモニターする。

【００７２】

ＰＰＰ分枝４０は、ＰＰＰポンプＰ７を作動することにより、処理チャンバ１６の第二ステージ３２からＰＰＰを運搬する。バルブＶ５を開くことにより、このＰＰＰの全部または一部は、ポンプＰ７の流速に依存して、収集容器Ｃ４に向けることができる。重量スケール７４は、容器Ｃ４で収集されたＰＰＰの容量をモニターする。収集されなかったＰＰＰは、リターンレザバ６８へと流入し、この場所で、それは、このＲＢＣと混ざる。

【００７３】

第二作動モード（これは、後に説明する）中にて、比較的に多量のＰＰＰ（すなわち、約５０％～７５％のＰＰＰ$_{Goal}$）は、典型的には、ドナーに戻ることなく、収集される。このことを見込んで、制御装置１６は、第一モード中にＰＰＰが収集される速度を制限する。これにより、この手順の最後において、余剰容量

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のＰＰＰが収集されることが避けられる。第一作動モード中にＰＰＰが収集される速度を制限することにより、制御装置１８は、引き続いた血液容量トリミング機能の時間を短くし、それにより、全体的な処置時間を短くする。少量の余剰ＰＰＰにより、また、この血液容量トリミング機能中にドナーに戻る抗凝血剤（これは、ＰＰＰで運ばれる）の量が少なくなるので、血液容量トリミング機能中において、より高いリターン流速を使用することが可能となる。

【００７４】

制御装置１８は、重量スケール７２から処理情報を受信し、リターンレザバ６８内のＲＢＣおよびＰＰＰの容量をモニターする。予め設定した容量があるとき、制御装置１８は、システム１０の作動を、ドローサイクルからリターンサイクルへとシフトする。

【００７５】

リターンサイクル（図４）では、制御装置１８は、全血入口ポンプＰ１および抗凝血剤ポンプＰ３を停止し、そして血液リターンポンプＰ６を始動する。リターン分枝４２は、針２２を通って、リターンレザバ６８にあるＲＢＣおよびＰＰＰをドナーへと運搬する。

【００７６】

一方では、制御装置１８は、このリターンサイクルにある間、ＷＢ処理ポンプＰ２、ＰＲＰポンプＰ４および再循環ポンプＰ５を作動状態に保って、チャンバ１６の第一ステージ２４および第二ステージ３２を通ってドローレザバ６６にプールされたＷＢを連続的に処理する。

【００７７】

重量スケール７２が、リターンレザバ６８の内容物がドナーに運搬されたことを表示したとき、制御装置１８は、システム１０の操作を別のドローサイクルへとシフトする。

【００７８】

制御装置１８は、$V_{brem} = V_{bRBC}$となるまで、連続ドローサイクルとリターンドローサイクルとの間で切り換える。$V_{brem} = V_{bRBC}$のとき、制御装置１８は、リターンレザバ６８の内容物をドナーに戻す最終リターンサイクルを命令す

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る。リターンレザバ６８の内容物を戻すとすぐに、制御装置１８は、第一作動モードから第二作動モードへと切り換える。

【００７９】

（ｉｖ）同時収集モード

第二または同時収集モード（図５）では、制御装置１８は、システム１０を調整して、持続ドローサイクルで作動して、全血を処理し、そして付随した追加容量のＰＣおよびＰＰＰと共に、目標容量のＲＢＣを同時に収集する。この同時収集モード中にて、制御装置１８は、システム１０の操作をリターンサイクルには切り換えない。この同時収集モード中にて、ただ１つの持続ドローサイクルだけが存在し、そして成分はドナーへは戻されない。

【００８０】

同時収集モードの持続ドローサイクルの間、制御装置１８は、ドローレザバ６６にある全血の大余剰容量が収集されることを避ける。図示した実施形態では、制御装置１８は、非同時収集モードのドローサイクル中に維持される差と比較して、全血入口ポンプＰ１と全血処理ポンプＰ２との間で低い流速差を維持することにより、この目的を達成する。例えば、図示した実施形態では、全血入口ポンプＰ１は、全血処理ポンプＰ２の上方で、例えば、僅か１ｍＬ／分の最小差で、作動される。

【００８１】

僅かな緩衝容量の全血のみが、同時収集モードの持続ドローサイクルの間、ドローレザバ６６内で、維持されることをさらに保証するために、重量スケール７０は、ドローレザバ６６内で感知された容量の血液が特定の最低緩衝容量（例えば、５ｇ）を超えるときはいつでも、全血入口ポンプＰ１および抗凝血剤ポンプＰ３をオフに切り換える。

【００８２】

同時収集モードの持続ドローサイクルの間、赤血球は、バルブＶ４（これは、この目的のために開いており、バルブＶ３は閉じていて、それにより、リターンレザバ６８では、ＲＢＣは集まらない）を経由して、収集容器Ｃ４へと向けられる。重量スケール１０８は、収集容器Ｃ４の重量をモニターする。

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【００８３】

チャンバ１６の第二ステージ３２では、付随容量のＰＣが集まり、その間、（ＰＰＰポンプＰ７およびバルブＶ５（これは、開いている）を作動することにより）、収集容器Ｃ３では、付随容量のＰＰＰが集まる。バルブＶ３は、閉じられ、そのようにして、リターンレザバ６８には、ＰＰＰが集まらない。

【００８４】

制御装置１８は、同時収集モードの持続ドローサイクルの間、Ｖｂｒｅｍを誘導する。Ｖｂｒｅｍがゼロになるとき、制御装置１８は、この同時収集モードを終了する。

【００８５】

（（ｉｖ）血液容量トリミング機能）

図示した実施形態（図６を参照）では、この同時収集モードの最後に、制御装置１８は、重量スケール１０８および７４を使用して、それぞれ、収集したＲＢＣおよびＰＰＰの容量を評価する。

【００８６】

収集したＲＢＣの容量がＲＢＣ$_{Goal}$を超える場合、制御装置１８は、インラインリターンポンプＰ６を作動することにより、収集容器Ｃ４から、分枝経路４３（バルブＶ６は開いている）を通って、リターン経路４２（バルブＶ２は開いている）へと、過剰なＲＢＣ容量をドナーに戻すリターンサイクルに入るように、システム１０に命令を出す。

【００８７】

同様に、もし、収集したＰＰＰの容量がＰＰＰ$_{Goal}$を超えるなら、制御装置１８は、インラインリターンポンプＰ６を作動することにより、収集容器Ｃ３から、分枝経路４５（バルブＶ７は開いており、バルブＶ５は閉じている）を通って、リターン経路４２へと、過剰なＰＰＰ容量をドナーに戻すリターンサイクルに入るように、システム１０に命令を出す。

【００８８】

この血液容量トリミング機能の最後に、制御装置１８は、所定流体交換容量と共に、システム１０にある残留血液をドナーに戻すように、生理食塩水再注入操

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作の命令を出す。

【００８９】

（（ｖ）収集後処理）

（（１）ＰＰＰ）

ＰＰＰの保持は、この成分分離プロセス中およびその後において、複数の目的に役立ち得る。

【００９０】

ＰＰＰの保持は、処理の間、治療目的に役立つ。ＰＰＰは、この成分分離プロセスの間、ＷＢに計量して供給された抗凝血剤の殆どを含有する。ＰＰＰの全部をドナーに戻す代わりに、その一部を保持することにより、処理中にドナーが受容する抗凝血剤の全体容量は、少なくなる。この減少は、大量の血液を処理する場合、特に重要である。処理中におけるＰＰＰの保持はまた、処理中において、ドナーの循環血小板数を高くかつ均一に保つ。

【００９１】

システム１０はまた、保持したＰＰＰから処理利益を誘導できる。例えば、システム１０は、代替再循環モードにおいて、第一隔室２４に入ってくるＷＢと混合するために、ＰＲＰの代わりに、保持したＰＰＰの一部を再循環できる。さもなければ、処理の間、ＷＢの流れが一時的に停止するなら、システム１０は、流体ラインを開いた状態で保つために、抗凝血「キープオープン（ｋｅｅｐ－ｏｐｅｎ）」流体として、保持容量のＰＰＰを利用できる。それに加えて、この分離プロセスの最後に、システム１０は、リターン経路４２を通ってＲＢＣをドナーに戻すために第一ステージ隔室２４から再懸濁し一掃するように、「リンスバック（ｒｉｎｓｅ－ｂａｃｋ）」流体として、保持容量のＰＰＰを利用できる。

【００９２】

（（２）ＰＣ）

この分離プロセス後、システム１０はまた、再懸濁モードでは、収集容器Ｃ５において、移動および保存用の第二ステージ２４で、ＰＣを再懸濁するために、保持したＰＰＰの一部を利用するように作動する。ＰＣの再懸濁および収集容器Ｃ５への移動は、手動でまたはオンラインで、達成できる。

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【００９３】

好ましくは、ＰＣを保存する容器Ｃ５は、ＤＥＨＰ可塑化ポリ塩化ビニル材料と比較した場合、血小板の保存に有利な高い気体透過性を有する材料から製造される。例えば、（Ｇａｊｅｗｓｋｉらの米国特許第４，１４０，１６２号で開示されているような）ポリオレフィン材料、またはトリメリト酸トリ－２－エチルヘキシル（ＴＥＨＴＭ）が使用できる。

【００９４】

（（２）ＲＢＣ）

図示した実施形態（図７を参照）では、保存用に収集したＲＢＣ容量を処理するために、使い捨て収集セット７６が提供される。

【００９５】

セット７６は、移動経路７８を含む。移動経路７８は、密封自由端８０を有し、これは、無菌様式で、ＲＢＣ収集容器Ｃ４（図７を参照）上の密封チューブセグメント８２に連結されるように設計される。Ｓｐｅｎｃｅｒの米国特許第４，４１２，８３５号で示されたもののような公知の無菌連結機構（図示せず）は、移動経路７８をチューブセグメント８２に連結するのに使用できる。これらの機構は、配管末端間において、溶融シールを形成し、これは、一旦、冷却すると、無菌溶接を形成する。

【００９６】

第一バッグ８４は、一定長の試料配管８６を通って、移動経路７８と連絡している。第一バッグ８４は、赤血球添加剤溶液Ｓ、例えば、ＳＡＧ－ＭまたはＡＤＳＯＬＩＤ（登録商標）Ｓｏｌｕｔｉｏｎ（Ｂａｘｔｅｒ　Ｈｅａｌｔｈｃａｒｅ　Ｃｏｒｐｏｒａｔｉｏｎ）を含有する。収集セット７６をＲＢＣ収集容器Ｃ４に連結することに続いて、試料配管８６にある通常のインライン脆弱カニューレ１０６が開かれ、赤血球添加剤溶液Ｓは、収集したＲＢＣ容量と混合するために、第一バッグ８４から収集容器Ｃ４へと移動される。添加剤溶液とＲＢＣとの混合物は、次いで、第一バッグ８４に戻って移動できる。

【００９７】

第一バッグ８４内の残留空気はインライン通気チャンバ８８に排出でき、これ

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は、移動経路７８と連絡している。同時に、第一バッグ８４内に存在している収集したＲＢＣ容量のアリコートは、試料配管８６に急送できる。

【００９８】

配管８６は、好ましくは、識別コード９０を有し、これは、第一バッグ８４上に印刷または塗布されたコード９０と同じである。配管８６は、次いで、通常のスナップアパート（ｓｎａｐ－ａｐａｒｔ）シールで閉じられ、第一バッグ８４は、このＲＢＣ容量を保存するために、収集セット７６から引き離される。配管８６は、さらに、通常のチューブシーラーを使用してセグメントで密封されて、分析および交差試験用に、このＲＢＣの複数の試料を単離できる。

【００９９】

セット７６はまた、第二バッグ９２を含み、これは、分枝経路９４を通って、第一バッグ８４の下流にある移動経路７８と連絡している。分枝経路９４は、インラインフィルター９６を含む。インラインフィルター９６は、赤血球から白血球を選択的に除去する濾過材９８を運ぶ。このフィルターは、例えば、Ｒ－３０００ Ｒｅｄ Ｂｌｏｏｄ Ｃｅｌｌ Ｆｉｌｔｅｒ（Ａｓａｈｉ Ｍｅｄｉｃａｌ）から構成できる。

【０１００】

赤血球および添加剤溶液の混合物は、第一バック８４をバイパスして、収集バッグＣ４から、インラインフィルター９６を通って、第二バッグ９２へと移動できる。このようにして、セット７６は、白血球を事実上含まない赤血球（これは、長期間の保存に適当である）を供給する。

【０１０１】

通気経路１００は、インラインフィルター９６をバイパスして、第二バッグ９２から移動経路７８へと伸長している。経路１００で通常の剥離カニューレ１０６を開くことにより、第二バッグ９２内の残留空気は、経路１００を通って、インライン通気チャンバ８８へと排出できる。経路１００内の逆止め弁１０４により、経路１００内の空気および液体の流れは、バッグ９２から離れることができるが、逆方向には行かない。

【０１０２】

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同時に、第二バッグ９２内に存在している収集したＲＢＣのアリコートは、通気経路１００内へと急送できる。通気経路１００は、識別コード１０２を有し、これは、第二バッグ９２上に印刷または塗布されたコード１０２と同じである。通気経路１００および分枝経路９４は、通常のスナップアパートシールで閉じられ、第二バッグ９２は、移動経路７８から引き離すことができる。経路１００もまた、セグメントで密封され、分析および交差試験用に、このＲＢＣの複数の試料を密封できる。

【０１０３】

収集セット７６は、長期間の保存に適当な赤血球産物（これは、保存前には、白血球を含まないか白血球が少ないかいずれかである）を供給するために、可撓性を与える。

【０１０４】

（ＩＶ．種々の処理ユーティリティー機能の要約）

（Ａ．誘導血小板の収量）

ユーティリティ機能Ｆ１は、システム１０の血小板分離効率（η_{Plt}）の連続的な計算を行う。ユーティリティ機能Ｆ１は、全血中で利用できる全血漿容量に対して、ドナーの全血から分離した血漿容量の割合と同じであるように、血小板分離効率η_{Plt}を処理する。ユーティリティ機能Ｆ１は、それにより、ドナーの全血から分離した血漿容量中の各血小板が収穫されたと仮定している。

【０１０５】

ドナーの血球容量は、処理中に抗凝血剤希釈および血漿枯渇効果が原因で変化し、そのようにして、分離効率η_{Plt}は、一定値には留まらず、この手順全体を通して変化する。ユーティリティ機能Ｆ１は、収量を漸進的にモニターすることにより、これらのプロセス依存的な変化と競争する。これらの収量は、増分精算容量（ｉｎｃｒｅｍｅｎｔａｌ　ｃｌｅａｒｅｄ　ｖｏｌｕｍｅｓ）（ΔＣｌｒＶｏｌ）と呼ばれているが、以下のようにして、現在の分離効率η_{Plt}を、ドナー全血（これは、抗凝血剤で希釈し処理した）の現在の増分容量と掛けることにより、計算される：

式（１）

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【０１０６】

【数３】

$$\Delta ClrVol = ACDil \times \eta_{Plt} \times \Delta VOL_{Proc}$$

ここで、

ΔＶｏｌ$_{proc}$は、処理される増分全血容量であり、そして

ＡＣＤｉｌは、この増分全血容量に対する抗凝血剤希釈因子であり、以下のようにして計算される：

式（２）

【０１０７】

【数４】

$$ACDil = \frac{AC}{AC+1}$$

ここで：

ＡＣは、全血容量と抗凝血剤容量との選択比（例えば、１０：１または「１０」）である。ＡＣは、この処理期間中の一定値を含み得る。あるいは、ＡＣは、この処理期間中において、所定の規準に従って、段階様式で変わり得る。

【０１０８】

例えば、ＡＣは、初期設定時間の間、処理の着手時では、より小さい比で設定でき、次いで、引き続いた期間の後、段階的に上昇できる；例えば、ＡＣは、処理の最初の１分間では、６：１に設定でき、次いで、次の２．５～３分間では、８：１に上昇でき、最後に、１０：１の処理レベルまで上昇できる。

【０１０９】

抗凝血剤の導入はまた、第二処理ステージ３２に入るＰＲＰの入口圧力をモニターすることにより、行い得る。例えば、ＡＣは、その初期圧力（例えば、５０

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０ｍｍＨｇ）が設定閾値レベル（例えば、２００ｍｍＨｇ～３００ｍｍＨｇ）まで落ちるまで、６：１に設定できる。ＡＣは、次いで、１０：１の処理レベルまで段階的に上昇できるのに対して、その圧力をモニタリングすることで、それが所望のレベルのままになることを保証する。

【０１１０】

ユーティリティ機能Ｆ１もまた、ドナーの現在の循環血小板数（Ｐｌｔ$_{circ}$）（これは、１マイクロリットル（μｌ）の血漿容量（またはｋ／μｌ）あたり、１０００個の血小板によって、表わされる）の連続的な概算を行う。η_{Plt}と同様に、Ｐｌｔ$_{circ}$は、その希釈効果および枯渇効果のために、処理の間、変化する。ユーティリティ機能Ｆ１はまた、各増分精算血漿容量（ΔＣｌｒＶｏｌ）（これは、η_{Plt}の瞬間的な計算に基づいている）を循環血小板数Ｐｌｔ$_{circ}$と掛けることにより、少しずつ漸進的に、この血小板収量をモニターする。その積は、増分血小板収量（Δｙｌｄ）であり、これは、典型的には、e^nとして表わされ、ここで、e^n＝０．５×１０^{n}個の血小板（e^{11}＝０．５×１０^{11}個の血小板）である。

【０１１１】

任意の一定時間では、増分血小板収量ΔＹｌｄの合計は、現在の血小板収量Ｙｌｄ$_{current}$を構成し、これはまた、以下のようにして表わすことができる：式（３）

【０１１２】

【数５】

$$Yld_{Current} = Yld_{Old} + \frac{\Delta ClrVol \times Plt_{Cur}}{100,000}$$

ここで：

Ｙｌｄ$_{old}$は、最後に計算したＹｌｄ$_{current}$であり、そして

式（４）

【０１１３】

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【数６】

$$\Delta Yld=\frac{\Delta ClrVol\times Plt_{Current}}{100,000}$$

であり、ここで：

Ｐｌｔcurrentは、ドナーの循環血小板数の現在の（瞬間的な）概算値である。

【０１１４】

ΔＹｌｄは、ユニットを均衡させるために、式（４）において、１００，０００で割っている。

【０１１５】

以下は、ユーティリティー機能Ｆ１による上記処理変数の誘導でのさらに詳細な説明を提供する。

【０１１６】

（ｉ）全体的な分離効率η_{Plt}の誘導

全体的なシステム効率η_{Plt}は、以下で表わすように、このシステムの部品の個々の効率の積である：

式（５）

【０１１７】

【数７】

$$\eta_{plt}=\eta_{1stSep}\times\eta_{2ndSep}\times\eta_{Anc}$$

ここで：

η_{1stSep}は、第一分離段階においてＷＢからＰＲＰを分離する効率である。

【０１１８】

η_{2ndSep}は、第二分離段階においてＰＲＰからＰＣを分離する効率である。

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【０１１９】

η_{Anc}は、このシステムの他の補助処理段階の効率の積である。

【０１２０】

（１．第一段階分離効率η_{1stSep}）

ユーティリティー機能Ｆ１は、以下の式を使用して、測定および実験処理値に基づいて、処理の過程で、η_{1stSep}を連続的に誘導する。

式（６）

【０１２１】

【数８】

$$\eta_{Sep}=\frac{Q_p}{(1-H_b)Q_b}$$

ここで：

Q_bは、測定した全血流速（ｍｌ／分）である。

【０１２２】

Q_pは、測定したＰＲＰ流速（ｍｌ／分）である。

【０１２３】

H_bは、第一段階分離隔室に入る抗凝血全血の見かけ血球容量である。H_bは、感知した流動要件および理論要件に基づいて、このユーティリティーにより誘導した値である。ユーティリティー機能Ｆ１には、従って、実際のＷＢ血球容量を測定するためのオンライン血球容量センサを必要としない。

【０１２４】

ユーティリティー機能Ｆ１は、以下の関係に基づいて、H_bを誘導する：

式（７）

【０１２５】

【数９】

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$$H_b = \frac{H_{rbc}(Q_b - Q_p)}{Q_b}$$

ここで：

Ｈｒｂｃは、第一段階分離チャンバの感知した作動条件および物理的寸法に基づいて、第一段階分離チャンバ内でのＲＢＣ床の見かけ血球容量である。Ｈｂと同様に、ユーティリティー機能Ｆ１には、以下の式に従ってユーティリティー機能により誘導したＨｒｂｃを決定する物理的センサを必要としない：

式（８）

【０１２６】

【数１０】

$$H_{rbc} = 1 - \left(\frac{\beta}{gAkS_r}(q_b - q_p)\right)^{\frac{1}{k-1}}$$

ここで：

ｑｂは、入口血流速度（ｃｍ³／秒）であり、これは、既知量であり、ｍｌ／分に変換したとき、式（６）にて、Ｑｂに一致している。

【０１２７】

ｑｐは、測定したＰＲＰ流速（ｃｍ³／秒）であり、これは、既知量であり、ｍｌ／分に変換したとき、式（６）にて、Ｑｐに一致している。

【０１２８】

βは、剪断速度依存項であり、そしてＳｒは、赤血球沈降係数（秒）である。実験データに基づいて、式（８）は、β／Ｓｒ＝１５．８×１０⁶秒⁻¹と仮定する。

【０１２９】

Ａは、既知寸法の分離チャンバの面積（ｃｍ²）である。

【０１３０】

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ｇは、遠心加速度（ｃｍ／秒^3）であり、これは、第一分離チャンバの半径（既知量）を回転速度の二乗Ω^2（ｒａｄ／秒^2）（他の既知量）と掛けた値である。

【０１３１】

ｋは、粘性定数＝０．６２５であり、κは、ｋおよび他の粘性定数α＝４．５に基づいた粘性定数であり、ここで：

式（９）

【０１３２】

【数１１】

$$\kappa=\frac{k+2}{\alpha}\left[\frac{k+2}{k+1}\right]^{k+1}=1.272$$

式（８）は、以下の式（１０）で表わされる関係から誘導される：

式（１０）

【０１３３】

【数１２】

$$H_{rbc}(1-H_{rbc})^{(k+1)}=\frac{\beta H_b q_b}{g A \kappa S_Y}$$

これは、ＢｒｏｗｎのＴｈｅ Ｐｈｙｓｉｃｓ ｏｆ Ｃｏｎｔｉｎｕｏｕｓ Ｆｌｏｗ Ｃｅｎｔｒｉｆｕｇａｌ Ｃｅｌｌ Ｓｅｐａｒａｔｉｏｎ，「Ａｒｔｉｆｉｃｉａｌ Ｏｒｇａｎｓ」 １９８９；１３（１）：４～２０））で示されている。式（８）は、H_{rbc}について、式（１０）を解く。

【０１３４】

（２．第二ステージ分離効率η_{2ndSep}）

ユーティリティー機能Ｆ１はまた、アルゴリズムに基づいて、処置の過程にわたって、η_{2ndSep}を連続的に誘導し、これは、コンピューターモデル化により誘

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導され、それらのサイズ（平均血小板容量、またはＭＰＶ）、流速（Q_p）、分離ステージ３２の面積（Ａ）、および遠心加速度（ｇ、これは、第二ステージのスピン半径を回転速度の二乗Ω２と掛けた値である）の関数として、常用対数（ｌｏｇ－ｎｏｒｍａｌｌｙ）分布した血小板のどの部分が第二分離ステージ３２で収集されたかを計算する。

【０１３５】

このアルゴリズムは、ある関数によって表わすことができ、これは、単一無次元パラメータｇＡS_p／Q_pによって、η_{2ndSep}を表したが、

ここで：

S_p＝１．８×１０$^{-9}$ＭＰＶ$^{2/3}$（秒）であり、そして

ＭＰＶは、平均血小板容量（フェムトリットル、ｆｌ、または立方ミクロン）であり、これは、処理前に収集されたドナーの血液試料から、通常の方法により、測定できる。異なるカウンタを使用することが原因で、ＭＰＶは変動し得る。このユーティリティー機能は、従って、使用するカウンタの種類に従って、その関数で使用するためのＭＰＶを標準化する探索表を含み得る。あるいは、ＭＰＶは、臨床血小板プレカウントPlt_{PRE}の統計的な評価から誘導した関数に基づいて概算でき、これは、このユーティリティー機能を使用できる。本発明者は、このような臨床データの評価に基づいて、このＭＰＶ関数を以下のようにして表わすことができると考えている：

ＭＰＶ（ｆｌ）＝１１．５－０．００９Plt_{PRE}（ｋ／μｌ）

【０１３６】

【数１３】

$$MPV\ (fl) \approx 11.5 - 0.009Plt_{PRE}\ (k/\mu l)$$

（３．補助分離効率η_{Anc}）

η_{Anc}は、この処理システムの他の部分の効率（血小板損失による）を考慮に入れている。η_{Anc}は、第一ステージチャンバから第二ステージチャンバへと血

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小板（ＰＲＰ中）を輸送する効率；この白血球除去フィルターによって血小板（これもまた、ＰＲＰ中）を輸送する効率；処理後、第二ステージチャンバから血小板（ＰＣ中）を再懸濁し輸送する効率；および単一針または二重針のいずれかの構成で先に処理した血液を再処理する効率を考慮に入れている。

【０１３７】

これらの補助プロセス工程の効率は、臨床データに基づいて評価できるか、またはコンピューターモデル化に基づいて概算できる。これらの要件に基づいて、η_{Anc}について予測した値を割り当てることができ、等式（５）は、これを、所定の手順の過程にわたって、定数として処理する。

【０１３８】

（Ｂ．ドナー血小板数（Ｐｌｔ$_{circ}$）の誘導）

ユーティリティー機能Ｆ１は、処理中のドナーの現在の循環血小板数Ｐｌｔ$_{circ}$を予測する動力学的モデルに依存している。このモデルは、ドナーの血液容量を概算し、次いで、以下の関係に従って、処理中の希釈効果および枯渇効果を概算して、Ｐｌｔ$_{Circ}$を誘導する：

等式（１１）

【０１３９】

【数１４】

$$Plt_{Circ}=[(Dilution)\times Plt_{pre}]-(Depletion)$$

ここで：

Ｐｌｔ$_{pre}$は、処理が始まる前のドナーの循環血小板数（ｋ／μｌ）であり、これは、処理前にドナーから取り出した全血の試料から、通常の方法により、測定できる。異なるカウンタを使用することが原因で、Ｐｌｔ$_{pre}$には、変動があり得る。（例えば、Ｐｅｏｐｌｅｓら、「Ａ Ｍｕｌｔｉ－Ｓｉｔｅ Ｓｔｕｄｙ ｏｆ Ｖａｒｉａｂｌｅｓ Ａｆｆｅｃｔｉｎｇ Ｐｌａｔｅｌｅｔ Ｃｏｕｎｔｉｎｇ ｆｏｒ Ｂｌｏｏｄ Ｃｏｍｐｏｎｅｎｔ Ｑｕａｌｉｔｙ Ｃ

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ｏｎｔｒｏｌ」 Ｔｒａｎｓｆｕｓｉｏｎ（Ｓｐｅｃｉａｌ Ａｂｓｔｒａｃｔ Ｓｕｐｐｌｅｍｅｎｔ，４７ｔｈ Ａｎｎｕａｌ Ｍｅｅｔｉｎｇ），３４巻、１０Ｓ号、１９９４年１０月　補遺を参照）。このユーティリティー機能は、従って、使用するカウンタの種類に従って、その関数で使用するための全ての血小板数（例えば、Plt_{pre}およびPlt_{post}（下記））を標準化する探索表を含み得る。

【０１４０】

Ｄｉｌｕｔｉｏｎは、ドナーの見かけ循環血液容量の上昇（これは、このシステムの感作容量および抗凝血剤の送達により、引き起こされる）が原因で、ドナーの処理前循環血小板数Plt_{pre}を低下させる因子である。Ｄｉｌｕｔｉｏｎはまた、この手順の間、腎臓による血管空間からの流体の連続除去を考慮に入れる。

【０１４１】

Ｄｅｐｌｅｔｉｏｎは、処理によるドナーの利用できる循環血小板プールの枯渇を考慮に入れる因子である。Ｄｅｐｌｅｔｉｏｎはまた、処理中にて、この循環血液容量へと血小板を戻す際の脾臓のカウンタ流動化を考慮に入れている。

【０１４２】

（１．希釈の概算）

ユーティリティー機能Ｆ１は、以下の式に基づいて、この希釈因子を概算する：

等式（１２）

【０１４３】

【数１５】

$$Dilution = 1 - \frac{Prime + \frac{2ACD}{3} - PPP}{DonVol}$$

ここで：

Ｐｒｉｍｅは、このシステムの感作容量（ｍｌ）である。

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【０１４４】

ＡＣＤは、使用する抗凝血剤の容量（この誘導が行われる時間に依存して、現在または終点）（ｍｌ）である。

【０１４５】

ＰＰＰは、収集されるＰＰＰの容量（現在または目標）（ｍｌ）である。

【０１４６】

ＤｏｎＶｏｌ（ｍｌ）は、ドナーの身長、体重および性別を考慮に入れたモデルに基づいたドナーの血液容量である。これらのモデルは、回帰によって線形化したドナーの体重に対する血液容量をプロットする実験データを使用して、以下のさらに簡素化した式へとさらに簡単にされる：

等式（１３）

【０１４７】

【数１６】

$$DonVol=1024+51Wgt(r^2=0.87)$$

ここで：

Ｗｇｔは、ドナーの体重（ｋｇ）である。

【０１４８】

（２．枯渇の概算）

血小板の連続収集は、利用できる循環血小板プールを枯渇させる。一次モデルは、ドナーの血小板数がドナーの循環血液容量（ＤｏｎＶｏｌ）で割った血小板収量（Ｙｌｄ）（現在または目標）だけ少なくなることを予測しており、これは、以下のようにして表わされる：

等式（１４）

【０１４９】

【数１７】

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$$Depl=\frac{100,000Yld}{DonVol}$$

ここで：

Ｙｌｄは、現在の瞬間的な血小板収量または目標血小板収量（ｋ／μｌ）である。等式（１４）では、Ｙｌｄは、単位を均衡させるために、１００，０００を掛けられている。

【０１５０】

等式（１４）は、代替血小板の脾臓流動化（これは、脾臓流動化因子（またはＳｐｌｅｅｎ）と呼ばれている）を考慮していない。Ｓｐｌｅｅｎは、少ない血小板数のドナーが、それにもかかわらず、脾臓で、多くの血小板蓄積を有する。処理中にて、循環血小板をドナーの血液から引き出すにつれて、脾臓は、それが蓄積している血小板を血液中に放出し、それにより、循環血小板の低下を部分的に相殺する。本発明者は、血小板プレカウントがドナー間で広範囲に変わるものの、利用できる全血小板容量は、ドナー間で極めて一定に保たれることを発見した。平均の見かけドナー容量は、血液１リットルあたり、３．１０±０．２５ｍｌの血小板である。その変動計数は、８．１％であり、これは、正常なドナーで見られる血球容量の変動係数よりも僅かに高いにすぎない。

【０１５１】

この流動化因子Ｓｐｌｅｅｎは、実際に測定した枯渇とＤｅｐｌ（等式（１４））とを比較することから誘導され、これは、Ｐｌｔ$_{Pre}$の関数として、プロットされ線形化される。Ｓｐｌｅｅｎ（これは、１の下限に制限される）は、以下のようにして示される：

等式（１５）

【０１５２】

【数１８】

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$$Spleen=[2.25-0.004Plt_{Pre}]\geq 1$$

等式（１４）および（１５）に基づいて、このユーティリティー機能は、以下のようにして、Ｄｅｐｌｅｔｉｏｎを誘導する：

等式（１６）

【０１５３】

【数１９】

$$Depletion=\frac{100,000Yld}{Spleen\times DonVol}$$

（Ｃ．リアルタイム手順の改良）

オペレータは、この手順の開始時にて、どのドナーについても、常に現在の血小板プレカウントＰｌｔPreを知っている訳ではない。ユーティリティー機能Ｆ１は、初期設定パラメータ下にて、このシステムを起動させるか、または先の手順から評価する。ユーティリティー機能Ｆ１は、この手順中にて、後に、オペレータにより、実際の血小板プレカウントＰｌｔPreを入力させる。ユーティリティー機能Ｆ１は、新たに入力した値を反映するように、１セットの条件下にて決定した血小板収量を再計算する。ユーティリティー機能Ｆ１は、有効クリアード容量を計算するために現在の収量を使用し、次いで、その容量を使用して新たな現在の収量を計算して、脾臓流動化の血小板プレカウント依存特性を維持する。

【０１５４】

ユーティリティー機能Ｆ１は、現在の収量を使用して、以下のようにして、有効クリアード容量を計算する：

等式（１７）

【０１５５】

【数２０】

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$$ClrVol=\frac{100,000\times DonVol\times Yld_{Current}}{[DonVol-Prime-\frac{ACD}{3}+\frac{PPP}{2}]\times Pre_{old}-\frac{50,000\times Yld_{current}}{Spleen_{old}}}$$

ここで：

ＣｌｒＶｏｌは、クリアード血漿容量である。

【０１５６】

ＤｏｎＶｏｌは、等式（１３）に従って計算したドナーの循環血液容量である。

【０１５７】

$Yld_{Current}$は、現在の処理条件に基づいて等式（３）に従って計算した現在の血小板収量である。

【０１５８】

Ｐｒｉｍｅは、血液側感作容量（ｍｌ）である。

【０１５９】

ＡＣＤは、使用した抗凝血剤の容量（ｍｌ）である。

【０１６０】

ＰＰＰは、収集した低血小板血漿の容量（ｍｌ）である。

【０１６１】

Pre_{old}は、処理開始前に入力した処理前ドナー血小板数（ｋ／μｌ）である。

【０１６２】

$Spleen_{old}$は、Pre_{old}に基づいて等式（１６）を使って計算した脾臓流動化因子である。

【０１６３】

ユーティリティー機能Ｆ１は、以下のようにして、新たな現在の収量を計算するために、等式（１７）を使って計算したＣｌｒＶｏｌを使用する。

【０１６４】

等式（１８）

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【０１６５】

【数２１】

$$Yld_{New}=\left[\frac{DonVol\text{-}Prime\text{-}\frac{ACD}{3}+\frac{PPP}{2}}{DonVol+\frac{ClrVol}{2\times Spleen_{New}}}\right]\times\left[\frac{ClrVol\times Pre_{New}}{100,000}\right]$$

ここで：

ＰｒｅNewは、処理中に入力した修正ドナー血小板プレカウント（ｋ／μｌ）である。

【０１６６】

ＹｌｄNewは、修正ドナー血小板プレカウントＰｒｅNewを考慮に入れた新たな血小板収量である。

【０１６７】

ＣｌｒＶｏｌは、等式（１７）に従って計算したクリアード血漿容量である。

【０１６８】

ＤｏｎＶｏｌは、等式（１３）に従って計算したドナーの循環血液容量であり、等式（１７）のものと同じである。

【０１６９】

Ｐｒｉｍｅは、血液側感作容量（ｍｌ）であり、等式（１７）のものと同じである。

【０１７０】

ＡＣＤは、使用した抗凝血剤の容量（ｍｌ）であり、等式（１７）のものと同じである。

【０１７１】

ＰＰＰは、収集した低血小板血漿の容量（ｍｌ）であり、等式（１７）のものと同じである。

【０１７２】

ＳｐｌｅｅｎNewは、ＰｒｅNewに基づいて等式（１５）を使って計算した脾臓

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流動化因子である。

【０１７３】

（Ｄ．残りの手順の時間）

ユーティリティー機能Ｆ２はまた、以下のようにして、残りの収集時間（ｔｒｅｍ）（分）を計算できる：

等式（１９）

【０１７４】

【数２２】

$$t_{rem}=\frac{Vb_{rem}}{Q_b}$$

ここで：

Ｖｂｒｅｍは、処理すべき残留容量であり、これは、現在の処理条件に基づいて、等式（１９）を使って計算される。

【０１７５】

Ｑｂは、全血の流速であり、これは、ユーザーにより設定されるか、またはそうでなければ制御装置１８により誘導されるかのいずれかである。

【０１７６】

（Ｅ．血漿の収集）

ユーティリティー機能Ｆ２は、以下のようにして、血漿収集容量（ＰＰＰ$_{Goal}$、ｍｌ）を誘導するための種々の血漿収集要件を加える：

等式（２０）

【０１７７】

【数２３】

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$$PPP_{Goal}=PPP_{PC}+PPP_{Source}+PPP_{Reinfuse}+PPP_{Waste}+PPP_{CollCham}$$

ここで：

ＰＰＰPCは、ＰＣ産物から選択される低血小板血漿の容量であり、これは、２５０ｍｌの典型的な初期設定値を有することができるか、またはそうでなければ、現在の処理条件に基づいて、制御装置１８により計算できる。

【０１７８】

ＰＰＰSourceは、血漿源として収集用に選択される低血小板血漿の容量である。

【０１７９】

ＰＰＰWasteは、種々の処理目的のために蓄積するように選択された低血小板血漿の容量（初期設定値＝３０ｍｌ）である。

【０１８０】

ＰＰＰCollChamは、血漿収集チャンバの容量（初期設定値＝４０ｍｌ）である。

【０１８１】

ＰＰＰReinfuseは、処理中に再注入する低血小板血漿の容量である。

【０１８２】

（Ｆ．血漿収集速度）

ユーティリティー機能Ｆ２は、以下のようにして、血漿収集速度（QPPP）（ｍｌ／分）を計算する：

等式（２１）

【０１８３】

【数２４】

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$$Q_{PPP}=\frac{PPP_{Goal}-PPP_{Current}}{t_{rem}}$$

ここで：

ＰＰＰGoalは、所望の低血小板血漿の収集容量（ｍｌ）である。

【０１８４】

ＰＰＰCurrentは、収集した低血小板血漿の現在の容量（ｍｌ）である。

【０１８５】

ｔremは、現在の処理条件に基づいて等式（１９）を使って計算した収集残留時間である。

【０１８６】

（Ｇ．見込み全ＡＣ用途）

ユーティリティー機能Ｆ２はまた、以下のようにして、処理中に使用することが予想される抗凝血剤の全容量（ＡＣＤEnd）を計算できる：

等式（２２）

【０１８７】

【数２５】

$$ACD_{End}=ACD_{Current}+\frac{Q_b\times t_{rem}}{1+AC}$$

ここで：

ＡＣＤCurrentは、使用した抗凝血剤の現在の容量（ｍｌ）である。

【０１８８】

ＡＣは、選択した抗凝血剤の割合である。

【０１８９】

Q_bは、全血の流速であり、これは、現在の処理条件に基づいて、ユーザーにより設定されるか、またはそうでなければ制御装置１８により計算されるかのい

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ずれかである。

【０１９０】

ｔｒｅｍは、現在の処理条件に基づいて等式（１９）を使って計算した収集残留時間である。

【０１９１】

本発明の種々の特徴は、上記の特許請求の範囲で述べている。

【０１９２】

【図面の簡単な説明】

【図１】

図１は、オンライン血液処理システムの概略図である。

【図２】

図２は、図１で示した血液処理システムの操作を管理する制御装置の概略図である。

【図３】

図３は、図１で示した血液処理システムの概略図であり、このシステムは、非同時収集モード中にドローサイクルを実行するように、この制御装置で調整される。

【図４】

図４は、図１で示した血液処理システムの概略図であり、このシステムは、非同時収集モード中にリターンサイクルを実行するように、この制御装置で調整される。

【図５】

図５は、図１で示した血液処理システムの概略図であり、このシステムは、非同時収集モードを実行するように、この制御装置で調整される。

【図６】

図６は、図１で示した血液処理システムの概略図であり、このシステムは、血液容量トリミング機能を実行するように、制御装置で調整される。

【図７】

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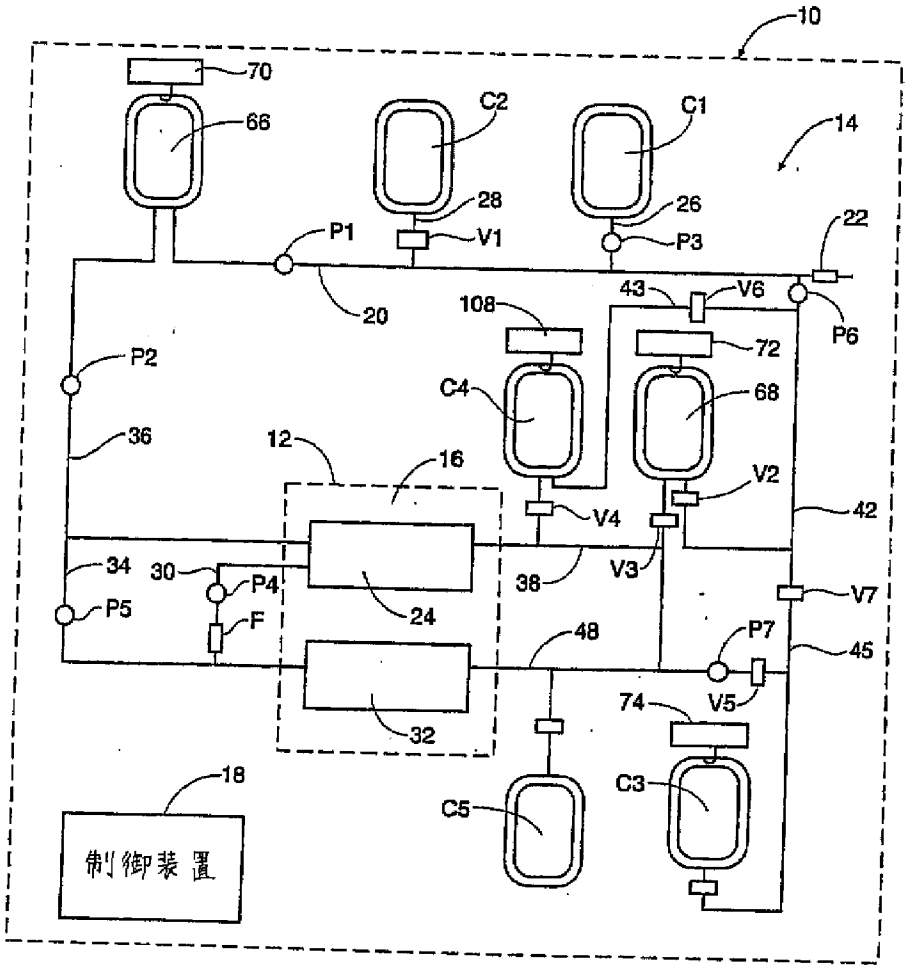
図７は、血液収集セットの正面図であり、これは、使用中にて、図１で示したシステムで収集した後の赤血球を、保存前にさらに処理するために受容する。

【図１】



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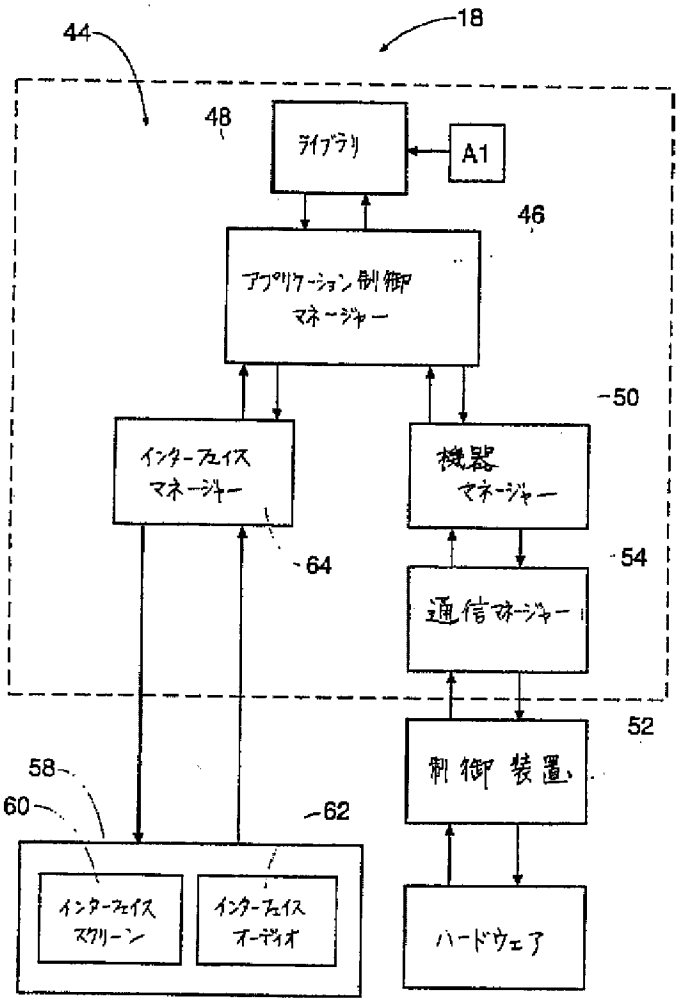
【図２】



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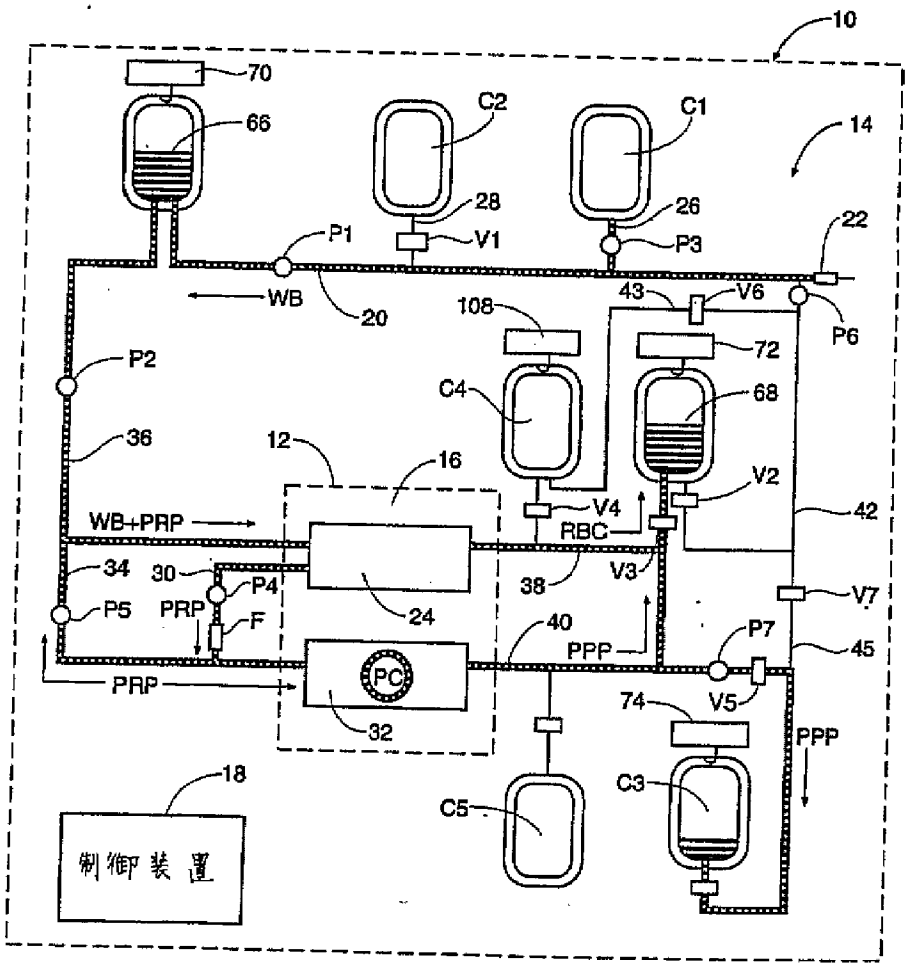
【図３】



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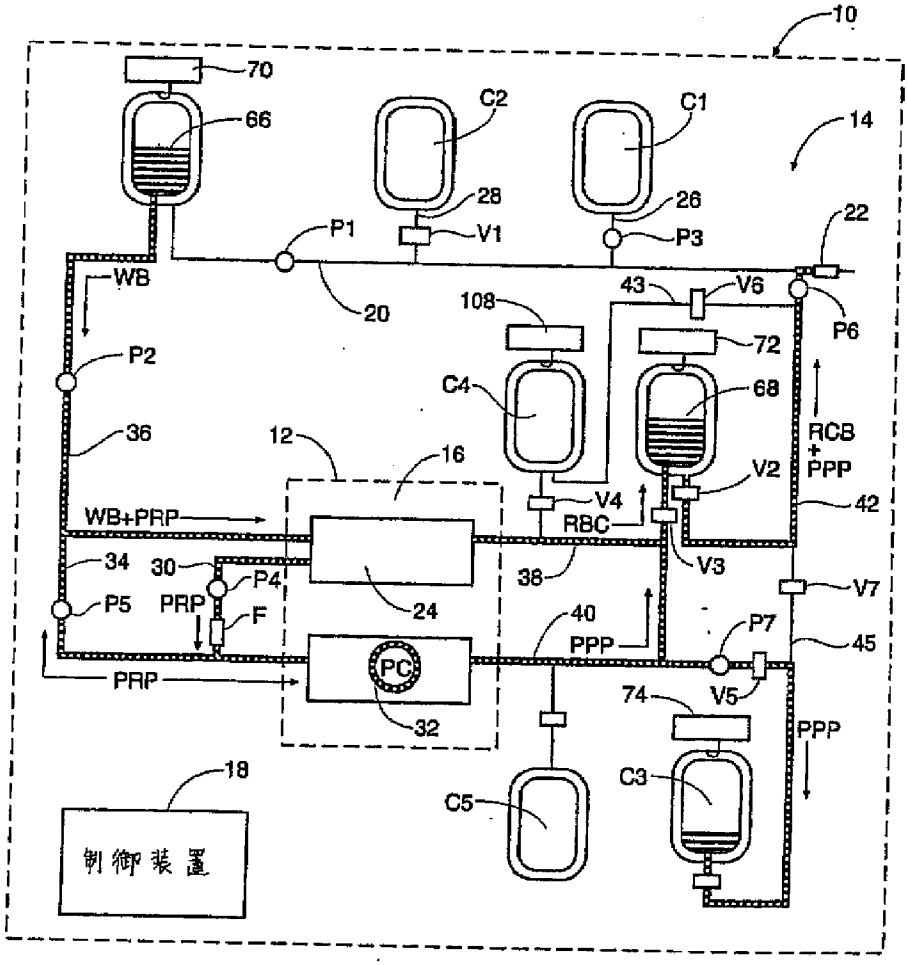
【図４】



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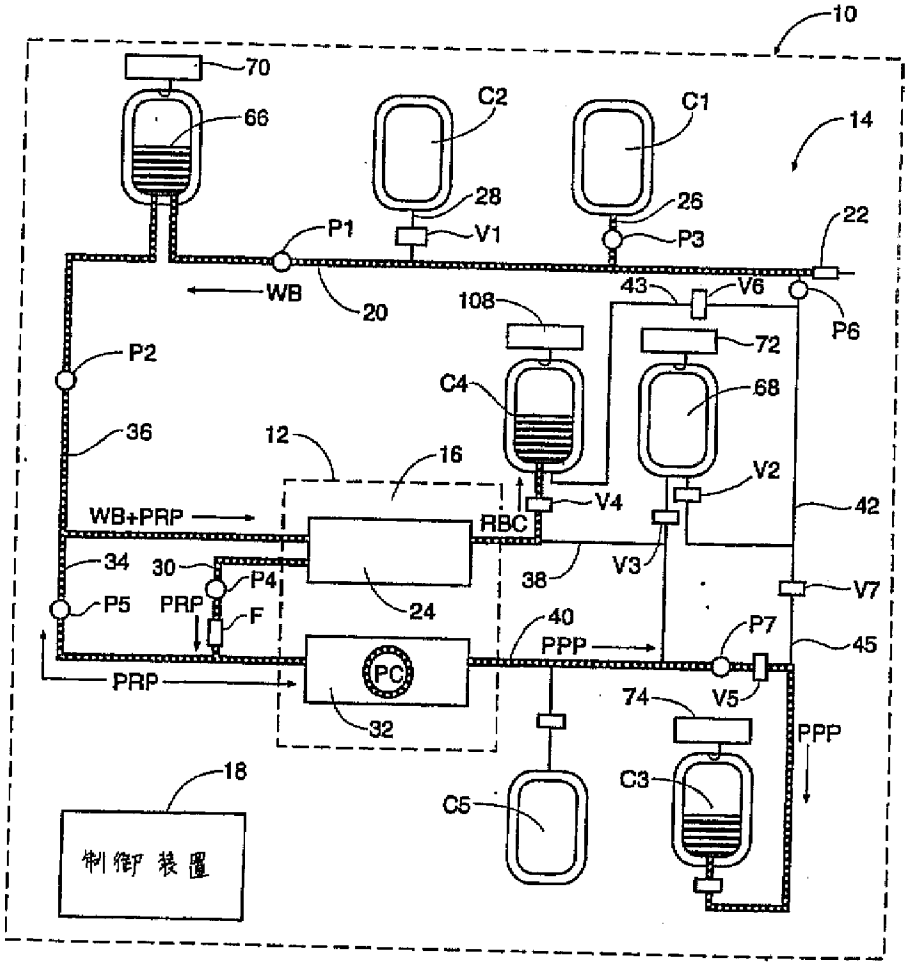
【図５】



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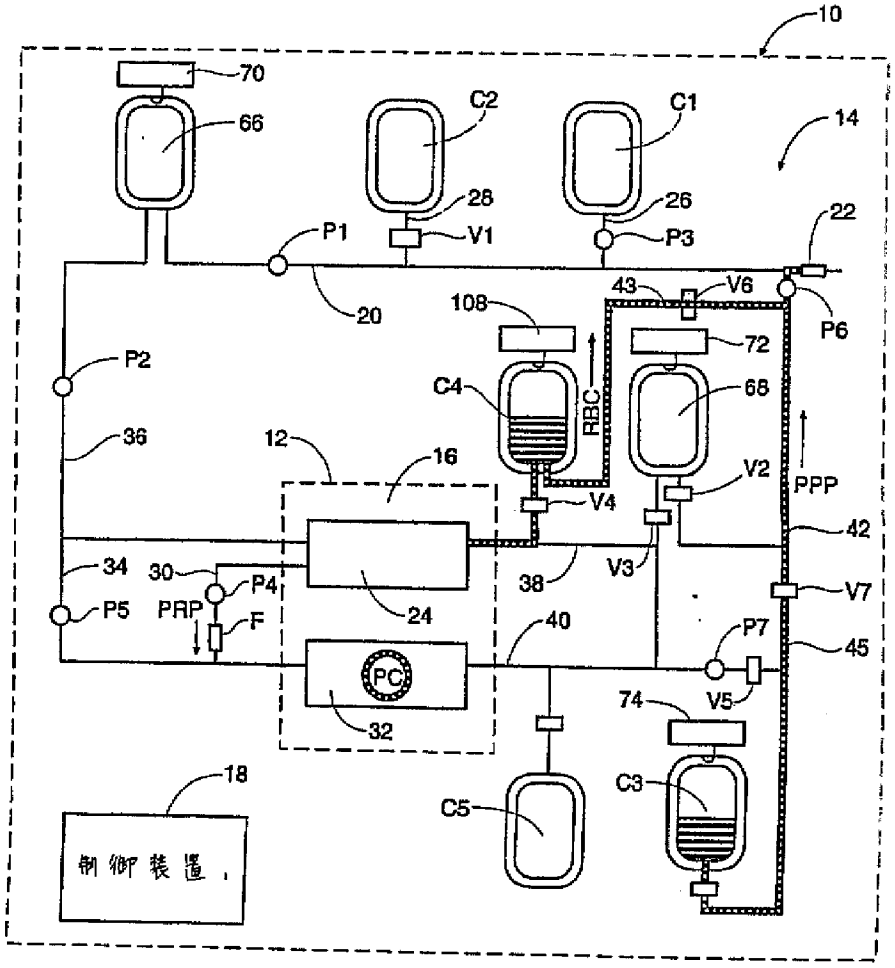
【図６】



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【図７】

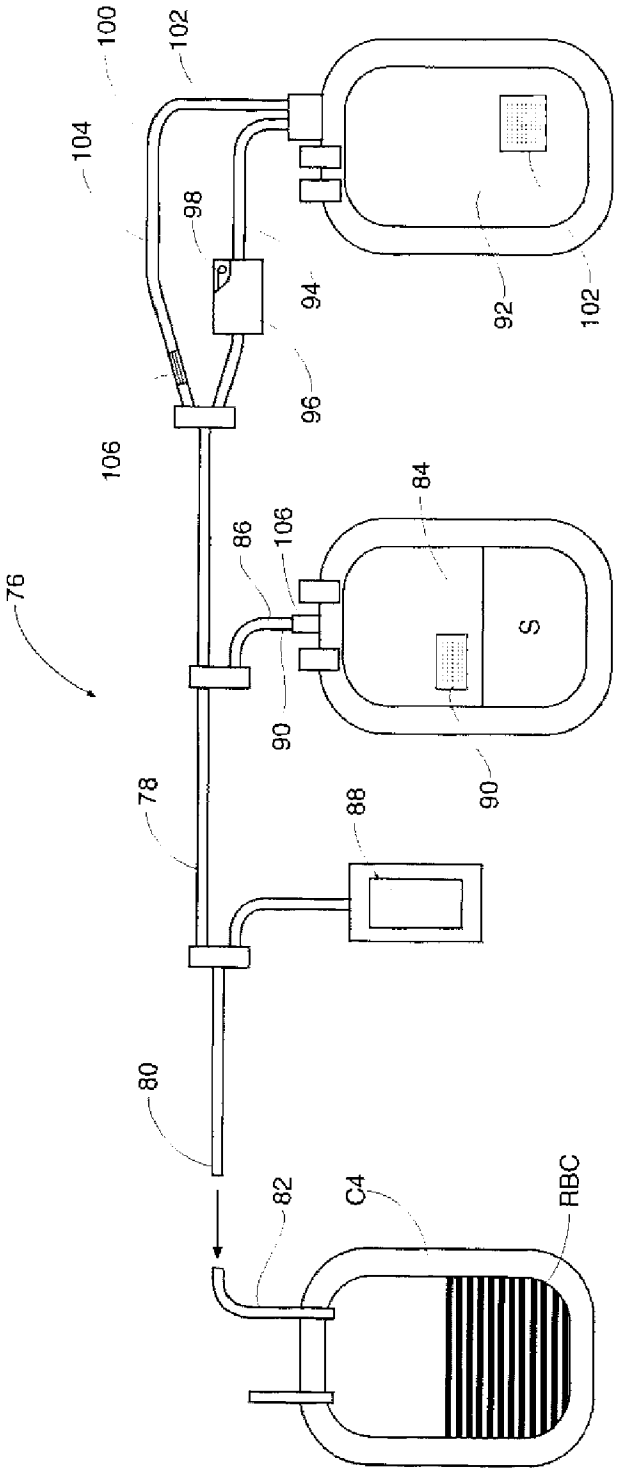

Fig. 7

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【国際調査報告】

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/28206

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61M 37/00; B01D 33/15; C02F 1/68
US CL : 604/4.01, 6.09, 6.02; 210/767, 782
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 604/4.01, 5.01-5.04, 6.01-6.05, 6.07, 6.09, 6.15, 6.16; 210/767, 782, 651, 85, 88, 109, 739, 745

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,730,883 A (Brown) 24 May 1998 (24.05.1998) entire document.	1-6, 10-16
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Y		7-9, 17-21
Y	US 5,849,203 A (Brown et al.) 15 December 1998 (15.12.1998) entire document.	1-23
A,P	US 6,051,147 A (Bischof) 18 April 2000 (18.04.2000) entire document.	1-23
A,P	US 6,071,421 A (Brown) 06 June 2000 (06.06.2000) entire document.	1-23
X,P	US 6,071,413 A (Brown et al.) 06 June 2000 (06.06.2000) entire document.	1-23

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 January 2001 (29.01.2001)	22 MAR 2001
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Angie Sykes Telephone No. (703) 308-0858

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SYSTEM AND METHOD FOR COLLECTING PLATELETS AND ANTICIPATING PLASMA RETURN

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Classification: - international: *A61M37/00*
- cooperative: **A61M1/0272 (EP)**; **A61M1/3603 (EP)**; **A61M1/3696 (EP)**; **A61M1/38 (EP)**; A61M2202/0415 (EP); A61M2202/0427 (EP)

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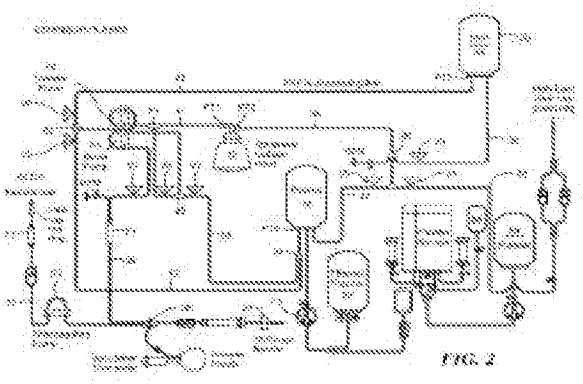
Abstract of WO2012091720 (A1)



A blood processing system for collecting plasma reduced platelets and anticipating plasma return includes a venous access device, a blood component separation device, a first return line, a recirculation line, and a second return line. The venous access device draws whole blood from a subject and returns blood components to the subject using a first pump. The blood component separation device separates the drawn blood into a first blood component and a second blood component, and sends the first blood component to a first blood component bag. The first return line fluidly connects the venous-access device and the blood component separation device. The recirculation line connects the first blood component container and the separation device. The second return line fluidly connects the first blood component container and the first return line and is

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configured to return the first blood component within the first blood container to the subject.

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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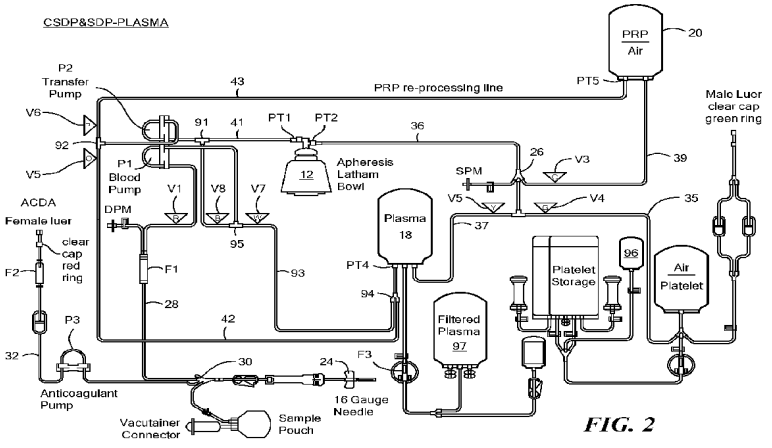

FIG. 2

(57) Abstract: A blood processing system for collecting plasma reduced platelets and anticipating plasma return includes a venous access device, a blood component separation device, a first return line, a recirculation line, and a second return line. The venous access device draws whole blood from a subject and returns blood components to the subject using a first pump. The blood component separation device separates the drawn blood into a first blood component and a second blood component, and sends the first blood component to a first blood component bag. The first return line fluidly connects the venous-access device and the blood component separation device. The recirculation line connects the first blood component container and the separation device. The second return line fluidly connects the first blood component container and the first return line and is configured to return the first blood component within the first blood container to the subject.

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System and Method for Collecting Platelets and Anticipating Plasma Return

Technical Field

The present invention relates to systems and methods for blood processing and blood component collection, and particularly to systems and methods for collecting platelets and anticipating plasma return.

Background Art

Apheresis is a procedure in which individual blood components can be separated and collected from whole blood temporarily withdrawn from a subject. Typically, whole blood is withdrawn through a needle inserted into a vein of the subject's arm and into a cell separator, such as a centrifugal bowl. Once the whole blood is separated into its various components, one or more of the components can be removed from the centrifugal bowl. The remaining components can be returned to the subject along with optional compensation fluid to make up for the volume of the removed component. The process of drawing and returning continues until the quantity of the desired component has been collected, at which point the process is stopped. A central feature of apheresis systems is that the processed but unwanted components are returned to the donor. Blood components separated may include, for example, a high density component such as red blood cells, an intermediate density component such as platelets or white blood cells, and a lower density component such as plasma.

Among various blood component products obtainable through apheresis, the demand for plasma reduced platelet products is rapidly growing. This is particularly because, with the improvement in cancer therapy, there is a need to administer more and more platelets to patients with lowered hemopoietic function, but the same patients may not need to be transfused with the plasma used to suspend platelets. Platelets are fragments of a large cell located in the marrow called a megakaryocyte and primarily contribute to hemostasis by performing aggregation function. Platelets also have a role in

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tissue healing. Normal platelet counts in adults are 150,000-400,000/mm^3. Platelet counts under 20,000/mm^3 can cause various troubles such as spontaneous bleeding.

Platelets have a short half-life of 4-6 days and the number of donors is limited. Therefore, in producing plasma reduced platelet products, it is important to harvest platelets from the whole blood supplied by a donor at a maximum yield and in a required amount. Further, it is known that the contamination of plasma reduced platelet product by white blood cells can lead to serious medial complications, such as GVH reactions. Therefore, it is also very important to keep the level of contamination by white blood cells as low as possible, while efficiently collecting platelets. To this end, various techniques have been developed. For example, using "surge" technology, after whole blood is collected and concentrically separated within a centrifuge into higher density, intermediate density and lower density components and plasma is harvested (so-called "draw" step), plasma is supplied through the centrifuge at a surge flow rate (e.g., a flow rate that increases with time). By performing the surge, platelets can be preferentially displaced from the intermediate density components (which exist as a buffy coat mainly comprising a mixture of platelets and white blood cells), and plasma reduced platelet products can be produced at an increased yield.

Instead of using surge technology, the platelet layer can also be extracted from the centrifuge by means of a layer "push" in which anticoagulated whole blood is introduced into the bowl until the platelet layer is pushed out, or by using a combination of surge and push methodologies. After harvesting a desired component or components, the residual blood components mostly comprising red blood cells and citrated plasma are returned to the donor (so-called "return" step).

As mentioned above, in many blood apheresis procedures and applications, unwanted components (e.g., the components that are not collected) are returned to the donor. In addition to contamination concerns (e.g., contamination, particulates, etc. being returned to the donor), the comfort of the subject must be taken into consideration. For example, returning citrated plasma to the subject too quickly or returning too much citrated plasma to the subject at one time can cause significant discomfort to the patient. Additionally, care must be taken to limit the volume of fluid outside of the body (e.g.,

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extra-corporeal volume) and/or the reduction of fluid in the body (e.g., intra-vascular deficit).

Summary of the Invention

In accordance with one embodiment of the invention, a method for collecting plasma reduced platelets and anticipating plasma return is presented. Whole blood is first drawn from the donor, anticoagulated, and introduced into a separation chamber. The separation chamber separates the anticoagulated whole blood into a number of blood components. The method then transfers plasma separated from the anticoagulated whole blood to a plasma container, and returns a first volume of the plasma from the plasma container back to the donor. The method then repeats the drawing, anticoagulating, introducing, and transferring steps to fill the separation device with additional anticoagulated whole blood.

Once the anticoagulated whole blood is introduced into the separation chamber (e.g., to fill the chamber), the method extracts platelet rich plasma ("PRP") from the separation chamber (e.g., using a surge elutriation method and/or surging with plasma) and into a PRP container. The method may then return the blood components remaining within the separation chamber to the donor and repeat the drawing, anticoagulating, and introducing steps to, once again, partially fill the separation device with anticoagulated whole blood. Once the separation device is partially filled, the method may then reintroduce PRP from the PRP container into the separation chamber, transfer plasma from the separation chamber to the plasma container, and reprocess the reintroduced PRP to create an enlarged layer of platelets within the separation device.

In accordance with some embodiments, the method may anticipate plasma return and return plasma within the plasma container to the donor while reintroducing the PRP into the separation chamber and/or reprocessing the PRP. The method may then, once again repeat the drawing, anticoagulating, and introducing steps to fill the separation chamber, remove the enlarged layer of platelets within the separation device using a surge elutriation method such that the platelets are transferred to a platelets container. The method may then return the blood components remaining within the separation chamber to the donor.

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In accordance with related embodiments, the method may also return plasma from the plasma container to the donor during dead times (times during which current apheresis procedures neither draw nor return blood or blood components to the donor). Additionally, the method may calculate an extra-corporeal volume and/or an intra-vascular deficit, and the first volume of plasma returned to the donor may be based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

In accordance with another embodiment of the present invention, a system for collecting plasma reduced platelets and anticipating plasma return includes a venous access device, a blood component separation device, a first return line, a recirculation line, and a second return line. The venous access device is configured to draw a first volume of whole blood from a subject and return blood components to the subject using a first pump. The blood component separation device (e.g., a centrifuge bowl) separates the drawn blood into a first blood component (e.g., plasma) and a second blood component (e.g., platelets), and is configured to send the first blood component to a first blood component bag and the second blood component to a second blood component bag.

The first return line fluidly connects the venous-access device and the blood component separation device and is configured to return blood components remaining in the separation device to the subject. The recirculation line connects the first blood component container and the separation device. The second return line fluidly connects the first blood component container and the first return line, and is configured to return the first blood component within the first blood container to the subject. The first blood component within the first blood component container may also be reintroduced into the separation chamber through the recirculation line and a recirculation pump.

The first pump may be used to return the first blood component within the first blood component container, and the blood components remaining in the separation device to the subject. The separation device may also separate the whole blood into a third blood component (e.g., red blood cells) in addition to the first and second blood components, and the blood components remaining in the separation device may include the third blood component.

In some embodiments, the second blood component may be removed from the separation device using a surge elutriation method. The surge elutriation method includes

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reintroducing the first blood component into the blood component separation device through the recirculation line at an increasing rate until the second blood component is removed from the blood component separation device. The second blood component may be platelets and may be reintroduced into the blood component separation device after a predetermined amount of platelets is collected within the second blood component container so as to extract a plasma reduced platelet product from the separation device.

The system may also include an anticoagulant line and a reintroduction line. The anticoagulant line may be connected to an anticoagulant source, and may introduce anticoagulant into the drawn blood. The reintroduction line may fluidly connect the second blood component bag and the blood component separation device. The second blood component within the second blood component bag may be reintroduced into the blood component separation device when a second volume of whole blood is withdrawn from the subject to create an enlarged layer of the second blood component within the blood component separation device. The enlarged layer of second blood component may be removed from the blood component separation device using a surge elutriation method.

The system may return the first blood component to the subject as the second blood component is reintroduced into the blood component separation device and/or during dead times. The system may also include a controller that calculates at least one of an extra-corporeal volume and an intra-vascular deficit. The system may then return a volume of first blood component via the second return line based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

In accordance with still further embodiments of the present invention, a system for collecting plasma reduced platelets may include (1) means for drawing a first volume of whole blood from a subject and returning blood components to the subject, (2) a blood component separation means for separating the drawn blood into a first blood component and a second blood component, (3) a first return means fluidly connecting the means for drawing a first volume of whole blood and the blood component separation means and for returning blood components remaining in the separation means to the subject, (4) a recirculation means connecting the second blood component container and the separation means, and (5) a second return means fluidly connecting the first blood component

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container and the first return means. The blood component separation means may be configured to send the first blood component to a first blood component bag and the second blood component to a second blood component bag. The recirculation means may reintroduce the second blood component within the second blood component container into the separation means. The second return means may be configured to return the first blood component within the first blood container to the subject.

The means for drawing whole blood may include a first pump that is configured to return the first blood component within the first blood component container to the subject. The first pump may also return the blood components remaining in the separation means to the subject.

In accordance with additional embodiments, the system may also include a controller for controlling the flow of fluids through the system. The controller may repeatedly draw whole blood from the donor into the separation means, extract first and second blood components from the separation means, return first blood components to the subject using the second return means, and return remaining components in the separation means back to the subject using the first return means. Additionally, after a predetermined volume of second blood component has been sequestered in the second blood component container, the second blood component from the second blood component container may be reintroduced into the separation means. The controller may also calculate an extra-corporeal volume and/or an intra-vascular deficit, and the amount of plasma returned using the second return means may be based (at least in part) on the extra-corporeal volume and/or an intra-vascular deficit.

Moreover, the system may also include means for introducing anticoagulant into the drawn whole blood, and a reintroduction means fluidly connecting the second blood component bag and the blood component separation means. The second blood component within the second blood component bag may be reintroduced into the blood component separation means when a second volume of whole blood is withdrawn from the subject to create an enlarged layer of the second blood component within the blood component separation means. The enlarged layer of second blood component may be removed from the blood component separation means using a surge elutriation method. Additionally or alternatively, the second blood component may be platelets and may be reintroduced into

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the blood component separation means after a predetermined amount of platelets is collected within the second blood component container so as to extract a plasma reduced platelet product from the separation means.

In accordance with additional embodiments, a method for collecting plasma reduced platelets and anticipating plasma return is presented. Whole blood is first drawn from a source, anticoagulated, and introduced into a separation chamber. The separation chamber separates the anticoagulated whole blood into a number of blood components. The method then transfers plasma separated from the anticoagulated whole blood to a plasma container, and returns a first volume of the plasma from the plasma container to the source. The method then repeats the drawing, anticoagulating, introducing, and transferring steps to fill the separation device with additional anticoagulated whole blood.

Once the anticoagulated whole blood is introduced into the separation chamber (e.g., to fill the chamber), the method extracts platelet rich plasma ("PRP") from the separation chamber (e.g., using a surge elutriation method and/or surging with plasma) and into a PRP container. The method may then return the blood components remaining within the separation chamber to the source, and repeat the drawing, anticoagulating, and introducing steps to, once again, partially fill the separation device with anticoagulated whole blood. Once the separation device is partially filled, the method may then reintroduce PRP from the PRP container into the separation chamber, transfer plasma from the separation chamber to the plasma container, and reprocess the reintroduced PRP to create an enlarged layer of platelets within the separation device.

In accordance with some embodiments, the method may anticipate plasma return and return plasma within the plasma container to the source while reintroducing the PRP into the separation chamber and/or reprocessing the PRP. The method may then, once again repeat the drawing, anticoagulating, and introducing steps to fill the separation chamber, remove the enlarged layer of platelets within the separation device using a surge elutriation method such that the platelets are transferred to a platelets container. The method may then return the blood components remaining within the separation chamber to the source.

In accordance with related embodiments, the method may also return plasma from the plasma container to the source during dead times. Additionally, the method may

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calculate an extra-corporeal volume and/or an intra-vascular deficit, and the first volume of plasma returned to the source may be based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

In still further embodiments, a method for collecting plasma reduced platelets may include drawing whole blood from a source, introducing anticoagulant into the whole blood drawn from the source, and introducing the anticoagulated whole blood into a separation chamber. The separation chamber, in turn, may separate the anticoagulated whole blood into a number of blood components. The method may then transfer plasma separated from the anticoagulated whole blood to a plasma container, return a first volume of the plasma from the plasma container back to the source, and repeat the above steps. Additionally, the method may also extract platelet rich plasma from the separation chamber into a platelet rich plasma container, and remove the remaining blood components from the separation chamber.

Brief Description of the Drawings

The foregoing features of the invention will be more readily understood by reference to the following detailed description, taken with reference to the accompanying drawings, in which:

Fig. 1 is a schematic diagram of an apheresis machine, in accordance with one embodiment of the invention;

Fig. 2 is a schematic diagram of a disposable system for use with the machine of Fig. 1, in accordance with one embodiment of the invention;

Fig. 3 is a side view of a centrifuge bowl for use with the machine of Fig. 1, in accordance with one embodiment of the invention; and

Fig. 4 is a flow chart depicting a method for collecting plasma reduced platelets from a donor and anticipating plasma return, in accordance with one embodiment of the invention.

Detailed Description of Specific Embodiments

Referring to Figs. 1 and 2, an apheresis apparatus 10 uses a blood component separation device, such as a standard Latham type centrifuge 11 for separating

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anticoagulated whole blood into its constituent components, as described in US Patent No. 3,145,713, which is hereby incorporated by reference. Other types of separation chambers and devices may be used, such as, without limitation, an integral blow-molded centrifuge bowl, as described in U.S. Pat. Nos. 4,983,156 and 4,943,273, which are hereby incorporated by reference. The centrifuge 11 includes a rotating bowl 12 and stationary input and output ports PT1 and PT2 that are typically closely coupled to the bowl interior by a rotary seal 74 (see Fig. 3). The input port PT1 of the centrifuge 11 is in fluid communication with a venous access device 24 (e.g., a phlebotomy needle) via a blood micro-aggregate filter F1, a tube 28 and a Y-connector 30 when a valve V1 is open. The venous access device 24 may be replaced with a whole blood bag (not shown) in case the whole blood is to be first pooled and then supplied. The tube 28 has compatibility with blood, as is all the tubing in the apparatus 10. The outlet port PT2 of the centrifuge 11 is selectively coupled by a tube 36, a valve V2 and a tube 37 with a first container 18 labeled plasma suspended from a weight scale 33. A second container 20 labeled platelets is selectively coupled via the tube 36, a valve V3 and a tube 39 to the outlet port PT2. Additionally, a third container 22 labeled platelet storage is selectively coupled via the tube 36, a valve V4 and a tube 35 to the outlet port PT2. Both second container 20 and third container 22 may also be suspended by weight scales 67 and 77, respectively. As discussed in greater detail below, some embodiments may also include a tube 93 fluidly connected to the plasma container 18 at one end (via connector 94) and tube 41 at the other end (e.g. via connector 95). The tube 93 may be used to return citrated plasma within the plasma container 18 to the donor during dead times and/or while processing the whole blood within the centrifuge 11.

A bag or container 16 for storing an anticoagulant is in fluid communication with the venous access device/phlebotomy needle 24 via a bacteria filter F2, a tube 32 and the Y-connector 30. The bacteria filter F2 prevents any bacteria in the anticoagulant (ACD) container 16 from entering the system. Containers 16, 18, 20, and 22 are preferably plastic bags made of a blood compatible material. Peristaltic pumps P1, P2 and P3, together with the valves V1, V2, V3, and V4 control the direction and duration of flow through the apparatus 10 in response to signals generated by a line sensor 14, a donor pressure monitor (DPM) M1, a system pressure monitor (SPM) M2 and air detectors D1,

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D2 and D3. The air detectors D1, D2 and D3 detect the absence or presence of fluid. The pressure monitors M1 and M2 monitor pressure levels within the apparatus 10. The line sensor 14 is an optical sensor and detects the presence of blood components passing through the line sensor 14 from the output port PT2.

In initial operation, the pumps P1 and P3 are energized to prime the tube 28 of the apparatus 10 with the anticoagulant from the container 16. The anticoagulant passes through the filter F2 and Y-connector 30 before reaching the air detector D1. The air detector D1 senses the presence of the anticoagulant at D1 and terminates the anticoagulant priming operation. During the priming operation, the valve V2 is open and sterile air displaced from bowl 12 by the anticoagulant enters the top port PT3 of the plasma container 18. The venous access device 24 is then inserted into the donor and the draw step is ready to be commenced.

Fig. 4 is a flowchart depicting a method for collecting blood components (e.g., platelets) from a subject and anticipating return of citrated plasma to the subject, in accordance with one embodiment of the invention. During draw step 401, whole blood is drawn from the subject, typically at a rate of about 80 ml/min. and mixed with the anticoagulant using the pumps P1 and P3 (Step 402) (referring back to Figs. 1-2). The pump P3 mixes the anticoagulant from the container 16 with the whole blood drawn from the subject or a bag in which it is pooled. The valve V1 is open, allowing the anticoagulated whole blood to pass through the tube 28 and blood filter F1 before being pumped into the separation device 12 through the inlet port PT1.

The whole blood is introduced into the bottom of the separation device 12 through a feed tube (not shown), step 403 of Fig. 4. The ratio of the anticoagulant to whole blood is typically about 1:10. The operation of each of the pumps and valves in the apheresis apparatus 10 can be performed in accordance with desired protocols under the control of a controller (not shown), which may be, for example, a microprocessor.

Referring to FIG. 3, the centrifuge 11 has the fixed inlet port PT1 and the fixed outlet port PT2. The rotary seal 74 fluidly couples the stationary inlet port PT1 to the lower interior portion of the bowl 12, and the outlet port PT2 to an upper portion of the bowl interior for collecting separated fractions. A core 72 occupies a volume coaxial

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with the interior of bowl 12 and provides a separation region between the wall of the core 72 and the outer bowl wall 70.

As the bowl 12 is rotated, centrifugal forces separate the anticoagulated whole blood admitted into the bottom of the bowl into red blood cells (RBC), white blood cells (WBC), platelets and plasma. The number of rotations of the bowl 12 can be selected, for example, within a range of 4,000 to 6,000 rpm, and is typically 4,800 rpm. The blood is separated into different fractions in accordance with the component densities. The higher density component, i.e., RBC 60, is forced to the outer wall 70 of the bowl 12 while the lower density plasma 66 lies nearer the core 72. A buffy coat 61 is formed between the plasma 66 and the RBC 60. The buffy coat 61 is made up of an inner layer of platelets 64, a transitional layer 68 of platelets and WBC, and an outer layer of WBC 62. The plasma 66 is the component closest to the outlet port from the separation region and is the first fluid component displaced from the bowl 12 via the outlet port PT2 as additional anticoagulated whole blood enters the bowl 12 through the inlet port PT1. As the plasma 66 is displaced from the bowl 12, it is transferred to the plasma container 18 through lines 36 and 37 (Step 404 of Fig. 4).

Returning to Fig. 1, the displaced plasma passes through the line sensor 14, the tube 36, a 3-way T-connector 26, and the valve V2 (in the open position) and enters the first container 18. The plasma entering the first container 18 is drawn from the container 18 by the pump P2 via tube 42, valve V5 (in the open position), Y-connector 92 and tube 40 from the lower port PT4 and is recirculated into the bowl 12 through the inlet port PT1 via Y-connector 91 and line 41. The recirculated plasma dilutes the anticoagulated whole blood entering the bowl 12 and allows the blood components to separate more readily. An optical sensor 21 is applied to a shoulder portion of the bowl 12 for monitoring each layer of the blood components as they gradually and coaxially advance toward the core 72 from the outer wall 70 of the bowl 12. The optical sensor 21 may be mounted in a position at which it can detect the buffy coat reaching a particular radius, and the steps of drawing the whole blood from the donor 401 and introducing the whole blood into the bowl 402 may be terminated in response to the detection.

The amount of whole blood processed by the bowl 12 may be varied in response to at least one characteristic associated with the whole blood, such as the hematocrit

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value, the number of platelets, the total amount of blood or the like of the whole blood, as described in copending U.S. patent application 09/392,880, filed September 9, 1999, entitled Apheresis Apparatus and Method for Producing Blood Products, which is hereby incorporated by reference. This variable control can be implemented under the control of a microcomputer, as aforementioned. Alternatively, each of them can be implemented manually.

As mentioned above, some embodiments of the present invention return plasma within the plasma container (e.g., citrated plasma) at various intervals during the apheresis process in order to anticipate plasma return and avoid returning a large volume at the end of the apheresis process (e.g., to improve patient comfort). To that end, the system 10 may pause the draw step (Step 401), and return some or all of the plasma contained within plasma container 18 to the donor. In particular, once the draw step (Step 401) is paused, the apheresis system 10 may reverse the direction of the draw/return pump P1, open valve V6, draw plasma from the plasma container 18 through outlet port PT4, and return the plasma to the patient/donor via lines 93 and 28.

The volume of plasma returned to the patient/donor during this step may depend upon a number of factors including, but not limited to the extra-corporeal volume ("ECV") and/or intra-vascular deficit ("IVD"). For example, the controller may calculate the ECV or IVD based upon data from previous cycles (e.g., previous cycles in a given apheresis procedure or cycles from a prior procedure), and determine if the ECV/IVD exceeds a predetermined percentage of estimated total blood volume ("TBV") (e.g., as estimated from donor characteristics such as gender, size, and weight). If the system 10 (e.g., the controller/microprocessor) determines that the ECV/IVD exceeds the predetermined percentage of TBV, then the system 10 may pause the draw (e.g., Step 401) and return plasma as discussed above. Additionally or alternatively, the system 10 may initiate the plasma return (Step 405) if the volume of plasma separated from the current cycle is equal to the volume of whole blood still to be drawn to complete the bowl filling. In order to preserve and/or improve blood separation during the plasma return step (Step 405), the centrifuge 11 may continue to spin and plasma may be circulated through the bowl 12 (e.g., using pump P2 and line 42).

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By pausing the draw step (Step 401) and initiating the anticipated plasma return step (Step 405), the system 10 is able to greatly reduce the ECV and IVD. Additionally, the anticipated plasma return process also ensures that the return of citrated plasma to the patient/donor occurs over multiple steps with a significant time interval (e.g., several minutes) between. As discussed above, this helps improve patient comfort and reduces the risks associated with returning citrated plasma to the patient/donor.

Once the plasma return step is complete, the system may continue to draw whole blood from the patient/donor (e.g., in order to complete bowl filling) (Step 406) and extract platelets from the separation chamber 11/bowl 12. The platelets are extracted from the bowl 12 into a container, step 407 of Fig. 4. When extracting the platelets from the bowl 12, various methodologies may be employed, including, without limitation, dwell, surge, and/or push methodologies. For illustrative purposes, platelet extraction based on a dwell and surge technique will now be described in detail.

After the whole blood has been introduced into the centrifuge 11, step 406 of Fig.4, the valve V1 is closed and the pump P1 is stopped so that blood is no longer drawn from the donor, and dwell is commenced. During the dwell, the pump P2 recirculates plasma 66 through the bowl 12 at a moderate rate (for example, about 100 ml/min. in Fig. 4) for about 20 to 30 seconds. At this flow rate, the buffy coat 61 is diluted by the plasma and widens but the platelets do not leave the bowl 12. The dilution of the buffy coat allows the heavier white blood cells to sediment to the outer side of the buffy coat, resulting in a better separation between the lighter platelets layer 64 and the heavier white blood cells layer 62. As a result, the transitional layer 68 is reduced. The dwell period also allows the flow patterns in the bowl 12 to stabilize and allows more time for microbubbles to leave the bowl 12 and be purged.

After dwell, the surge step is commenced. In the surge, the speed of the pump P2 is increased in 5-10 ml/min. increments to recirculate plasma until reaching a platelet surge velocity of about 200-250 ml/min. The platelet surge velocity is the velocity at which platelets can leave the bowl 12 but not red blood cells or white blood cells. The plasma exiting the bowl becomes cloudy with platelets and this cloudiness is detected by the line sensor 14. The line sensor 14 consists of an LED which emits light through blood components leaving the bowl 12 and a photo detector which receives the light after

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it passes through the components. The amount of light received by the photo detector is correlated to the density of the fluid passing through the line.

When platelets first start leaving the bowl 12, the line sensor output starts to decrease. The valve V3 is opened and the valve V2 is closed and the platelets are collected in container 20. Once the majority of the platelets are removed from the bowl 12, the fluid exiting the bowl becomes less cloudy. This lessening of cloudiness is detected by the line sensor 14, whereupon valve V3 is closed.

It is important to note that during any "dead" times (e.g., time during which whole blood is not being drawn from the patient/donor, any time during which the centrifuge 11 is stopped, etc), the system 10 may return plasma contained within the plasma bag 18 to the patient/donor. For example, while the system 10 removes/extracts the platelets from the centrifuge bowl 12 and/or during the dwell step described above, the system 10 may also return plasma contained within the container 18 to the patient/donor in a manner similar to that described above (e.g., by reversing the pump P1 and drawing the plasma through line 93.

If the plasma return occurs during the surge process (e.g., the recirculation of plasma through the bowl 12), both the draw/return pump P1 and the recirculation pump P2 may draw plasma from the plasma container 18 and both valves V5 and V7 may be open. The draw/return pump P1 may draw the plasma through tube 93 and the recirculation pump P2 may draw plasma through tube 42. To prevent the separate plasma flows from mixing and interfering with one another, valve V8 (Fig. 2), located between connectors 91 and 95 may be closed.

After the platelets have been collected, return step 409 (see Fig. 4) is initiated. During return step 409, the rotation of the bowl 12 is stopped and the remaining blood components in the bowl 12 are returned to the donor by reversal of rotation of the pump P1 via the venous access device 24 with the valve V1 open. The valve V2 is also opened to allow air to enter the centrifuge bowl during the return. The plasma from the container 18 dilutes the remaining blood components in the bowl 12. Namely, the pump P2 mixes the plasma with the returning components in the bowl 12 with the valve V2 open, diluting the returning red blood cells component with plasma to speed up the return time. When

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the remaining blood components in the bowl have been returned to the donor, the return step 409 is terminated.

Referring to Fig. 4, the steps of drawing whole blood from the donor (Step 401), introducing anticoagulant into the whole blood (Step 402), introducing the whole blood into a separation chamber (Step 403), transferring plasma to the plasma container 18 (Step 404), returning plasma to the patient/donor (Step 405), continuing whole blood draw (Step 406), extracting platelets from the separation chamber (Step 407), returning plasma (Step 408), and returning the remaining components back to the donor (Step 409), are repeated until a desired volume of platelets is sequestered in the container 20, step 410. Typically, steps 401-409 are repeated two to four times, with about 450-500 ml of whole blood processed per cycle. The sequestered platelet concentration is typically about 1.5 $x10^6/\mu L$.

The system may then re-process the platelets within container 20 by re-introducing the platelets (platelet rich plasma) in container 20 into the bowl 12, step 412 of Fig. 4. Reintroducing the platelets forms a layer of platelets that is several times larger than that obtained by processing only one cycle of whole anticoagulated blood. For example, in some embodiments, the platelet layer volume is approximately equal to the average volume of one cycle multiplied by the number of platelet sequestering cycles plus one. The platelets are drawn from port PT5 of container 20 by pump P2 via tube 43, valve V6 (in the open position), Y-connector 92, and tube 40, and input into bowl 12 through the inlet port PT1 via Y-connector 91 and line 41. To minimize contact between the platelets and bowl 12, the bowl 12 may be partly filled with anticoagulated whole blood drawn from the donor 401 prior to re-introduction of the platelets, step 411 of Fig. 4. The whole blood forms a cell bed at the periphery of the bowl 12 that serves as a buffer between the periphery of the bowl and the platelets, reducing platelet clumping. Additionally or alternatively, whole anticoagulated blood may be added to the separation chamber during platelet reintroduction so as to bring platelet layer towards the elutriation radius, or after platelet reintroduction for perfecting platelet separation and standardizing conditions of initiating platelet extraction.

It is worth noting that, if the platelets being reintroduced into the bowl 12 and reprocessed are in the form of platelet rich plasma ("PRP")(platelets suspended within

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plasma), the centrifugal forces within the bowl 12 will cause the PRP to abandon the suspended platelets, thereby freeing the plasma. This freed plasma will be displaced from the bowl 12 and sent to the plasma container 18 as additional fluid (e.g., additional PRP, plasma, anticoagulated whole blood, etc.) enters the bowl 12.

As the platelets are reprocessed to form the plasma reduced platelet product (discussed in greater detail below), the system 10 may, once again, return plasma within the container 18 to the patient/donor (Step 413). For example, as the platelets from container 20 are being reintroduced into the bowl 12, the system 10 may open valve V7 and use the draw/return pump P1 to draw plasma from port PT4 of container 18 through line 93, and return the plasma to the patient/donor through line 28 and the venous access device 24. The system 10 may then draw whole blood from the patient/donor and fill the bowl 12 with anticoagulated whole blood, step 414.

Using, for example, surge or push methodologies, the plasma reduced platelet concentrate is then extracted from the layer of platelets that now reside in bowl 12, step 415 of Fig. 4. The plasma reduced platelet product is sequestered in container 22 via line sensor 14, tube 36, 3-way T-connector 26 and valve V4 (in the open position). Platelet product concentration is typically in the range of $2.6x10^6/\mu L$ to $5.2x10^6/\mu L$, which is 2-3 times that of platelets sequestered when processing only one cycle of whole anticoagulated blood. Once the plasma reduced platelet concentrate is extracted from the bowl 12 and collected within container 22, the system 10 may then return any blood components remaining within the bowl 12 and any plasma still remaining within the plasma container 18, step 416 of Fig. 4.

It should be noted that the surge elutriation technique may use a variety of fluids other than plasma to extract the platelets and/or the reduced plasma platelet product from the separation chamber (e.g., saline solution may be used). Additionally, the platelets that are reintroduced into the separation chamber may be re-anticoagulated to prevent the platelets from coagulating and/or clumping. For example, the platelet collection bag 20 or the reduced plasma platelet product bag 22 may be pre-loaded with a quantity of anticoagulant so that the platelets and/or reduced plasma platelet product mix with the anticoagulant as they are drawn from the separation chamber. Additionally or alternatively, sufficient anticoagulant may be added as the whole blood is withdrawn

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from the subject such that enough anticoagulant is still present in the platelets prior to re-processing. In either scenario, the amount of anticoagulant added the whole blood and/or extracted platelets must be weighed against the safety of the subject. In particular, the amount of anticoagulant should be limited so as to prevent a large quantity of anticoagulant being returned to the subject.

It should also be noted that once the platelets and the reduced plasma platelet product are collected, a platelet preservative solution may be added to help preserve and store the platelets for later use. The preservative solution can be added to the platelets and platelet product after collection (e.g., from a separate bag or storage container 96), or the platelet collection bag 20 and the reduced plasma platelet product bag 22 may be pre-loaded with the additive solution.

By anticipating the total amount of plasma that will be returned to the donor and returning the plasma in multiple steps, various embodiments of the present invention are able to provide numerous advantages over the prior art. For example, by not returning all of the plasma at the end of the procedure, various embodiments of the present invention are able to greatly reduce patient discomfort and the risks associated with returning large volumes of citrated plasma. Additionally, by returning plasma during "dead" times, some embodiments of the present invention are able to reduce the overall procedure time, and the ECV/IVD at any given time during the procedure. Furthermore, because plasma may be returned during processing and the EVC/IVD is significantly reduced, various embodiments of the present invention do not need to return saline (or other compensation fluid) to the patient to reduce the ECV.

Although the embodiments described above discuss returning the plasma to the patient/donor, not all of the plasma needs to be returned. For example, some embodiments of the present invention may save a portion of the collected plasma. In such embodiments, the plasma may be filtered using F3 and stored within filtered plasma container 97.

If additional reduced plasma platelet product is required, each of the steps described above may now be repeated until a desired quantity of plasma reduced platelet product is collected. In various embodiments, plasma may be added to the plasma

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reduced platelet product so as to adjust the plasma reduced product to a predetermined volume or concentration.

Although the above embodiments are described as withdrawing whole blood from a patient/donor and returning unwanted components back to the donor, other embodiments of the present invention may be used for donor-free processing. For example, as discussed above, the venous access device 24 may be replaced with a whole blood bag (not shown) in cases in which the whole blood is to be first pooled and then supplied to the separation device 11. In such embodiments, the plasma from the plasma container 18 and the blood components remaining in the separation device 11 may be returned to one or more storage bags/containers (e.g., all into one container or into separate containers) or returned to the whole blood bag. Such embodiments would still have advantages over the prior art systems because of the greatly reduced processing time (e.g., because plasma is sent to the containers during dead times, etc.)

The described embodiments of the invention are intended to be merely exemplary and numerous variations and modifications will be apparent to those skilled in the art. All such variations and modifications are intended to be within the scope of the present invention.

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We claim:

1. A method for collecting plasma reduced platelets and anticipating plasma return comprising:

a) drawing whole blood from a donor;

b) introducing anticoagulant into the whole blood drawn from the donor;

c) introducing the anticoagulated whole blood into a separation chamber, the separation chamber separating the anticoagulated whole blood into a number of blood components;

d) transferring plasma separated from the anticoagulated whole blood to a plasma container;

e) returning a first volume of the plasma from the plasma container back to the donor;

f) repeating steps a through d;

g) extracting platelet rich plasma from the separation chamber into a platelet rich plasma container; and

h) returning the remaining blood components within the separation chamber to the donor.

2. A method according to claim 1 further comprising:

i) repeating steps a through c to partially fill the separation device with anticoagulated whole blood;

j) reintroducing platelet rich plasma from the platelet rich plasma container into the separation chamber;

k) transferring plasma from the separation chamber to the plasma container; and

l) reprocessing the reintroduced platelet rich plasma to create an enlarged layer of platelets within the separation device.

3. A method according to claim 2, further comprising

m) returning plasma from the plasma container to the donor while reprocessing the platelet rich plasma.

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4. A method according to claim 2, further comprising

m) returning plasma from the plasma container to the donor while reintroducing the platelet rich plasma into the separation chamber.

5. A method according to claim 2 further comprising:

m) removing the enlarged layer of platelets within the separation device using a surge elutriation method such that the platelets are transferred to a platelets container; and

n) returning the blood components remaining within the separation chamber to the donor.

6. A method according to claim 5, further comprising returning plasma from the plasma container to the donor during dead times.

7. A method according to claim 1, further comprising:

calculating at least one of an extra-corporeal volume and an intra-vascular deficit, the volume of plasma returned during step (e) being based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

8. A method according to claim 1, wherein extracting platelet rich plasma from the separation chamber includes extracting the platelet rich plasma by surge elutriation.

9. A method according to claim 8, wherein extracting the platelet rich plasma from the separation chamber by surge elutriation includes surging with plasma.

10. A system for collecting plasma reduced platelets and anticipating plasma return comprising:

a venous access device for drawing a first volume of whole blood from a subject and returning blood components to the subject using a first pump;

a blood component separation device for separating the drawn blood into a first blood component and a second blood component, the blood component separation device

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configured to send the first blood component to a first blood component bag and the second blood component to a second blood component bag;

a first return line fluidly connecting the venous-access device and the blood component separation device for returning blood components remaining in the separation device to the subject;

a recirculation line connecting the first blood component container and the separation device, wherein the first blood component within the first blood component container is reintroduced into the separation chamber through the recirculation line and a recirculation pump; and

a second return line fluidly connecting the first blood component container and the first return line and configured to return the first blood component within the first blood container to the subject.

11. A system according to claim 10, wherein the first pump returns the first blood component within the first blood component container to the subject.

12. A system according to claim 10, wherein the first pump returns the blood components remaining in the separation device to the subject.

13. A system according to claim 10, wherein the separation device is a centrifuge bowl.

14. A system according to claim 10, wherein the first blood component is plasma and the second blood component is platelets.

15. A system according to claim 10, wherein the separation device separates the whole blood into a third blood component in addition to the first and second blood components.

16. A system according to claim 15, wherein blood components remaining in the separation device includes the third blood component.

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17. A system according to claim 15, wherein the third blood component is red blood cells.

18. A system according to claim 10, wherein the second blood component is removed from the separation device using a surge elutriation method.

19. A system according to claim 18, wherein the surge elutriation method includes reintroducing the first blood component into the blood component separation device through the recirculation line at an increasing rate until the second blood component is removed from the blood component separation device.

20. A system according to claim 10, further comprising an anticoagulant line connected to an anticoagulant source, the anticoagulant line introducing anticoagulant into the drawn blood.

21. A system according to claim 10, wherein the second blood component is platelets and is reintroduced into the blood component separation device after a predetermined amount of platelets is collected within the second blood component container so as to extract a plasma reduced platelet product from the separation device.

22. A system according to claim 10, further comprising a reintroduction line fluidly connecting the second blood component bag and the blood component separation device, wherein the second blood component within the second blood component bag is reintroduced into the blood component separation device when a second volume of whole blood is withdrawn from the subject, thereby creating an enlarged layer of the second blood component within the blood component separation device, the enlarged layer of second blood component being removed from the blood component separation device using a surge elutriation method.

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23. A system according to claim 22, wherein the first blood component within the first blood component container is returned to the subject as the second blood component is reintroduced into the into the blood component separation device.

24. A system according to claim 10, wherein the first blood component within the first blood component container is returned to the subject during dead times.

25. A system according to claim 10, further comprising a controller, the controller calculating at least one of an extra-corporeal volume and an intra-vascular deficit, the system returning a volume of first blood component via the second return line based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

26. A system for collecting plasma reduced platelets and anticipating plasma return comprising:

means for drawing a first volume of whole blood from a subject and returning blood components to the subject;

a blood component separation means for separating the drawn blood into a first blood component and a second blood component, the blood component separation means configured to send the first blood component to a first blood component bag and the second blood component to a second blood component bag;

a first return means fluidly connecting the means for drawing a first volume of whole blood and the blood component separation means, the first return means configured to return blood components remaining in the separation means to the subject;

a recirculation means connecting the second blood component container and the separation means, wherein the recirculation means reintroduces the second blood component within the second blood component container into the separation means; and

a second return means fluidly connecting the first blood component container and the first return means and configured to return the first blood component within the first blood container to the subject.

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27. A system according to claim 26, wherein the means for drawing whole blood includes a first pump, the first pump configured to return the first blood component within the first blood component container to the subject.

28. A system according to claim 27, wherein the first pump is also configured to return the blood components remaining in the separation means to the subject.

29. A system according to claim 26, further comprising a controller for controlling the flow of fluids through the system, the controller repeatedly drawing whole blood from the donor into the separation means, extracting first and second blood components from the separation means, returning first blood components within the first blood component container to the subject using the second return means, and returning remaining components in the separation means back to the subject using the first return means, wherein after a predetermined volume of second blood component has been sequestered in the second blood component container, the second blood component from the second blood component container is reintroduced into the separation means.

30. A system according to claim 29, wherein the controller calculates at least one of an extra-corporeal volume and an intra-vascular deficit, the amount of first blood component returned using the second return means being based at least in part on the at least one of an extra-corporeal volume and an intra-vascular deficit.

31. A system according to claim 26, wherein the first blood component is plasma and the second blood component is platelets.

32. A system according to claim 26, wherein the separation means separates the whole blood into a third blood component in addition to the first and second blood components.

33. A system according to claim 32, wherein blood components remaining in the separation means includes the third blood component.

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34. A system according to claim 32, wherein the third blood component is red blood cells.

35. A system according to claim 26, wherein the second blood component is removed from the separation device using a surge elutriation method.

36. A system according to claim 35, wherein the surge elutriation method includes reintroducing the first blood component into the blood component separation means through the recirculation means at an increasing rate until the second blood component is removed from the blood component separation means.

37. A system according to claim 26, further comprising means for introducing anticoagulant into the drawn whole blood.

38. A system according to claim 26, wherein the second blood component is platelets and is reintroduced into the blood component separation means after a predetermined amount of platelets is collected within the second blood component container so as to extract a plasma reduced platelet product from the separation means.

39. A system according to claim 26, further comprising a reintroduction means fluidly connecting the second blood component bag and the blood component separation means, wherein the second blood component within the second blood component bag is reintroduced into the blood component separation means when a second volume of whole blood is withdrawn from the subject, thereby creating an enlarged layer of the second blood component within the blood component separation means, the enlarged layer of second blood component being removed from the blood component separation means using a surge elutriation method.

40. A method for collecting plasma reduced platelets and anticipating plasma return comprising:

a) drawing whole blood from a source;

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b) introducing anticoagulant into the whole blood drawn from the source;

c) introducing the anticoagulated whole blood into a separation chamber, the separation chamber separating the anticoagulated whole blood into a number of blood components;

d) transferring plasma separated from the anticoagulated whole blood to a plasma container;

e) returning a first volume of the plasma from the plasma container the source;

f) repeating steps a through d;

g) extracting platelet rich plasma from the separation chamber into a platelet rich plasma container; and

h) returning the remaining blood components within the separation chamber to the source.

41. A method according to claim 40 further comprising:

i) repeating steps a through c to partially fill the separation device with anticoagulated whole blood;

j) reintroducing platelet rich plasma from the platelet rich plasma container into the separation chamber;

k) transferring plasma from the separation chamber to the plasma container; and

l) reprocessing the reintroduced platelet rich plasma to create an enlarged layer of platelets within the separation device.

42. A method according to claim 41, further comprising

m) returning plasma from the plasma container to the source while reprocessing the platelet rich plasma.

43. A method according to claim 41, further comprising

m) returning plasma from the plasma container to the source while reintroducing the platelet rich plasma into the separation chamber.

44. A method according to claim 41 further comprising:

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m) removing the enlarged layer of platelets within the separation device using a surge elutriation method such that the platelets are transferred to a platelets container; and

n) returning the blood components remaining within the separation chamber to the source.

45. A method according to claim 44, further comprising returning plasma from the plasma container to the source during dead times.

46. A method according to claim 40, further comprising:

calculating at least one of an extra-corporeal volume and an intra-vascular deficit, the volume of plasma returned during step (e) being based, at least in part, upon the calculated extra-corporeal volume or intra-vascular deficit.

47. A method according to claim 40, wherein extracting platelet rich plasma from the separation chamber includes extracting the platelet rich plasma by surge elutriation.

48. A method according to claim 47, wherein extracting the platelet rich plasma from the separation chamber by surge elutriation includes surging with plasma.

49. A method for collecting plasma reduced platelets comprising:

a) drawing whole blood from a source;

b) introducing anticoagulant into the whole blood drawn from the source;

c) introducing the anticoagulated whole blood into a separation chamber, the separation chamber separating the anticoagulated whole blood into a number of blood components;

d) transferring plasma separated from the anticoagulated whole blood to a plasma container;

e) returning a first volume of the plasma from the plasma container back to the source;

f) repeating steps a through d;

g) extracting platelet rich plasma from the separation chamber into a platelet rich plasma container; and

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h) removing the remaining blood components from the separation chamber.

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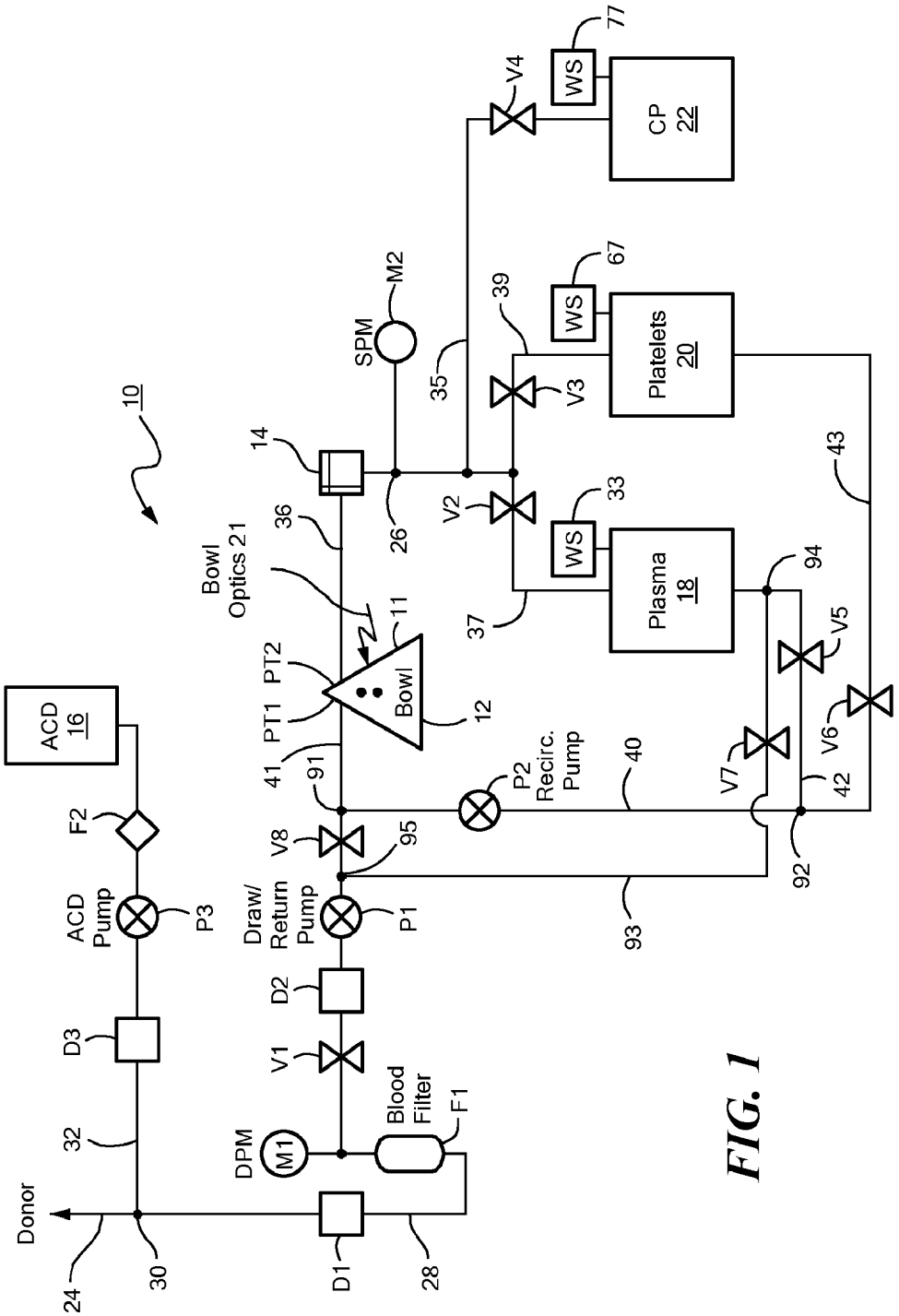

FIG. 1

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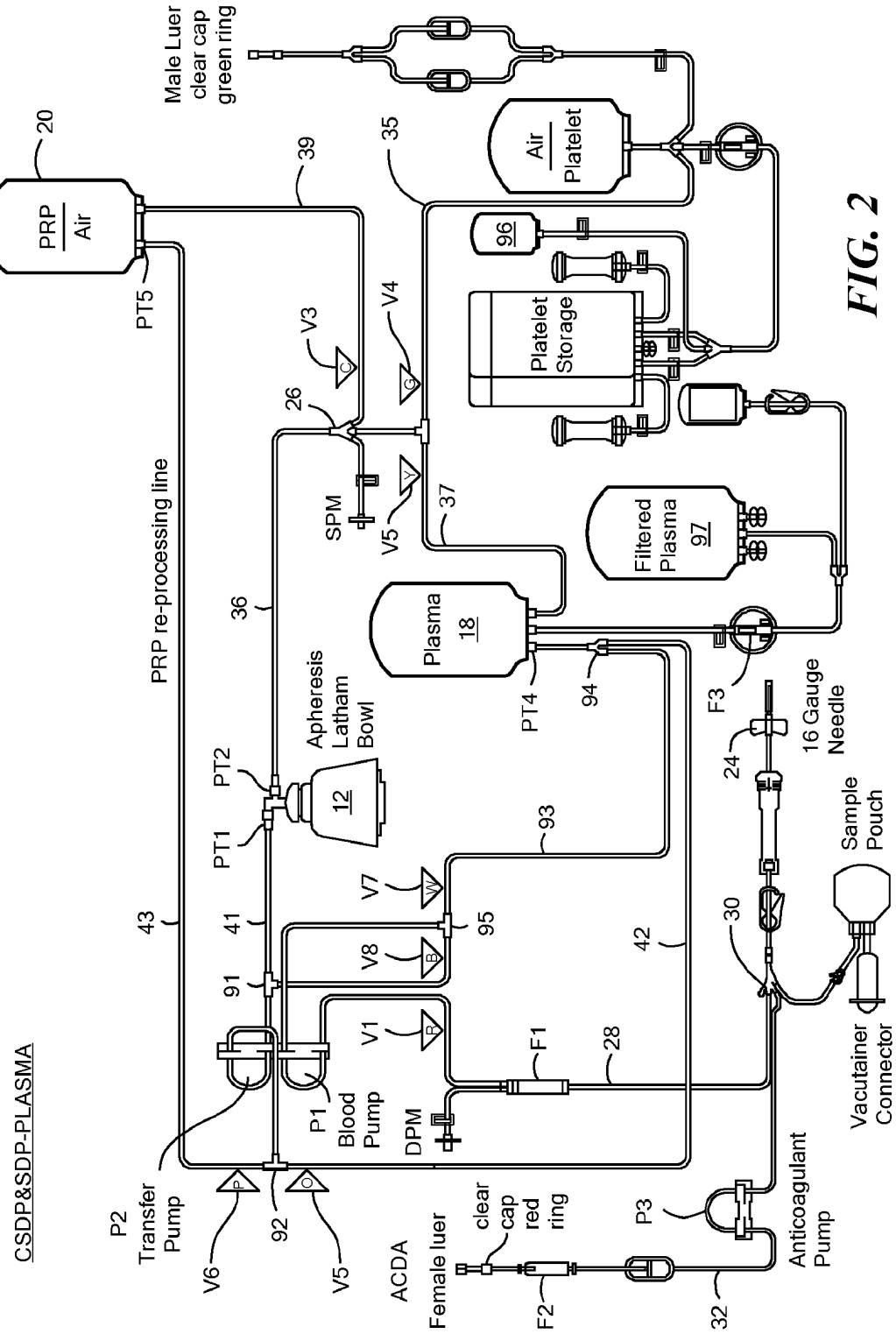
CSDP&SDP-PLASMA
PRP re-processing line
PRP
Air
20
PT5
39
35
Male Luer
clear cap
green ring
Air
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96
Platelet
Storage
V3
V4
26
SPM
V5
37
Filtered
Plasma
97
Plasma
18
36
Apheresis
Latham
Bowl
12
PT2
PT1
PT4
94
F3
16 Gauge
Needle
24
Sample
Pouch
93
V7
95
V8
41
43
91
42
30
V1
F1
28
P1
Blood
Pump
DPM
Vacutainer
Connector
P2
Transfer
Pump
V6
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clear
cap
red
ring
F2
P3
Anticoagulant
Pump
32

FIG. 2

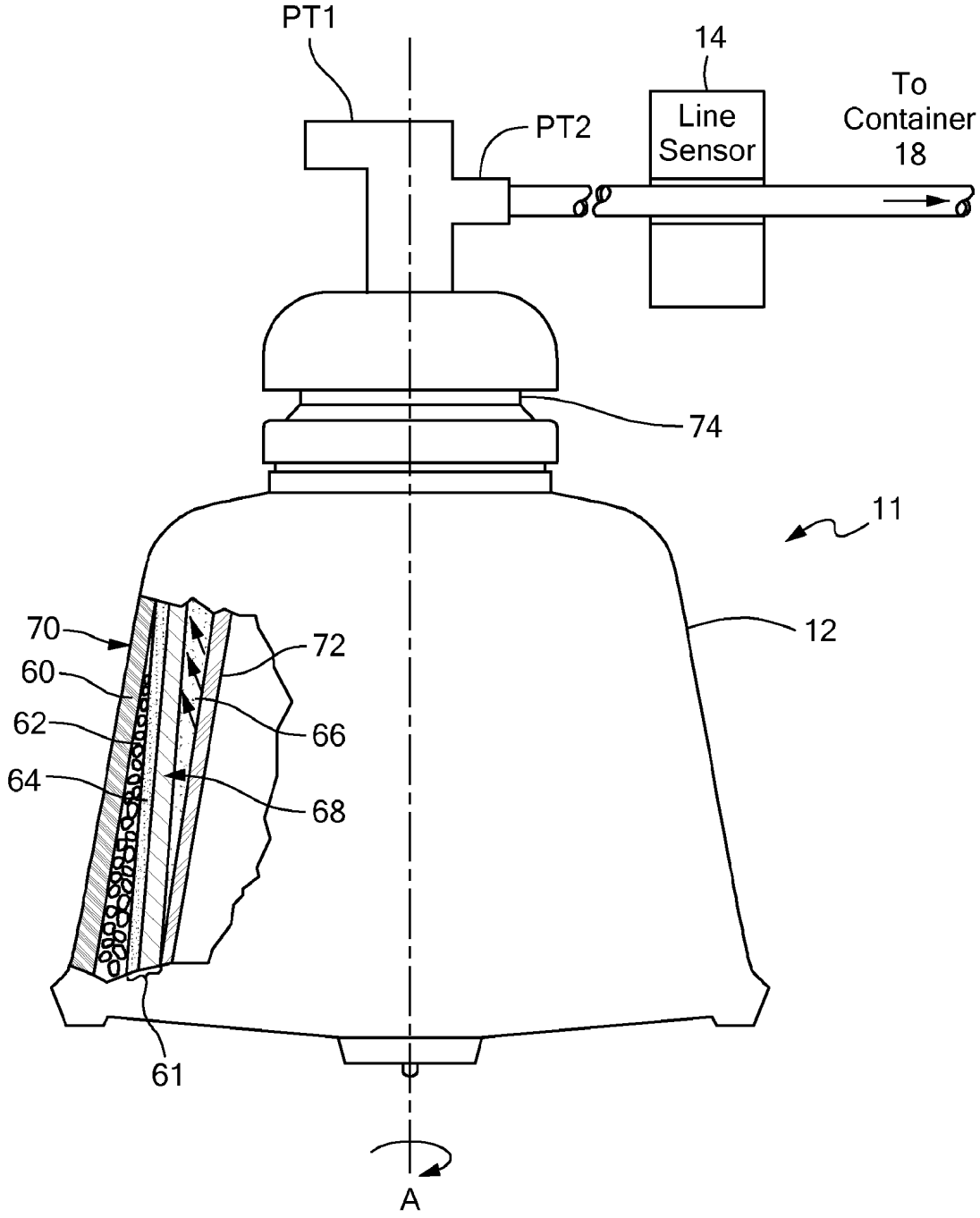

FIG. 3

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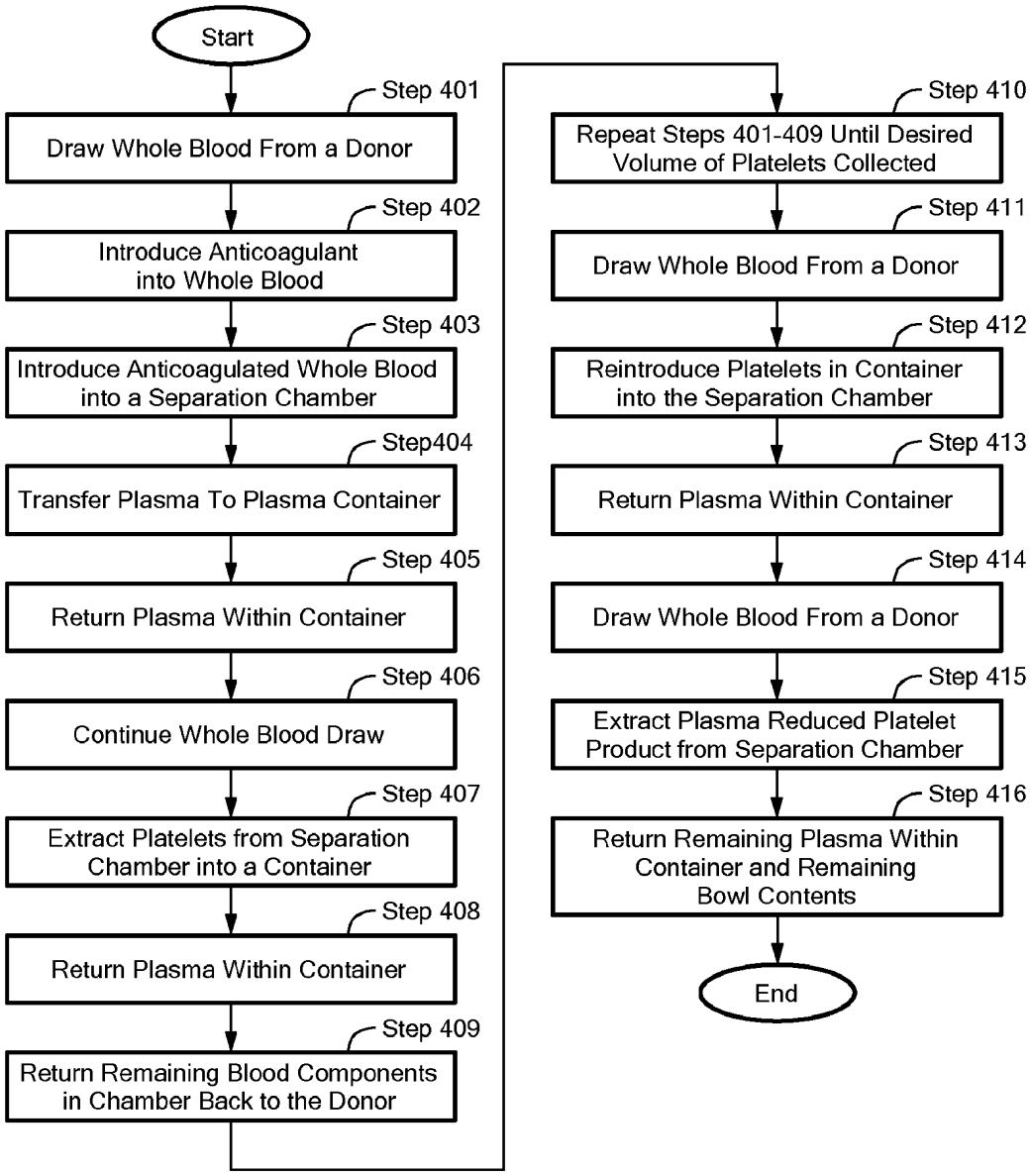
Start
Step 401
Draw Whole Blood From a Donor
Step 402
Introduce Anticoagulant into Whole Blood
Step 403
Introduce Anticoagulated Whole Blood into a Separation Chamber
Step404
Transfer Plasma To Plasma Container
Step 405
Return Plasma Within Container
Step 406
Continue Whole Blood Draw
Step 407
Extract Platelets from Separation Chamber into a Container
Step 408
Return Plasma Within Container
Step 409
Return Remaining Blood Components in Chamber Back to the Donor
Step 410
Repeat Steps 401-409 Until Desired Volume of Platelets Collected
Step 411
Draw Whole Blood From a Donor
Step 412
Reintroduce Platelets in Container into the Separation Chamber
Step 413
Return Plasma Within Container
Step 414
Draw Whole Blood From a Donor
Step 415
Extract Plasma Reduced Platelet Product from Separation Chamber
Step 416
Return Remaining Plasma Within Container and Remaining Bowl Contents
End

FIG. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 10/62540

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61M 37/00 (2011.01)
USPC - 604/6.04
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): A61M 37/00 (2011.01)
USPC: 604/6.04

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
IPC(8): A61M 37/00 (2011.01)
USPC: 604/6.04; 210/634, 644-646; 604/4.01, 5.01, 6.01, 6.04, 6.07, 6.11, 6.15

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPTO PubWEST (USPT, PGPUB, EPAB, JPAB); collect$, 'plasma reduced platelets', 'plasma return', 'whole blood', anticoagulant, separat$, chamber, container, 'platelet rich plasma', blood, plasma, calculat$, 'extra-corporeal volume', 'extracorporeal volume'
Google Scholar; 'collecting platelet reduced plasma anticipating plasma return'

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2010/0234788 A1 (PAGES, et al.) 16 September 2010 (16.09.2010), [Abstract], para[0005],[0010]-[0014], [0016], [0017], [0019], [0020], [0023], [0027], [0028], [0031], [0033], [0034], [0036]-[0038], [0040]-[0044], [0056]-[0060]; Fig. 1	1-6, 8-24, 26-29, 31-45, 47-49 ----- 7, 25, 30, 46
Y	US 2009/0217202 A1 (FOLEY, et al.) 27 August 2009 (27.08.2009), para[0056], [0069]-[0071]	7, 25, 30, 46

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 February 2011 (21.02.2011)	03 MAR 2011
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

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Espacenet

Bibliographic data: WO2019084278 (A1) — 2019-05-02

SYSTEM AND METHOD FOR COLLECTING PLASMA

Inventor(s): RAGUSA MICHAEL [US] ± (RAGUSA, Michael)

Applicant(s): HAEMONETICS CORP [US] ± (HAEMONETICS CORPORATION)

Classification: **- international:** ***A61M1/36***
- cooperative: **A61M1/3496 (EP, KR)**; **A61M1/36 (KR)**; **A61M1/3672 (EP, KR)**; **A61M1/3693 (EP, KR)**; **A61M1/385 (EP, KR)**; A61M2202/0415 (EP, KR); A61M2205/3306 (EP, KR); A61M2205/3393 (EP, KR); A61M2230/207 (EP, KR)

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Priority number(s): US201715793339 20171025

Also published as: AU2018355417 (A1) CA3079851 (A1) CN111465421 (A) EP3700606 (A1) EP3700606 (A4) more

Abstract of WO2019084278 (A1)

A method for collecting plasma includes determining the weight, height, and hematocrit of a donor, and calculating a donor plasma volume and a target plasma collection volume. The target plasma collection volume is based on the donor plasma volume and a target percentage of plasma. The method then withdraws blood from the donor through a line connected to a blood component separation device, and introduces anticoagulant into the withdrawn blood. The blood component separation device separates the blood into a plasma component and a second blood component, and the plasma component is collected from the blood component separation device and into a plasma collection container. The method may then calculate the volume of pure plasma collected within the plasma collection container, and continue processing/collecting until the calculated volume of pure plasma equals the target plasma collection volume.

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(74) Agent: **LOVELY, Jonathan, C.** et al.; McCarter & English, LLP, 265 Franklin Street, Boston, MA 02110 (US).

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(54) **Title:** SYSTEM AND METHOD FOR COLLECTING PLASMA

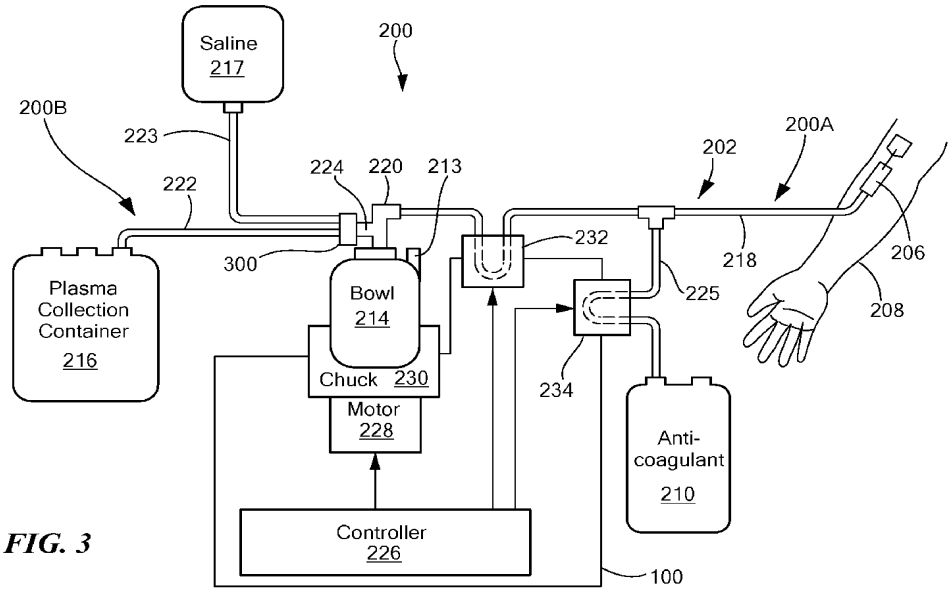

FIG. 3

(57) **Abstract:** A method for collecting plasma includes determining the weight, height, and hematocrit of a donor, and calculating a donor plasma volume and a target plasma collection volume. The target plasma collection volume is based on the donor plasma volume and a target percentage of plasma. The method then withdraws blood from the donor through a line connected to a blood component separation device, and introduces anticoagulant into the withdrawn blood. The blood component separation device separates the blood into a plasma component and a second blood component, and the plasma component is collected from the blood component separation device and into a plasma collection container. The method may then calculate the volume of pure plasma collected within the plasma collection container, and continue processing/collecting until the calculated volume of pure plasma equals the target plasma collection volume.

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[Continued on next page]

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— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

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System and Method for Collecting Plasma

Priority

[0001] This patent application claims priority from United States Patent Application No. 15/793,339, entitled "System and Method for Collecting Plasma," filed October 25, 2017, attorney docket number 130670-08003 (formerly 1611/C86), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

[0002] United States Application No. 15/793,339, in turn, is a continuation-in-part of and claims priority from all priority dates of U.S. Patent Application No. 15/608,183, entitled "System and Method for Collecting Plasma," filed May 30, 2017, attorney docket number 130670-08002 (formerly 1611/C80), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

Technical Field

[0003] The present invention relates to systems and methods for blood apheresis, and more particularly system and methods for collecting a plasma product.

Background Art

[0004] Apheresis is a procedure in which individual blood components can be separated and collected from whole blood temporarily withdrawn from a subject. Typically, whole blood is withdrawn through a needle inserted into a vein of the subjects arm and into a cell separator, such as a centrifugal bowl. Once the whole blood is separated into its various components, one or more of the components (e.g., plasma) can be removed from the centrifugal bowl. The remaining components can be returned to the subject along with optional compensation fluid to make up for the volume of the removed component. The process of drawing and returning continues until the quantity of the desired component has been collected, at which point the process is stopped. A central feature of apheresis systems is that the processed but unwanted components are returned to the donor. Separated blood components may include, for example, a high density

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component such as red blood cells, an intermediate density component such as platelets or white blood cells, and a lower density component such as plasma.

[0005] Many jurisdictions have regulations regarding the amount of whole blood and/or blood components that can be removed from a donor. For example, the U.S. Food and Drug Administration ("the FDA") sets both an upper limit on the volume of plasma that may be collected (e.g., 800 ml for an adult weighing more than 175 pounds) as well as an upper limit on the total collection volume (e.g., 880 ml for an adult weighing more than 175 pounds). Prior art plasma collection systems are unable to determine the total volume of plasma that has been collected (e.g., because the product collected is a mixture of plasma and anticoagulant) and, therefore collect based on the total collection volume, even if the total volume of plasma that has been collected is below the limit prescribed by the FDA. Additionally, prior art collection systems do not tailor the amount of plasma collected to the individual (e.g., other than what weight group they fall into) and, therefore, the percentage of the patient's plasma that is collected varies widely from patient to patient (e.g., only 23% percent of the plasma is collected for some patients and 29% - or greater – of the plasma is collected for others).

Summary of the Invention

[0006] In accordance with some embodiments of the present invention, a method for collecting plasma includes determining the weight and hematocrit of a donor, and inserting a venous-access device into the donor. Once the venous access device is inserted, the method may withdraw whole blood from the donor through the venous-access device and a draw line that is connected to a blood component separation device. The method may then introduce anticoagulant into the withdrawn whole blood through an anticoagulant line and separate, using the blood component separation device, the withdrawn whole blood into a plasma component and at least a second blood component. Once separated, the plasma component may be collected from the blood component separation device and into a plasma collection container. During processing, the method may calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma collection container. The volume of pure plasma may be based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component. The method may continue the process (e.g., withdrawing whole blood, introducing anticoagulant into the whole blood, separating the blood, collecting the plasma, and calculating the percentage of

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anticoagulant and volume of pure plasma) until a target volume of pure plasma is collected within the plasma collection container.

[0007] In some embodiments, the method may determine a change in volume within an anticoagulant container, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant container. Additionally or alternatively, the method may determine a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump. The method may also determine a volume of anticoagulant within the blood component separation device, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the volume of anticoagulant within the blood component separation device.

[0008] In further embodiments, the method may monitor the volume and/or weight of the plasma component collected within the plasma collection container (e.g., using a weight sensor), and the calculated volume of pure plasma collected within the plasma collection device may be based, at least in part, on the monitored volume and/or weight of the collected plasma component. Additionally or alternatively, determining the hematocrit of the donor may include monitoring a volume of red blood cells collection within the blood separation device. In such embodiments, the determined hematocrit of the donor may be based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor.

[0009] The target volume of pure plasma may be based, at least in part, on the weight of the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant that is added to the system during a priming step. After collecting at least a portion of the target volume of pure plasma, the method may return the second blood component to the donor through a return line.

[0010] In accordance with additional embodiments, a system for collecting plasma includes a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and a blood component separation device for separating the drawn blood into a plasma component and a second blood component. The blood component separation device has an outlet and is configured to send the plasma

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component to a plasma container. The system may also include a blood draw line fluidly connected to the venous-access device and an anticoagulant line connected to an anticoagulant source. The blood draw line transports drawn whole blood to the blood component separation device, and the flow through the blood draw line may be controlled by a blood draw pump. The anticoagulant line may introduce anticoagulant into the drawn whole blood.

[0011] Additionally, the system may include a controller that controls the operation of the centrifuge bowl. The controller may also calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma container. The volume of pure plasma may be based, at least in part, upon the percentage of anticoagulant in the collected plasma component. The controller may stop the blood draw pump when a target volume of pure plasma (e.g., based, at least in part, on the weight of the donor) is collected within the plasma container. In some embodiments, the percentage of anticoagulant in the collected plasma component may be based, at least in part, on the volume of anticoagulant added to the drawn whole blood and the subject's hematocrit.

[0012] The system may also include an anticoagulant source weight sensor that measures the weight of the anticoagulant source. The controller may monitor the change in volume within the anticoagulant container based on the measured weight of the anticoagulant source, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant source. Additionally or alternatively, the controller may monitor the number of rotations of an anticoagulant pump to determine a volume of anticoagulant introduced into the whole blood. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump.

[0013] In some embodiments, the system may include an optical sensor located on the blood component separation device. The optical sensor may monitor the contents of the blood component separation device and determine if a volume of anticoagulant remains within the blood component separation device. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the volume of anticoagulant within the blood component separation device.

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[0014] In additional embodiments, the system may also include a plasma container weight sensor that monitors a volume and/or weight of the plasma component collected within the plasma collection container. The calculated volume of pure plasma collected within the plasma collection container may be based, at least in part, on the monitored volume and/or weight of collected plasma component. The system may also have an optical sensor located on the blood component separation device. The optical sensor may monitor the volume of red blood cells collected within the blood separation device. The controller may then determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added to the system during a priming step.

[0015] In accordance with additional embodiments, a method for collecting plasma determines the weight, height, and hematocrit of a donor, and calculates a donor plasma volume based, at least in part, on the weight, height and hematocrit of the donor. The method then calculates a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma (e.g., between 26.5 and 29.5 percent of the donor's plasma volume), and withdraws whole blood from the donor through the venous-access device and a first line that is connected to a blood component separation device. As the whole blood is withdrawn, the method may introduce anticoagulant into the withdrawn whole blood through an anticoagulant line.

[0016] The blood component separation device separates the withdrawn whole blood into a plasma component and at least a second blood component, and the method may collect the plasma component from the blood component separation device and into a plasma collection container. During processing, the method may calculate a volume of pure plasma collected within the plasma collection container. The method continues the withdrawing, introduction of anticoagulant, separating, collecting, and calculating steps until the volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

[0017] In some embodiments, after collecting at least a portion of the target plasma collection volume, the method may return the contents of the blood component separation device to the donor through the first line. Additionally or alternatively, the method may calculate an intravascular deficit based, at least in part on, the volume of

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pure plasma collected and the volume of the contents of the blood component separation device that are returned to the donor. The method may also return a volume of saline to the donor to obtain a target intravascular deficit. The target intravascular deficit may be between -250 and 500 milliliters (e.g., it may be 0 milliliters or 250 milliliters).The donor plasma volume may be calculated based, at least in part, on the donor's body mass index that, in turn, is calculated based on the donor's weight and height.

[0018] In further embodiments, the method may include calculating a percentage of anticoagulant in the collected plasma component. In such embodiments, the volume of pure plasma may be based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on a change in volume within the anticoagulant container, the number of rotations of the anticoagulant pump, and/or the volume of anticoagulant within the blood component separation device. The method may determine the change in volume within the anticoagulant container, the volume of anticoagulant introduced into the whole blood, and/or the volume of anticoagulant within the blood component separation device. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

[0019] In some embodiments, the method may include monitoring a volume or and/or weight of the plasma component collected within the plasma collection container. In such embodiments, the calculated volume of pure plasma collected within the plasma collection device may be based, at least in part, on the monitored volume and/or weight of collected plasma component. To determine the donor's hematocrit, the method may monitor the volume of red blood cells collected within the blood separation device. The hematocrit of the donor may be based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor.

[0020] In accordance with still further embodiments, a system for collecting plasma includes a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and a blood component separation device for separating the drawn blood into a plasma component and a second blood component. The blood component separation device may have an outlet and may send the plasma component to a plasma container. The system may also have a first line and an

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anticoagulant line. The first line may be fluidly connected to the venous-access device and may (1) transport drawn whole blood to the blood component separation device and (2) return fluid within the blood component separation device to the subject. The flow through the first line may be controlled by a first pump. The anticoagulant line may be connected to an anticoagulant source and may introduce anticoagulant into the drawn whole blood.

[0021] The system may also include a controller that controls the operation of the centrifuge bowl and the first pump. The controller may calculate (1) a donor plasma volume, (2) a target plasma collection volume, and (3) a volume of pure plasma collected within the plasma container. The donor plasma volume may be based, at least in part, on a weight and height of the donor and a hematocrit of the donor. The target plasma collection volume may be based, at least in part, on the calculated donor plasma volume and a target percentage of plasma. The volume of pure plasma collected within the plasma container may be based, at least in part, upon a percentage of anticoagulant in the collected plasma component. The controller may stop the first pump when the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

[0022] In further embodiments, the controller may return, after collecting at least a portion of the target plasma collection volume, fluid remaining within the blood component separation device via the first line. Additionally or alternatively, the controller may calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and the volume of the contents of the blood component separation device returned to the donor. The system may also include a saline line that fluidly connects to a saline source and the blood component separation device. The controller may return a volume of saline to the donor to obtain a target intravascular deficit (e.g., between -250 and 500 milliliters).

[0023] The controller may calculate the donor's body mass index based, at least in part, on the weight and height of the donor. The donor plasma volume may, in turn, be calculated based, at least in part, on the donor's body mass index. The target percentage of plasma may be between 26.5 and 29.5 percent (e.g., 28.5 percent) of the donor's plasma volume.

[0024] In additional embodiments, the controller may calculate the percentage of anticoagulant in the collected plasma component, for example, based on the volume of anticoagulant added to the drawn whole blood, and the subject's hematocrit. The system

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may also include an anticoagulant source weight sensor that measures the weight of the anticoagulant source. The controller may then monitor a change in volume within the anticoagulant container based on the measured weight of the anticoagulant source. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant source. Additionally or alternatively the controller may monitor a number of rotations of the anticoagulant pump to determine the volume of anticoagulant introduced into the whole blood. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump.

[0025] The system may also include an optical sensor and/or a plasma container weight sensor. The optical sensor may be located on the blood component separation device and may monitor the contents of the blood component separation device to determine if a volume of anticoagulant remains within the blood component separation device. The calculated percentage of anticoagulant in the collected plasma may then be based, at least in part, on the volume of anticoagulant within the blood component separation device. The plasma container weight sensor may monitor a volume and/or weight of the plasma component collected within the plasma container. The calculated volume of pure plasma collected within the plasma collection device may then be based, at least in part, on the monitored volume and/or weight of collected plasma component. The optical sensor may also monitor the volume of red blood cells collected within the blood separation device, and the controller may determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

Brief Description of the Drawings

[0026] The foregoing features of the invention will be more readily understood by reference to the following detailed description, taken with reference to the accompanying drawings, in which:

[0027] Fig. 1 schematically shows a perspective view of a blood processing system in accordance with some embodiments of the present invention.

[0028] Fig. 2 schematically shows a top view of the blood processing system of Figure 1, in accordance with some embodiments of the present invention;

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[0029] Fig. 3 schematically shows a disposable set installed within the blood processing system of Figure 1, in accordance with some embodiments of the present invention.

[0030] Fig. 4 is a flowchart depicting a method of collecting plasma, in accordance with embodiments of the present invention.

[0031] Fig. 5 is a flowchart depicting an alternative method of collecting plasma, in accordance with further embodiments of the present invention.

Detailed Description of Specific Embodiments

[0032] Illustrative embodiments of the present invention provide blood processing systems and methods for collecting a target volume of pure plasma. The system and method calculate a percentage of anticoagulant collected within a plasma collection container (e.g., in addition to the plasma that is collected within the container) based on the amount of anticoagulant added to the system and the hematocrit of the donor. The system/method may then calculate the volume of pure plasma (e.g., plasma without anticoagulant) that has been collected within the container. Further embodiments may tailor the volume of plasma collected based on the donor's plasma volume and a target percentage of plasma to collect. Details of the illustrative embodiments are discussed below.

[0033] As shown in Figures 1 and 2, the blood processing system 100 includes a cabinet 110 that houses the main components of the system 100 (e.g., the non-disposable components). Within the cabinet 110, the system 100 may include a first/blood pump 232 that draws whole blood from a subject, and a second/anticoagulant pump 234 that pumps anticoagulant through the system 100 and into the drawn whole blood. Additionally, the system 100 may include a number of valves that may be opened and/or closed to control the fluid flow through the system 100. For example, the system 100 may include a donor valve 120 that may open and close to selectively prevent and allow fluid flow through a donor line 218 (e.g., an inlet line; Fig. 3), and a plasma valve 130 that selectively prevents and allows fluid flow through an outlet/plasma line 222 (Fig. 3). Some embodiments may also include a saline valve 135 that selectively prevents and allows saline to flow through a saline line 223.

[0034] To facilitate the connection and installation of a disposable set and to support the corresponding fluid containers, the system 100 may include an anticoagulant pole 150 on which the anticoagulant solution container 210 (Fig. 3) may be hung, and a

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saline pole 160 on which a saline solution container 217 (Fig. 3) may be hung (e.g., if the procedure being performed requires the use of saline). Additionally, in some applications, it may be necessary and/or desirable to filter the whole blood drawn from the subject for processing. To that end, the system 100 may include blood filter holder 170 in which the blood filter (located on the disposable set) may be placed.

[0035] As discussed in greater detail below, apheresis systems 100 in accordance with embodiments of the present invention withdraw whole blood from a subject through a venous access device 206 (Fig. 3) using the blood pump 232. As the system 100 withdraws the whole blood from the subject, the whole blood enters a blood component separation device 214, such as a Latham type centrifuge (other type of separation chambers and devices may be used, such as, without limitation, an integral blow-molded centrifuge bowl, as described in U.S. Patent Nos. 4,983,158 and 4,943,273, which are hereby incorporated by reference). The blood component separation device 214 separates the whole blood into its constituent components (e.g., red blood cells, white blood cell, plasma, and platelets). Accordingly, to facilitate operation of the separation device 214, the system 100 may also include a well 180 in which the separation device 214 may be placed and in which the separation device 214 rotates (e.g., to generate the centrifugal forces required to separate the whole blood).

[0036] To allow the user/technician to monitor the system operation and control/set the various parameters of the procedure, the system 100 may include a user interface 190 (e.g., a touch screen device) that displays the operation parameters, any alarm messages, and buttons which the user/technician may depress to control the various parameters. Additional components of the blood processing system 100 are discussed in greater detail below (e.g., in relation to the system operation).

[0037] FIG. 3 is a schematic block diagram of the blood processing system 100 and a disposable collection set 200 (with an inlet disposable set 200A and an outlet disposable set 200B) that may be loaded onto/into the blood processing system 100, in accordance with the present invention. The collection set 200 includes a venous access device 206 (e.g., a phlebotomy needle) for withdrawing blood from a donor's arm 208, a container of anti-coagulant 210, a centrifugation bowl 214 (e.g., a blood component separation device), a saline container 217, and a final plasma collection bag 216. The blood/inlet line 218 couples the venous access device 206 to an inlet port 220 of the bowl 214, the plasma/outlet line 222 couples an outlet port 224 of the bowl 214 to the plasma collection bag 216, and a saline line 223 connects the outlet port 224 of the bowl 214 to

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the saline container 217. An anticoagulant line 225 connects the anti-coagulant container 210 to the inlet line 218. In addition to the components mentioned above and as shown in Figure 3, the blood processing system 100 includes a controller 226, a motor 228, and a centrifuge chuck 230. The controller 226 is operably coupled to the two pumps 232 and 234, and to the motor 228, which, in turn, drives the chuck 230. The controller 226 may be operably coupled to and in communication with the user interface 190.

[0038] In operation, the disposable collection set 200 (e.g., the inlet disposable set 200A and the outlet disposable set 200B) may be loaded onto/into the blood processing system 100 prior to blood processing. In particular, the blood/inlet line 218 is routed through the blood/first pump 232 and the anticoagulant line 225 from the anti-coagulant container 210 is routed through the anticoagulant/second pump 234. The centrifugation bowl 214 may then be securely loaded into the chuck 230. Once the bowl 214 is secured in place, the technician may install the outlet disposable set 200B. For example the technician may connect a bowl connector 300 to the outlet 224 of the bowl 214, install the plasma container 216 into the weight senor 195, run the saline line 223 through valve 135, and run the plasma/outlet line 222 through valve 130 and the line sensor 185. Once the disposable set 200 is installed and the anticoagulant and saline containers 210/217 are connected, the system 100 is ready to begin blood processing.

[0039] Figure 4 is a flowchart depicting an exemplary method of collecting plasma in accordance with various embodiments of the present invention. Prior to connecting the donor to the blood processing device 100, it is beneficial (and perhaps necessary in some instances) to obtain/determine some information regarding the donor, namely, the donor's weight (Step 410) and hematocrit (Step 415). Not only does this information help determine if the individual is a viable donor and the volumes of blood components that may be withdrawn/collected (e.g., per the FDA guidelines), the hematocrit may be used during processing to help collect a target volume of plasma. The technician may obtain/determine the donor's weight by weighing the donor (e.g., on a scale). To obtain/determine the donor's hematocrit, the technician may draw a blood sample from the donor and test the sample of blood. Additionally or alternatively, as discussed in greater detail below, the system may determine the hematocrit during blood processing. For example, the blood processing device 100 may include a hematocrit sensor (not shown) that determines the hematocrit of the blood flowing into the blood processing device 100 and/or the system 100 may determine the hematocrit based on a volume of red blood cells collected within the bowl 214.

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[0040] Once the lines 222/223 are in place and the technician has determined the donor's weight and/or hematocrit (if needed), the user/technician may insert the venous access device 206 into the donor's arm 208 (Step 420). Next, the controller 226 activates the two pumps 232, 234 and the motor 228. Operation of the two pumps 232, 234 causes whole blood to be drawn from the donor (step 425), anticoagulant from container 210 to be introduced into the drawn whole blood (step 430), and the now anticoagulated whole blood to be delivered to the inlet port 220 of the bowl 214.

[0041] It should be noted that the anticoagulant line 225 may also include a bacteria filter (not shown) that prevents any bacteria in the anticoagulant source 210, the anticoagulant, or the anticoagulant line 225 from entering the system 100 and/or the subject. Additionally, the anticoagulant line 225 may include an air detector 140 that detects the presence of air within the anticoagulant. The presence of air bubbles within any of the system 100 lines can be problematic for the operation the system 100 and may also be harmful to the subject if the air bubbles enter the blood stream. Therefore, the air detector may be connected to an interlock that stops the flow within the anticoagulant line 225 in the event that an air bubble is detected (e.g., by stopping the anticoagulant pump 234), thereby preventing the air bubbles from entering the subject.

[0042] As the anti-coagulated whole blood is withdrawn from the subject and contained within the blood component separation device 214, the blood component separation device 214 separates the whole blood into several blood components (Step 435). For example, the blood component separation device 214 may separate the whole blood into a first, second, third, and, perhaps, fourth blood component. More specifically, the blood component separation device 214 (and the centrifugal forces created by rotation of the separation device 214) can separate the whole blood into plasma, platelets, red blood cells ("RBC"), and, perhaps, white blood cells ("WBC"). The higher density component, i.e., RBC, is forced to the outer wall of the bowl 214 while the lower density plasma lies nearer the core. A buffy coat is formed between the plasma and the RBC. The buffy coat is made up of an inner layer of platelets, a transitional layer of platelets and WBC and an outer layer of WBC. The plasma is the component closest to the outlet port and is the first fluid component displaced from the bowl 214 via the outlet port 224 as additional anticoagulated whole blood enters the bowl 214 through the inlet port 220.

[0043] As shown in Figure 3, the system 100 may also include an optical sensor 213 that may be applied to a shoulder portion of the bowl 214. The optical sensor monitors each layer of the blood components as they gradually and coaxially advance

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toward the core from the outer wall of the bowl 214. The optical sensor 213 may be mounted in a position (e.g., within the well 180) at which it can detect the buffy coat and/or the red blood cells reaching a particular radius, and the steps of drawing the whole blood from the subject/donor and introducing the whole blood into the bowl 12 may be altered and/or terminated in response to the detection.

[0044] Additionally, in some embodiments, the optical sensor 213 may be used to determine the hematocrit of the donor during processing. For example, as the bowl 214 fills with red blood cells and the optical sensor 213 detects the layer of red blood cells, the system 100 (e.g., the controller) can determine the volume of red blood cells within bowl 214 based on the location of the red blood cell layer and the fixed/known bowl volume. The system 100 may then calculate the donor hematocrit based on the volume of red blood cells within the bowl and the volume of whole blood that has been processed to that point.

[0045] Once the blood component separation device 214 has separated the blood into the various components, one or more of the components can be removed from the blood component separation device 214. For instance, the plasma may be removed to a plasma container 216 (e.g., a plasma bottle) through line 222 (Step 440). As noted above, some embodiments of the system 100 may include a weight sensor 195 (Fig. 1) that measures the amount of plasma collected. The plasma collection process may continue until a target volume of pure plasma (discussed in greater detail below) is collected within the plasma collection container 216. Although not shown, if the blood processing system 100 and/or the disposable set 200 include platelet, red blood cell, and/or white blood cell bags, each of the bags/containers may include similar weight sensors (e.g., load cells).

[0046] In some embodiments, the system 100 may also include a line sensor 185 (mentioned above) that can determine the type of fluid (e.g., plasma, platelets, red blood cells etc.) exiting the blood component separation device 214. In particular, the line sensor 185 consists of an LED which emits light through the blood components leaving the bowl 214 and a photo detector which receives the light after it passes through the components. The amount of light received by the photo detector is correlated to the density of the fluid passing through the line. For example, if plasma is exiting the bowl 214, the line sensor 185 will be able to detect when the plasma exiting the bowl 214 becomes cloudy with platelets (e.g., the fluid existing the bowl 214 is changing from plasma to platelets). The system 100 may then use this information to either stop the

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removal of blood components from the bowl 214, stop drawing whole blood from the subject, or redirect the flow by, for example, closing one valve an opening another.

[0047] It is important to note that during processing, the osmolarity of the red blood cells prevents the anticoagulant introduced into the whole blood from entering/remaining with the red blood cells (e.g., within the bowl 214). Rather, the anticoagulant mixes with the plasma component. Therefore, the anticoagulant exits the bowl 214 with the plasma and is collected within collection container 216 along with the plasma. In other words, the weight of the product measured by the weight senor 195 is the weight of the plasma, as well as any anticoagulant that is mixed with the plasma – the weight provided by the weight sensor 195 is not the weight of pure plasma.

[0048] Additionally, whole blood contains a variable amount of plasma, as determined by the donor's hematocrit. The hematocrit for typical donors can vary from 38% to 54%, which means that for 100 ml of whole blood, the volume of plasma can vary from 36 to 62 ml. Furthermore, the amount of anticoagulant added to the withdrawn whole blood is fixed (e.g., it does not depend on the hematocrit of the donor), meaning that the percentage of anticoagulant in the collected plasma may vary from 9.7% to 12.7% for donor hematocrits between 38% to 54%, respectively. Therefore, not only does the volume measured by the weight sensor 195 include the volume of anticoagulant, that volume of anticoagulant may vary from donor to donor based on the hematocrit.

[0049] As mentioned above, some embodiments of the present invention continue the blood processing/separation procedure until a target volume of pure plasma (e.g., plasma only – without the volume of any anticoagulant mixed with the plasma included in the target volume) is collected within the plasma collection container 216. To that end, some embodiments of the present invention may calculate the volume of pure plasma within the plasma collection container 216. For example, the technician or the system 100 (e.g., the controller) may calculate the percentage of anticoagulant within the collected plasma (Step 455) (e.g., the plasma contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor. The technician and/or system can calculate the percentage of anticoagulant according to the following equation, where AC is the amount of anticoagulant added to the system 100. As noted above, because the osmolarity of the red blood cells prevents the anticoagulant from mixing with it, essentially all of the anticoagulant exits the bowl 214 and is collected within the plasma collection container 216 along with the plasma.

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$$\%AC = \frac{1}{1 + (AC - 1)(1 - Hct_D)}$$

[0050] The amount of anticoagulant that is added to the system 100 can be determined in a number of ways. For example, the system 100 can base the amount of anticoagulant (e.g., the value of "AC" in the above equation) on the predetermined ratio of anticoagulant per unit of anticoagulated whole blood. In some embodiments, the value of "AC" may be the inverse of the predetermined ratio (e.g., "AC" would be 16 if the ratio of anticoagulant to anticoagulated whole blood was 1:16). Additionally or alternatively, the technician/system 100 can monitor the volume of anticoagulant added to the system. In such embodiments, the technician/system can monitor the volume of anticoagulant added to the system 100 based on the number of rotations of the anticoagulant pump (e.g., each rotation of the anticoagulant pump introduces a set volume of anticoagulant into the system 100) and/or based on the change in weight of the anticoagulant container 210 as measured by a weight sensor (discussed in greater detail below).

[0051] Once the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 465). For example, the technician/system 100 may determine the volume of anticoagulant within the container (based on the percentage of anticoagulant within the container 216) and subtract this volume from the total volume of fluid within the container 216 as measured by the weight sensor 195. The system 100 may continue to monitor the volume of pure plasma collected within the container 216 and continue processing whole blood (e.g., continue performing Steps 425, 430, 435, 440, 455, 460 and 465) until a target volume of pure plasma is collected within the plasma collection container 216 (Step 470) (e.g., 800 mL for an adult donor weighing more than 175 pounds or other limit prescribed by the FDA or similar governing body).

[0052] Once the system 100 has collected the target volume of pure plasma within the plasma collection container 216, the system 100 can return the remaining components (e.g., the components remaining within the bowl 214) to the subject (Step 475). For example, when all the plasma has been removed and the bowl 214 is full of RBCs (and any other blood component not collected), the controller 226 stops the draw of whole blood from the subject and reverses the direction of the blood/first pump 232 to draw the

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RBCs (and other components) from the bowl 214 directly back to the subject. Alternatively, if the system 100 is so equipped, the system may return the components to the subject via a dedicated return line.

[0053] In addition to the non-collected blood components (e.g., the components remaining in the bowl 214), the system 100 may also return saline to the patient/subject. The saline may be used as a compensation fluid to make up for the volume of the blood component (e.g., plasma) that was removed and collected, and is not being returned to the patient. To that end, during the return step (e.g., Step 475), the saline valve 135 may be opened to allow saline from the saline container 217 to flow through the saline line 223 and into the bowl 214 (via outlet 224), where it can be returned to the patient/donor with or after the remaining blood components.

[0054] It should be noted that some embodiments may perform some additional and optional steps to help determine the volume of pure plasma within the plasma collection container 216. For example, as mentioned above, some embodiments may monitor the change in weight of the anticoagulant container 210 (e.g., as measured by a weight sensor/load cell on the anticoagulant container 210) (step 445). This measurement provides an indication of the volume of anticoagulant that has been added to the system 100, and may be used help determine the percentage of anticoagulant within the plasma collection container 216. Additionally or alternatively, some embodiments may similarly, monitor the change in weight and/or volume of the plasma and anticoagulant collected within the plasma collection container 216 (e.g., via weight sensor 195) (step 450). This measurement may be used to calculate of the total volume of pure plasma collected within the plasma collection container 216 (e.g., to obtain the total weight from which to subtract the calculated volume of anticoagulant).

[0055] Some embodiments may also (optionally) monitor the volume of anticoagulant remaining in the bowl 214 (step 460) (e.g., anticoagulant that did not mix with the plasma and/or otherwise remained in the bowl). For example, the system 100 may utilize the optical sensor on the bowl 214 to determine whether any anticoagulant remains within the bowl 214. If it does, the method 400/system 100 may modify the calculation of the amount of pure plasma collected within the plasma collection container (e.g., either increase the calculated amount or decreased the calculated amount), based on the volume of anticoagulant remaining within the bowl 214.

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[0056] The various embodiment of the present invention described above provide numerous benefits over prior art plasma collection systems. In particular, as noted above, prior art plasmapheresis devices end plasma collection based on a total volume of anticoagulated plasma (e.g., pure plasma plus the added anticoagulant). Although this is the easiest method because it requires only that the product collection container be weighed, the amount of true product – the pure plasma – is dependent on the donor's hematocrit. In other words, prior art systems will collect more plasma from low hematocrit donors than from high hematocrit donors because of the variation of the percentage of anticoagulant in the product. Various embodiments of the present invention address the issues of prior art systems by collecting a standard volume (e.g., a target volume) of pure plasma from each donor. As noted above, embodiments of the present invention accomplish this by using knowledge of the donor's hematocrit and the amount of anticoagulant collected within the plasma collection container 216 (e.g., by counting pump rotations and/or using scale/weight sensors, etc.) to determine the percentage of anticoagulant in the product. Additionally, by stopping the plasma collection process based on a volume of pure plasma collected, embodiments of the present invention are able to collect a greater volume of plasma as compared to prior art systems that stop based on a plasma/anticoagulant mixture.

[0057] Figure 5 shows an alternative method for collecting plasma, using the system (or similar system) shown within Figures 1-3, that bases the total volume of plasma to collect on the individual donor (e.g., based on their height, weight, hematocrit, blood volume and/or plasma volume). In a manner similar to that described above for the method shown in Figure 4, prior to connecting the donor to the blood processing device 100, the system/method may obtain/determine some information regarding the donor, namely, the donor's weight and height (Step 505) and hematocrit (Step 510). For example, the technician may obtain/determine the donor's weight by weighing the donor (e.g., on a scale) and the donor's height by measuring the donor. To obtain/determine the donor's hematocrit (e.g., in a manner similar to that described above), the technician may test a blood sample or the system may determine the hematocrit during blood processing using a hematocrit sensor and/or based on the volume of red blood cells collected within the bowl 214.

[0058] Using the donor height and weight, and the hematocrit, the system 100/method 500 may calculate the donor's plasma volume (e.g., the volume of plasma within the donor's blood) (Step 515). For example, the system 100/method 500 may

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calculate the donor/subject's body mass index ("BMI") using the donor's height and weight (e.g., BMI = weight/height^2), and then the total blood volume within the donor/subject using the calculated BMI (e.g., see Lemmens et al., *Estimating Blood Volume in Obese and Morbidly Obese Patients*, Obesity Surgery, 2006:16, 773-776, the subject matter incorporated herein by reference). The total blood volume may be calculated using the following equation:

[0059] $InBV = \frac{70}{\sqrt{BMIp/22}}$

[0060] In the above equation, InBV is the indexed blood volume (e.g., the donor's total blood volume), BMIp is the patient's BMI (e.g., kg/ m^2), 22 is the BMI value (e.g., also in kg/m^2) for an ideal body weight (IBW), and 70 is the total blood volume (in mL/kg) for a donor at their ideal weight (BMI = 22 kg/ m^2). Once the system 100 has calculated the total blood volume within the donor/subject, the system 100 (e.g., the controller) may then determine/calculate the volume of plasma within the donor's blood (Step 515) based, for example, on the donor's hematocrit.

[0061] As mentioned above, the embodiment shown in Figure 5 bases the volume of plasma to collect on the individual donor. To that end, once the system 100/method 500 has determined the donor's plasma volume, the system 100/method 500 may then calculate the target volume of plasma to collect (Step 520). For example, the system 100/method 500 may multiply the total plasma volume within the patient by a target percentage of plasma to collect to obtain the target plasma volume to collect (e.g., if the total plasma volume is 2700 ml and the target percentage to collect is 28.5%, then the target plasma volume to collect is 769.5 ml). The target percentage of plasma to collect may depend on the application and/or the donor, and may be input directly into the system 100 (e.g., using the user interface 190) or may be preset from the factory. In some embodiments, the target percentage may be between 26.5 and 30%, and preferably may be 28.5%. However, in other embodiments, the target percentage may be below 26.5% or above 30%.

[0062] Once the lines 222/223 are in place and the system 100/method 500 has calculated the target plasma volume, the user/technician may insert the venous access device 206 into the donor's arm 208 (Step 525). Next, in a manner similar to that described above for the method shown in Figure 4, the controller 226 activates the two pumps 232, 234 and the motor 228. Operation of the two pumps 232, 234 causes whole

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blood to be drawn from the donor (step 530), anticoagulant from container 210 to be introduced into the drawn whole blood (step 535), and the now anticoagulated whole blood to be delivered to the inlet port 220 of the bowl 214.

[0063] As the anti-coagulated whole blood is withdrawn from the subject and introduced into the blood component separation device 214, the blood component separation device 214 separates the whole blood into the respective blood components (e.g., into plasma, platelets, RBC, and, perhaps, WBC) (Step 540). As discussed above, the higher density component, i.e., RBC, is forced to the outer wall of the bowl 214 and the plasma is the component closest to the outlet port and, therefore, is the first fluid component displaced from the bowl 214 via the outlet port 224 as additional anticoagulated whole blood enters the bowl 214 through the inlet port 220. During separation and processing, the optical sensor 213 monitors each layer of the blood components as they gradually and coaxially advance toward the core from the outer wall of the bowl 214, and the steps of drawing the whole blood from the subject/donor and introducing the whole blood into the bowl 12 may be altered and/or terminated in response to the detection. Additionally, as discussed above, the optical sensor 213 may be used to determine the hematocrit of the donor during processing (e.g., if it is not known and/or determined prior to the start of processing).

[0064] Once the blood component separation device 214 has separated the blood into the various components, the plasma may be removed to a plasma container 216 (e.g., a plasma bottle) through line 222 (Step 545). As noted above, some embodiments of the system 100 may include a weight sensor 195 (Fig. 1) that measures the amount of plasma collected. The plasma collection process may continue until the target plasma collection volume (discussed in greater detail below) is collected within the plasma collection container 216. If equipped with the line sensor 185, the system 100 may then use the information from the sensor 185 to either stop the removal of blood components from the bowl 214, stop drawing whole blood from the subject, or redirect the flow by, for example, closing one valve an opening another.

[0065] As mentioned above, some embodiments of the present invention continue the blood processing/separation procedure until a target plasma collection volume is collected. In order to ensure that this volume does not include the volume of any anticoagulant collected within the container 216, the target plasma collection volume should only include the volume of pure plasma (e.g., plasma only – without the volume of any anticoagulant mixed with the plasma included in the target volume). To that end and

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in a manner similar to that described above, some embodiments of the present invention may calculate the volume of pure plasma within the plasma collection container 216. To determine the volume of pure plasma, the technician or the system 100 (e.g., the controller) may calculate the percentage of anticoagulant within the collected plasma (Step 560) (e.g., the plasma contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor (see equation provided above). The amount of anticoagulant that is added to the system 100 can be determined in any of the ways mentioned above (e.g., based on the predetermined ratio of anticoagulant per unit of anticoagulated whole blood, by monitoring the volume of anticoagulant added to the system, etc.).

[0066] Once the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 570). For example, as discussed above, the technician/system 100 may determine the volume of anticoagulant within the container (based on the percentage of anticoagulant within the container 216) and subtract this volume from the total volume of fluid within the container 216 as measured by the weight sensor 195. The system 100 may continue to monitor the volume of pure plasma collected within the container 216 and continue processing whole blood (e.g., continue performing Steps 530, 535, 540, 545, 560, 570 and, possibly, steps 550, 555 and 565) until the volume of pure plasma collected within the plasma collection container 216 reaches the target plasma volume (Step 575) (e.g., as calculated based on the individual plasma volume of the donor and the target percentage of plasma to collect).

[0067] Once the system 100 has collected the target plasma volume within the plasma collection container 216, the system 100 can return the remaining components (e.g., the components remaining within the bowl 214) to the subject (Step 580) by stopping the draw of whole blood from the subject and reversing the direction of the blood/first pump 232 to draw the RBCs (and other components) from the bowl 214 and back to the subject (e.g., directly via the blood/inlet line 218 or, if so equipped, via a dedicated return line.

[0068] It is important to note that, because the system 100/method 500 collect and do not return some of the blood components (e.g., the plasma), the volume of fluid that is returned to the donor/subject is less than the volume that was removed. This, in turn, creates an intravascular deficit that is equal to the amount of plasma collected (e.g., the

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volume of whole blood removed from the donor minus the volume of plasma collected/not returned). In instances in which the intravascular deficit is too large, the donor is at risk of fainting when the procedure is complete and they get up to leave the facility. To reduce the intravascular deficit (and the risk of donor injury), as noted above, some embodiments of the present invention return saline to the patient/subject (Step 585). The saline may be used as a compensation fluid to make up for the volume of the blood component (e.g., plasma) removed. To that end, during the return step (e.g., Step 580), the controller 226 (or the technician) may open the saline valve to allow saline from the saline container 217 to flow through the saline line 223 and into the bowl 214 (via outlet 224), where it can be returned to the patient/donor with or after the remaining blood components.

[0069] As mentioned above, the volume of plasma that is collected from the donor varies from donor to donor (e.g., because it is based on the donor's height, weight, hematocrit, and blood volume). Therefore, the volume of saline that is returned to the donor to reduce the intravascular deficit may similarly be dependent on the donor. To that end, when returning the contents of the separation device and the saline (Steps 580 and 585) to the donor, the system 100/method 500 may calculate the intravascular deficit (Step 590) based on the total volume of whole blood removed from the donor and the volume of blood components and saline that has been returned (or based on the volume of plasma collected and the volume of blood components and saline that have been returned). The system 100/method 500 may continue returning saline until the donor's intravascular deficit reaches a target intravascular deficit (Step 595).

[0070] The target intravascular deficit may be any intravascular deficit that reduces the donor's risk for fainting and may be the same for each donor. For example, the target intravascular deficit may be set to 0 mL or 250 mL for each donor. Alternatively, like the target plasma volume to collect, the target intravascular deficit may be different for each donor. In other words, the target intravascular deficit may be set to 0 mL for some donors and 250 mL for others. It should be noted that 0 and 250 mL are provided as examples only and other embodiments may have target intravascular deficits between 0 and 250, or greater than 250 mL. Additionally, in some instances, it may be beneficial to return more fluid to the donor than was removed/collected. In such instances, the target intravascular deficit may be set less than zero (e.g., -1 to -250 mL) so that the donor has more fluid/volume after the procedure than they did before the procedure.

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[0071] Like the method 400 shown in Figure 4, the method 500 may similarly perform some additional and optional steps to help determine the volume of pure plasma within the plasma collection container 216. For example, some embodiments may monitor the change in weight of the anticoagulant container 210 (e.g., as measured by a weight sensor/load cell on the anticoagulant container 210) (step 550). This measurement provides an indication of the volume of anticoagulant that has been added to the system 100, and may be used help determine the percentage of anticoagulant within the plasma collection container 216. Additionally or alternatively, some embodiments may similarly, monitor the change in weight and/or volume of the plasma and anticoagulant collected within the plasma collection container 216 (e.g., via weight sensor 195) (step 555). This measurement may be used to calculate of the total volume of pure plasma collected within the plasma collection container 216 (e.g., to obtain the total weight from which to subtract the calculated volume of anticoagulant). Also, some embodiments may also monitor the volume of anticoagulant remaining in the bowl 214 (step 565) (e.g., anticoagulant that did not mix with the plasma and/or otherwise remained in the bowl) using the optical sensor on the bowl 214 to determine whether any anticoagulant remains within the bowl 214 and modify the calculation of the amount of pure plasma collected within the plasma collection container (e.g., either increase the calculated amount or decreased the calculated amount), based on the volume of anticoagulant remaining within the bowl 214.

[0072] As noted above, prior art systems that follow the current FDA nomogram for plasma collection collect a volume of plasma product (e.g., anticoagulant and plasma mixed together) based solely on the weight of the donor – the same volume is collected from every donor at the same weight. However, the total blood volume and plasma volume for two donors may vary greatly. For example, when comparing two donors in the same weight grouping according to the FDA nomogram – one obese and one not obese – the obese donor will effectively have a lower blood volume that the non-obese donor. Furthermore, with respect to the total plasma volume, donors with high hematocrit will have lower plasma volumes. In other words, because the total blood volume and total plasma volume vary from donor to donor (even among donors that weight the same), the percentage of the donor's plasma that is ultimately collected may vary widely from donor to donor. By tailoring the plasma collection to the donor (e.g., based on the donor's height, weight, BMI, hematocrit, total blood volume, and/or total plasma volume) and collecting a predetermined percent of plasma from each donor, embodiments of the preset

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invention are able to collect a greater volume of plasma (e.g., pure plasma) from some donors but less plasma from more vulnerable donors (e.g., smaller donors with high hematocrit, donors with lower plasma volume, etc.), as compared to systems that do not base the collection volume on the individual donor.

[0073] Similarly, current systems do not tailor the saline return volume to the patient (e.g., each donor at a given level receives the same volume of saline, for example, if the target plasma product volume is 800 mL, the donor will receive 500 mL of saline). However, because prior art systems collect based on the volume of the plasma product (which includes both plasma and anticoagulant) and the volume of pure plasma that is actually collected (and therefore, the volume removed from the donor) varies based on the donor hematocrit, the intravascular deficit for each donor will vary. In other words, the volume of saline returned to the donor may be sufficient for some, but insufficient for others. By tailoring the saline return to the individual donor, embodiments of the present invention are able to ensure that each donor has the same intravascular deficit (if any) once the procedure is complete. This, in turn, allows embodiments of the present invention to achieve isovolemia for each donor and greatly reduce any adverse reactions that the donor may experience (e.g., falling, fainting, light-headedness, vasovagal reactions, etc.).

[0074] It is also important to note that, although the various embodiments discussed above are in relation to a blood processing system that collects plasma, the features discussed herein may be applied to any type of blood processing system. For example, the features described herein may be implemented on blood processing systems that collect and/or process red blood cells, platelets and/or white blood cells.

[0075] The embodiments of the invention described above are intended to be merely exemplary; numerous variations and modifications will be apparent to those skilled in the art. All such variations and modifications are intended to be within the scope of the present invention as defined in any appended claims.

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What is claimed is:

1. A method for collecting plasma comprising:

(a) determining a weight and height of a donor;

(b) determining a hematocrit of the donor;

(c) calculating a donor plasma volume based, at least in part, on the weight and height of the donor and the hematocrit of the donor;

(d) calculating a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma;

(e) withdrawing whole blood from the donor through the venous-access device and a first line, the first line connected to a blood component separation device;

(f) introducing anticoagulant into the withdrawn whole blood through an anticoagulant line;

(g) separating the withdrawn whole blood into a plasma component and at least a second blood component using the blood component separation device;

(h) collecting the plasma component from the blood component separation device and into a plasma collection container;

(i) calculating a volume of pure plasma collected within the plasma collection container; and

(j) continuing steps (e) through (i) until the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

2. A method according to claim 1, further comprising:

returning, after collecting at least a portion of the target plasma collection volume, the contents of the blood component separation device to the donor through the first line.

3. A method according to claim 2, further comprising:

calculating an intravascular deficit based, at least in part on, the volume of pure plasma collected and a volume of the contents of the blood component separation device returned to the donor.

4. A method according to claim 3, further comprising:

returning a volume of saline to the donor to obtain a target intravascular deficit.

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5. A method according to claim 4, wherein the target intravascular deficit is 0 milliliters.

6. A method according to claim 4, wherein the target intravascular deficit is between -250 and 500 milliliters.

7. A method according to claim 1, further comprising:

calculating the donor's body mass index based, at least in part on the weight and height of the donor, the donor plasma volume calculated based, at least in part, on the donor's body mass index.

8. A method according to claim 1, wherein the target percentage of plasma is between 26.5 and 29.5 percent of the donor's plasma volume.

9. A method according to claim 1, further comprising:

inserting a venous-access device into the donor prior to step (e).

10. A method according to claim 1, further comprising:

calculating a percentage of anticoagulant in the collected plasma component, the volume of pure plasma based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component.

11. A method according to claim 10, further comprising:

determining a change in volume within an anticoagulant container, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the change in volume within the anticoagulant container.

12. A method according claim 10, further comprising:

determining a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the number of rotations of the anticoagulant pump.

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13. A method according to claim 10, further comprising:

determining a volume of anticoagulant within the blood component separation device, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the volume of anticoagulant within the blood component separation device.

14. A method according to claim 10, wherein the percentage of anticoagulant in the collected plasma component includes at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

15. A method according to claim 1, further comprising:

monitoring a volume of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection device based, at least in part, on the monitored volume of collected plasma component.

16. A method according to claim 1, further comprising:

monitoring a weight of plasma component collected within the plasma collection container, the calculated volume of pure plasma collected within the plasma collection device based, at least in part, on the monitored weight of collected plasma component.

17. A method according to claim 1, wherein step (b) includes monitoring a volume of red blood cells collected within the blood separation device, the determined hematocrit of the donor based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and a volume of whole blood withdrawn from the donor.

18. A system for collecting plasma comprising:

a venous-access device for drawing whole blood from a subject and returning blood components to the subject;

a blood component separation device for separating the drawn blood into a plasma component and a second blood component, the blood component separation device having an outlet and being configured to send the plasma component to a plasma container;

a first line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device and return fluid within the

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blood component separation device to the subject, the flow through the first line being controlled by a first pump;

an anticoagulant line connected to an anticoagulant source, the anticoagulant line configured to introduce anticoagulant into the drawn whole blood; and

a controller configured to control the operation of the centrifuge bowl and the first pump, the controller configured to calculate (1) a donor plasma volume based, at least in part, on a weight and height of the donor and a hematocrit of the donor, (2) a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma, and (3) a volume of pure plasma collected within the plasma container based, at least in part, upon a percentage of anticoagulant in the collected plasma component, the controller configured to stop the first pump when the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

19. A system according to claim 18, wherein the controller is further configured to:

return, after collecting at least a portion of the target plasma collection volume, fluid remaining within the blood component separation device via the first line.

20. A system according to claim 19, wherein the controller is further configured to:

calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and a volume of the contents of the blood component separation device returned to the donor.

21. A system according to claim 20, further comprising:

a saline line configured to fluidly connect to a saline source and the blood component separation device, the controller configured to return a volume of saline to the donor to obtain a target intravascular deficit.

22. A system according to claim 21, wherein the target intravascular deficit is between -250 and 500 milliliters.

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23. A system according to claim 18, wherein the controller is further configured to:

calculate the donor's body mass index based, at least in part, on the weight and height of the donor, the donor plasma volume calculated based, at least in part, on the donor's body mass index.

24. A system according to claim 18, wherein the target percentage of plasma is between 26.5 and 29.5 percent of the donor's plasma volume.

25. A system according to claim 18, wherein the controller is further configured to:

calculate the percentage of anticoagulant in the collected plasma component.

26. A system according to claim 25, wherein the percentage of anticoagulant in the collected plasma component is based, at least in part, on a volume of anticoagulant added to the drawn whole blood and the subject's hematocrit.

27. A system according to claim 25, further comprising:

an anticoagulant source weight sensor configured to measure the weight of the anticoagulant source, the controller further configured to monitor a change in volume within the anticoagulant container based on the measured weight of the anticoagulant source, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the change in volume within the anticoagulant source.

28. A system according to claim 25, wherein the controller is configured to monitor a number of rotations of an anticoagulant pump to determine a volume of anticoagulant introduced into the whole blood, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the number of rotations of the anticoagulant pump.

29. A system according to claim 25, further comprising:

an optical sensor located on the blood component separation device and configured to monitor the contents of the blood component separation device and determine if a volume of anticoagulant remains within the blood component separation device, the calculated percentage of anticoagulant in the collected plasma being based, at least in part, on the volume of anticoagulant within the blood component separation device.

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30. A system according to claim 18, further comprising:

a plasma container weight sensor configured to monitor a volume of plasma component collected within the plasma container, the calculated volume of pure plasma collected within the plasma collection device based, at least in part, on the monitored volume of collected plasma component.

31. A system according to claim 18, further comprising:

a plasma container weight sensor configured to monitor a weight of plasma component collected within the plasma container, the calculated volume of pure plasma collected within the plasma collection device based, at least in part, on the monitored weight of collected plasma component.

32. A system according to claim 18, further comprising:

an optical sensor located on the blood component separation device and configured to monitor a volume of red blood cells collected within the blood separation device, the controller configured to determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and a volume of whole blood withdrawn from the donor.

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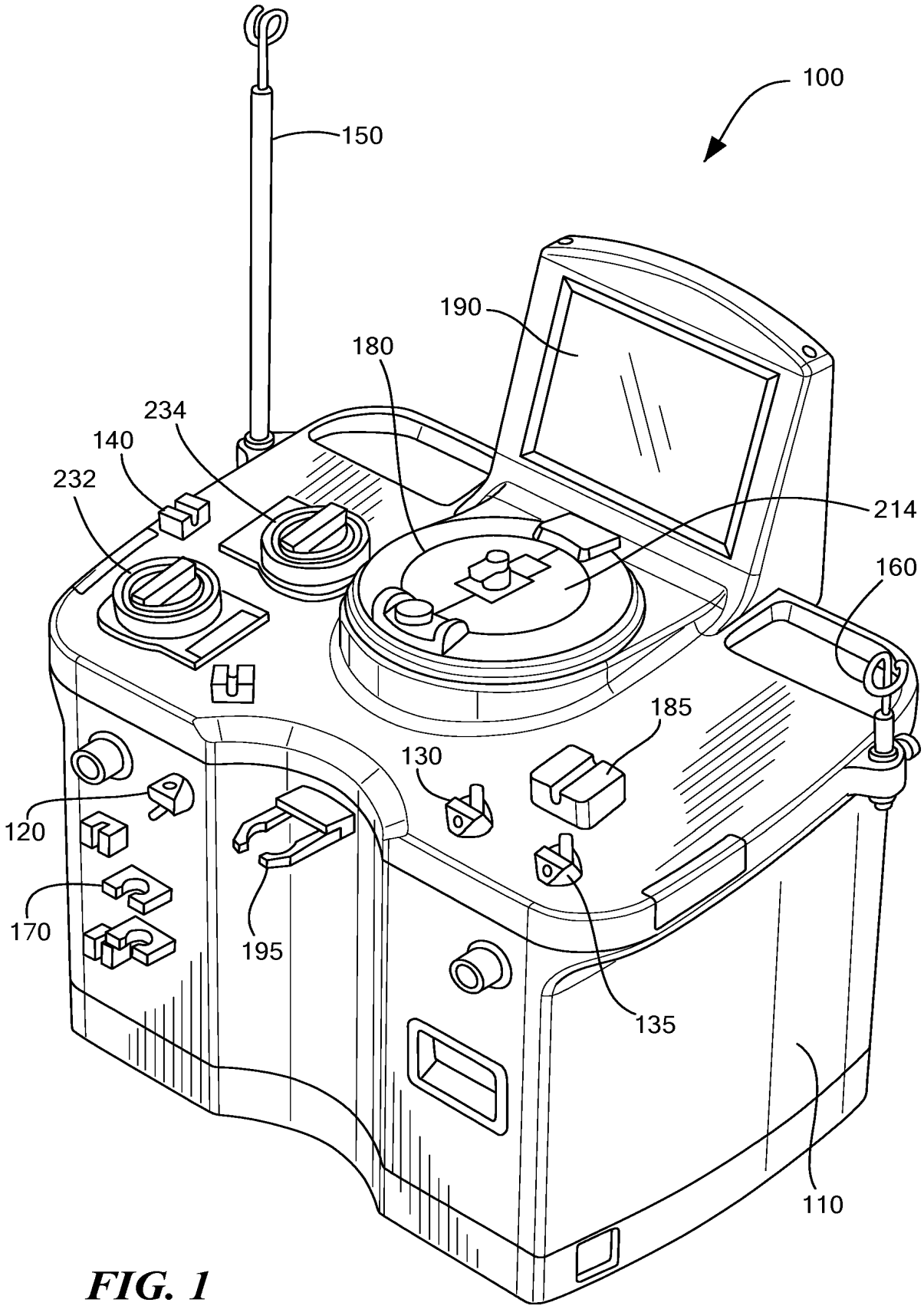

FIG. 1

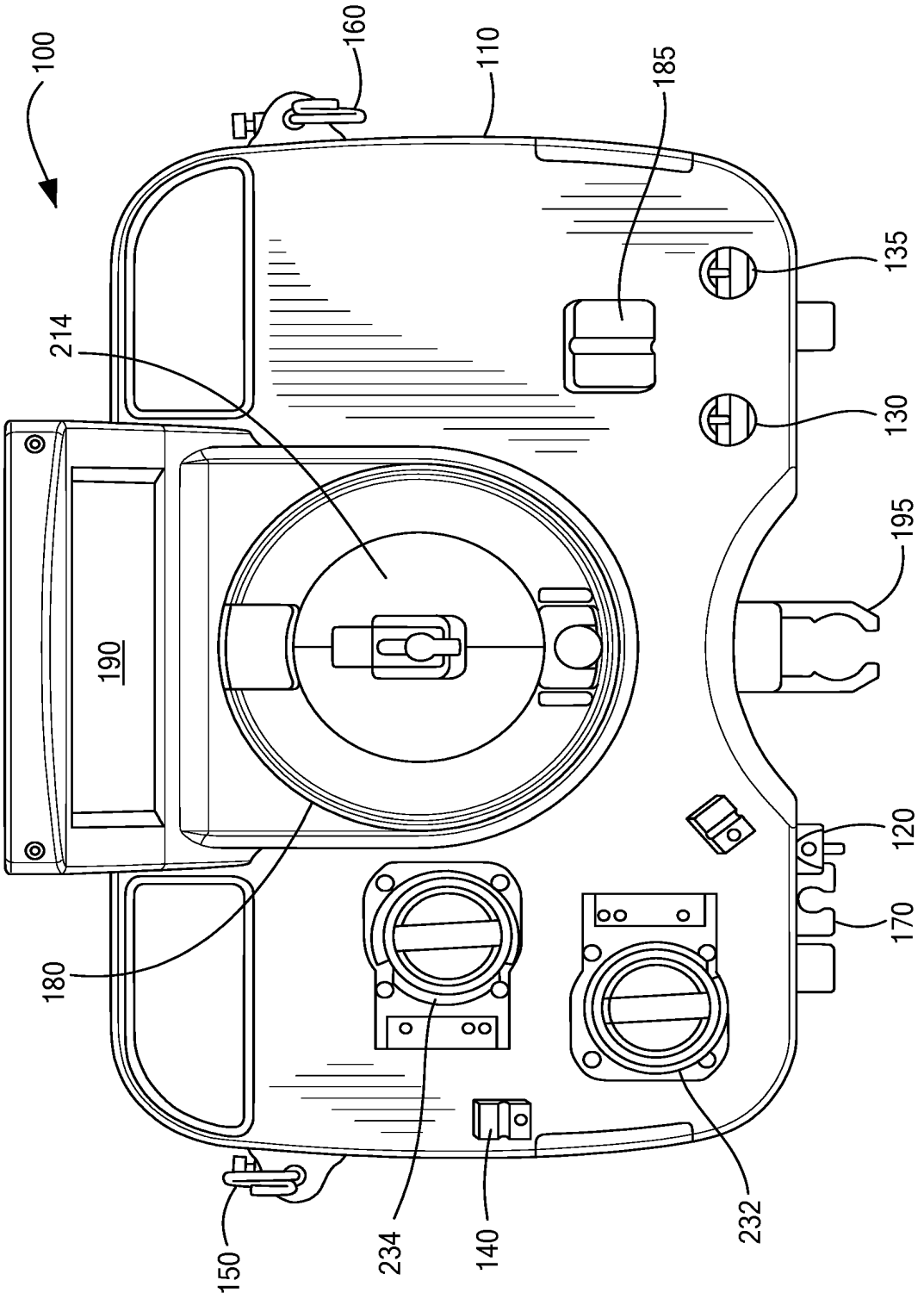

FIG. 2

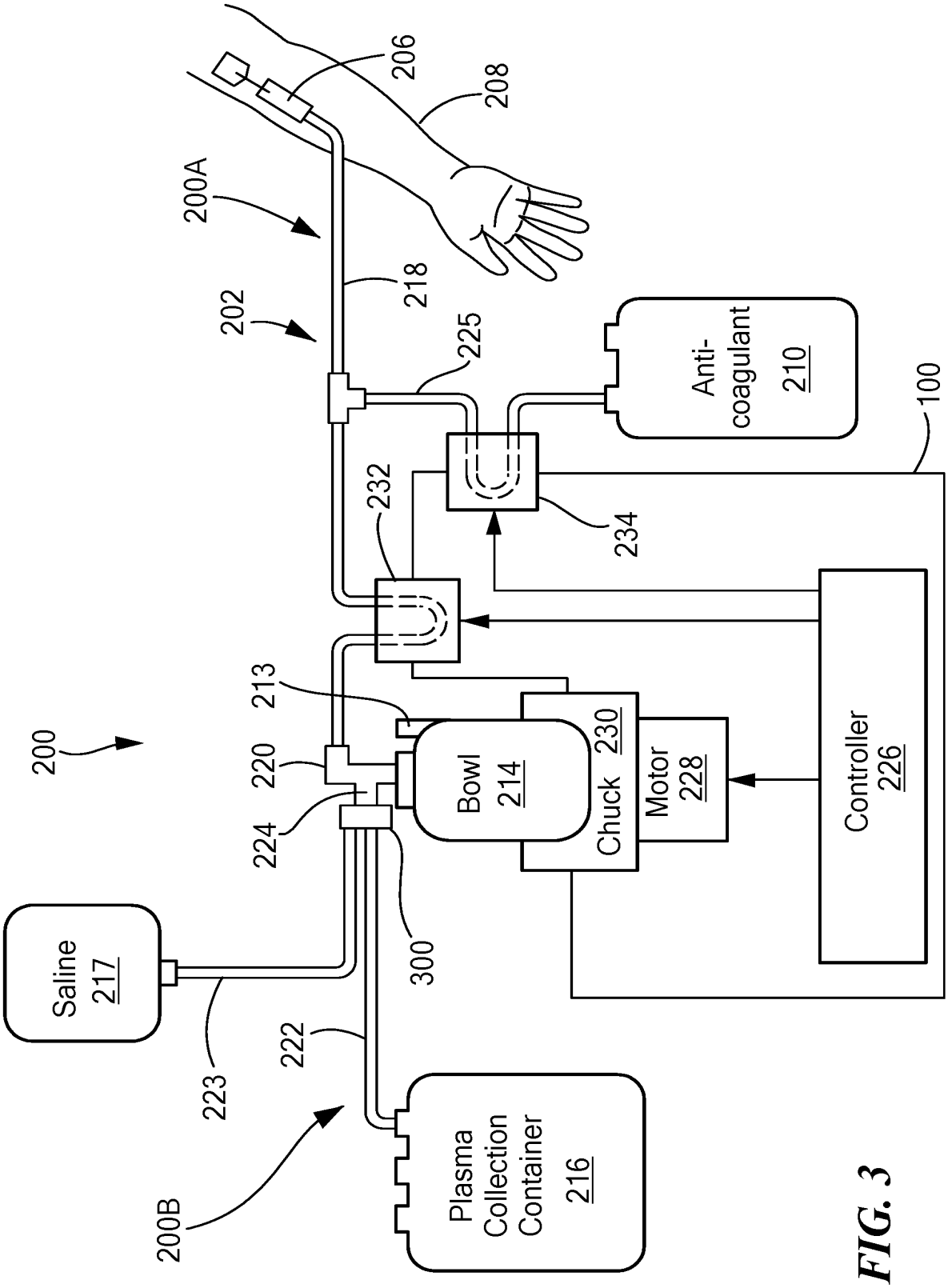
206
208
200A
218
202
225
Anti-coagulant 210
100
232
234
213
200
220
Bowl 214
Chuck 230
Motor 228
Controller 226
224
300
Saline 217
222
223
Plasma Collection Container 216
200B

FIG. 3

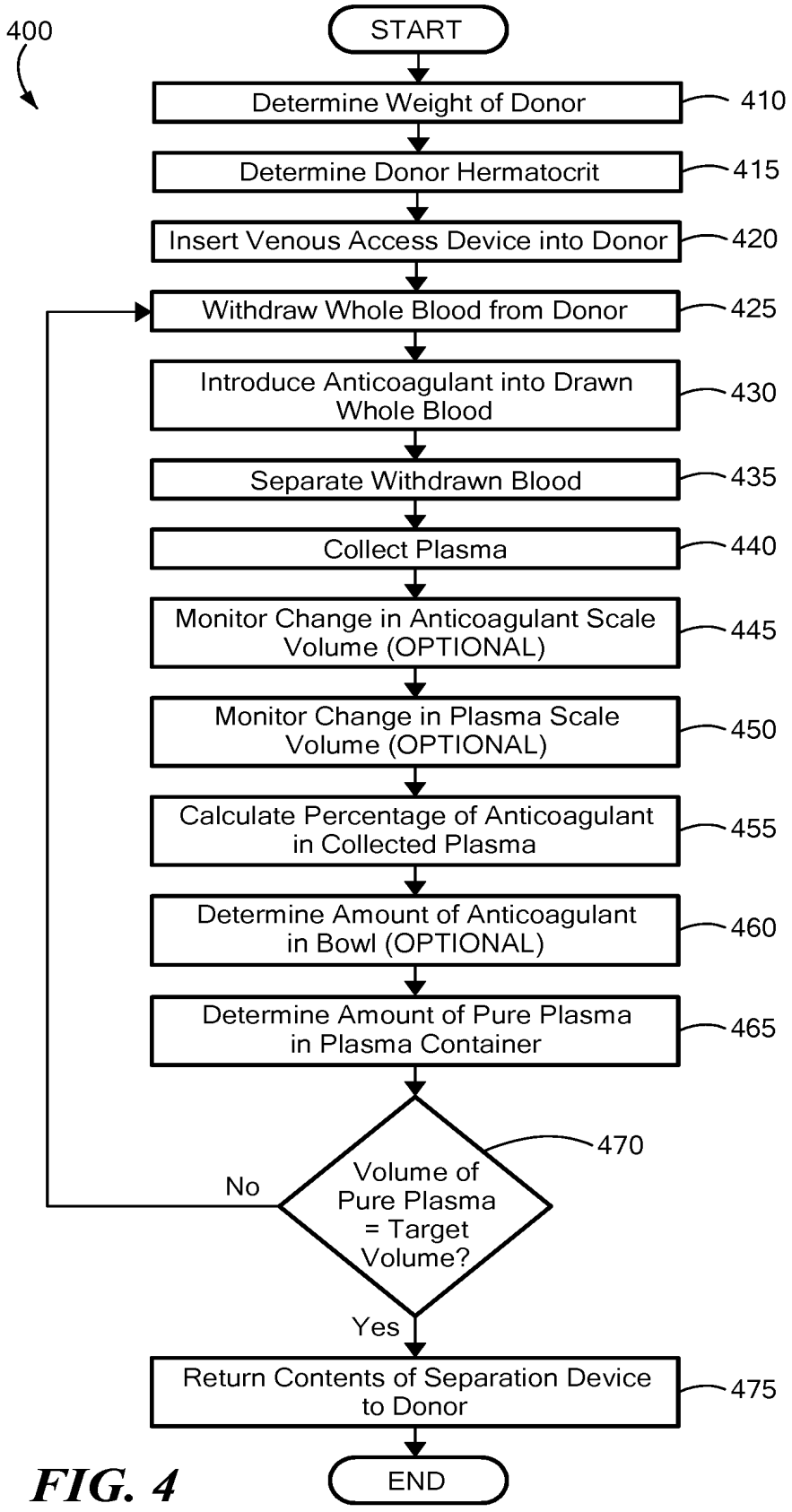
400
START
Determine Weight of Donor
410
Determine Donor Hermatocrit
415
Insert Venous Access Device into Donor
420
Withdraw Whole Blood from Donor
425
Introduce Anticoagulant into Drawn Whole Blood
430
Separate Withdrawn Blood
435
Collect Plasma
440
Monitor Change in Anticoagulant Scale Volume (OPTIONAL)
445
Monitor Change in Plasma Scale Volume (OPTIONAL)
450
Calculate Percentage of Anticoagulant in Collected Plasma
455
Determine Amount of Anticoagulant in Bowl (OPTIONAL)
460
Determine Amount of Pure Plasma in Plasma Container
465
Volume of Pure Plasma = Target Volume?
470
No
Yes
Return Contents of Separation Device to Donor
475
END

FIG. 4

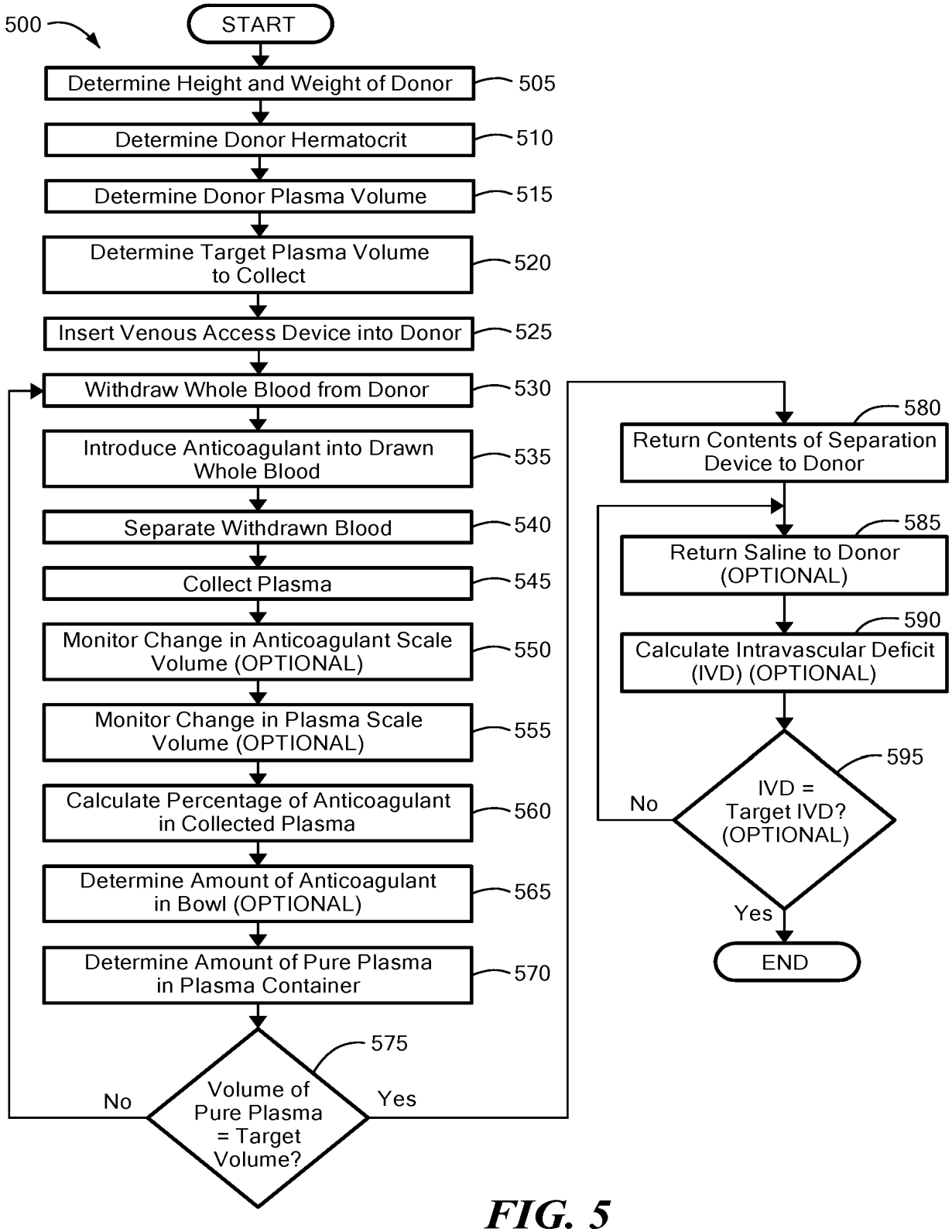
500
START
Determine Height and Weight of Donor
505
Determine Donor Hermatocrit
510
Determine Donor Plasma Volume
515
Determine Target Plasma Volume to Collect
520
Insert Venous Access Device into Donor
525
Withdraw Whole Blood from Donor
530
Introduce Anticoagulant into Drawn Whole Blood
535
Separate Withdrawn Blood
540
Collect Plasma
545
Monitor Change in Anticoagulant Scale Volume (OPTIONAL)
550
Monitor Change in Plasma Scale Volume (OPTIONAL)
555
Calculate Percentage of Anticoagulant in Collected Plasma
560
Determine Amount of Anticoagulant in Bowl (OPTIONAL)
565
Determine Amount of Pure Plasma in Plasma Container
570
575
Volume of Pure Plasma = Target Volume?
No
Yes
580
Return Contents of Separation Device to Donor
585
Return Saline to Donor (OPTIONAL)
590
Calculate Intravascular Deficit (IVD) (OPTIONAL)
595
IVD = Target IVD? (OPTIONAL)
No
Yes
END

FIG. 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/57528

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61M 1/36 (2018.01)
CPC - A61M 1/3496

According to International Patent Classification (IPC) or to both national classification and IPC

B FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y -- A	US 2001/0000185 A1 (KELLER et al.); 5 April 2001 (05.04.2001); entire document, especially Abstract, para. [0115]-[0116], [0264], [0269], [0272], [0275], [0280], [0316]-[0319], [0329].	1-2, 9, 15, 17 --- 3-6, 8, 10, 11-14, 16, 18-22, 24-28, 30-31 --- 7, 23, 29, 32
Y -- A	US 2003/0125881 A1 (RYAN); 3 July 2003 (03.07.2003); entire document, especially Abstract, para. [0011]-[0012], [0014], [0019], [0021], [0026]-[0027], [0044].	1, 8, 10-14, 16, 18-22, 24-28, 30-31 --- 7, 23, 29, 32
Y	US 2002/0062100 A1 (PIERCE et al.); 23 May 2002 (23.05.2002); entire document, especially Abstract, para. [0111], [0137].	3-6, 20-22
Y	US 2012/0175313 A1 (BARRY et al.); 12 July 2012 (12.07.2012); entire document, especially Abstract, para. [0057].	11, 13
Y	US 2014/0356851 A1 (HAEMONETICS CORPORATION); 4 December 2014 (04.12.2014); entire document, especially Abstract, para. [0030]-[0031].	14

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 December 2018	07 JAN 2019
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0335

PTO/SB/08a (01-22)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2002-282352	JP	A	2002-10-02	Terumo Corp		X

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0336

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17205400
	Filing Date	2021-03-18
	First Named Inventor	Michael Ragusa
	Art Unit	N/A
	Examiner Name	Not Yet Assigned
	Attorney Docket Number	130670-80104

	1		

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0337

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2022-04-04
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0338

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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Petitioner Terumo Exhibit 1014-0339

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 4, 2022
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 | Confirmation No.: 4686

Filed: March 18, 2021 | Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING PLASMA | Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional document. A PTO Form SB/08 and a full copy of the document required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

Applicant submits herewith a copy of the cited foreign patent in accordance with 37 C.F.R. § 1.98(a)(2).

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	10,980,926	Issued	130670-08005
17/205,374	March 18, 2021	2021-0205509	Published	130670-08006
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	10,980,934	Issued	130670-80103

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed reference.

Applicant believes no fee is due with this response.

Dated: April 4, 2022

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0341

Electronic Acknowledgement Receipt

EFS ID:	45379223
Application Number:	17205400
International Application Number:	
Confirmation Number:	4686
Title of Invention:	SYSTEM AND METHOD FOR COLLECTING PLASMA
First Named Inventor/Applicant Name:	Michael Ragusa
Customer Number:	86738
Filer:	Jonathan Lovely
Filer Authorized By:	
Attorney Docket Number:	130670-80104
Receipt Date:	04-APR-2022
Filing Date:	18-MAR-2021
Time Stamp:	07:24:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	130670-08006_-_JP2002282352A.pdf	767249 f6c8cd708d8e9564bfa68fe940aa69f5e55ac7ac	no	14

Warnings:

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0342

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	130670-80104_-_Information_Disclosure_Statement_Fillable_PDF.pdf	1263150 9a7e6a6ef7f4fb8fa219f580a9c5c9399e5d13bd	no	4
Warnings:					
Information:					
A U.S. Patent Number Citation or a U.S. Publication Number Citation is required in the Information Disclosure Statement (IDS) form for autoloading of data into USPTO systems. You may remove the form to add the required data in order to correct the Informational Message if you are citing U.S. References. If you chose not to include U.S. References, the image of the form will be processed and be made available within the Image File Wrapper (IFW) system. However, no data will be extracted from this form. Any additional data such as Foreign Patent Documents or Non Patent Literature will be manually reviewed and keyed into USPTO systems.					
3	Transmittal Letter	Information_Disclosure_Statement.pdf	25198 3c73fb2d710f2c94677cd369f97368f032005195	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	2055597		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Espacenet

Bibliographic data: JP2002282352 (A) — 2002-10-02

BLOOD COMPONENT COLLECTING DEVICE

Inventor(s): TAKAGI YOSHIMI ± (TAKAGI YOSHIMI)

Applicant(s): TERUMO CORP ± (TERUMO CORP)

Classification: **- international:** ***A61M1/02;*** (IPC1-7): A61M1/02
- cooperative:

Application number: JP20010087773 20010326

Priority number(s): JP20010087773 20010326

Abstract of JP2002282352 (A)

PROBLEM TO BE SOLVED: To provide a blood component collecting device that can perform an appropriate collection of blood component according to a donor.
SOLUTION: The blood component collecting device 1 shown in a figure 1 is the device that collects mainly plasma as a specific blood component and comprising a needle for collecting blood (means for collecting device) 29 that collects blood from a donor, an anticoagulant providing means that adds anticoagulant into the blood (23 in the third line and liquid feeding pump 12 in the second), a centrifuge 20 that centrifuges the blood that is collected by the needle 29 and to which anticoagulant is added by the anticoagulant providing means into multiple blood components, a plasma collecting bag (a blood component collecting bag) 25 that collects plasma to which the anticoagulant is contaminated, an input means 3 to which information on the donor is inputted, and a control unit (a control means) that controls the movement of the blood component collecting device 1, and a specific condition of the blood component collecting device 1 is set according to information on the donor. The above setting condition is preferably to be an aimed collecting volume for plasma itself not including anticoagulant.

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Petitioner Terumo Exhibit 1014-0344

(19)日本国特許庁（ＪＰ）　(12) **公開特許公報**（Ａ）　(11)特許出願公開番号
特開2002－282352
（P2002－282352A）
(43)公開日　平成14年10月２日(2002.10.2)

(51)Int.Cl.[7]	識別記号	ＦＩ		テーマコード（参考）
Ａ６１Ｍ　1/02	５７５	Ａ６１Ｍ　1/02	５７５	４Ｃ０７７

審査請求　未請求　請求項の数６　ＯＬ　（全 13 頁）

(21)出願番号　特願2001－87773(P2001－87773)

(22)出願日　平成13年３月26日(2001.3.26)

(71)出願人　000109543
テルモ株式会社
東京都渋谷区幡ヶ谷２丁目44番１号
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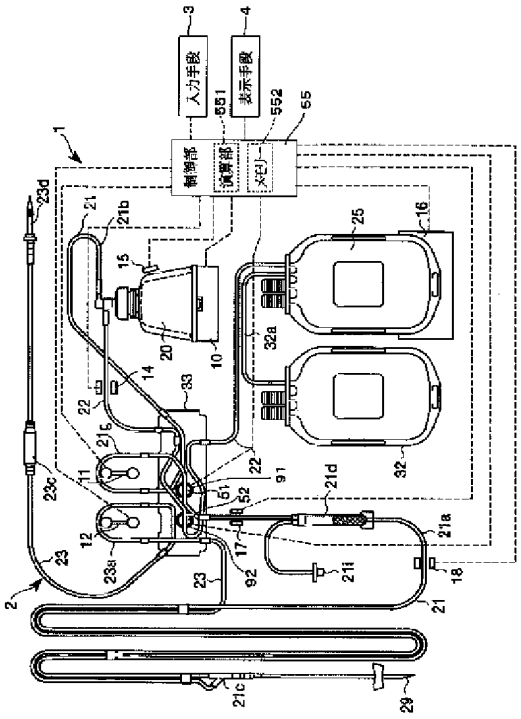
静岡県富士宮市三園平818番地　テルモ株式会社内
(74)代理人　100091292
弁理士　増田　達哉

Ｆターム(参考)　4C077 AA13 BB04 DD13 HH03 HH16 JJ03 JJ17 JJ28 KK27 NN03

(54)【発明の名称】　血液成分採取装置

(57)【要約】
【課題】　供血者に応じた適正な血液成分採取操作を行なうことができる血液成分採取装置を提供すること。
【解決手段】　図１に示す血液成分採取装置１は、所定の血液成分として、主に血漿を採取する装置であり、ドナー（供血者）から血液を採取する採血針（採血手段）２９と、血液中に抗凝固剤を添加する抗凝固剤供給手段（第３のライン２３および第２の送液ポンプ１２）と、採血針２９により採血され、抗凝固剤供給手段により抗凝固剤が添加された血液を複数の血液成分に遠心分離する遠心分離器２０と、抗凝固剤が混入した血漿を採取する血漿採取バッグ（血液成分採取バッグ）２５と、ドナーに関する情報を入力する入力手段３と、血液成分採取装置１の作動を制御する制御部（制御手段）とを有し、ドナーに関する情報に基づき、血液成分採取装置１の所定の条件を設定する。また、前記所定の条件は、抗凝固剤を除く血漿自体の目標とする採取量とするのが好ましい。



Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0345

【特許請求の範囲】
【請求項１】　供血者から採取した血液を複数の血液成分に分離するとともに分離された血液成分を採取する血液成分採取装置であって、
供血者から血液を採取する採血手段と、
前記血液中に抗凝固剤を添加する抗凝固剤供給手段と、
内部に貯血空間を有するローターと、該ローターの回転により前記採血手段により採取された血液を前記貯血空間内で複数の血液成分に遠心分離する遠心分離器と、
前記貯血空間に連通し、所定の血液成分を採取する血液成分採取バッグと、
前記所定の血液成分の採取量を検出する検出手段と、
前記供血者に関する情報を入力する入力手段と、
前記血液成分採取装置の作動を制御する制御手段とを有し、
前記供血者に関する情報に基づき、前記血液成分採取装置の所定の条件を設定することを特徴とする血液成分採取装置。
【請求項２】　前記所定の条件は、前記所定の血液成分の目標とする採取量である請求項１に記載の血液成分採取装置。
【請求項３】　前記供血者から採取された血液を遠心分離し、前記所定の血液成分を、前記血液成分採取バッグ内に移送する血液成分採取工程と、
残りの血液成分を前記供血者に返還する血液成分返還工程とを有する血液成分採取操作を複数サイクル行なうよう作動し、
前記所定の血液成分の目標とする採取量に基づき、前記血液成分採取操作のサイクル数を決定する請求項２に記載の血液成分採取装置。
【請求項４】　前記血液成分採取バッグ内に採取された前記所定の血液成分の現在の採取量が、前記所定の血液成分の目標とする採取量の７０～１００％に到達した場合、あるいは、前記血液成分採取操作を前記サイクル数行なった場合には、前記血液成分採取操作を終了する請求項３に記載の血液成分採取装置。
【請求項５】　前記所定の血液成分の採取量には、抗凝固剤の混入量が含まれていない請求項２ないし４のいずれかに記載の血液成分採取装置。
【請求項６】　前記所定の血液成分は、主に血漿である請求項１ないし５のいずれかに記載の血液成分採取装置。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】本発明は、血液中から所定の血液成分を採取する血液成分採取装置に関する。
【０００２】
【従来の技術】採血を行う場合、現在では、血液の有効利用および供血者の負担軽減などの理由から、採血血液を遠心分離などにより各血液成分に分離し、輸血者に必要な成分だけを採取し、その他の成分は供血者に返還する成分採血が行われている。
【０００３】このような成分採血では、例えば、血漿製剤を得る場合、供血者から採取した血液を血液成分採取回路に導入し、該血液成分採取回路に設置された遠心ボウルと呼ばれる遠心分離器により、血漿、バフィーコートおよび赤血球に分離し、その内の血漿は容器に回収されて血漿製剤とし、残りのバフィーコート（白血球、血小板）および赤血球は、供血者に返血（返還）することが行われる。
【０００４】ところで、従来、成分採血を行なう場合、供血者に関する情報（例えば、身長、体重、性別等）を考慮せず、例えば、目標とする血漿の採取量（目標血漿採取量）を設定している。この場合、供血者に応じた適正な採取量を得るのが困難である。
【０００５】また、通常、採取される血漿中には、抗凝固剤が混入しており、目標血漿採取量も、抗凝固剤の混入量を含んで設定されている。
【０００６】このため、操作者は、血漿自体の採取量を把握することができず、供血者によっては、許容される量以上の血漿を採取してしまったり、あるいは、許容される量にはるかに満たない量で血漿採取を終了してしまったりすることがあり、好ましくない。
【０００７】
【発明が解決しようとする課題】本発明の目的は、供血者に応じた適正な血液成分採取操作を行なうことができる血液成分採取装置を提供することにある。
【０００８】
【課題を解決するための手段】このような目的は、下記（１）～（９）の本発明により達成される。
【０００９】（１）　供血者から採取した血液を複数の血液成分に分離するとともに分離された血液成分を採取する血液成分採取装置であって、供血者から血液を採取する採血手段と、前記血液中に抗凝固剤を添加する抗凝固剤供給手段と、内部に貯血空間を有するローターと、該ローターの回転により前記採血手段により採取された血液を前記貯血空間内で複数の血液成分に遠心分離する遠心分離器と、前記貯血空間に連通し、所定の血液成分を採取する血液成分採取バッグと、前記所定の血液成分の採取量を検出する検出手段と、前記供血者に関する情報を入力する入力手段と、前記血液成分採取装置の作動を制御する制御手段とを有し、前記供血者に関する情報に基づき、前記血液成分採取装置の所定の条件を設定することを特徴とする血液成分採取装置。
【００１０】（２）　前記所定の条件は、前記所定の血液成分の目標とする採取量である上記（１）に記載の血液成分採取装置。
【００１１】（３）　前記供血者から採取された血液を遠心分離し、前記所定の血液成分を、前記血液成分採取バッグ内に移送する血液成分採取工程と、残りの血液成

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分を前記供血者に返還する血液成分返還工程とを有する血液成分採取操作を複数サイクル行なうよう作動し、前記所定の血液成分の目標とする採取量に基づき、前記血液成分採取操作のサイクル数を決定する上記（２）に記載の血液成分採取装置。

【００１２】（４）　前記血液成分採取バッグ内に採取された前記所定の血液成分の現在の採取量が、前記所定の血液成分の目標とする採取量の７０～１００％に到達した場合、あるいは、前記血液成分採取操作を前記サイクル数行なった場合には、前記血液成分採取操作を終了する上記（３）に記載の血液成分採取装置。

【００１３】（５）　前記所定の血液成分の採取量には、抗凝固剤の混入量が含まれていない上記（２）ないし（４）のいずれかに記載の血液成分採取装置。

【００１４】（６）　前記所定の条件を表示する表示手段を有する上記（１）ないし（５）のいずれかに記載の血液成分採取装置。

【００１５】（７）　前記表示手段は、前記血液成分採取バッグ内に採取された前記所定の血液成分の現在の採取量を表示する上記（６）に記載の血液成分採取装置。

【００１６】（８）　前記供血者に関する情報は、前記供血者の性別、体重および身長のうちの少なくとも１つを含む上記（１）ないし（７）のいずれかに記載の血液成分採取装置。

【００１７】（９）　前記所定の血液成分は、主に血漿である上記（１）ないし（８）のいずれかに記載の血液成分採取装置。

【００１８】

【発明の実施の形態】以下、本発明の血液成分採取装置を添付図面に示す好適な実施形態に基づいて詳細に説明する。

【００１９】図１は、本発明の血液成分採取装置の構成例を示す平面図であり、図２は、本発明の血液成分採取装置が備える遠心分離器に遠心分離器駆動装置が装着された状態の部分破断断面図であり、図３は、本発明の血液成分採取装置の作用を説明するためのフローチャートである。

【００２０】以下、血液成分採取装置１を、所定の血液成分として、主に血漿を採取する血漿採取装置に適用した場合を一例として説明する。

【００２１】図１に示す血液成分採取装置１は、ドナー（供血者）から血液を採取する採血針（採血手段）２９と、内部に貯血空間１４６を有するローター１４２を備え、ローター１４２の回転により採血針２９により採取された血液を貯血空間１４６内にて遠心分離する遠心分離器２０と、遠心分離器２０により分離された血漿を採取する血漿採取バッグ（血液成分採取バッグ）２５とを備える血液成分採取回路（血漿採取回路）２を有し、ドナーから採取した血液を遠心分離し、血漿を採取した後、主に白血球、血小板および赤血球等の血漿以外の血液成分（残りの血液成分）をドナーに返還する装置である。

【００２２】血液成分採取装置１は、内部に貯血空間１４６を有するローター１４２と、貯血空間１４６に連通する流入口１４３および流出口１４４とを有し、ローター１４２の回転により流入口１４３より導入された血液を貯血空間１４６内で遠心分離する遠心分離器２０と、採血手段である採血針２９と遠心分離器２０の流入口１４３とを接続するための第１のライン２１と、遠心分離器２０の流出口１４４に接続された第２のライン２２と、第１のライン２１に接続され、抗凝固剤注入のための第３のライン２３と、第２のライン２２と接続された血漿採取バッグ２５と、血漿採取バッグ２５とチューブ３２ａにより接続されたサブバッグ３２とを備える血液成分採取回路２を有している。

【００２３】また、血液成分採取装置１は、遠心分離器２０のローター１４２を回転させるための遠心分離器駆動装置１０と、第１のライン２１のための第１の送液ポンプ１１と、第３のライン２３のための第２の送液ポンプ１２と、血液成分採取回路２の流路の開閉を行うための第１の流路開閉手段５１および第２の流路開閉手段５２と、遠心分離器駆動装置１０、第１の送液ポンプ１１、第２の送液ポンプ１２、第１の流路開閉手段５１および第２の流路開閉手段５２を制御するための制御部（制御手段）５５と、濁度センサ１４と、光学式センサ１５と、重量センサ（検出手段）１６と、第１の気泡センサ１７と、第２の気泡センサ１８と、入力手段３と、表示手段４とを備えている。

【００２４】なお、本実施形態では、第３のライン２３と第２の送液ポンプ１２とで、ドナーから採取された血液中に抗凝固剤を添加する抗凝固剤供給手段が構成される。

【００２５】以下、各部の構成について説明する。採血針２９としては、例えば、金属針が使用される。

【００２６】第１のライン２１は、採血針２９が接続された採血針側第１ライン２１ａと、遠心分離器２０の流入口１４３とを接続された遠心分離器側第１ライン２１ｂと、これらの間に配置された第１のポンプチューブ２１ｇとを有している。

【００２７】採血針側第１ライン２１ａは、気泡およびマイクロアグリゲート除去のためのチャンバー２１ｄを備える。チャンバー２１ｄには、通気性かつ菌不透過性のフィルター２１ｉが接続されている。

【００２８】第２のライン２２は、一端が遠心分離器２０の流出口１４４に接続され、他端が血漿採取バッグ２５に接続されている。

【００２９】第３のライン２３は、一端が第１のライン２１に設けられた接続用分岐コネクター２１ｃに接続されている。第３のライン２３は、接続用分岐コネクター２１ｃ側より、第２のポンプチューブ２３ａ、気泡除去

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用チャンバー２３ｃ、抗凝固剤容器接続用針２３ｄを備えている。

【００３０】上述した第１のライン２１、第２のライン２２および第３のライン２３の形成に使用されるチューブ、各ポンプチューブ２１ｇ、２３ａ、さらに、バッグに接続されているチューブ３２ａの構成材料としては、ポリ塩化ビニルが好ましい。

【００３１】各チューブがポリ塩化ビニル製であれば、十分な可撓性、柔軟性が得られるので取り扱いがし易く、また、クレンメ等による閉塞にも適するからである。

【００３２】なお、各ポンプチューブ２１ｇ、２３ａとしては、ローラーポンプにより押圧されても損傷を受けない程度の強度を備えるものが使用されている。

【００３３】また、上述した分岐コネクター２１ｃの構成材料についても、前記チューブの構成材料と同様のものを用いることができる。

【００３４】血漿採取バッグ２５は、血漿を採取するための容器であり、第２のライン２２を介して、遠心分離器２０に接続され、これにより、血漿採取バッグ２５の内部は、ローター１４２の貯血空間１４６に連通している。

【００３５】サブバッグ３２は、血漿採取操作（血液成分採取操作）の終了後に、血漿採取バッグ２５内から空気（エアー）を排出し、これを貯留するための容器である。このサブバッグ３２は、チューブ３２ａを介して血漿採取バッグ２５に接続され、それらの内部同士が連通している。

【００３６】これらの血漿採取バッグ２５、サブバッグ３２は、それぞれ、樹脂製の可撓性を有するシート材を重ね、その周縁部を融着（熱融着、高周波融着等）または接着して袋状にしたものが使用される。

【００３７】血漿採取バッグ２５、サブバッグ３２に使用される材料としては、例えば、軟質ポリ塩化ビニルが好適に使用される。この軟質ポリ塩化ビニルにおける可塑剤としては、例えば、ジ（エチルヘキシル）フタレート（ＤＥＨＰ）、ジ－（ｎ－デシル）フタレート（ＤｎＤＰ）等が使用される。なお、このような可塑剤の含有量は、ポリ塩化ビニル１００重量部に対し、３０～７０重量部程度とするのが好ましい。

【００３８】そして、血液成分採取回路２の主要部分は、図１に示すように、カセット式となっている。血液成分採取回路２は、すべてのライン（第１のライン２１、第２のライン２２、第３のライン２３）を部分的に収納しかつ部分的にそれらを保持し、言い換えれば、部分的にそれらが固定されたカセットハウジング３３を備えている。

【００３９】カセットハウジング３３には、第１のポンプチューブ２１ｇの両端部および第２のポンプチューブ２３ａの両端部が固定され、これらのポンプチューブ２１ｇ、２３ａは、それぞれ、カセットハウジング３３より、後述する各送液ポンプ（例えば、ローラーポンプ等）１１、１２の形状に対応したループ状に突出している。このため、第１のポンプチューブ２１ｇおよび第２のポンプチューブ２３ａは、各送液ポンプ１１、１２への装着が容易である。

【００４０】さらに、カセットハウジング３３は、カセットハウジング３３内に位置する複数の開口部を備えている。具体的には、第１のポンプチューブ２１ｇより採血針２９側の第１のライン２１を露出させかつ、第１の流路開閉手段５１の侵入が可能な第１の開口部９１、第２のライン２２を露出させかつ第２の流路開閉手段５２の侵入が可能な第２の開口部９２を備えている。

【００４１】血液成分採取装置１は、このカセットハウジング３３を装着するカセットハウジング装着部（図示せず）を備えている。このため、カセットハウジング３３を血液成分採取装置１のカセットハウジング装着部に装着することにより、カセットハウジング３３の各開口部９１、９２より露出する部分の各ラインおよび各チューブが、自動的に対応する各流路開閉手段５１、５２に装着される。これにより血液成分採取回路２の装着が容易であるとともに、血漿採取（血液成分採取）の準備も迅速に行える。

【００４２】また、血液成分採取装置１には、カセットハウジング装着部に近接して２つの送液ポンプ１１、１２が設けられている。このため、カセットハウジング３３より露出する各ポンプチューブ２１ｇ、２３ａの各送液ポンプ１１、１２への装着も容易である。

【００４３】血液成分採取回路２に設けられている遠心分離器２０は、通常、遠心ボウルと呼ばれており、遠心力により血液を分離する。遠心分離器２０としては、図２に示すものが使用される。

【００４４】第１の流路開閉手段５１は、ポンプチューブ２１ｇより採血針側において第１のライン２１の流路の途中を開閉するために設けられている。

【００４５】第２の流路開閉手段５２は、第２のライン２２の流路の途中を開閉するために設けられている。

【００４６】第１の流路開閉手段５１および第２の流路開閉手段５２は、ラインもしくはチューブの挿入部を備え、挿入部には、例えば、ソレノイド、電動モーター、シリンダ（油圧または空気圧）等の駆動源で作動するクランプを有する。具体的には、ソレノイドで作動する電磁クランプが好適である。

【００４７】遠心分離器駆動装置１０は、図２に示すように、遠心分離器２０を収納するハウジング１５１と、脚部１５２と、駆動源であるモータ１５３と、遠心分離器２０を保持する円盤状の固定台１５５とで構成されている。ハウジング１５１は、脚部１５２の上部に載置、固定されている。

【００４８】また、ハウジング１５１の下面には、ボル

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ト１５６によりスペーサー１５７を介してモータ１５３が固定されている。モータ１５３の回転軸１５４の先端部には、固定台１５５が回転軸１５４と同軸でかつ一体的に回転するように嵌入されており、固定台１５５の上部には、ローター１４２の底部が嵌合する凹部が形成されている。

【００４９】また、遠心分離器２０の上部１４５は、図示しない固定部材により、ハウジング１５１に固定されている。遠心分離器駆動装置１０では、モータ１５３を駆動すると、固定台１５５およびそれに固定されたローター１４２が、あらかじめ設定された所定の遠心条件（例えば、回転数１０００～６０００ｒｐｍ）で回転する。この遠心条件により、ローター１４２内の血液の分離パターン（例えば、分離する血液成分数）を設定することができる。

【００５０】なお、ローター１４２において、貯血空間１４６の容積は、例えば、１００～３５０ｍＬ程度とされる。

【００５１】また、ハウジング１５１の内壁には、遠心分離器２０（貯血空間１４６）内で分離された血液成分の界面（例えば、血漿層１３１とバフィーコート層１３２との界面Ｂ、バフィーコート層１３２と赤血球層１３３との界面、血漿層と血球層の界面）の位置を光学的に検出する光学式センサ１５が、取付部材１５８により設置、固定されている。

【００５２】この光学式センサ１５は、遠心分離器２０の肩の部分に向けて光を照射する光源と、遠心ボウルから反射して戻ってくる光を受光する受光部で構成されている。つまり、ＬＥＤ（半導体レーザー等）のような発光素子と、フォトダイオードまたはＣＣＤのような受光素子とが列状に配置され、発光素子から発せられた光の血液成分での反射光を受光素子により受光し、その受光光量を光電変換するように構成されている。分離された血液成分（例えば、血漿層１３１とバフィーコート層１３２）により反射光の強度が異なるため、受光光量が変化した受光素子に対応する位置が、界面Ｂの位置として検出される。

【００５３】より具体的には、遠心分離器２０の光が通過する位置が透明な液体（血漿や水）で充填されている時と、バフィーコート層１３２で充填されている時の、受光部での受光量の差から、バフィーコート層１３２が光通過部に到達したことが検知される。

【００５４】バフィーコート層１３２を検出する位置は、光が遠心分離器（遠心ボウル）２０内を通過する位置を変えることで調節され、通常は、光線通過位置を決めたら、そこで固定する。

【００５５】重量センサ１６は、血漿採取バッグ２５内に採取された血漿の採取量を検出する検出手段を構成する。

【００５６】濁度センサ１４は、第２のライン２２中を流れる流体の濁度を検知するためのものであり、濁度に応じた電圧値を出力する。具体的には、濁度が高い時には低電圧値、濁度が低い時には高電圧値を出力する。

【００５７】第１の気泡センサ１７および第２の気泡センサ１８は、それぞれ、第１のライン２１内に空気が流れたことを検知するためのものである。

【００５８】これらの濁度センサ１４および各気泡センサ１７、１８としては、それぞれ、例えば、超音波センサ、光学式センサ、赤外線センサなどが使用できる。

【００５９】第１のライン２１の第１のポンプチューブ２１ｇが装着される第１の送液ポンプ１１ならびに第３のライン２３の第２のポンプチューブ２３ａが装着される第２の送液ポンプ１２としては、ローラーポンプなどの非血液接触型ポンプが好適である。

【００６０】また、第１の送液ポンプ（血液ポンプ）１１としては、いずれの方向にも血液を送ることができるものが使用される。具体的には、正回転と逆回転が可能なローラーポンプが用いられている。

【００６１】制御部５５は、例えば、マイクロコンピューター等で構成されており、図１に示すように、遠心分離器駆動装置１０、第１の送液ポンプ１１、第２の送液ポンプ１２、第１の流路開閉手段５１、第２の流路開閉手段５２、濁度センサ１４、光学式センサ１５、重量センサ１６、第１の気泡センサ１７および第２の気泡センサ１８と、それぞれ、電気的に接続されている。

【００６２】濁度センサ１４、光学式センサ１５、重量センサ１６、第１の気泡センサ１７および第２の気泡センサ１８からの検出信号は、それぞれ、制御部５５へ随時入力される。制御部５５は、これらからの各検出信号に基づき、予め設定されたプログラムに従って、血液成分採取装置１の作動、すなわち、各送液ポンプ１１、１２の回転、停止、あるいは、回転方向（正転／逆転）を制御するとともに、必要に応じ、各流路開閉手段５１、５２の開閉および遠心分離器駆動装置１０の作動を制御する。

【００６３】また、この制御部５５は、演算部５５１とメモリー５５２とを内蔵している。さらに、制御部５５には、例えばキーボード等で構成された入力手段３と、例えば液晶ディスプレイ等で構成された表示手段４が、それぞれ電気的に接続されている。

【００６４】このような制御部５５は、ドナーから血液を採取し、その血液の成分（血液成分）のうち、血漿を採取するように血液成分採取装置１の作動を制御する。

【００６５】具体的には、制御部５５は、ドナーから採取された血液を遠心分離器２０（貯血空間１４６）内に流入させ、遠心分離器２０により分離された血漿を血漿採取バッグ２５内に採取（移送）する血漿採取工程（血液成分採取工程）と、血液成分採取回路２内に残った血漿以外の血液成分（残りの血液成分）をドナーへ返還する血液成分返還工程とを有する血漿採取操作を行うよう

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に、血液成分採取装置１の作動を制御する。

【００６６】なお、本実施形態では、血漿採取工程において、血漿採取バッグ２５内には、抗凝固剤が混入した血漿が採取され、重量センサ１６では、この抗凝固剤が混入した血漿の重量が検出される。

【００６７】以下の説明では、抗凝固剤が混入した血漿を「見かけの血漿」、その採取量を「見かけの血漿採取量」と言い、抗凝固剤を除いた血漿自体を「真の血漿」、その採取量を「真の血漿採取量」と言う。

【００６８】また、制御部５５は、必要に応じて、前記血漿採取操作を複数サイクル行なう。以下の説明では、各サイクルにおける血漿の採取量を「サイクル当たりの血漿採取量」と言う。

【００６９】さらに、以下の説明では、目標とする血漿の採取量を、「目標血漿採取量」と言い、実際に採取された血漿の採取量を、「現在血漿採取量」と言う。

【００７０】以下、血液成分採取装置１の使用方法および作用について、図３を参照しつつ説明する。

【００７１】なお、以下の説明では、血液成分採取装置１の所定の条件を、抗凝固剤を除いた血漿自体の目標とする採取量（真の目標血漿採取量）とする場合を一例として説明する。

【００７２】まず、オペレーター（操作者）は、入力手段３を操作して、真の目標血漿採取量（表１参照）およびサイクル当たりの見かけの血漿採取量（表２参照）を入力する。これらのテーブルは、メモリー５５２に記憶される。なお、これらのテーブルは、予めメモリー５５２に記憶させておくこともできる。

【００７３】

【表１】

表１

（真の目標血漿採取量Ｄ［ｍＬ］）

	男性	女性
４０～４４ｋｇ	－	３００
４５～４９ｋｇ	３５０	３５０
５０～５４ｋｇ	４００	４００
５５～５９ｋｇ	４５０	４５０
６０～６４ｋｇ	５００	５００
６５～６９ｋｇ	５５０	５５０
７０ｋｇ～	６００	６００

【００７４】

【表２】

表２

（サイクル当たりの見かけの血漿採取量Ａ［ｍＬ］）

	男性	女性
４０～４４ｋｇ	－	１２０
４５～４９ｋｇ	１３０	１３０
５０～５４ｋｇ	１４０	１４０
５５～５９ｋｇ	１５０	１５０
６０～６４ｋｇ	１６０	１６０
６５～６９ｋｇ	１７０	１７０
７０ｋｇ～	１８０	１８０

【００７５】また、オペレーターは、入力手段３を操作して、例えば、性別、体重、身長、年齢、ヘマトクリット値等のドナーに関する情報（以下、「ドナー情報」と言う。）、および、後述する抗凝固剤の採血血液に対する添加比率を入力する。

【００７６】次に、オペレーターは、第３のライン２３と採血針２９とを抗凝固剤でプライミングし、その後、採血針２９をドナーの血管に穿刺する。これにより、血漿の採取準備を完了する。

【００７７】次に、オペレーターが図示しない採取開始スイッチをオンする。これにより、図３に示すプログラムが実行され、血漿の採取が行われる。

【００７８】（１）　まず、血液成分採取装置１は、条件設定工程を行なう。この条件設定工程では、制御部５５は、真の目標血漿採取量Ｄ［ｍＬ］を採取するのに必要なサイクル数Ｅ［回］、および、見かけの目標血漿採取量Ｇ［ｍＬ］を求める（図３のステップＳ１０１）。

【００７９】（１１）　まず、制御部５５は、サイクル当たりの真の血漿採取量Ｂ［ｍＬ］を求める。

【００８０】具体的には、制御部５５の演算部５５１は、ドナー情報（性別および体重）に基づき、メモリー５５２に記憶されているテーブル（表２）から、サイクル当たりの見かけの血漿採取量Ａ［ｍＬ］を得、次いで、このＡを、メモリー５５２に予め記憶されている下

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記式（Ｉ－２）に代入して、Ａ中の抗凝固剤混入量Ｃ［ｍＬ］を求め、さらに、これらのＡおよびＣを下記式（Ｉ－１）に代入して、サイクル当たりの真の血漿採取量Ｂ［ｍＬ］を求める。

【００８１】なお、この式（Ｉ－２）は、第１サイクルと第２サイクル以降とでは、適用する式が異なり、また、この式（Ｉ－２）は、適宜変更することもできる。

【００８２】

$$B = A - C \quad \cdots \quad \text{式（Ｉ－１）}$$

$$C[\text{第１サイクル}] = -0.0003A^2 + 0.3A + 0.4$$

$$[\text{第２サイクル以降}] = 0.2A \quad \cdots \quad \text{式（Ｉ－２）}$$

【００８３】また、サイクル当たりの見かけの血漿採取量Ａ［ｍＬ］は、ドナーのヘマトクリット値（Ｈｃｔ）に基づき、下記式（Ｉ－０）から求めることもできる。

【００８４】なお、この式（Ｉ－０）は、第１サイクルと第２サイクル以降とでは、適用する式が異なり、また、この式（Ｉ－０）は、適宜変更することもできる。

【００８５】

$$A[\text{第１サイクル}] = 670 - 10 \times Hct$$

$$[\text{第２サイクル以降}] = 530 - 8 \times Hct \quad \cdots \quad \text{式（Ｉ－０）}$$

【００８６】（１２）　次いで、制御部５５は、真の目標血漿採取量Ｄ［ｍＬ］を得るのに必要となるサイクル数Ｅ［回］を求める。すなわち、制御部５５は、真の目標血漿採取量Ｄ［ｍＬ］に基づき、血漿採取操作（血液成分採取操作）のサイクル数Ｅ［回］を決定する。

【００８７】具体的には、制御部５５の演算部５５１は、ドナー情報（性別および体重）に基づき、メモリー５５２に記憶されているテーブル（表１）から、真の目標血漿採取量Ｄ［ｍＬ］を得、次いで、サイクル当たりの真の血漿採取量Ｂ［ｍＬ］の合計が、真の目標血漿採取量Ｄ［ｍＬ］に最も近づき、かつ、真の目標血漿採取量Ｄ［ｍＬ］を超える最も少ないサイクル数Ｅ［回］を求める。すなわち、下記式（II－１）を満たすようなサイクル数Ｅ［回］を求める。

【００８８】

$$D \leqq B[\text{第１サイクル}] + B[\text{第２サイクル}] + \cdots + B[\text{第Ｅサイクル}] \quad \cdots \quad \text{式（II－１）}$$

【００８９】なお、制御部５５の演算部５５１は、真の目標血漿採取量Ｄ［ｍＬ］を、ドナー情報（性別、体重および身長）に基づき、メモリー５５２に予め記憶されている下記式（II－０）から求めることもできる。なお、この式（II－０）は、性別により適用する式が異なる。

【００９０】

$$D[\text{男性}] = (0.168Hi^3 + 0.050Wt + 0.444) \times 120$$

$$[\text{女性}] = (0.250Hi^3 + 0.063Wt + 0.662) \times 120 \quad \cdots \quad \text{式（II－０）}$$

Ｈｉ：身長［ｍ］、Ｗｔ：体重［ｋｇ］

【００９１】（１３）　次いで、制御部５５は、最終サイクルでのサイクル当たりの真の血漿採取量Ｆ［ｍＬ］を求める。

【００９２】具体的には、制御部５５の演算部５５１は、真の目標血漿採取量Ｄ［ｍＬ］およびサイクル当たりの真の血漿採取量Ｂ［ｍＬ］を、下記式（III）に代入して、最終サイクル（第Ｅサイクル）でのサイクル当たりの真の血漿採取量Ｆ［ｍＬ］を求める。

【００９３】

$$F = D - \Sigma B \quad \cdots \quad \text{式（III）}$$

ΣＢ：Ｂ［第１サイクル］からＢ［第（Ｅ－１）サイクル］までの和

【００９４】（１４）　次いで、制御部５５は、見かけの目標血漿採取量Ｇ［ｍＬ］を求める。

【００９５】具体的には、制御部５５の演算部５５１は、サイクル当たりの真の血漿採取量Ｂ［ｍＬ］、Ａ中の抗凝固剤混入量Ｃ［ｍＬ］および最終サイクル（第Ｅサイクル）でのサイクル当たりの真の血漿採取量Ｆ［ｍＬ］を、下記式（IV）に代入して、見かけの目標血漿採取量Ｇ［ｍＬ］を求める。

【００９６】

$$G = \Sigma(B + C) + (F + C[\text{第Ｅサイクル}]) \quad \cdots \quad \text{式（IV）}$$

Σ（Ｂ＋Ｃ）：（Ｂ＋Ｃ）［第１サイクル］から（Ｂ＋Ｃ）［第（Ｅ－１）サイクル］までの和

【００９７】なお、この条件設定工程で得られた真の目標血漿採取量Ｄ［ｍＬ］は、表示手段４に表示される。これにより、オペレーターが設定条件を視認することができ、便利である。

【００９８】また、サイクル当たりの見かけの血漿採取量Ａ［ｍＬ］、サイクル当たりの真の血漿採取量Ｂ［ｍＬ］、あるいは、見かけの目標血漿採取量Ｇ［ｍＬ］を、必要に応じて、表示手段４に表示するようにしてもよい。

【００９９】（２）　次に、血液成分採取装置１は、血

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漿採取工程を行なう。この血漿採取工程では、ローター１４２の貯血空間１４６内に、採血針（採血手段）２９によりドナーから採血され、抗凝固剤供給手段により抗凝固剤が混入された血液を導入し、かかる血液を遠心分離することにより分離された抗凝固剤が混入した血漿（見かけの血漿）を血漿採取バッグ２５内に採取する。

【０１００】（２１）　制御部５５は、ドナーから見かけの血漿の採取を行なう（図３のステップＳ１０２）。

【０１０１】具体的には、制御部５５は、第１の流路開閉手段５１および第２の流路開閉手段５２を開放し、第１の送液ポンプ１１を所定の回転速度（好ましくは２５０ｍＬ／min以下程度、より好ましくは４０～１５０ｍＬ／min程度、例えば、６０ｍＬ／min）で作動（正転）するよう制御する。

【０１０２】また、この採血と同時に、制御部５５の制御により、第２の送液ポンプ１２を作動して、第３のライン２３を介して、例えばＡＣＤ－Ａ液のような抗凝固剤を供給し、この抗凝固剤を採血血液中に混入させる。

【０１０３】このとき、第２の送液ポンプ１２の回転速度は、制御部５５により、オペレーターにより入力された所定比率（添加比率）で抗凝固剤が添加されるように制御される。

【０１０４】なお、この所定比率としては、好ましくは１／２０～１／６程度とされ、例えば１／１２とされる。

【０１０５】これにより、血液（抗凝固剤加血液）は、第１のライン２１を介して移送され、遠心分離器２０の流入口１４３より管体１４１を経てローター１４２の貯血空間１４６内に導入される。

【０１０６】このとき、遠心分離器２０内の空気（滅菌空気）は、第２のライン２２を介して血漿採取バッグ２５内に送り込まれる。

【０１０７】また、前記採血と同時にまたはこれと前後して、制御部５５は、遠心分離器駆動装置１０を作動し、ローター１４２を所定の回転数で回転するよう制御する。

【０１０８】このローター１４２の回転により、貯血空間１４６内に導入された血液は、内側から血漿層（ＰＰＰ層）１３１、バフィーコート層（ＢＣ層）１３２、赤血球層（ＣＲＣ層）１３３の３層に分離される。

【０１０９】なお、ローター１４２の回転数としては、好ましくは３０００～６０００ｒｐｍ程度、より好ましくは４０００～５７００ｒｐｍ程度とされる。

【０１１０】さらに、前記採血および前記抗凝固剤の供給を継続し、貯血空間１４６の容量を越える血液（約２７０ｍＬ）が貯血空間１４６内に導入されると、貯血空間１４６内は完全に血液により満たされ、遠心分離器２０の流出口１４４から見かけの血漿がオーバーフローする。

【０１１１】これにより、第２のライン２２を介して、見かけの血漿を血漿採取バッグ２５内に導入、採取する。

【０１１２】なお、血漿採取バッグ２５は、その重量が重量センサ１６により計測されており、計測された重量信号は制御部５５に入力される。

【０１１３】（２２）　次いで、制御部５５は、血漿採取バッグ２５内にサイクル当たりの見かけの血漿採取量Ａ［ｍＬ］が採取されたか否かを判断する（図３のステップＳ１０３）。

【０１１４】具体的には、制御部５５は、重量センサ１６からの情報（重量信号）に基づき、後述する手順に従って、そのサイクルが開始されてから採取された見かけの血漿採取量Ｗ［ｍＬ］を求め、かかるＷ［ｍＬ］がＡ［ｍＬ］に到達したか否かを判断する。

【０１１５】なお、このサイクル当たりの見かけの血漿採取量Ａ［ｍＬ］は、前記条件設定工程で得られたものである。

【０１１６】このステップＳ１０３において、血漿採取バッグ２５内にサイクル当たりの見かけの血漿採取量Ａ［ｍＬ］が採取されていない場合には、制御部５５は、ステップＳ１０２に戻り、再度、ステップＳ１０２以降を繰り返す。

【０１１７】また、ステップＳ１０３において、血漿採取バッグ２５内にサイクル当たりの見かけの血漿採取量Ａ［ｍＬ］が採取された場合には、制御部５５は、血漿採取工程を終了する。

【０１１８】具体的には、制御部５５は、ローター１４２の回転および第１の送液ポンプ１１の作動を停止するよう制御し、この血液成分採取工程を終了する。

【０１１９】この血漿採取工程では、制御部５５の演算部５５１は、そのサイクルが開始されてから採取された見かけの血漿採取量Ｗ［ｍＬ］、および、真の現在血漿採取量Ｚ［ｍＬ］を、血漿採取バッグ２５の重量が１ｇ増加する毎に、次の手順に従って算出する。以下に、その手順を示す。

【０１２０】１：　まず、制御部５５の演算部５５１は、重量センサ１６からの重量信号に基づいて、実際に採取された見かけの血漿の重量（見かけの現在血漿重量）Ｕ［ｇ］を得、次いで、このＵ、前サイクルまでに採取された見かけの血漿の重量Ｖ［ｇ］を、下記式（Ｖ－１）に代入して、そのサイクルが開始されてから採取された見かけの血漿採取量Ｗ［ｍＬ］を求める。

【０１２１】なお、この式（Ｖ－１）において、定数「１．０３」は、見かけの血漿の比重［ｇ／ｍＬ］を表す。

【０１２２】

$$W=(U-V)/1.03 \quad \cdots\cdots\cdots\cdots\cdots \text{式（Ｖ－１）}$$

【０１２３】２：　次いで、制御部５５の演算部５５１は、そのサイクルが開始されてから採取された見かけの

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血漿採取量Ｗ［ｍＬ］を、下記式（Ｖ－２）に代入して、Ｗ中の抗凝固剤混入量Ｘ［ｍＬ］を求める。

【０１２４】なお、この式（Ｖ－２）は、第１サイクルと第２サイクル以降とでは、適用する式が異なり、また、この式（Ｖ－２）は、適宜変更することもできる。

【０１２５】

$$X[\text{第１サイクル}] = -0.0003W^2 + 0.3W + 0.4$$

$$X[\text{第２サイクル以降}] = 0.2W \quad \cdots\cdots\cdots \text{式（Ｖ－２）}$$

【０１２６】３：　次いで、制御部５５の演算部５５１は、前サイクルまでに採取された真の血漿採取量Ｙ［ｍＬ］と、そのサイクルが開始されてから採取された見かけの血漿採取量Ｗ［ｍＬ］およびＷ中の抗凝固剤混入量Ｘ［ｍＬ］を、下記式（Ｖ－３）に代入して、真の現在血漿採取量Ｚ［ｍＬ］を求める。

【０１２７】

$$Z = Y + (W - X) \quad \cdots\cdots\cdots\cdots\cdots \text{式（Ｖ－３）}$$

【０１２８】なお、この真の現在血漿採取量Ｚ［ｍＬ］は、表示手段４に表示される。これにより、オペレーターが真の現在血漿採取量Ｚ［ｍＬ］をリアルタイムで視認することができ、便利である。

【０１２９】また、表示手段４には、Ｗ中の抗凝固剤混入量Ｘ［ｍＬ］等を表示するようにしてもよいし、さらに、制御部５５の演算部５５１において、ドナーに返還される抗凝固剤の量を求め、かかる量を表示するようにしてもよい。

【０１３０】（３）　次に、血液成分採取装置１は、血漿採取操作を終了するか否かを判断する。

【０１３１】具体的には、制御部５５は、①真の現在血漿採取量Ｚ［ｍＬ］が真の目標血漿採取量Ｄ［ｍＬ］のＭ［％］に到達したか否か、あるいは、②血漿採取操作をサイクル数Ｅ［回］行なったか否かを判断する（図３のステップＳ１０４）。

【０１３２】なお、①におけるＭとしては、好ましくは７０～１００％程度、より好ましくは８０～１００％とされる。

【０１３３】また、血漿採取操作の終了条件①または②は、オペレーターが適宜選択することができる。

【０１３４】このステップＳ１０４において、①または②の条件を満足すると判断した場合には、制御部５５は、終了工程に移行する。なお、この終了工程については、後に説明する。

【０１３５】また、ステップＳ１０４において、①または②の条件を満足していないと判断した場合には、制御部５５は、血液成分返還工程に移行する。

【０１３６】（４）　次に、血液成分採取装置１は、血液成分返還工程を行なう。この血液成分採取工程では、血液成分採取回路２（主に、ローター１４２の貯血空間１４６）内に残った血液成分（残りの血液成分）をドナーへ返還する。

【０１３７】（４１）　まず、制御部５５は、ドナーへ残りの血液成分の返還を行なう（図３のステップＳ１０５）。

【０１３８】具体的には、制御部５５は、第１の流路開閉手段５１および第２の流路開閉手段５２を開放した状態を維持しつつ、第１の送液ポンプ１１を所定の回転速度（好ましくは、３０～１００ｍＬ／min程度、例えば４５ｍＬ／min）で作動（逆転）するよう制御する。

【０１３９】これにより、ローター１４２の貯血空間１４６内の残りの血液成分は、遠心分離器側第１ライン２１ｂ、採血針側第１ライン２１ａおよび採血針２９を介して、ドナーへ返還される。

【０１４０】（４２）　次いで、制御部５５は、第１の気泡センサ１７が空気を検出したか否かを判断する（図３のステップＳ１０６）。

【０１４１】このステップＳ１０６において、第１の気泡センサ１７が空気を検出していない場合には、制御部５５は、ステップＳ１０５に戻り、再度、ステップＳ１０５以降を繰り返す。

【０１４２】また、ステップＳ１０６において、第１の気泡センサ１７が空気を検出した場合には、制御部５５は、次サイクルの血漿採取操作の血漿採取工程に移行する。

【０１４３】具体的には、制御部５５は、第１の気泡センサ１７が第２のライン２２の流路内の空気（気泡）の存在を検出すると、第１の送液ポンプ１１を所定の回転速度に低下（変更）するように制御する。

【０１４４】そして、制御部５５は、第１の送液ポンプ１１を前記所定の回転速度で所定の回数、回転させた後、第１の流路開閉手段５１および第２の流路開閉手段５２を閉塞させ、かつ、第１の送液ポンプ１１を停止するよう制御する。

【０１４５】なお、この第１の送液ポンプ１１の回転速度としては、好ましくは１～８０ｍＬ／min程度、より好ましくは２０～５０ｍＬ／min程度とされる。

【０１４６】また、第１の送液ポンプ１１を所定の回転速度で回転させる回数としては、好ましくは１～１５回程度、より好ましくは５～１２回程度とされる。

【０１４７】これにより、血液成分採取回路２内の残りの血液成分が、ほぼ全てドナーへ返還される。

【０１４８】（５）　また、前記ステップＳ１０４において、①または②の条件を満足すると判断した場合には、制御部５５は、終了工程を行なう。この終了工程では、血液成分採取回路２（主に、ローター１４２の貯血空間１４６）内に残った血液成分（残りの血液成分）をドナーへ返還する。

【０１４９】すなわち、この終了工程（図３のステップ

Ｓ１０７、１０８）では、前記血液成分返還工程（ステップＳ１０５、１０６）と同様の工程を行なう。

【０１５０】これにより、血液成分採取回路２内の残りの血液成分が、ほぼ全てドナーへ返還され、血漿採取操作を終了する。

【０１５１】このような血液成分採取装置１では、ドナーの性別、体重および身長のうちの少なくとも１つを含むドナー情報に基づき、血液成分採取装置１の所定の条件を設定するので、ドナーに応じた適正な血漿採取操作を行なうことができる。

【０１５２】また、血液成分採取装置１では、この所定の条件として、目標血漿採取量を設定するように構成されているので、ドナーに応じた適正な量の血漿を採取することができる。

【０１５３】特に、本実施形態の血液成分採取装置１では、抗凝固剤を除いた血漿自体の目標血漿採取量（真の目標血漿採取量）を設定するように構成され、さらに、前述したような終了条件①または②に基づき、血漿採取操作を終了するように構成されているので、ドナーからの血漿採取量が許容血漿採取量（通常、体内血液量の１２％以下）から逸脱してしまうのを好適に防止し、安全性の向上を図ることができ、また、ドナーからの採取が許容される量に近い量の血漿（真の血漿）を採取することができるので、経済面での向上も図ることができる。

【０１５４】以上、本発明の血液成分採取装置を図示の実施形態に基づいて説明したが、本発明は、これらに限定されるものではなく、各部の構成は、同様の機能を有する任意の構成のものに置換することができる。

【０１５５】また、供血者に関する情報としては、前述したものの他、例えば、年齢、人種、国籍、血液型、病歴等の情報を適宜、追加することもできる。

【０１５６】また、供血者に関する情報に基づき、設定される血液成分採取装置の条件としては、実施形態で示したものに限定されないことは、言うまでもない。

【０１５７】また、本発明では、血液成分採取装置は、血漿を採取する血漿採取装置に適用する場合に限らず、血小板や、血小板および血漿を採取する血液成分採取装置にも適応することができる。

【０１５８】

【発明の効果】以上説明したように、本発明の血液成分採取装置によれば、供血者に関する情報に基づき、血液成分採取装置の所定の条件を設定するので、供血者に応じた適正な血液成分採取操作を行なうことができる。

【０１５９】また、この所定の条件として、所定の血液成分の目標とする採取量を設定した場合には、供血者に応じた適性な量の所定の血液成分を採取することができる。

【０１６０】特に、所定の条件を、抗凝固剤を除いた所定の血液成分自体の目標とする採取量とすることにより、供血者の体外血液循環量が許容体外循環量から逸脱してしまうのを好適に防止し、安全性の向上を図ることができ、また、供血者からの採取が許容される量に近い量の血液成分を採取することができるので、経済面での向上も図ることができる。

【図面の簡単な説明】

【図１】本発明の血液成分採取装置の構成例を示す平面図である。

【図２】本発明の血液成分採取装置に使用される遠心分離器駆動装置の断面を示す図である。

【図３】血液成分採取工程の際の制御部の制御動作を示すフローチャートである。

【符号の説明】

１	血液成分採取装置
２	血液成分採取回路
１０	遠心分離器駆動装置
１１	第１の送液ポンプ
１２	第２の送液ポンプ
１４	濁度センサ
１５	光学式センサ
１６	重量センサ
１７	第１の気泡センサ
１８	第２の気泡センサ
２０	遠心分離器
２１	第１のライン
２２	第２のライン
２３	第３のライン
２５	血漿採取バッグ
２９	採血針
３２	サブバッグ
３３	カセットハウジング
５１	第１の流路開閉手段
５２	第２の流路開閉手段
５５	制御部
５５１	演算部
５５２	メモリー
９１	第１の開口部
９２	第２の開口部
１３１	血漿層
１３２	バフィーコート層
１３３	赤血球層
１４２	ローター
１４３	流入口
１４４	流出口
１４５	上部
１４６	貯血空間
１５１	ハウジング
１５２	脚部
１５３	モータ
１５４	回転軸
１５５	固定台

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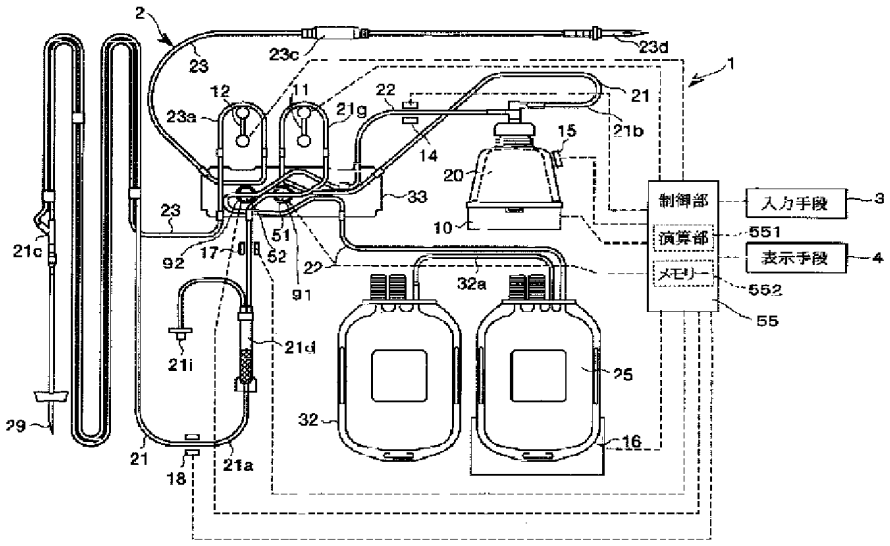
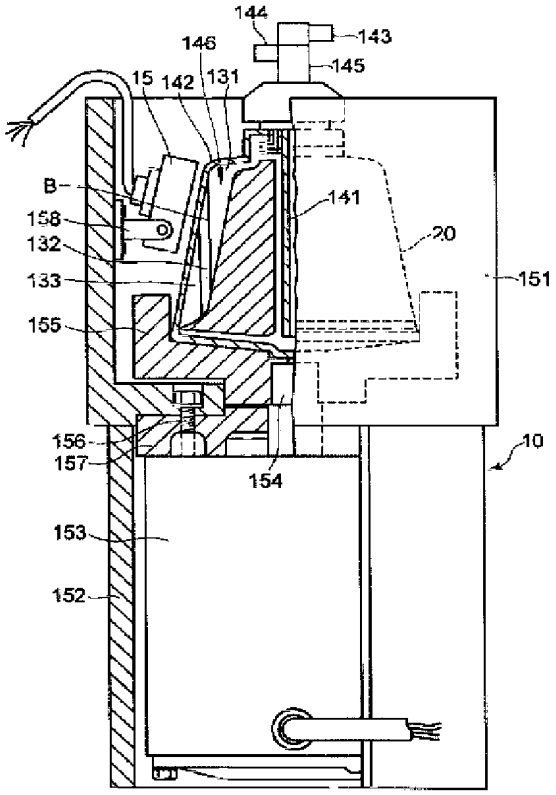
１５６	ボルト	２１ｇ	第１のポンプチューブ
１５７	スペーサー	２１ｉ	フィルター
１５８	取付部材	２３ａ	第２のポンプチューブ
２１ａ	採血針側第１ライン	２３ｃ	気泡除去用チャンバー
２１ｂ	遠心分離器第１ライン	２３ｄ	抗凝固剤溶器接続用針
２１ｃ	接続用分岐コネクター	３２ａ	チューブ
２１ｄ	チャンバー		

【図１】



【図2】


144
143
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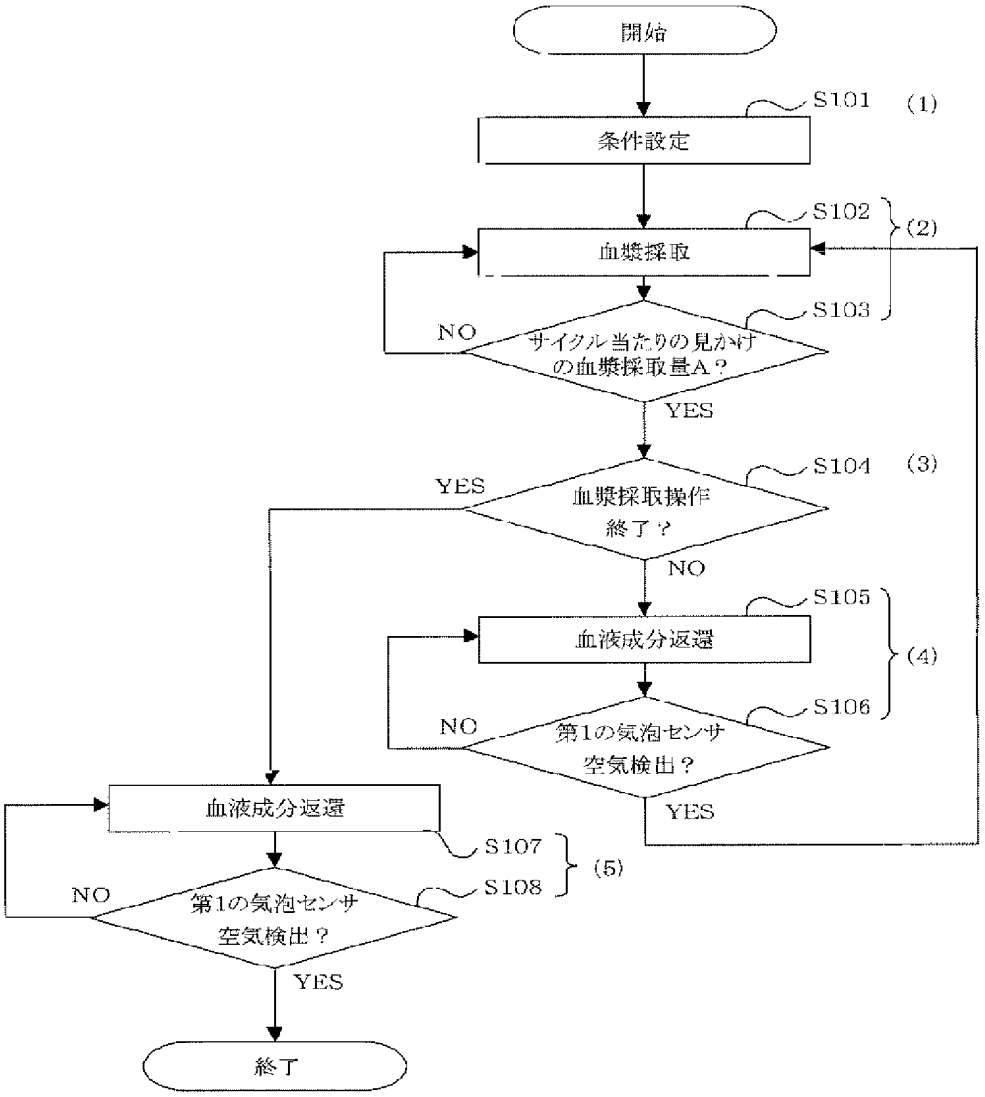
152

【図3】


開始
S101
(1)
条件設定
S102
(2)
血漿採取
S103
NO
サイクル当たりの見かけの血漿採取量A？
YES
S104
(3)
YES
血漿採取操作終了？
NO
S105
血液成分返還
(4)
S106
NO
第1の気泡センサ空気検出？
YES
血液成分返還
S107
(5)
S108
NO
第1の気泡センサ空気検出？
YES
終了

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(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

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	2	8454548	B2	2013-06-04	Ohashi et al.	

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	2	2601449	RU	C2	2016-11-10	Fenval Ink		☒

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

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That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2021-11-18
Name/Print	Jonathan C. Lovely	Registration Number	60,821

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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 18, 2021
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 | Confirmation No.: 4686

Filed: March 18, 2021 | Art Unit: N/A

For: SYSTEM AND METHOD FOR COLLECTING PLASMA | Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents. Applicant submits herewith copies of foreign patents in accordance with 37 C.F.R. § 1.98(a)(2).

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Petitioner Terumo Exhibit 1014-0362

The Examiner is advised that the following applications contain subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	10,980,926	Issued	130670-08005
17/205,374	March 18, 2021	2021-0205509	Published	130670-08006
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	10,980,934	Issued	130670-80103

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: November 18, 2021

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
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Attorney/Agent For Applicant

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Petitioner Terumo Exhibit 1014-0363

Electronic Acknowledgement Receipt

EFS ID:	44313564
Application Number:	17205400
International Application Number:	
Confirmation Number:	4686
Title of Invention:	SYSTEM AND METHOD FOR COLLECTING PLASMA
First Named Inventor/Applicant Name:	Michael Ragusa
Customer Number:	86738
Filer:	Jonathan Lovely
Filer Authorized By:	
Attorney Docket Number:	130670-80104
Receipt Date:	18-NOV-2021
Filing Date:	18-MAR-2021
Time Stamp:	11:53:56
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	130670-08006_-_RU2252788C1.pdf	422749 3640de119a28c833667e0871c7c0ff792e2f799e	no	8

Warnings:

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0364

Information:					
2	Foreign Reference	135975-80102_-_RU2601449C2.pdf	3861185 bbc25aa687bdf8db3cf28ebb3f777b6c2a83dc97	no	72
Warnings:					
Information:					
3	Information Disclosure Statement (IDS) Form (SB08)	130670-80104_-_Information_Disclosure_Statement_Fillable_PDF.pdf	1034321 2901e85445d9f2a85cd32fac2eedecb43a1972b7	no	4
Warnings:					
Information:					
4	Transmittal Letter	Information_Disclosure_Statement_IDS.pdf	25166 2280d74d6e8226bd9d215e1c30030562e6e78d9c	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	5343421	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Espacenet

Bibliographic data: RU2003131033 (A) — 2005-04-10

DEVICE FOR CARRYING OUT MEMBRANE-TYPE PLASMAPHERESIS IN SINGLE-NEEDLE MODE

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Applicant(s): Общество с ограниченной ответственностью научно-технический центр "Мепотекс" (RU)

Classification: **- international:** ***A61M1/16;*** (IPC1-7): A61M1/16
- cooperative:

Application number: RU20030131033 20031021

Priority number(s): RU20030131033 20031021

Also published as: RU2252788 (C1)

Abstract of RU2252788 (C1)

FIELD: medical engineering. ^ SUBSTANCE: device has line for taking blood and returning erythrocytic mass with air trap, line for supplying anticoagulant and hemodilution agent and forceps. Dosing member is mounted on anticoagulant line being chamber manufactured from plastic film-like material having an opening on one side for anticoagulant to be supplied and another opening for discharging it. Pump segment is set on line collecting blood as a flexible tube having an opening for supplying blood and another opening for delivering the blood to plasma filter connected to pressure control line having valve filter mounted thereon. Unit for supplying drug and discharging air is mounted on the air trap. It is manufactured as a tube with clamp. ^ EFFECT: enhanced effectiveness in applying continuous and safe plasmapheresis. ^ 1 dwg

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Petitioner Terumo Exhibit 1014-0367

РОССИЙСКАЯ ФЕДЕРАЦИЯ

(19) **RU** (11) **2 252 788** (13) **C1**

(51) МПК[7] **A 61 M 1/16**

ФЕДЕРАЛЬНАЯ СЛУЖБА
ПО ИНТЕЛЛЕКТУАЛЬНОЙ СОБСТВЕННОСТИ,
ПАТЕНТАМ И ТОВАРНЫМ ЗНАКАМ

(12) ОПИСАНИЕ ИЗОБРЕТЕНИЯ К ПАТЕНТУ

(21), (22) Заявка: 2003131033/14, 21.10.2003

(24) Дата начала действия патента: 21.10.2003

(45) Опубликовано: 27.05.2005 Бюл. № 15

(56) Список документов, цитированных в отчете о поиске: RU 2113863 C1, 27.06.1998. RU 2033188 C1, 20.04.1995. RU 2153389 C1, 27.07.2000. SU 685294 A, 15.09.1979. SU 487642 A, 15.10.1975.

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(54) УСТРОЙСТВО ДЛЯ ПРОВЕДЕНИЯ МЕМБРАННОГО ПЛАЗМАФЕРЕЗА ПО ОДНОИГОЛЬНОЙ СХЕМЕ

(57) Реферат:

Изобретение относится к медицинским изделиям и может быть использовано для лечебного и донорского плазмафереза, т.е. разделения крови на эрмассу и плазму, отвод плазмы, возврат эрмассы пациенту и введения плазмазаменяющих растворов и антикоагулянта. Устройство включает магистраль забора крови и возврата эрмассы с ловушкой воздуха, магистрали для подачи гемодилютанта и антикоагулянта и зажимы. На магистрали для подачи антикоагулянта установлен дозирующий элемент в виде камеры, выполненной из пленочного пластичного материала и имеющей с одной стороны отверстие для входа антикоагулянта, а с другой - отверстие для его выхода. На магистрали забора крови установлен насосный сегмент в виде трубки, выполненный из эластичного материала и имеющий отверстие для входа крови, отверстие для подачи крови к плазмафильтру, соединенное с магистралью контроля давления с расположенным на ней фильтром - клапаном. На ловушке воздуха установлен узел подачи лекарств и отвода воздуха, выполненный в виде трубки с зажимом. Изобретение позволит осуществить непрерывный и безопасный лечебный плазмаферез. 1 ил.

RU 2252788 C1

RU 2252788 C1

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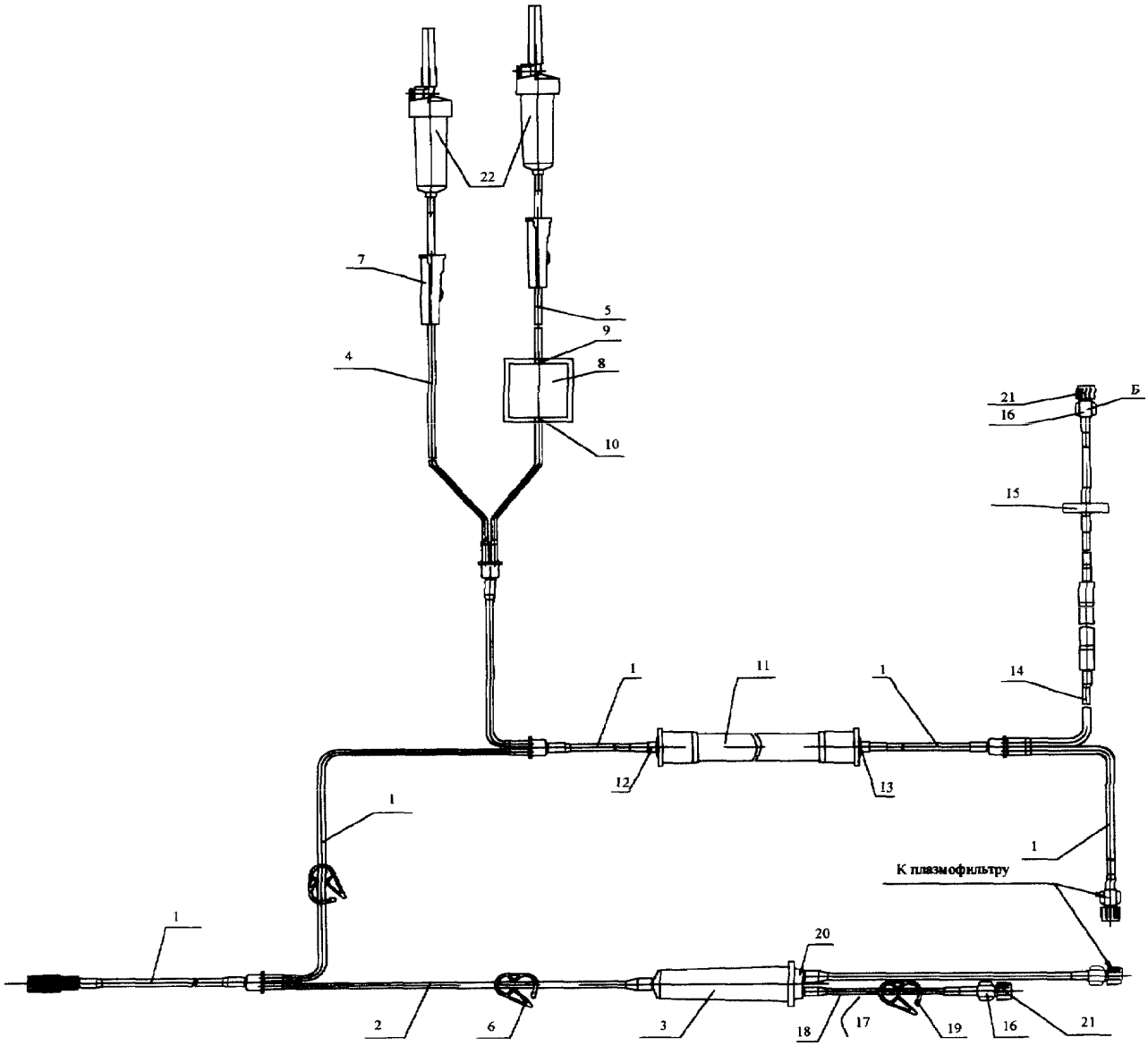
RU 2252788 C1



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Petitioner Terumo Exhibit 1014-0369

RUSSIAN FEDERATION

(19) **RU** (11) **2 252 788** (13) **C1**

(51) Int. Cl.[7] **A 61 M 1/16**

FEDERAL SERVICE
FOR INTELLECTUAL PROPERTY,
PATENTS AND TRADEMARKS

(12) ABSTRACT OF INVENTION

(21), (22) Application: 2003131033/14, 21.10.2003

(24) Effective date for property rights: 21.10.2003

(45) Date of publication: 27.05.2005 Bull. 15

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(73) Proprietor(s):
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otvetstvennost'ju nauchno-tekhnicheskij
tsentr "Mepoteks" (RU)

(54) DEVICE FOR CARRYING OUT MEMBRANE-TYPE PLASMAPHERESIS IN SINGLE-NEEDLE MODE

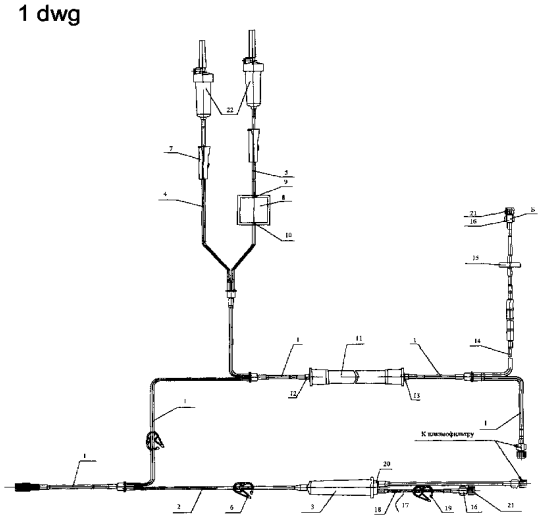
(57) Abstract:

FIELD: medical engineering.

SUBSTANCE: device has line for taking blood and returning erythrocytic mass with air trap, line for supplying anticoagulant and hemodilution agent and forceps. Dosing member is mounted on anticoagulant line being chamber manufactured from plastic film-like material having an opening on one side for anticoagulant to be supplied and another opening for discharging it. Pump segment is set on line collecting blood as a flexible tube having an opening for supplying blood and another opening for delivering the blood to plasma filter connected to pressure control line having valve filter mounted thereon. Unit for supplying drug and discharging air is mounted on the air trap. It is manufactured as a tube with clamp.

EFFECT: enhanced effectiveness in applying continuous and safe plasmapheresis.

1 dwg



RU 2252788 C1

RU 2252788 C1

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Petitioner Terumo Exhibit 1014-0370

Предлагаемое устройство для проведения мембранного плазмафереза по одноигольной схеме относится к медицинским изделиям и может быть использовано для лечебного и донорского мембранного плазмафереза, т.е. разделения крови на эрмассу и плазму, отвод плазмы, возврат эрмассы пациенту и введение плазмозамещающих растворов и антикоагулянта. Плазмаферез признан наиболее эффективным методом, обеспечивающим радикальное удаление токсинов из организма вместе с плазмой.

Известно устройство для отделения плазмы под действием силы тяжести, включающее магистраль забора крови, мембранный плазмофильтр, накопительную емкость, соединенную с плазмофильтром второй магистралью, емкость для плазмы, соединенную с плазмофильтром магистралью плазмы, емкость для гемодилютанта с магистралью и средство ввода антикоагулянта, подсоединенное к магистрали забора крови. Емкость для гемодилютанта подсоединена магистралью непосредственно к накопительной емкости [1].

Недостатком известного устройства является отсутствие возможности дозированной подачи антикоагулянта, что ведет к серьезным осложнениям при плазмаферезе, т.к. при малом количестве антикоагулянта возможно тромбирование плазмофильтра, а при избыточном количестве - возможность противотока потоку отбираемой крови. Кроме того, использование этого устройства для лечебного плазмафереза затруднительно из-за осуществления возврата эрмассы пациенту только один раз. Конструкция устройства не обеспечивает устойчивого режима отбора крови, особенно при спадании вены.

Наиболее близким по технической сущности к предлагаемому устройству является устройство для осуществления мембранного плазмафереза по одноигольной схеме [2].

Известное устройство включает средство для отбора крови, мембранный плазмофильтр, накопительную емкость в виде шприца, емкости для гемодилютанта и сбора плазмы, магистрали с зажимами и капельницами, средство ввода антикоагулянта и средство контроля давления.

Недостатком этой конструкции устройства является отсутствие возможности непрерывной дозированной подачи антикоагулянта синхронно с забором крови при проведении донорского и лечебного плазмафереза, отсутствие защиты средства контроля давления от возможности заброса в него крови при увеличении давления в магистрали забора крови. Кроме того, конструкция устройства не позволяет медперсоналу в процессе проведения плазмафереза регулировать высоту заполнения кровью ловушки воздуха и вводить дополнительно необходимые для пациента лекарства при возврате эрмассы, что создает неудобства в работе медперсонала и не обеспечивает безопасность пациента при проведении плазмафереза.

Цель изобретения - обеспечение непрерывной дозированной подачи антикоагулянта синхронно с забором крови при проведении донорского и лечебного плазмафереза, а также обеспечение безопасности пациента, надежности работы устройства и удобства в работе при проведении плазмафереза.

Для достижения поставленной цели предложено устройство для проведения мембранного плазмафереза по одноигольной схеме, включающее магистраль забора крови и возврата эрмассы с ловушкой воздуха, магистрали для подачи гемодилютанта и антикоагулянта и зажимы.

На магистрали для подачи антикоагулянта установлен дозирующий элемент в виде камеры, выполненной из пленочного эластичного материала и имеющей с одной стороны отверстие для входа антикоагулянта, а с другой - отверстие для его выхода.

На магистрали забора крови установлен насосный сегмент в виде трубки, выполненной из эластичного материала, и имеющего отверстие для входа крови и отверстие для подачи крови к плазмофильтру, соединенное с магистралью контроля давления с расположенным на ней фильтром-клапаном.

На ловушке воздуха установлен узел подачи лекарств и отвода воздуха, выполненный в виде трубки с зажимом, один конец которой соединен с крышкой ловушки воздуха, а другой с коннектором типа “Луэр”.

Для пояснения изобретения ниже приводится пример конкретного выполнения

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Petitioner Terumo Exhibit 1014-0371

устройства для проведения мембранного плазмафереза по одноигольной схеме со ссылками на чертеж, на котором изображен общий вид устройства.

Устройство содержит магистраль забора крови 1, магистраль возврата эрмассы 2 с ловушкой воздуха 3, магистраль подачи гемодилютанта 4, магистраль подачи антикоагулянта 5 и зажимы 6 и 7.

На магистрали подачи антикоагулянта установлен дозирующий элемент 8, выполненный в виде камеры из пленочного эластичного материала и имеющий с одной стороны отверстие 9 для входа антикоагулянта, а с другой - отверстие 10 для его выхода. Вместимость камеры составляет 2 мл антикоагулянта и рассчитана исходя из максимально возможной дозы антикоагулянта, вводимой за один цикл забора крови.

На магистрали забора крови 1 установлен насосный сегмент 11 в виде трубки из эластичного материала со специальными упруго-эластичными свойствами и имеющий отверстие 12 для входа крови и отверстие 13 для подачи крови к плазмофильтру, соединенное с магистралью контроля давления 14, имеющей фильтр-клапан 15. Введение насосного сегмента в магистраль забора крови позволяет осуществлять беспрерывный синхронный отбор крови из вены пациента и смешение ее с определенной дозой антикоагулянта перед насосным сегментом, что позволяет избежать осложнений, вызванных недостатком или избытком антикоагулянта, особенно при проведении донорского плазмафереза. Кроме того, беспрерывная дозированная подача антикоагулянта в эксфузат ускоряет отбор плазмы из плазмофильтра. Введение насосного сегмента позволяет осуществлять беспрерывный возврат эрмассы после плазмофильтра с одновременным введением пациенту гемодилютанта. Магистраль контроля давления 14 соединена при помощи коннектора типа “Луэр” 16 с прибором для измерения давления крови на входе в плазмофильтр. Для исключения попадания крови в прибор для измерения давления на магистрали установлен фильтр-клапан 15, представляющий собой герметично соединенные крышку, корпус и расположенную внутри них мембрану, физические показатели которой позволяют беспрепятственно пропускать воздух, не создавая дополнительного сопротивления и в то же время удерживать столб жидкости, не давая ей попасть в прибор контроля давления, что обеспечивает надежность работы устройства и безопасность проведения процедуры плазмафереза.

Для создания удобства пользования устройством и обеспечения безопасности пациента при проведении плазмафереза на ловушке воздуха 3 установлен узел подачи лекарств и отвода воздуха 17, выполненный в виде трубки 18 с зажимом 19, один конец которой соединен с крышкой ловушки воздуха 20, а другой с коннектором типа “Луэр” 16 закрытый колпачком 21.

Такая конструкция устройства позволяет медперсоналу в процессе проведения плазмафереза, немного приоткрывая колпачок 21, регулировать высоту заполнения кровью ловушки воздуха за счет сбрасывания или подачи в нее воздуха и вводить дополнительно при помощи шприца, подсоединяя его к коннектору 16, необходимые для пациента лекарства.

Устройство для проведения мембранного плазмафереза по одноигольной схеме работает следующим образом.

Предварительно необходимо заполнить устройство, соединенное с плазмофильтром и прибором контроля давления физраствором и вытеснить из устройства имеющийся воздух. Затем магистраль подачи антикоагулянта 5 подсоединяют при помощи капельницы 22 к емкости с антикоагулянтом, а магистраль подачи плазмозамещающего раствора 4 к емкости с раствором. Магистраль забора крови 1 соединяют с внутривенным катетером, который вводят в вену пациента. При помощи насосного сегмента 11 за один цикл производят забор дозы крови от пациента с одновременным забором дозы антикоагулянта (например, глюгицира) из дозирующего элемента 8 и подачей дозы антикоагулянта в магистраль забора крови 1 перед насосным сегментом. Кровь, смешанная с антикоагулянтом, подается насосным сегментом к плазмофильтру. Давление крови в магистрали забора крови на выходе из насосного сегмента определяется прибором

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контроля давления, к которому при помощи коннектора 16 подсоединяется магистраль контроля давления, с расположенным на ней фильтр-клапаном 15, позволяющим избежать попадание крови в прибор для измерения давления при резком повышении давления, что обеспечивает надежность работы устройства. Эрмасса после плазмофильтра при помощи насосного сегмента 11 возвращается пациенту по магистрали возврата эрмассы 2. В зависимости от состояния пациента в процессе проведения плазмафереза медперсонал может вводить необходимые лекарства, подсоединяясь шприцем к коннектору 16 узла подачи лекарств 17. При значительном изменении уровня крови в ловушке воздуха, опасном для пациента, медперсонал может регулировать уровень крови за счет возможности отвода воздуха приоткрывая колпачок 21 коннектора 16. Осуществление таких манипуляций обеспечивает безопасность пациента при проведении плазмафереза, создает удобство в работе медперсонала.

Таким образом, предложенное устройство, используемое для проведения мембранного плазмафереза по одноигольной схеме, позволит осуществлять донорский и лечебный плазмаферез безопасно для пациента с возможностью точного дозирования и подачи антикоагулянта с одновременным забором крови при помощи насосного сегмента, обеспечит удобство в работе медперсонала.

Использованная литература

1. Япония, заявка №60-7852, A 61 M 1/04,1985 г.

2. Россия, патент РФ №2113863, A 61 M 1/36, 1998 г.

Формула изобретения

Устройство для проведения мембранного плазмафереза по одноигольной схеме, включающее магистраль забора крови и возврата эритромассы с ловушкой воздуха, магистраль для подачи гемодилютанта и магистраль для подачи антикоагулянта, отличающееся тем, что на магистрали для подачи антикоагулянта установлен дозирующий элемент в виде емкости, выполненной из эластичного пленочного материала и имеющий с одной стороны отверстие для входа антикоагулянта, с другой - отверстие для его выхода, на магистрали забора крови установлен насосный сегмент в виде трубки из эластичного материала, имеющий отверстие для входа крови и отверстие для подачи крови к плазмофильтру, соединенное с магистралью контроля давления, имеющей фильтр-клапан, при этом на ловушке воздуха установлен узел подачи лекарств и отвода воздуха, выполненный в виде трубки с зажимом.

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Espacenet

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DEVICE FOR MEMBRANE SEPARATION, SYSTEMS AND METHODS USING SAID DEVICES, AND DATA MANAGEMENT SYSTEMS AND METHODS

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Applicant(s): Фенвал, Инк.

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Abstract of RU2601449 (C2)

FIELD: medicine.SUBSTANCE: invention relates to membrane separation devices for use in blood processing procedures. Filtration device comprises: cylindrical body; internal element installed inside the body; porous membrane, located at distance from the body wall or internal element surface to make annular clearance between them, wherein body and internal element can rotate in relation to each other; inlet for direction of whole blood in annular gap, first outlet to direct plasma passing through membrane to container for collection; and second outlet for direction of remaining blood

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components from annular gap, wherein device also has a high perfusion area, covered with membrane, and static area and includes radial projection, which separates area of high perfusion from static area.EFFECT: technical result is increased degree and rate of blood separation.9 cl, 2 tbl, 33 dwg

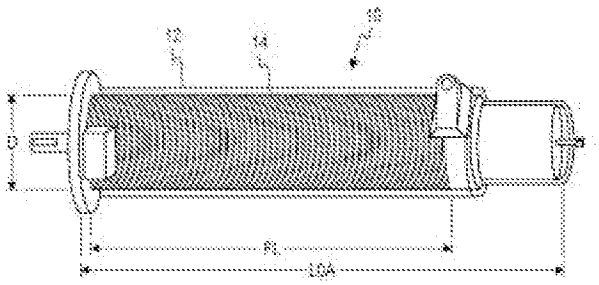

Fig. 7

РОССИЙСКАЯ ФЕДЕРАЦИЯ

ФЕДЕРАЛЬНАЯ СЛУЖБА
ПО ИНТЕЛЛЕКТУАЛЬНОЙ СОБСТВЕННОСТИ

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RU 2601449 C2

RU 2601449 C2

(54) УСТРОЙСТВА МЕМБРАННОГО РАЗДЕЛЕНИЯ, СИСТЕМЫ И СПОСОБЫ, ПРИМЕНЯЮЩИЕ УКАЗАННЫЕ УСТРОЙСТВА, И СИСТЕМЫ И СПОСОБЫ УПРАВЛЕНИЯ ДАННЫМИ

(57) Реферат:

Изобретение относится к мембранным устройствам разделения для применения в процедурах обработки крови. Устройство фильтрации крови содержит: цилиндрический корпус; внутренний элемент, установленный внутри корпуса; пористую мембрану, расположенную на расстоянии от стенки корпуса или поверхности внутреннего элемента с образованием кольцевого зазора между ними, при этом корпус и внутренний элемент могут вращаться друг относительно друга; впуск для направления цельной крови, в кольцевой зазор, первый выпуск для направления плазмы, проходящей через мембрану в контейнер для сбора; и второй выпуск для направления из кольцевого зазора оставшихся компонентов крови, причем устройство дополнительно содержит область высокой перфузии, покрытую мембраной, и непроточную область и содержит радиальный выступ, который отделяет область

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высокой перфузии от непроточной области. Технический результат заключается в повышении степени и скорости сепарации крови. 2 н. и 7 з.п. ф-лы, 2 табл., 33 ил.

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RU 2601449 C2

(54) DEVICE FOR MEMBRANE SEPARATION, SYSTEMS AND METHODS USING SAID DEVICES, AND DATA MANAGEMENT SYSTEMS AND METHODS

(57) Abstract:

FIELD: medicine.

SUBSTANCE: invention relates to membrane separation devices for use in blood processing procedures. Filtration device comprises: cylindrical body; internal element installed inside the body; porous membrane, located at distance from the body wall or internal element surface to make annular clearance between them, wherein body and internal element can rotate in relation to each other; inlet for direction of whole blood in annular gap, first outlet to direct plasma passing through membrane to container for collection; and second outlet for direction of remaining blood components from annular gap, wherein device also has a high perfusion area, covered with membrane, and static area and includes radial projection, which separates area of high perfusion from static area.

EFFECT: technical result is increased degree and rate of blood separation.

9 cl, 2 tbl, 33 dwg

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ОБЛАСТЬ ТЕХНИКИ, К КОТОРОЙ ОТНОСИТСЯ ИЗОБРЕТЕНИЕ

Настоящая заявка относится, частично, к типу устройств разделения, использующих взаимно вращающиеся поверхности, по меньшей мере одна из которых содержит мембрану для фильтрации компонента от жидкости, проходящей между поверхностями; к контурам и системам потока жидкости, включающим в себя такой сепаратор; и к применению таких систем для отделения биологических клеток, таких как эритроциты, плазма или лейкоциты, от цельной крови, среды для хранения, среды взвеси, супернатанта и т.п.

УРОВЕНЬ ТЕХНИКИ

Традиционное взятие крови продолжает опираться на ручное взятие цельной крови у здоровых доноров на станциях сдачи крови, при визитах доноров в центры крови или больницы и т.п. При типичном ручном взятии, цельная кровь берется путем ее простого протекания под воздействием силы тяжести и венозного давления из вены донора в контейнер для сбора. Объем забранной цельной крови обычно составляет "единицу", которая составляет около 450 мл.

Конкретнее, при таком взятии обычно применяется предварительно собранная конструкция трубок и контейнеров или пакетов, включая первичный контейнер из эластичного пластика или пакет для приема единицы цельной крови от донора и один или более вспомогательных контейнеров или пакетов. Кровь сначала собирается в первичный контейнер, который также содержит противосвертывающее средство (обычно содержащее цитрат натрия, фосфат и декстрозу - часто называемое CPD). Консервант (часто называемый “раствор добавки” или AS, и обычно содержащий среду из физиологического раствора, аденина и глюкозы, которая называется SAG) может быть включен в качестве элемента большей по размеру конструкции пакетов и трубок, которые используются при обработке после сбора крови.

После сбора единицы цельной крови общепринятой практикой в банках крови является транспортировка единицы цельной крови, с помощью подсоединенных трубок и контейнеров, в лабораторию обработки компонентов крови, обычно называемую “вспомогательная лаборатория”, для дальнейшей обработки. Дальнейшая обработка обычно включает в себя ручную загрузку первичного контейнера и связанных с ним трубок и вспомогательных контейнеров в центрифугу для разделения цельной крови на компоненты, такие как концентрированные эритроциты и обогащенная тромбоцитами плазма или обедненная тромбоцитами плазма. Данные компоненты затем вручную отжимаются из первичного контейнера в другие предварительно подсоединенные вспомогательные контейнеры, и могут опять центрифугироваться для выделения тромбоцитов из плазмы. После этого компоненты крови могут подвергаться лейкоредукции посредством фильтрации для дальнейшей обработки или хранения. Коротко говоря, данный процесс требует больших временных затрат, является трудоемким и подвержен возможным ошибкам, связанным с человеческим фактором.

Другой типовой задачей, выполняемой банками крови и центром переливания крови, является “промывание клеток”. Оно может выполняться с целью удаления и/или замещения жидкой среды (или ее части), в которой суспендированы клетки, с целью концентрирования или дальнейшего концентрирования клеток в жидкой среде, и/или с целью очистки взвеси клеток путем удаления нежелательного клеточного или другого материала.

В предшествующих системах промывания клеток чаще всего применялось центрифугирование взвеси клеток, слив суперанатанта, ресуспендирование концентрированных клеток в новых средах, а также возможное повторение данных

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этапов до тех пор, пока клетки во взвеси не будут представлены в достаточно высокой или желательной по другим признакам концентрации. Центробежные сепараторы, используемые в обработке крови и компонентов крови, обычно использовались в таких способах промывания клеток.

Данные процессы также требуют достаточно больших временных затрат, поскольку требуют повторяющихся ручных манипуляций с кровью или компонентами крови и сборки или разборки различных устройств обработки жидкостей. Это, естественно, повышает не только стоимость, но и потенциал для связанной с человеческим фактором ошибки или погрешности. Соответственно, несмотря на десятилетия развития устройств и процессов разделения крови, продолжает существовать потребность в лучших и/или более эффективных устройствах, системах и способах разделения, применимых к базовым методикам взятия и обработки крови.

Хотя во многих предшествующих устройствах и процедурах разделения крови применялись принципы разделения центрифугированием, существует другой класс устройств, основанных на применении мембран, которые использовались для плазмафереза, то есть отделения плазмы от цельной крови. Конкретнее, устройства этого типа используют вращающиеся друг относительно друга поверхности, одна из которых содержит пористую мембрану. Обычно устройство имеет внешний неподвижный корпус и внутренний вращающийся ротор, покрытый пористой мембраной.

Одним из таких хорошо известных устройств для плазмафереза является сепаратор Autopheresis-C®, поставляемый Fenwal, Inc. из Lake Zurich, штат Иллинойс. Подробное описание сепаратора с вращающейся мембраной можно найти в патенте США No. 5194145, выданном Schoendorfer, который включен в настоящее описание посредством ссылки. В данном патенте описывается покрытый мембраной вращатель, имеющий внутреннюю систему сбора, размещенную в неподвижной оболочке. Кровь подается в кольцевое пространство или зазор между вращателем и оболочкой. Кровь перемещается вдоль продольной оси оболочки в направлении выходной области, при этом плазма проходит через мембрану за пределы оболочки в пакет для сбора. Оставшиеся компоненты крови, в основном, эритроциты, тромбоциты и лейкоциты, переходят в выходную область между вращателем и оболочкой, и затем обычно возвращаются донору.

Было обнаружено, что сепараторы с вращающейся мембраной обеспечивают отличную скорость фильтрации плазмы, в основном благодаря уникальным схемам потока (“вихри Тейлора”), возбуждаемым в зазоре между вращающейся мембраной и оболочкой. Вихри Тейлора помогают удерживать клетки крови от осаждения на мембрану и ее загрязнения или закупоривания.

Несмотря на то, что сепараторы с вращающейся мембраной широко использовались для сбора плазмы, они обычно не использовались для сбора других компонентов крови, в частности, эритроцитов. Сепараторы с вращающейся мембраной также обычно не использовались для промывания клеток. Один из примеров сепаратора с вращающейся мембраной, примененного для промывания клеток, таких как эритроциты, описан в патенте США No. 5053121, который также включен в настоящее описании посредством ссылки во всей своей полноте. Однако в системе, описанной в этом патенте, используется два отдельных вращателя, соединенных последовательно или параллельно, для промывания “выделенной” крови пациента. Другие описания применения сепараторов с вращающейся мембраной для разделения крови или компонентов крови, также можно найти в патентах США No. 5376263; 4776964; 4753729; 5135667 и 4755300.

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Объект изобретения, изложенный в настоящей заявке, предоставляет дополнительные достижения в области мембранных сепараторов, потенциального снижения стоимости и различных других достижений и преимуществ по сравнению с предшествующим ручным сбором и обработкой крови.

СУЩНОСТЬ ИЗОБРЕТЕНИЯ

Настоящий объект изобретения имеет ряд аспектов, которые могут быть применены в различных комбинациях, и изложение одного или более конкретных вариантов осуществления приведено в целях изложения и описания, а не ограничения. В изложении сущности выделено только несколько аспектов данного объекта изобретения, и дополнительные аспекты изложены на чертежах и в приведенном ниже более подробном описании.

Посредством настоящего изложения, представлен мембранный сепаратор, который более эффективно разделяет цельную кровь на ее компоненты и может быть успешно применен в различных системах и процедурах обработки крови.

В частности, представлено устройство фильтрации крови, имеющее по существу цилиндрический корпус с внутренней стенкой и внутренним элементом, установленным внутри корпуса и имеющим внешнюю поверхность. Внутренняя стенка корпуса и/или внешняя поверхность внутреннего элемента включает в себя пористую мембрану, расположенную на расстоянии от передней стенки корпуса или поверхности внутреннего элемента, с образованием кольцевого зазора между ними, при этом корпус и внутренний элемент могут вращаться друг относительно друга. Впуск представлен для направления цельной крови, содержащей плазму и эритроциты, в кольцевой зазор, тогда как второй выпуск представлен для направления из кольцевого зазора оставшихся компонентов крови. Мембрана имеет площадь поверхности, достаточную для отделения плазмы с такой скоростью потока, что время нахождения эритроцитов в пределах кольцевого зазора является недостаточным для того, чтобы вызвать ненадлежащий гемолиз эритроцитов. В одном из вариантов осуществления, это достигается посредством предоставления внутреннего элемента, который имеет длину и/или диаметр, превышающий длину и диаметр внутренних элементов устройств предшествующего уровня техники. Конкретнее, внутренний элемент по настоящей заявке содержит ротор, который имеет длину, вплоть до 2,5 раз превышающую длину роторов предшествующих устройств с вращающейся мембраной, и диаметр, вплоть до 2,0 раз превышающий диаметр предшествующих устройств с вращающейся мембраной. Было обнаружено, что такие сепараторы обеспечивают улучшенную скорость отделения плазмы и также обеспечиваю приемлемо низкие уровни гемолиза в сохраняемой крови. В одном конкретном варианте осуществления, длина внутреннего элемента составляет около 14 см и диаметр составляет около 3,8 см.

Также изложен способ создания мембранного устройства разделения. Способ включает в себя разработку модели, использующей входные данные, полученные полуэмпирически для существующего устройства фильтрации, имеющего пористую мембрану с заданными размерами, с целью получения заданных выходных данных. Модель применяется к гипотетическим устройствам фильтрации, имеющим мембраны с различными размерами, с тем чтобы получить спрогнозированные значения для заданных выходных данных. Спрогнозированные значения рассматриваются, и размеры мембраны выбираются на основании сравнения спрогнозированных значений заданных выходных данных. В одном из аспектов способ обеспечивает площадь поверхности мембраны, которая улучшает одну или более характеристик фильтрации. В конкретном примере, устройство фильтрации содержит внутренний элемент, имеющий

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установленную на него мембрану, при этом внутренний элемент установлен с возможностью вращения относительно по существу цилиндрического корпуса, и внутренний элемент имеет диаметр и/или длину мембраны, позволяющие осуществлять фильтрацию без ненадлежащего лизиса эритроцитов в крови. В конкретном применении модели внутренний элемент имеет диаметр, вплоть до около 2,0 раз превышающий диаметр существующих устройств фильтрации и/или длину мембраны, вплоть до около 2,5 раз превышающую длину мембраны существующих устройств фильтрации.

В другом аспекте изложения представлен мембранный сепаратор в котором по меньшей мере две зоны или области созданы в зазоре между внутренним элементом и оболочкой таким образом, что это препятствует смешиванию жидкостей между двумя областями. Конкретнее, представлен мембранный сепаратор, в котором внутренняя стенка наружной структуры и/или внешняя поверхность внутренней структуры содержит радиальное ребро или выступ, который уменьшает зазор между двумя поверхностями, при этом задавая две области жидкостей, и выступ изолирует жидкости в двух областях с целью минимизации их смешивания.

КРАТКОЕ ОПИСАНИЕ ЧЕРТЕЖЕЙ

Указанные и другие характеристики объекта настоящего изобретения описаны в приведенном ниже подробном описании и показаны на прилагаемых фигурах, среди которых:

Фиг. 1 представляет собой вид в перспективе сепаратора с вращающейся мембраной, в парциальном сечении и с удалением частей для демонстрации деталей.

Фиг. 2 представляет собой продольный вид в поперечном сечении сепаратора с вращающейся мембраной с фиг. 1.

Фиг. 3 представляет собой контурное изображение выходных значений гематокрита и напряжения сдвига на стенке выпуска как функции относительной длины фильтрации и радиуса вращателя на основании теоретической проектной модели.

Фиг. 4 представляет собой контурное изображение выходных значений гематокрита и концентрации гемоглобина в плазме для выпуска как функции относительной длины фильтрации и радиуса вращателя на основании теоретической проектной модели, в которой тангенциальная скорость мембраны является постоянной.

Фиг. 5 представляет собой контурное изображение выходных значений гематокрита и числа Тейлора как функции относительной длины фильтрации и радиуса вращателя на основании теоретической проектной модели.

Фиг. 6 представляет собой трехмерный график концентрации гемоглобина в плазме как функции относительной длины фильтрации и радиуса вращателя на основании теоретической проектной модели.

Фиг. 7 представляет собой вид в перспективе устройства или сепаратора с вращающейся мембраной по настоящей заявке.

Фиг. 8 представляет собой схематический поперечный разрез сепаратора с вращающейся мембраной по настоящей заявке, при этом вращатель содержит радиально направленный выступ для задания отдельных областей жидкости.

Фиг. 9 представляет собой схематическое изображение автоматизированной системы разделения цельной крови для обработки ранее собранной цельной крови, содержащей одноразовый модуль контура циркуляции жидкости и долговременный контроллер или управляющий модуль, на который установлен модуль контура циркуляции жидкости.

Фиг. 10 представляет собой схему циркуляции, демонстрирующую один из вариантов осуществления потока жидкости через контур циркуляции жидкости, в соответствии с описанным в настоящем описании, для переработки единицы цельной крови в

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концентрированный продукт эритроцитов и продукт плазмы.

Фиг. 11 аналогична фиг. 9, но демонстрирует несколько более подробное изображение компонентов одноразового контура, или модуля циркуляции жидкости, и долговременного модуля контроллера.

Фиг. 12 представляет собой схематическое изображение альтернативного варианта осуществления системы в соответствии с настоящим изложением, в котором система применяется для разделения ранее собранной цельной крови.

Фиг. 12A представляет собой схематическое изображение еще одного альтернативного варианта осуществления, аналогичного фиг. 12.

Фиг. 13 представляет собой вид в перспективе системы разделения крови с двумя насосами, такой как показана на фиг. 9, 11, 12 и 12A.

Фиг. 14 представляет собой схематическое изображение еще одной альтернативы, аналогичной фиг. 12, за исключением того, что она включает в себя три насоса, иллюстрирующей систему в фазе заполнения.

Фиг. 15 представляет собой схематическое изображение системы с фиг. 14, иллюстрирующее систему в фазе разделения.

Фиг. 15A представляет собой схематическое изображение еще одной альтернативной системы с тремя насосами, аналогичной фиг. 14 и 15.

Фиг. 16 представляет собой схематическое изображение автоматизированной системы сбора цельной крови в соответствии с настоящим изложением, демонстрирующее конфигурацию системы для автоматизированного кабинетного сбора и обработки цельной крови донора в режима заполнения.

Фиг. 17 представляет собой схематическое изображение системы с фиг. 16, демонстрирующее конфигурацию системы для сбора и разделения цельной крови на эритроциты и плазму.

Фиг. 18 представляет собой схематическое изображение системы с фиг. 16, демонстрирующее конфигурацию системы для прополаскивания системы противосвертывающим средством после завершения взятия крови у донора.

Фиг. 19 представляет собой схематическое изображение системы с фиг. 16, демонстрирующее конфигурацию системы в конце процедуры сбора крови.

Фиг. 20 представляет собой схематическое изображение системы с фиг. 16, демонстрирующее конфигурацию системы в необязательной конфигурации для фильтрации собранных эритроцитов через лейкоцитный фильтр.

Фиг. 21 представляет собой схематическое изображение альтернативного варианта осуществления автоматизированной системы сбора цельной крови относительно систем, показанных на фиг. 16-20, в которой компонент контура циркуляции жидкости одноразового использования содержит встроенный фильтр лейкоредукции как часть линии извлечения устройства доступа к донору.

Фиг. 22 представляет собой схематическое изображение альтернативного варианта осуществления контура циркуляции жидкости одноразового использования с фиг. 21, в котором фильтр лейкоредукции размещен в линии извлечения по ходу потока относительно входной точки, в которой противосвертывающее средство вводится в цельную кровь.

На фиг. 23 показан одноразовый набор, подходящий для промывания клеток в соответствии со способом, изложенным в настоящем описании.

На фиг. 24 показан другой вариант осуществления одноразового набора, подходящего для промывания клеток в соответствии с альтернативным способом, изложенным в настоящем описании.

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На фиг. 25 показан вариант осуществления панели управления устройства, подходящего для промывания клеток в соответствии со способом, изложенным в настоящем описании.

Фиг. 26-28 представляют собой блок-схемы этапов способа промывания клеток, изложенного в настоящем описании.

Фиг. 29 представляет собой блок-схему, иллюстрирующую способ управления данными в соответствии с настоящим изложением.

Фиг. 30 представляет собой схематическое изображение системы управления данными в соответствии с настоящим изложением в комбинации с контейнером для сбора и набором для обработки.

Фиг. 31 представляет собой блок-схему, иллюстрирующую различные этапы, которые включает в себя способ для управления данными в соответствии с настоящим изложением.

ПОДРОБНОЕ ОПИСАНИЕ

Более подробное описание сепаратора с вращающейся мембраной в соответствии с настоящим изложением и его применения в различных автоматизированных системах приведено ниже. Следует понимать, что приведенное ниже описание конкретных устройств и способов предлагается в качестве примера, и не является исчерпывающим описанием всех возможных вариаций или применений. Таким образом, не предполагается, что объем изложения является ограничивающим, и должен пониматься как включающий вариации или варианты осуществления, которые будут понятны специалистам.

Обратимся к фиг. 1 и 2, на которых показана система разделения или фракционирования крови с вращающейся мембраной, обозначенная в общем как 10. Такая система 10 обычно применяется для извлечения плазмы из цельной крови, полученной у отдельного донора-человека. В целях облегчения понимания, показано только устройство выделения плазмы и связанный с ним блок привода, хотя следует понимать, что такой сепаратор образует часть одноразовой системы, содержащей пакеты для сбора, пакеты с добавками, такими как физиологический раствор или ACD, возвратные пакеты, трубки, и т.д., и что также имеются ассоциированные системы управления и система контрольно-измерительных средств для функционирования устройства.

Система 10 содержит по существу цилиндрический корпус 12, установленный концентрически вокруг продольной вертикальной центральной оси. Внутренний элемент 14 установлен концентрически с центральной осью. Корпус и внутренний элемент имеют возможность вращения друг относительно друга. В предпочтительном варианте осуществления, в соответствии с проиллюстрированным, корпус является неподвижным, и внутренний элемент является вращающимся, при этом он вращается концентрически в пределах цилиндрического корпуса 12. Границы маршрута тока крови в общем случае определены зазором 16 между внутренней поверхностью корпуса 12 и внешней поверхностью ротационного вращателя 14. Пространство между корпусом и вращателем иногда называется зазором сдвига. Типовой зазор сдвига может составлять приблизительно 0,025-0,050 дюйма (0,067-0,127 см) и может иметь равномерный размер вдоль оси, например, когда ось вращателя и корпуса совпадают. Зазор сдвига также может изменяться, например, по окружности, когда оси корпуса и вращателя смещены друг относительно друга.

Зазор сдвига также может изменяться вдоль направления оси, например, предпочтительно, ширина зазора может увеличиваться в направлении потока с целью

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ограничения гемолиза. Такая ширина зазора может изменяться в диапазоне от 0,025 до около 0,075 дюйма (0,06-0,19 см). Например, оси корпуса и ротора могут совпадать, и диаметр ротора может уменьшаться в направлении оси (направлении потока), тогда как диаметр внутренней поверхности корпуса остается постоянным, или диаметр корпуса увеличивается, и диаметр ротора остается постоянным, или диаметр обеих поверхностей изменяется. Например, ширина зазора может составлять около 0,035 дюйма (0,088 см) в конце зазора со стороны начала потока, или у конца зазора около впуска, и около 0,059 дюйма (0,15 см) в конце зазора со стороны конца потока. Ширина зазора может изменяться путем изменения внешнего диаметра ротора и/или внутреннего диаметра передней поверхности корпуса. Ширина зазора может изменяться линейно или пошагово, или некоторым другим желаемым образом. В любом случае, размер ширины зазора предпочтительно выбирается таким образом, чтобы при желаемой относительной скорости вращения поток Тейлора-Куэтта, такой как вихри Тейлора, создавался в зазоре, и при этом ограничивался гемолиз.

Цельная кровь подается из впускной трубки 20 через впускное отверстие 22, которое направляет кровь во входную область тока крови по маршруту, касательному к окружности вокруг верхнего конца вращателя 14. В нижнем конце цилиндрического корпуса 12 внутренняя стенка корпуса имеет выпускное отверстие 34.

Цилиндрический корпус 12 заканчивается крышкой 40 верхнего конца, имеющей концевую втулку 42, стенки которой являются немагнитными, и нижний конец 44 корпуса заканчивается выпускным отверстием 46 плазмы, концентрическим с центральной осью.

Вращатель 14 установлен с возможностью вращения между крышкой 40 верхнего конца и нижним концом 44 корпуса. Вращатель 14 содержит формованный центральный сердечник или ротор 50, внешняя поверхность которого отформована для задания ряда разнесенных в пространстве кольцевых каналов или выступов 52, разделенных кольцевыми перемычками 54. Поверхностные каналы, задаваемые кольцевыми каналами 52, соединены друг с другом посредством продольных каналов 56. На каждом конце сердечника 50 эти каналы 56 связаны с центральным отверстием или трубой 58.

В проиллюстрированном варианте осуществления поверхность ротационного вращателя 14, по меньшей мере, частично, и, предпочтительно, по существу или полностью покрыта цилиндрической пористой мембраной 62. Мембрана 62 обычно имеет номинальный размер поры 0,6 мкм, но альтернативно могут использоваться другие размеры пор. Мембраны, подходящие для способов промывания, описанных в настоящем описании, могут представлять собой волокнистые сетчатые мембраны, литые мембраны, трековые мембраны или мембраны других типов, которые будут известны квалифицированным специалистам в данной области техники. Например, в одном из вариантов осуществления, мембрана может содержать полиэфирную сетку (подложку) с частицами нейлона, отвержденными на ней, посредством чего создается извилистый путь, через который пройдут только компоненты определенного размера. В другом варианте осуществления мембрана может быть сделана из тонкого (толщиной приблизительно 15 мкм) листа, например, поликарбоната. В данном варианте осуществления, поры (отверстия) могут быть больше, чем описанные выше. Например, поры могут составлять приблизительно 3-5 мкм. Размер пор может быть таким, чтобы допускать прохождение небольших сформированных компонентов (например, тромбоцитов, микрочастиц, и т.д.), и чтобы при этом собирались нужные клетки (например, лейкоциты).

Ротационный вращатель устанавливается в крышку верхнего конца для вращения

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вокруг стержня 64, который запрессован в крышку 40 конца с одной стороны и размещен внутри цилиндрической несущей поверхности 65 в концевом цилиндре 66, образующем часть ротационного вращателя 14. Внутренний вращатель или внешний корпус может вращаться посредством любого устройства или системы привода вращения. В соответствии с проиллюстрированным, концевой цилиндр 66 частично охвачен кольцом 68 из магнитного материала, используемым в косвенном управлении вращателем 14. Приводной двигатель 70, внешний по отношению к корпусу 12, подсоединен с целью поворота элемента 72 кольцевого магнитного привода, который содержит, по меньшей мере, пару внутренних постоянных магнитов 74. При вращении элемента 72 кольцевого магнитного привода магнитное притяжение между кольцом 68, расположенным внутри корпуса 12, и магнитами 74, расположенными вне корпуса, присоединяет вращатель 14 к внешнему приводу, вызывающему вращение вращателя 14.

На нижнем конце ротационного вращателя 14 центральное выпускное отверстие 58 связано с центральным каналом 76 в концевом подшипнике 78, который является концентрическим с центральной осью. Место установки концевого подшипника определяется внутренним фланцем 80, который формирует нижний край центрального отверстия 82. Центральное отверстие 82 соединено с выпускным отверстием 46 плазмы. Если поверхность внутренней стороны корпуса полностью или частично покрыта мембраной, пакет сбора жидкости или труба может размещаться под мембраной для сбора плазмы и направлять ее через впуск корпуса (не показано).

I. Конструкция мембранного сепаратора

В соответствии с одним из аспектов заявки, представлен сепаратор с вращающейся мембраной, который обеспечивает улучшенные скорости потока плазмы с приемлемо низким уровнем гемолиза в сохраняемой крови. Известны различные факторы, влияющие на скорость потока фильтрации через сепараторы с вращающейся мембраной, включающие в себя скорость вращения, размер зазора между вращающейся мембраной и оболочкой, эффективную площадь мембраны, концентрацию эритроцитов (или гематокрит) и вязкость крови. Предшествующие практики проектирования устройств с вращающейся мембраной были в значительной степени эмпирическими, и им до некоторой степени способствовали неясные феноменологические описания влияния различных параметров проектирования на производительность и гемолиз. Это оказалось неэффективным относительно времени разработки и затрат технических ресурсов.

Напротив, параметры сепаратора с вращающейся мембраной по настоящей заявке были определены на основании количественных дифференциальных моделей, которые принимают во внимание локальную скорость плазмы при прохождении через мембрану и локальную концентрацию гемоглобина. Данные дифференциальные модели интегрировались по длине устройства с целью получения суммарной скорости потока плазмы и концентрации гемоглобина в плазме на выходе устройства.

Способ включает операционные входные данные на основании геометрических параметров и условий функционирования существующего сепаратора Plasmacell-C, включая гематокрит донора, скорость входного потока крови, скорость вращения и эффективную площадь мембраны. Также учитывались геометрические входные данные для радиуса ротора, ширины кольцевого зазора и длины, по которой выполняется интегрирование. См. таблицу 1 ниже.

Для получения спрогнозированных значений для гипотетических сепараторов, радиус ротора и длина фильтрации изменялись от около 1,0 до около 2,0 раз по сравнению с текущими значениями Plasmacell-C с шагом 0,05, в результате чего была получена сетка пространства параметров проектирования размером 21×21 для каждой представляющей

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интерес выходной переменной. Для всех устройств срез корпуса и зазор в выпуске сохранялись постоянными, и зазор во впуске и скорость вращения изменялись соответственно. Также разрабатывались модели, которые связывали вязкость и плотность крови с гематокритом, температурой и концентрацией противосвертывающего средства.

Таблица 1
Входные данные для расчета моделей

Параметр, единицы измерения	Значение
Скорость входного потока крови, мл/мин	106
Входной гематокрит, %	42
Температура, °C	35
Концентрация цитрата, %	5,66
Длина фильтрации, см	7,600
Радиус ротора с мембраной, см	1,3551
Входной зазор, см	0,0673
Выходной зазор, см	0,0584
Эффективная доля мембраны	0,50
Ширина контактного участка мембраны, см	0,46
Скорость вращения, об/мин	3600
Гематокрит для стенок, %	0,90
Радиус эритроцитов, мкм	2,75
Концентрация гемоглобина в эритроцитах, мг/дл	335,60
Плотность плазмы, г/см^3	1,024
Плотность упакованных эритроцитов, г/см^3	1,096
Вязкость цитратной плазмы, сП	1,39

В одной из реализаций способа, выходные данные для скорости потока плазмы и концентрации гемоглобина были получены для различных значений радиуса ротора, скорости вращения и длины интегрирования. Результаты моделирования показаны в наложенных контурных изображениях выходного гематокрита и выходного напряжения сдвига на стенке (фиг. 3), выходного гематокрита и выходной концентрации гемоглобина в плазме (фиг. 4), и выходного гематокрита и числа Тейлора (фиг. 5), во всех случаях - как функция относительной длины фильтрации и радиуса вращателя. При использовании в настоящем документе, “длина фильтрации” понимается как осевая длина центрального сердечника ротора 50 от начала до конца каналов или выступов 52. В общем смысле, она представляет собой длину мембраны, доступную для фильтрации. “Радиус вращателя” или “диаметр вращателя” понимается как радиус или диаметр ротора с прикрепленной мембраной. На фиг. 6 показаны результаты как функция длины фильтрации и радиуса вращателя на трехмерном графике, демонстрирующем увеличение гемоглобина с увеличением размеров устройств. Данные результаты затем оценивались с целью обеспечения наилучшего баланса высокой скорости потока плазмы с приемлемо низкими уровнями гемолиза.

Модели показали, что эффективная площадь мембраны имеет наиболее сильное положительное влияние на производительность. Кроме того, хотя увеличение площади мембраны путем увеличения диаметра ротора более положительно влияет на скорости потоков, чем увеличение площади мембраны путем увеличения длины ротора, оно также увеличивает возможность гемолиза вследствие повышенной скорости мембраны, и, вследствие этого, повышения сдвигающих сил в зазоре.

Соответственно, моделирование позволило спрогнозировать длины и диаметры ротора, которые приведут к повышению площади мембран, применение которых также позволит иметь приемлемо низкие уровни гемолиза. Сепараторы-прототипы (на

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основании результатов моделирования) были сделаны и протестированы с целью проверки результатов, спрогнозированных посредством моделирования. Ниже в таблице 2 приведено сравнение имеющегося устройства для плазмафереза Plasmacell-C с двумя потенциальными альтернативами, основанными на моделях.

Таблица 2

Параметр, единицы измерения	Устройство		
	Plasmacell-C	RL 140-162	RL 140-185
Относительная длина фильтрации	1,00	1,62	1,85
Относительный радиус вращателя	1,00	1,40	1,40
Относительная скорость вращателя	1,00	0,70	0,75
Длина фильтрации, см	7,600	12,311	14,059
Радиус вращателя, см	1,3551	1,8971	1,8971
Скорость вращателя, об/мин	3600	2520	2700
Входной зазор, см	0,0673	0,0729	0,0749
Выходной зазор, см	0,0584	0,0584	0,0584
Скорость входного потока, мл/мин	106	106	106
Входной гематокрит, %	42	42	42
Концентрация цитрата, %	5,66	5,66	5,66
Скорость потока плазмы, мл/мин	36,33	47,42	50,57
Выходной гематокрит, %	63,90	76,00	80,32
Выходная концентрация гемоглобина в плазме, мг/дл	5,04	14,36	27,84
Время пребывания, с	2,98	7,99	9,77
Центростремительное давление, мм рт. ст.	100,22	96,25	110,50
Крутящий момент, Н·см	1,045	3,319	4,442
Выходное число Тейлора	89,07	51,00	46,96

Со ссылкой на таблицу 2 и фиг. 7, сепаратор с вращающейся мембраной 10 содержит ротационный вращатель 14, который имеет диаметр вращателя D, длину фильтрации FL и суммарную длину LOA. В типичном устройстве плазмафереза, таком как сепаратор Plasmacell-C, ротор имеет диаметр D, составляющий приблизительно 2,79 см, длину фильтрации FL, составляющую приблизительно 7,62 см, и суммарную длину LOA, составляющую приблизительно 12,7 см.

В соответствии с настоящей заявкой, было обнаружено, что диаметр мембраны может быть увеличен вплоть до около 2,0 раз относительно диаметра мембраны, имеющегося в типичном устройстве плазмафереза, тогда как длина может быть увеличена вплоть до около 2,5 раз относительно длины вращающейся мембраны в типичном устройстве плазмафереза. Увеличение размера ротора в пределах данных периметров достаточно увеличивает площадь мембраны фильтра для обеспечения высокого скорости потока плазмы, при этом обеспечивая приемлемо низкий уровень гемолиза. В конкретном примере сепаратор с вращающейся мембраной по настоящей заявке может, предпочтительно, иметь диаметр D, составляющий 4,19 см, длину фильтрации FL, составляющую 14,02 см, и суммарную длину LOA, составляющую 19,56 см.

Прототипы сепараторов с вращающейся мембраной тестировались с бычьей и человеческой кровью для проверки результатов, спрогнозированных по моделям. Скорости потоков крови, составляющие 100 мл/мин, были получены при скоростях вращателя, изменяющихся в диапазоне 1000-3500 об/мин. Выходные уровни гематокрита, составляющие 80% и выше, были получены до достижения высоких уровней загрязнения мембраны. Время сбора 880 мл плазмы изменялось в диапазоне приблизительно между 18 и 20 минутами.

Как отмечалось выше, время нахождения эритроцитов в зазоре сдвига напрямую связано с величиной гемолиза. В устройствах разделения с вращающейся мембраной

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существуют области потока вдоль осевой длины ротора, где поток жидкости является относительно стоячим, что приводит к образованию очагов гемолиза. Качество собранных эритроцитов ухудшается в той степени, в которой эритроциты из области с высоким гемолизом перемешиваются с потоком в области с низким гемолизом.

Соответственно, согласно другому аспекту заявки, представлен способ для создания отдельных областей потока жидкости в зазоре сепаратора с вращающейся мембраной без использования затворов. Отдельные области потока снижают или минимизируют влияние смешивания жидкостей между двумя областями потока. Отдельные области потока получают посредством наличия приподнятого ребра или выступа в зазоре для снижения или минимизации зазора между вращателем и внешним цилиндром. Предпочтительно, выступ или ребро представлено на поверхности ротора за пределами места, в котором к нему прикреплена вращающаяся мембрана.

Выступ, предпочтительно, расположен таким образом, чтобы задать границу области потока высокой перфузии. Радиальный размер выступа обратно пропорционален степени смешивания, допускаемой между двумя областями, которые он задает, при этом больший радиальный размер выступ допускает меньшее смешивание. Осевой размер или протяженность выступа также обратно пропорциональна допускаемой степени смешивания, при этом больший осевой размер допускает меньшее смешивание. Осевой размер выступа, предпочтительно, имеет размер, по меньшей мере, равный размеру зазора по длине в целях минимизации образования смежных потоков Тейлора, вызывающих нежелательное смешивание.

Обратимся к фиг. 8, на которой показано схематическое представление в поперечном сечении устройства 10 разделения с вращающейся мембраной. Устройство содержит неподвижный внешний цилиндр 12 и вращающийся внутренний цилиндр 14, на котором находится фильтрующий элемент. В соответствии с настоящей заявкой, внутренний цилиндр представлен с радиальным выступом 90. Этот выступ служит для разделения зазора 16 между вращателем и внешним корпусом на две области потока. Первая область 92 жидкости имеет стоячую, непроточную область потока, обычно в части вращателя, которая выходит за пределы мембраны фильтра. Вторая область 94 потока, которая обычно контактирует с мембраной фильтра, имеет область потока с высокой перфузией.

Поскольку первая область 92 потока является непроточной, кровь, находящаяся в ней, подвержена повышенным напряжениям сдвига в течение более продолжительных периодов времени, чем кровь во второй области 94 потока. Таким образом, кровь в первой области 92 потока часто может стать гемолизированной и имеет высокие концентрации свободного гемоглобина (Hb). Выступ 90 препятствует потоку жидкости между двумя областями потока, таким образом, минимизируя степень смешивания Hb-загрязненной крови в первой области 92 с кровью с низкой Hb во второй области 94.

Хотя показано, что выступ 90 составляет единой целое с ротором, он также может быть сформирован на внутренней стороне внешнего цилиндра для достижения того же самого эффекта. Как было отмечено выше, осевой размер выступа должен иметь длину, составляющую по меньшей мере одну величину зазора. Типичное устройство разделения с вращающейся мембраной для выполнения плазмафереза обычно имеет зазор между вращателем и герметизирующей стенкой, составляющий от 0,058 см до 0,0673 см, и выступ в соответствии с настоящей заявкой мог бы иметь осевой размер в пределах того же общего диапазона. Однако большие осевые размеры для выступа приведут к сниженному смешиванию и, в одном из примеров, было обнаружено, что ротор, имеющий радиально вытянутый выступ с осевым размером 0,234 см, является

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эффективным.

II. Системы и способы для обработки ранее собранной цельной крови

Устройство разделения с вращающейся мембраной в соответствии с описанным выше может быть выгодно использовано в различных системах и способах обработки крови, для которых предшествующие устройства обычно не подходили, особенно, в системах и процессе для получения эритроцитов. В одном из типов системы и способа, вращатель может быть использован для обработки во "вспомогательной лаборатории" ранее собранной цельной крови, как показано на фиг. 9-15A.

Обратимся к фиг. 9, на которой схематически проиллюстрированы одноразовый контур циркуляции жидкости, или модуль A, и многоразовый долговременный контроллер, или модуль B, сконфигурированный для взаимодействия с потоком через контур жидкости A и управления им. Одноразовый контур жидкости A, как проиллюстрировано на фиг. 9, содержит множество компонентов, соединенных между собой гибкими пластиковыми трубками, определяющими маршрут потока между компонентами. Контур, предпочтительно, заранее полностью собран и предварительно стерилизован, за исключением блока с контейнером цельной крови и контейнером клеточного консерванта. Конкретнее, проиллюстрированный одноразовый контур на фиг. 9 содержит контейнер 101 цельной крови и контейнер 102 с раствором клеточного консерванта, сепаратор 108 компонентов крови, контейнер 112 для сбора плазмы, необязательный фильтр 113 редукции лейкоцитов, и контейнер 115 для сбора эритроцитов. Хотя это и не проиллюстрировано на фиг. 9, многоразовый модуль B может иметь крепления и связанные с ними весы для поддержания любого или всех контейнеров 101, 102, 112 и 115. В различных других вариантах осуществления, обсуждаемых в настоящем описании, такие крепления/весы могут не быть проиллюстрированы, но понимается, что они являются частью описываемых систем.

Контейнер 101 для сбора цельной крови может представлять собой любой подходящий контейнер, но обычно он представляет собой гибкий пластиковый мешок или пакет, в который ранее было собрано приблизительно 450 мл цельной крови. Контейнер 101 может являться частью отдельной системы в процессе сбора, и затем может присоединяться к остальной части жидкостного контура A, или может фактически являться частью контура A во время сбора. Во время сбора, в соответствии с обычной процедурой, цельная кровь смешивается с противосвертывающим средством, размещенным в первичном контейнере, с целью предотвращения преждевременной коагуляции. Соответственно, "цельная кровь" при использовании в настоящем описании включает кровь, смешанную с противосвертывающим средством.

Гибкие пластиковые трубки 105 соединены с контейнером для сбора цельной крови, например, посредством стерильного соединительного устройства или другого подходящего механизма прикрепления, и задают маршрут потока цельной крови между контейнером 101 с цельной кровью и соединением с трубками 103 раствора клеточного консерванта, которые выступают из контейнера 102 с раствором клеточного консерванта в соединение маршрута потока. Соединение маршрута потока между маршрутом потока цельной крови и маршрутом потока всех консервантов располагается во входном фиксаторе 116. Из соединения маршрут потока проходит через трубки 107 к впускному отверстию сепаратора 108.

Как показано на фиг. 9 настоящего описания, корпус сепаратора имеет выпуск, который соединен с зазором между корпусом и ротором и с трубками 110 потока концентрированных эритроцитов для извлечения концентрированных эритроцитов из зазора сепаратора. Кроме того, корпус содержит выпуск из ротора, который соединен

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со стороной мембраны, направленной в другую сторону от зазора (например, внутренняя часть ротора) и соединен с трубками 111 маршрута потока плазмы.

В целях снижения числа лейкоцитов, которые могут присутствовать в эритроцитах, одноразовый контур циркуляции жидкости A, необязательно, содержит фильтр 113 редукции лейкоцитов, который может представлять собой любую хорошо известную конструкцию для удаления лейкоцитов из концентрированных эритроцитов без чрезмерного гемолиза эритроцитов или снижения числа эритроцитов в собранном продукте. Концентрированные эритроциты из фильтра 113 редукции эритроцитов проходят через удлинение 114 по маршруту потока концентрированных эритроцитов в контейнер 15 для хранения, который может быть сделан из любого подходящего пластикового материала, совместимого с хранением эритроцитов.

Многоразовый или долговременный модуль B контроллера, который схематически показан на фиг. 9, предпочтительно, содержит датчик 104 гематокрита для определения гематокрита и цельной крови, вытекающей из контейнера 101 цельной крови. Детектор гематокрита может иметь любую подходящую схему или конструкцию, предпочтительно, в соответствии с описанным в патенте США No. 6419822, который настоящим включен в данное описание посредством ссылки.

Долговременный контроллер многоразового использования, или модуль B управления, содержит входной фиксатор 116, которым можно управлять с целью контроля жидкости из контейнера 101 цельной крови или контейнера 102 клеточного консерванта, или, необязательно, одновременно и пропорционально из обоих контейнеров 101 и 102. Для контролирования потока крови в сепаратор, модуль многоразового использования содержит впускной насос 106, который также может иметь любую подходящую конструкцию и может, например, представлять собой насос перистальтического типа, который функционирует посредством постепенного сжатия или сдавливания трубок 107, образующих маршрут впускного потока в сепаратор, насос с гибкой диафрагмой или другой подходящий насос. Датчик 117 давления взаимодействует с маршрутом впускного потока между насосом 106 и сепаратором 108 с целью определения впускного давления насоса. Датчик может выдавать данные в систему управления для обеспечения функции тревоги в случае превышения давления, недостаточного давления, или и того, и другого.

В целях контроля скорости потока концентрированных эритроцитов от сепаратора 108, многоразовый модуль также содержит выпускной насос 109, который связан с маршрутом 110 выпускного потока и функционирует аналогичным описанному в отношении впускного насоса 106 образом. Он также может иметь любую подходящую конструкцию, такую как перистальтический насос, структуру с гибкой диафрагмой или другую подходящую структуру насоса. Маршрут 111 потока плазмы, выходящей из сепаратора, предпочтительно, не контролируется насосом, и объемная скорость потока через трубки маршрута потока плазмы представляет собой разность между впускной объемной скоростью потока из насоса 106 и выпускной объемной скоростью потока из насоса 109. Модуль B многоразового использования может, однако, также содержать фиксатор 118 для управления потоком плазмы через трубки 111 маршрута потока плазмы.

Одноразовый модуль A также может содержать контейнер 112 для сбора плазмы, имеющий жидкостное соединение с маршрутом потока плазмы, для приема плазмы, отделенной сепаратором 108. Поскольку плазма проходит через пористую мембрану в сепараторе 108, плазма, которая собирается в контейнере 112, является в значительной степени безклеточной плазмой, и может подходить для введения пациентам,

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замораживания с целью хранения или последующей обработки.

На фиг. 10 показан общий вид маршрута(-ов) потока жидкости через систему, проиллюстрированную на фиг. 9. В частности, на ней показан поток цельной крови из контейнера 101 с одной единицей цельной крови через детектор 104 гематокрита цельной крови к соединению в маршруте потока, расположенном в бинарном фиксаторе 116. Раствор для консервирования клеток, такой как раствор для консервирования эритроцитов, вытекает из контейнера 102 эритроцитов также к соединению в бинарном фиксаторе 116. В зависимости от этапов обработки, бинарный фиксатор допускает поток цельной крови или клеточного консерванта в остальную часть системы. Необязательно, фиксатор 116 может представлять собой пропорциональный фиксатор, допускающий выбранный одновременный пропорциональный поток цельной крови и консерванта эритроцитов.

Из бинарного фиксатора 116 цельная кровь или жидкость клеточного консерванта протекает через впускной насос 106 и в устройство 108 разделения. Как объяснялось ранее, устройство разделения использует вращающиеся друг относительно друга корпус и ротор, на одном из которых находится мембрана, через которую может проходить плазма.

В одном из вариантов осуществления, мембрана находится на поверхности ротора, и плазма проходит через мембрану и через внутренний лабиринт протоков в пределах ротора, выходя в итоге в контейнер 112 для сбора плазмы. В случае, когда мембрана установлена на роторе, устройство обычно называется сепаратором с вращающейся мембраной, как показано на фиг. 10. Однако следует понимать, что мембрана потенциально может быть установлена на внутренней поверхности корпуса в направлении зазора между внутренней поверхностью стенки корпуса и внешней поверхностью мембраны, или мембрана может находиться и на внешней поверхности ротора, и на внутренней поверхности корпуса, с тем чтобы плазма проходила через мембраны одновременно, что потенциально увеличивается скорость разделения или производительность сепаратора 108. Из сепаратора 108 концентрированные эритроциты протекают через выпуск корпуса, соединенный с зазором между ротором и корпусом, и через маршрут 110 потока эритроцитов и выпускной насос 109, который контролирует скорость объемного потока концентрированных эритроцитов.

Хотя гематокрит концентрированных эритроцитов, удаленных из сепаратора 108, может меняться, ожидается, что гематокрит концентрированных эритроцитов будет составлять приблизительно 80-85%. Выпускной насос 109 закачивает концентрированные эритроциты в контейнер 115 для сбора эритроцитов и, необязательно, через фильтр редукции лейкоцитов, расположенный на маршруте потока эритроцитов между насосом 109 и контейнером 115 для сбора. Воздействие насоса, выталкивающего концентрированные эритроциты через фильтр редукции лейкоцитов, помогает поддерживать время обработки в пределах целесообразного диапазона по сравнению, например, со временем, которое потребовалось бы для потока концентрированных эритроцитов через фильтр редукции лейкоцитов в ручной установке под воздействием гравитации.

Плазма, отделенная сепаратором 108, как показано на фиг. 10, протекает через устройство разделения, например, из выпуска, связанного с лабиринтом протоков внутри ротора, через единичный контрольный фиксатор 118 и в контейнер 112 для сбора плазмы. Как отмечалось ранее, поскольку плазма проходит через мембрану, она является в значительной степени безклеточной и подходящей для последующего введения пациентам, замораживания и/или для обработки, например, путем фракционирования,

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с целью получения компонентов плазмы, предназначенных для использования в терапевтических продуктах.

Система также может содержать фильтр, такой как фильтр редукции лейкоцитов, в линии 111 потока плазмы, если есть необходимость.

Фиг. 11 иллюстрирует одну из версий потенциальной системы, использующей и одноразовый модуль A жидкостного контура, и многоразовый или долговременный модуль B контроллера. Хотя они показаны собранными друг с другом, модуль A жидкостного контура и долговременный модуль B имеют отдельное и независимое назначение и могут также использоваться с другими системами. Как можно видеть на фиг. 11, одноразовый модуль A удобно установлен напротив многоразового модуля B, который имеет связанные с ним навесы или опоры, некоторые из которых могут быть связаны с весами, для поддержания различных контейнеров одноразовой системы. Одноразовый модуль предпочтительно является, как указывалось ранее, предварительно собранным и предварительно простерилизованным. Контейнер с раствором клеточного консерванта может быть предварительно присоединен как часть одноразовой системы или может быть добавлен позднее, например, с помощью стерильного соединительного устройства или другого подходящего приспособления. Контейнер цельной крови, который содержит единицу ранее собранной цельной крови, также может быть предварительно присоединен к предварительно собранному жидкостному контуру или может быть присоединен посредством стерильного соединительного устройства или другого подходящего приспособления для соединения.

Поверхность многоразового модуля B содержит, в данном варианте осуществления, отдельный фиксатор 116a раствора для управления потоком раствора для консервации клеток из контейнера 102 раствора, который свисает с поднятой поддерживающий штанги раствора. Контейнер 101 цельной крови подвешен к весам. Весы могут иметь обычную конструкцию и могут выдавать сигнал измерения веса, который может быть использован системой управления модуля B для измерения количества цельной крови, которое остается в контейнере, и/или количества цельной крови, которое было обработано системой. Одноразовая система содержит маршрут 105 потока эритроцитов, который проходит из контейнера цельной крови через детектор 104 гематокрита и через отдельный фиксатор 116b цельной крови для управления потоком цельной крови из контейнера в систему. Маршрут 103 потока раствора клеточного консерванта и маршрут 105 потока цельной крови объединяются в соединении, таком как v-участок или y-участок, выше по ходу потока от впускного насоса 106. Объединенный маршрут потока проходит через впускной насос на впуск устройства 108 разделения. Как видно на фиг. 11, многоразовый модуль B содержит блок привода, такой как магнитный блок привода, для выполнения вращения ротора в пределах корпуса сепаратора без необходимости физического прохождения элементов или компонентов привода через корпус. В данной схеме расположения ротор содержит магнитно подсоединенный элемент привода, который вращается посредством магнитного блока привода, соединенного с многоразовым модулем. Система подробнее описана в патенте США No. 5194145, выданном Schoendrofer, который включен в настоящее описание посредством ссылки.

Выпуск концентрированных эритроцитов из сепаратора 108 присоединен к маршруту 110 потока эритроцитов, который проходит через выпускной насос 109 к впуску необязательного фильтра 113 редукции лейкоцитов. Среда фильтра, расположенная между впуском и выпуском фильтра редукции лейкоцитов, по существу, удаляет лейкоциты из эритроцитов. Трубки 114 маршрута потока эритроцитов передают эритроциты с выпуска фильтра в контейнер 115 для сбора эритроцитов.

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Плазма пропускается из выпуска плазмы сепаратора через фиксатор 118 контроля потока плазмы в контейнер 112 для сбора плазмы. Аналогично контейнеру цельной крови, контейнер 115 концентрированных эритроцитов и контейнер 112 плазмы подвешиваются к весам, которые могут находиться в электронном взаимодействии с системой управления долговременного или многоразового модуля B с целью предоставления информации относительно количества концентрированных эритроцитов и/или плазмы, собранных из цельной крови, или относительно скорости сбора.

Хотя данная система была проиллюстрирована с определенными основными компонентами и свойствами в соответствии с описанным выше, не предполагается, что данное описание исключает добавление, при необходимости, других компонентов, таких как датчики, насосы, фильтры и т.п. Например, необязательно, может быть желательным проведение фильтрации плазмы до ее входа в контейнер для сбора плазмы, или может быть желательным исключение фильтра лейкроредукции для эритроцитов. Хотя плазма, удаленная из сепаратора 108, является в значительной степени безклеточной плазмой, может быть необходимой фильтрация плазмы с целью последующего введения или обработки. Не предполагается, что настоящее описание исключает возможное добавление дополнительных компонентов или удаление одного или более компонентов, описанных выше.

Обратимся теперь к обработке цельной крови в проиллюстрированной системе; процесс разделения начинается с заливки системы. “Заливка” относится к способу, посредством которого мембрана подготавливается (то есть, смачивается) до начала использования. Смачивание жидкостью помогает вытеснить воздух, присутствующий в матрице мембраны, до проведения индуцированного давлением потока через мембрану. Обычно небиологическая жидкость низкой вязкости, такая как раствор клеточного консерванта (раствор эритроцитов, такой как раствор Adsol), используется для смачивания с целью осуществления наиболее эффективного вытеснения воздуха. Во время заливки жидкость удаляется из пакета 102 раствора клеточного консерванта посредством впускного насоса 106 до тех пор, пока линия 103 раствора, линия 105 цельной крови, впускная линия 107 и устройство 108 с вращающейся мембраной не будут полностью заполнены раствором. Для обеспечения надлежащей заливки, впускной насос 106 может перемещаться по часовой стрелке и против часовой стрелки во время заливки. Цель заливки раствором состоит в предотвращении формирования поверхности раздела воздух-кровь посредством создания поверхности раздела раствор-кровь, а также в смачивании мембраны в устройстве разделения. Каждая из предпринимаемых мер позволяет снизить гемолиз эритроцитов.

После того как система была успешно залита, маршрут 103 потока клеточного раствора будет закрыт посредством впускного фиксатора 116. Проиллюстрированный впускной фиксатор представляет собой бинарный фиксатор, который может закрывать маршрут 103 потока раствора клеточной консервации или маршрут 107 потока цельной крови. Цельная кровь будет затем прокачана через маршрут 105 потока цельной крови и маршрут 107 впускного потока в сепаратор 108 посредством впускного насоса 106. Скорость потока впускного насоса 106 может изменяться от около 10 мл/мин до 150 мл/мин в зависимости от желаемого выхода продукта для конкретной процедуры. После того как цельная кровь выходит из контейнера 101, она проходит через детектор 104 гематокрита цельной крови, который генерирует оценку гематокрита цельной крови путем измерений отражения IR LED. Подробности относительно детектора гематокрита объяснены в патенте США No. 6419822 (Название: Systems and methods for sensing red blood cell hematocrit), включенном посредством ссылки. Значение гематокрита цельной

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крови требуется для исходного алгоритма управления проиллюстрированной системы, но может быть важным в других системах.

После того как цельная кровь заполнила сепаратор 108, система начинает перемещать плазму из сепаратора, который разделяет цельную кровь, входящую в устройство с вращающейся мембраной, на концентрат эритроцитов и практически безклеточную плазму. Упакованные эритроциты с гематокритом, составляющим приблизительно 80-85%, будут выкачаны из сепаратора 108 через маршрут 110 потока эритроцитов в лейкофильтр 113 эритроцитов посредством выпускного насоса 109. Выпускной насос пропускает упакованные эритроциты через лейкофильтр 113 эритроцитов, и концентрат эритроцитов, который выходит из лейкофильтра 113 эритроцитов через линию 114 эритроцитов в пакет 115 продукта эритроцитов, будет успешно обеднен лейкоцитами и также обеднен тромбоцитами. Также возможно выполнить автоматизированное разделение цельной крови без использования лейкофильтра 113 эритроцитов. В этом случае лейкофильтр 114 эритроцитов будет удален из системы, и продукт 115 эритроцитов не будет обеднен лейкоцитами или тромбоцитами.

В течение процедуры плазма проходит через маршрут 111 потока плазмы в пакет 112 плазмы со скоростью потока, равной разности между скоростью потока впускного насоса 106 и скоростью потока выпускного насоса 109, что в настоящее время выполняется в других приложениях разделения с вращающейся мембраной, таких как применяются в инструменте Autopheresis-C®, поставляемом компанией Fenwal, Inc. Давление на мембране, сгенерированное вследствие различия в скоростях потока, отслеживается датчиком 117 давления. Измерения давления используются для контроля скорости потока плазмы с применением алгоритма, описанного в заявке на патент США No. 13/095633, поданной 27 апреля 2011 (Название: SYSTEMS AND METHODS OF CONTROLLING FOULING DURING A FILTRATION PROCEDURE), настоящим включенной посредством ссылки.

Система на фиг. 9-11 будет продолжать разделять упакованные эритроциты и плазму до тех пор, пока пакет 101 цельной крови не станет пустым, что будет определено по прохождению воздуха через детектор 104 гематокрита цельной крови. В этот момент линия 105 цельной крови будет закрыта, и линия раствора клеточного консерванта будет открыта посредством впускного фиксатора 116 для запуска промывания раствором или спуска. Во время промывания раствором, раствор консерванта будет удален из пакета 102 раствора и будет закачан в сепаратор 108 посредством впускного насоса 106. Маршрут 111 потока плазмы закрывается посредством фиксатора 118 плазмы во время промывания раствором. Промывание раствором используется для спуска любой крови, остающейся в системе, в контейнер 115 продукта эритроцитов. Промывание раствором также повысит объем контейнера 115 продукта эритроцитов до уровня, необходимого для надлежащего хранения эритроцитов. После окончания промывания раствором разделение единицы цельной крови завершается.

Обратимся к фиг. 12, на которой показана еще одна альтернативная система с двумя насосами. Данный вариант осуществления отличается от показанного на фиг. 9 в основном тем, что жидкость из раствора консерванта для клеток крови добавляется после того как эритроциты были отделены от цельной крови. Конкретнее, контейнер/пакет 101, содержащий ранее собранную цельную кровь (предпочтительно уже объединенную с противосвертывающим средством), соединяется с одноразовой системой A через сегмент трубок 107, который ведет к сепаратору 108 крови. Насос 106 взаимодействует с трубками 107 с целью закачивания цельной крови в сепаратор 108. Контейнер 102, содержащий раствор добавки для консервации эритроцитов, соединяется

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с контейнером 115 для сбора отделенных эритроцитов через трубки 114, через которые отделенные эритроциты также направляются в контейнер 115 через фильтр 114 лейкоцитов.

Стерильное соединение контейнеров 101, 102 с одноразовой системой может быть достигнуто посредством ряда различных способов. Контейнер 102 для раствора добавки может быть представлен как часть одноразовой системы A, и может быть объединен с остальной одноразовой частью (после стерилизации посредством, например, обработки гамма- или электронным пучком) во время итоговой упаковки, после того как оставшаяся часть одноразовых элементов была стерилизована (посредством, например, обработки паром). Альтернативно, контейнер 102 может быть сформирован как единое целое с одноразовыми элементами. В еще одной альтернативе, и контейнер 102, и контейнер 101 цельной крови могут быть отдельными от остальных одноразовых элементов и могут подсоединяться в момент использования через, например, стерильные стержневые соединения 170, показанные схематически на фиг. 10. Такие стержневые соединения, предпочтительно, имеют фильтр 0,2 мкм для поддержания стерильности.

В другом аспекте данного варианта осуществления, трубки 103, соединяющие контейнер 102 с раствором добавки с фильтром 62 лейкоцитов, также могут быть совместно сцеплены посредством насоса 109. В частности, насос 109 может представлять собой насос с двойным напором, который производит поток раствора добавки и поток эритроцитов, выходящих из сепаратора 108, с целью контроля скорости каждого на основании внутреннего диаметра трубок 103 и 110.

В варианте осуществления с фиг. 12 также используется дополнительный датчик 117b давления для отслеживания встречного давления из фильтра 113 лейкоцитов. Если встречное давление станет чрезмерным, как в случае закупорки фильтра, датчик будет осуществлять управление скоростью потока с целью обеспечения того, чтобы одноразовые элементы не разрывались вследствие избыточного давления.

III. Заливка мембраны

В соответствии с другим аспектом изложения, представлен способ для заливки мембранного фильтра, посредством которого повышается вероятность того, что будет достигнуто смачивание максимальной величины площади поверхности мембранного фильтра, в результате чего максимизируется площадь мембраны, доступная для фильтрации/разделения. В частности, когда система фильтра с вращающейся мембраной заливается в соответствии с описанным выше, при этом вращающаяся мембрана ориентирована таким образом, что ось вращения является, по существу, вертикальной, раствор для заливки входит в верхний впускной канал вращающегося сепаратора, и гравитация направляет жидкость к выпуску на дне сепаратора. В таких обстоятельствах поверхностное натяжение жидкости заливки будет формировать поверхность раздела воздух-жидкость, которая может передвигаться неравномерно по поверхности мембраны, создавая нарушения. В результате этого определенные области мембраны фильтра не будут увлажняться во время заливки, что повышает потенциал захвата воздуха матрицей мембраны. Таким образом, неувлажненная область мембраны становится недоступной для разделения, что негативно сказывается на эффективности разделения мембраной, до тех пор пока не будет создано достаточное давление для вытеснения воздуха.

Соответственно, представлен способ для заливки мембранного сепаратора, который позволяет равномернее смочить поверхность мембраны посредством обеспечения более равномерной поверхности раздела воздух-жидкость во время заливки. С этой целью жидкость заливки вводится в сепаратор таким образом, что она работает против силы

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тяжести при продвижении поверхности раздела жидкость-воздух в верхнем направлении через поверхность мембраны. Это помогает обеспечить более равномерное смачивание мембраны, поскольку воздух, вытесненный во время заливки, может перемещаться в одном направлении, не будучи захваченным, при продвижении поверхности раздела воздух-жидкость через мембрану.

Таким образом, в соответствии с данным альтернативным способом для заливки, жидкость заливки вводится в сепаратор через канал на дне сепаратора. Раствор для заливки продвигается вверх в корпусе сепаратора против силы тяжести для смачивания поверхности мембраны, при этом воздух выталкивается из сепаратора через канал на верху сепаратора. Хотя такая заливка "снизу вверх" описывается в контексте сепаратора с вращающейся мембраной, оно также применима к мембранному сепаратору любого типа, которому требуется заливка жидкостью до начала использования.

В соответствии с фиг. 9 и 12, сепаратор 108 ориентирован вертикально, при этом мембранный сепаратор и корпус могут вращаться друг относительно друга вокруг, в общем смысле, вертикальной оси, при этом канал для приема цельной крови расположен на верху сепаратора и каналы, через которые выходят отделенные эритроциты и плазма, расположены внизу сепаратора. Таким образом, в соответствии с одним из путей выполнения данного альтернативного способа заливки, и в соответствии с фиг. 1 и 2, раствор для заливки может быть введен через выходное отверстие 34 или выпускное отверстие 46 плазмы сепаратора с вращающейся мембраной 10, при этом воздух выталкивается через впускное отверстие 22. В соответствии с другим путем выполнения данного альтернативного способа заливки, сепаратор 10 может быть инвертирован или перевернут для заливки, с тем чтобы выходное отверстие 34 и выпускное отверстие 46 плазмы находились на верху сепаратора 10, и впускное отверстие 22 находилось внизу сепаратора 10. Раствор для заливки может затем быть введен через впуск 22, при этом поверхность раздела жидкость-воздух продвигается вверх, и воздух выталкивается через выходное отверстие 34 или выпускное отверстие 46 плазмы, или через оба отверстия. После заливки, сепаратору 10 может быть возвращена его исходная ориентация, в которой впускное отверстие 22 находится наверху, и выходное отверстие 34 и выпускное отверстие 46 плазмы находятся внизу.

Еще одна альтернатива, в которой может быть использована заливка "снизу вверх" сепаратора 108 крови, описанная выше, показана на фиг. 12A. В отличие от фиг. 12, впускная линия 107 для цельной крови соединяется с более низким каналом сепаратора 108 (к которому была присоединена выпускная линия 110 в варианте осуществления с фиг. 12), тогда как выпускная линия 110 соединена с каналом на верху сепаратора 108 (к которому была присоединена впускная линия 107 в варианте осуществления с фиг. 12). Для заливки системы с фиг. 12A, фиксатор 116B открывается и насос 106 активируется для создания потока цельной крови (предпочтительно, с добавленным противосвертывающим средством) через впускную линию 107 таким образом, чтобы он входил в сепаратор 108 через канал в более низком конце корпуса. При заполнении цельной кровью корпуса сепаратора воздух выталкивается через верхний канал, с тем чтобы удалить, по существу, весь воздух из устройства и осуществить смачивание мембраны фильтра.

После завершения заливки, система продолжает функционировать, как показано на фиг. 12A, для разделения цельной крови на плазму, принимаемую в контейнере 112, и эритроциты, принимаемые в контейнере 115. В конце процедуры разделения сепаратор может промываться раствором добавки из контейнера 102.

Обратимся к фиг. 14 и 15, на которых показана еще одна альтернативная система

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разделения крови в соответствии с настоящим изложением. Система с фиг. 14 и 15 аналогична системам с фиг. 9, 11 и 12, за исключением того, что модуль B содержит третий насос 119 для избирательного закачивания раствора добавки в сепаратор 108 в течение фазы заливки (как показано на фиг. 14), или к отделенным эритроцитам во время фазы разделения (как показано на фиг. 15). Система с фиг. 14 и 15 также содержит дополнительный фиксатор 120 для избирательного разрешения или предотвращения потока жидкости (отделенных эритроцитов и раствора добавки) через лейкофильтр 113 и в контейнер 115 эритроцитов. До начала заливки фиксатор 20 может недолго оставаться открытым, и насос 109 может выкачивать остаточный воздух из контейнера 115 и фильтра 113, минимизируя объем воздуха, остающийся в контейнере 115 в конце данной процедуры. Как и на фиг. 12A, в системе с фиг. 14 и 15 используется заливка “снизу вверх” сепаратора 108, за исключением использования раствора добавки в качестве жидкости для заливки вместо цельной крови. В течение заливки системы, как показано на фиг. 14, воздух из одноразовой системы A выталкивается в контейнер 101 цельной крови.

В течение фазы разделения система функционирует как показано на фиг. 15.

При завершении фазы разделения раствор добавки закачивается в сепаратор 108 (как показано в фазе заливки, проиллюстрированной на фиг. 14) для промывания сепаратора.

Обратимся к фиг. 15A, на которой показана еще одна альтернативная система. Система с фиг. 15A аналогична системе с фиг. 14 и 15 в том, что многоразовый компонент B содержит три насоса 106, 109 и 119. Однако система с фиг. 15A аналогична системе с фиг. 12A в том, что впускная линия 107 для цельной крови соединена с каналом внизу сепаратора 108, тогда как выпускная линия для отделенных эритроцитов соединена с каналом на верху сепаратора. Таким образом, в системе с фиг. 15A цельная кровь используется для заливки системы аналогично системе с фиг. 12A.

IV. Системы и способы управления данными

Система, описанная в настоящем описании, также может включать в себя решения по управлению данными. Весы и добавление устройств печатания этикеток к системе позволило бы пользователям получать этикетки с весом продукта напрямую из системы разделения по завершении процедуры. Это устраняет ручное взвешивание и запись данных, используемые в текущих способах обработки. Модуль B может содержать подходящий пользовательский интерфейс, такой как сенсорный экран, кнопочную панель или клавиатуру, а также сканер, чтобы предоставить пользователям возможность ввода информации, такой как пользовательский номер идентификации донора, идентификатор банка крови, номера набора жидкостного контура, номера партии, и т.д., которая также может улучшить эффективность управления данными в центрах производства крови.

Конкретнее, и в соответствии с еще одним аспектом настоящего изложения, представлен способ для автоматизации передачи данных, ассоциированных с контейнером для сбора цельной крови, а также другой относящейся к делу информации, в устройство обработки данных, используемое для последующего разделения цельной крови и конечного хранения контейнера или контейнеров для такого отделенного компонента или компонентов крови. Данный способ схематически проиллюстрирован на блок-схеме с фиг. 29, где представлен исходный контейнер (этап 122), который обычно содержит единицу ранее собранной цельной крови, хотя исходный контейнер может содержать ранее обработанный продукт крови. Исходный контейнер обычно имеет ассоциированные с ним данные, относящиеся к идентификации донора и времени,

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места сбора и т.д., при этом такие данные предпочтительно находятся в машиночитаемом формате, таком как штрихкод или метка RFID. Эти данные затем извлекаются и передаются (этап 124), и затем ассоциируются с устройством обработки данных и контейнерами конечного хранения (этап 126).

Обратимся к фиг. 30, на котором показана одна из возможных систем для применения в качестве системы управления данными в соответствии с настоящим изложением. Представлен контейнер 128 для сбора крови и отдельное устройство 130 обработки данных, имеющее три контейнера 132, 134 и 136 для конечного хранения. Во время взятия цельной крови, информация идентификации донора кодируется и ассоциируется с контейнером для собранной цельной крови. Это может быть выполнено путем ручного помещения этикетки со штрихкодом для идентификатора донора на этикетку контейнера, иглу контейнера или трубки. Также это можно сделать посредством применения записывающего устройства RFID в месте сбора, передающего идентификатор донора с весов сбора или портативного устройства на метку RFID, прикрепленную к контейнеру для сбора. Использование RFID позволяет управлять большим объемом информации, включая такие данные, как тип контейнера, дата истечения срока годности, время сбора, объем сбора, идентификатор медсестры, место сбора и т.п.

Автоматизированная передача данных между контейнером 128 для сбора и комплектом 130 обработки/контейнерами 132, 134, 136 для хранения может происходить в контексте стерильного соединения контейнера 128 для сбора с комплектом 130 обработки. Например, может быть использована электромеханическая система, которая выполняет стерильное соединение контейнера для сбора цельной крови с комплектом обработки. Такая система изложена в предварительных заявках на патент США No. 61/578690 и 61/585467, поданных 21 декабря 2011 и 11 января 2012, соответственно, которые включены в настоящее описание посредством ссылки. Устройство стерильного соединения может являться отдельно стоящим, как показано в указанных выше предварительных заявках, или может быть интегрировано с многоразовым модулем B, описанным выше. Альтернативно, система управления данными может быть просто связана с многоразовым модулем B, без устройства стерильного соединения, ассоциированного с ними. В любом случае устройство стерильного соединения или многоразовый модуль содержит программируемый контроллер, сконфигурированный для автоматического выполнения, или запроса выполнения пользователем, различных этапов способа управления данными, в соответствии с подробнее описанным ниже.

Система управления данными 138 включает в себя блок обработки, экран 140 для предоставления информации пользователю (такой как запросы и подтверждения), сенсорную панель 142 для предоставления пользователю возможности ввода информации и сканер/считыватель 144 для извлечения и передачи информации между контейнером 128 для сбора и комплектом 130 обработки. Система 138 также обеспечивает печать этикеток со штрихкодом или передачу данных на одну или более меток RFID, ассоциированных с комплектом обработки. Обратимся теперь к фиг. 31, на которой показана блок-схема, иллюстрирующая в общих чертах способ управления данными. Способ включает в себя загрузку пакета для сбора и комплекта обработки на многоразовый модуль и/или в устройство стерильного соединения (этап 140). Извлекаются данные, ассоциированные с комплектом обработки и данные, ассоциированные с контейнером для сбора (этапы 142 и 144). Как можно понять, порядок, в котором выполняются данные этапы, не является критичным. Как отмечалось выше, эти данные могут принимать форму штрихкода, метки RFID или другую форму,

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при этом комплект обработки и ассоциированные с ним контейнеры для сбора имеют соответствующие данные из контейнера для сбора, ассоциированного с ними. Это может принимать форму печати этикеток со штрихкодами или записи данных на метку RFID (этапы 146 и 148). Контейнер для сбора и комплект обработки соединены друг с другом, предпочтительно в процедуре стерильного соединения (этап 150), при этом такое соединение происходит в период времени в течение последовательности выполнения описанных выше этапов.

Затем кровь в контейнере для сбора обрабатывается (этап 152). Затем информация комплекта обработки/контейнера для хранения извлекается и проверяется с использованием данных контейнера для сбора (этапы 154 и 156). После такой проверки контейнеры для хранения могут быть отсоединены от контейнера для сбора (этап 158).

Система по настоящему изложению помогает пользователю в выполнении этапов, описанных выше, тем, что она выдает запросы и подтверждения для различных этапов. Например, если идентифицирующая информация имеет форму штрихкода, то система запрашивает у пользователя сканирование идентификатора штрихкода комплекта обработки и идентификатора донора контейнера для сбора. Система будет затем печатать копии этикеток штрихкодов на принтере, который является частью системы или присоединен к ней, при этом тип и количество этикеток определяется типом загруженного комплекта обработки. Система затем запрашивает у пользователя нанесение этикеток со штрихкодом на контейнеры конечного хранения. После того как система разделяет кровь на ее компоненты, система запрашивает у пользователя сканирование идентификаторов штрихкода контейнера с конечными компонентами, с тем чтобы система могла проверить правильность информации штрихкода до отсоединения контейнеров для хранения от контейнера для сбора и комплекта обработки.

Если идентифицирующая информация ассоциирована с меткой RFID, то система автоматически сканирует метку RFID на контейнере для сбора и затем автоматически считывает информацию на RFID, включенной в комплект обработки. Затем система автоматически копирует информацию контейнера для сбора на метку или метки RFID, ассоциированные с контейнерами для хранения комплекта обработки. После того как система разделит кровь на ее компоненты, в соответствии с типом комплекта обработки, определенным инструментом, система будет считывать метку RFID на контейнерах конечных компонентов для обеспечения возможности проверки идентифицирующей информации до отсоединения контейнеров для хранения крови от комплекта обработки и контейнера для сбора.

Предполагается, что система может использовать и штрихкод, и RFID в качестве избыточных систем, и может включать некоторые или все этапы, описанные выше, в зависимости от конкретного случая. Хотя сканер штрихкодов/считыватель RFID описан как ассоциированный с многоразовым модулем B, он может представлять собой выделенную станцию, физически отдельную от самой машины обработки, но соединенную через программное обеспечение управления данными.

Хотя данный способ управления данными был описан в связи со сбором цельной крови в контейнер, отдельный от комплекта обработки и контейнеров для хранения, он с таким же успехом может использоваться в связи с системой или комплектом, в котором контейнер для сбора составляет одно целое с комплектом обработки и его контейнерами для хранения. Кроме того, способ может быть использован в связи с обработкой цельной крови, полученной напрямую у донора, как описано ниже, при этом данные идентификации донора предоставляются донором, а не контейнером для

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сбора, или в процедуре промывания клеток, при этом данные идентификации ассоциированы с исходным контейнером.

V. Системы и способы для обработки цельной крови донора

В соответствии с еще одним аспектом настоящего изложения, сепаратор с вращающейся мембраной, описанный выше, может быть выгодно использован в одном этапе или в "кабинетном" сборе и разделении цельной крови на компоненты крови. Как описано ниже, представлена автоматизированная система сбора цельной крови, которая разделяет цельную кровь на одну единицу эритроцитов и плазму одновременно при взятии цельной крови у донора. Предполагается, что система является системой сбора "за один проход", без реинфузии компонентов крови обратно донору. Система, предпочтительно, содержит одноразовый контур потока жидкости и долговременный многоразовый контроллер, который взаимодействует с контуром и управляет потоком жидкости через него. Контур потока, предпочтительно, представляет собой одноразовый предварительно простерилизованный контур потока жидкости, который, предпочтительно, содержит контейнеры для сбора эритроцитов и плазмы, противосвертывающее средство и растворы добавки эритроцитов, сепаратор и фистулу для обеспечения прохождения цельной крови от донора в жидкостный контур. Долговременный контроллер, предпочтительно, содержит управляемое микропроцессором электромеханическое устройство с механизмами клапанов, насосов и датчиков, сконфигурированными для управлениям потоком через контур, а также содержит системы безопасности и сигнальные функции, подходящие для процедуры взятия цельной крови.

Способ взятия крови с применением системы включает в себя выполнение прокола вены донора и извлечение цельной крови из донора в одноразовый контур, в котором она обрабатывается аппаратурой и компонентами жидкостного контура, в результате чего цельная кровь разделяется на желаемые компоненты эритроцитов и плазмы. Донор остается подключенным к системе в течение процедуры, и все жидкости остаются в линии тока одноразового набора до завершения процедуры. В "однопроходной" системе цельная кровь, предпочтительно, проходит через жидкостный контур только один раз, и ни один из компонентов крови не возвращается донору.

Эритроциты, получаемые в результате сбора, не обязательно должны подвергаться процессу лейкоредукции. Однако лейкоредукция посредством фильтрации может быть осуществлена с помощью фильтра лейкоредукции, предпочтительно, встроенного в одноразовый контур, или посредством использования отдельного контура обработки, который стерильно соединен с контейнером для сбора эритроцитов.

Аппаратура, предпочтительно, содержит интерфейс оператора, такой как сенсорный экран, кнопочная панель, мышь, клавиатура и т.д., для ввода информации и/или отображения информации. Индикатор сообщения позволяет оператору контролировать процедуру, собирать информацию о ее статусе и устранять любые сбойные ситуации при их появлении.

Обратимся к чертежам; на фиг. 16-19 можно видеть схематическое представление системы автоматизированного сбора цельной крови под общим обозначением 210, в соответствии с настоящим изложением, на различных стадиях или фазах функционирования. Система, предпочтительно, содержит многоразовый компонент 212 аппаратного обеспечения, который, предпочтительно, содержит насосы, фиксаторы и датчики давления для управления потоком жидкости, а также одноразовый предварительно собранный стерильный компонент 214 жидкостного контура, который может быть установлен на компонент аппаратного обеспечения и содержит различные

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контейнеры/мешки, устройство доступа к донору или фистулу, и камеру разделения крови, при этом все элементы соединены друг с другом через стерильный маршрут жидкости, такой как гибкие пластиковые трубки. Контейнеры/мешки обычно являются сгибаемыми и сделаны из подходящего пластикового материала, хорошо известного в технике. Материал контейнеров может различаться в зависимости от применения, и может содержать непластифицированные материалы, такие как не содержащие DEHP полимеры, в частности, но не только, для хранения эритроцитов.

Конкретнее, проиллюстрированный компонент или модуль 214 жидкостного контура содержит устройство 216 доступа к донору, которое содержит первый отрезок трубок 218 в качестве линии извлечения, через которую цельная кровь извлекается из донора и вводится в жидкостный контур 214. Устройство 216 доступа к донору, предпочтительно, содержит иглу, в частности, малокалиберную иглу (18-21 калибра) с целью повышения комфорта донора, с наличием предохранителя иглы, при необходимости, для предотвращения случайных проколов иглой. Трубки 218 взаимодействуют с устройством разделения крови под общим обозначением 220 и, как описано выше, используются для введения цельной крови в сепаратор.

Второй отрезок трубок 222 обеспечивает обмен жидкостями между сепаратором 220 и первым контейнером/мешком 224 для приема отделенных концентрированных эритроцитов, тогда как третий отрезок трубок 226 обеспечивает обмен жидкостями между сепаратором 220 и вторым контейнером/мешком 228 для приема плазмы.

Жидкостный контур 214 также содержит источник противосвертывающего средства (например, CPD), которое находится в третьем контейнере 230, который взаимодействует с первым отрезком трубок 218 посредством четвертого отрезка трубок 232, соединенного с трубками 218, например, посредством Y-соединителя. Жидкостный контур 214 также может содержать источник раствора консерванта для эритроцитов, которые должны быть доставлены в контейнер/мешок 224. Раствор консерванта может находиться в отдельном мешке, связанном с контейнером 224. Альтернативно, контейнер 224 может быть предварительно заполнен объемом раствора консерванта, соответствующим количеству эритроцитов, которые будут приняты им в течение процедуры сбора.

Жидкостный контур 214 также содержит встроенную систему 234 взятия проб для асептического взятия проб крови до и в течение процедуры сдачи крови. Система 234 взятия проб содержит мешок, который взаимодействует с первым отрезком трубок 218 устройства доступа к донору через пятый отрезок трубок 236, расположенный выше по ходу потока относительно соединения между трубками 218 и трубками 232, через которые вводится противосвертывающее средство. Трубки 236, предпочтительно, взаимодействуют с трубками 218 через Y-соединитель или аналогичное устройство.

Долговременный компонент 212 аппаратного обеспечения, предпочтительно, содержит первый насос 238, который взаимодействует с трубками 218 для закачивания цельной крови в устройство 220 разделения и второй насос 240, который взаимодействует с трубками 222 для транспортировки, по существу, концентрированных эритроцитов из камеры 220 разделения в первый контейнер 224 для сбора. Насосы 238, 240 являются, предпочтительно, перистальтическими, или роликовыми, насосами, которые включают в себя ротор с одним или более роликами для сжатия трубок с целью обеспечения движения жидкости через них, хотя также могут быть использованы другие подходящие конструкции насосов, такие как насосы с гибкой диафрагмой. Компонент аппаратного обеспечения также, предпочтительно, содержит третий насос 242, который взаимодействует с трубками 232 для транспортировки противосвертывающего средства к трубкам 218 линии извлечения, через которые цельная кровь транспортируется в

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сепаратор 220. Третий насос 242 обеспечивает дозирование потока противосвертывающего средства, и также способствует смачиванию и промыванию системы, как будет описано ниже. Однако третий насос 242 является необязательным, и противосвертывающее средство может дозироваться в линии извлечения 218 цельной крови посредством гравитационного потока, при этом трубки 232 имеют размер, обеспечивающий необходимую скорость потока в течение процедуры сбора.

Компонент 212 аппаратного обеспечения также, предпочтительно, содержит фиксаторы 244, 246, 248 и 250 для избирательной закупорки и открытия сегментов трубок 218, 232, 222 и 226, соответственно. Термин “фиксаторы” используется в настоящем документе в широком смысле, и включает в себя любой механизм, который взаимодействует с маршрутами потока, например, сегментами трубок жидкостного контура, с целью избирательного разрешения или предотвращения потока жидкости через них. Компонент 212 аппаратного обеспечения также, предпочтительно, содержит датчики 252, 254 давления в трубках 218 линии извлечения вблизи или смежно с иглой (датчик 252 давления) и вблизи или смежно с впуском сепаратора 220 (датчик 254 давления) для контроля впускного давления, например, для обнаружения коллапса вены. Также, предпочтительно, представлены весы (не показаны) по меньшей мере для первого контейнера 224 с целью предоставления обратной связи относительно объема собранных эритроцитов.

В соответствии с другим аспектом изложения, многоразовый компонент аппаратного обеспечения, предпочтительно, содержит программируемый контроллер 256 для приведения в действие насосов и фиксаторов и контроля датчиков давления и весов, с тем чтобы процедура сбора цельной крови могла быть, по существу, автоматизирована. Контроллер 256 содержит программируемый микропроцессор и, предпочтительно, включает в себя интерфейс оператора, такой как сенсорный экран и индикатор сообщения для обеспечения оператору возможности входа и просмотра данных и управления процедурой, сбора информации по ее статусу и устранение любых сбойных ситуаций при их появлении.

Для выполнения автоматизированной процедуры сборы и разделения с помощью автоматизированной системы 210 сбора крови, изложенной выше, одноразовый жидкостный контур 214 загружается в рабочее положение на многоразовом компоненте 212 аппаратного обеспечения, как показано на фиг. 16 в прилагаемых чертежах. В фазе или стадии, показанной на фиг. 16, система заливается жидкостью для существенного удаления воздуха и смачивания мембраны фильтра. На начальной стадии первый фиксатор 244 закрыт, с тем чтобы предотвратить обмен жидкостями между устройством 216 доступа к донору и камерой 220 разделения крови, и противосвертывающее средство прокачивается насосами 240 и 242 через трубки 218, сепаратор 212 и трубки 222 с целью заливки системы. Затем выполняется прокол вены донора с помощью иглы устройства доступа к донору с целью принятия цельной крови в трубки 218. В этот момент могут быть взяты пробы цельной крови посредством пакета 234 сбора проб.

Обратимся к фиг. 17; после заливки первый фиксатор 244 открывается для пропускания цельной крови через трубки 218 в сепаратор 220 крови, с помощью насоса 238, для начала фазы сбора/разделения процедуры сбора. Противосвертывающее средство продолжает дозироваться в линии извлечения сегмента 218 трубки через сегмент 232 трубки посредством третьего насоса 242. Эритроциты выходят из сепаратора 220 через трубки 222. Четвертый фиксатор 250 открывается для того, чтобы позволить плазме выйти из сепаратора 220 и пройти через трубку 226 во второй контейнер 228 для сбора. Первый насос 238 выдает поток цельной крови в сепаратор 220, при этом

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впускное давление контролируется датчиком 254, тогда как эритроциты закачиваются из камеры 220 для разделения посредством второго насоса 240. Перепад расхода между первым насосом 238 и вторым насосом 240 обеспечивает выход отделенной плазмы из сепаратора 220 во второй контейнер 228 для сбора.

Обратимся к фиг. 18; когда объем эритроцитов в первом контейнере 224 для сбора достигает предварительно определенного объема (измеренного через вес первого контейнера 224 для сбора, определенный посредством весов), весы выдают контроллеру 256 сигнал, который запрашивает у контроллера завершение процедуры сбора посредством закрытия первого фиксатора 244, вследствие чего происходит закупорка линии 218 извлечения. Устройство 216 доступа к донору может быть извлечено из донора в этот момент. Если система должна промываться, то четвертый фиксатор 250 закрывается с целью закупорки для плазмы линии 226 потока ко второму контейнеру 228 для сбора. Первый насос 238 деактивируется, тогда как третий насос 242 продолжает доставлять противосвертывающее средство в сепаратор 220, при этом противосвертывающее средство выпускается в первый контейнер 224 для сбора через сегмент 222 трубки.

Обратимся к фиг. 19; после завершения цикла промывания, второй фиксатор 246 и третий фиксатор 248 закрываются, и второй насос 240 и третий насос 242 деактивируются.

В этом момент первый контейнер 224 для сбора, содержащий, по существу, концентрированные эритроциты, может быть отсоединен от одноразового жидкостного контура 214 для хранения или для способствования лейкофильтрации. Это может быть выполнено путем простого подвешивания контейнера 224 для сбора и допущения гравитационной фильтрации эритроцитов через фильтр лейкоредукции в контейнер для конечного хранения. Однако, в соответствии с другим аспектом изложения, и как показано на фиг. 20, может быть представлен третий контейнер 258 для сбора, который находится в жидкостном взаимодействии со вторым контейнером 224 для сбора через сегмент 260 трубки, при этом сегмент 260 трубки находится в жидкостном взаимодействии с сегментом 220 трубки через Y-соединитель, расположенный на сегменте 222 трубки между выпуском сепаратора 220 и вторым насосом 240. Затем может быть открыт третий фиксатор 248 для разрешения выходного потока концентрированных эритроцитов из контейнера 224 для сбора, при этом второй насос 240 активируется и выполняет закачку в обратном направлении для обеспечения потока концентрированных эритроцитов через фильтр редукции лейкоцитов 262 и в контейнер для сбора 258. Давление, созданное насосом 240, значительно ускоряет процесс фильтрации по сравнению с вызываемой гравитацией лейкофильтрацией эритроцитов.

В качестве еще одной альтернативы, лейкоредукция может быть выполнена в отношении цельной крови в течение фазы извлечения в процессе эксплуатации. Обратимся к фиг. 21 и 22; линия извлечения трубки 218 может содержать фильтр 264 редукции лейкоцитов, который находится в одной линии с трубкой 218. Фильтр 264 расположен против направления потока от первого насоса 238, с тем чтобы насос прилагал достаточную силу извлечения к крови для ее извлечения через фильтр 264 во время сбора. Лейкофильтр 264 может быть расположен в сегменте 218 трубки, против направления потока относительно места, где противосвертывающее средство вводится в систему (как показано на фиг. 21) или по направлению потока относительно места, где противосвертывающее средство вводится в линию 218 извлечения (как показано на фиг. 22). Размещение по направлению потока от места подсоединения противосвертывающего средства позволяет использовать противосвертывающее

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средство для смывания любой остающейся цельной крови из фильтра 264 после завершения извлечения из донора. Кроме того, размещение фильтра лейкоредукции в трубках 218 линии извлечения устраняет необходимость отдельного этапа фильтрации лейкоредукцией внизу по направлению потока, таким образом, дополнительно оптимизируя процесс сбора крови.

Ожидается, что автоматизированные однопроходные система и способ сбора цельной крови, описанные в настоящем описании, улучшат эффективность центра сбора крови и снизят расходы по эксплуатации путем выполнения разделения цельной крови на компоненты эритроцитов и плазмы без необходимости последующих ручных операций. Кроме того, использование малокалиберных игл в устройствах доступа к донору, используемых в системе, должно повысить комфорт донора, тогда как использование вытяжного насоса позволяет системе достичь времени взятия, аналогичного обычному сбору цельной крови. Кроме того, за счет управления сбором цельной крови посредством микропроцессора предоставляется больше возможностей для управления данными, которых обычно не имеется в текущих способах ручного сбора цельной крови, включая использование интегрированных считывателей штрихкодов и/или технологии RFID, в соответствии с описанным выше.

В соответствии с другим аспектом изложения, ниже описаны способы, системы и устройства, пригодные для промывания биологических клеток, таких как клетки крови или другие компоненты крови или биологические компоненты.

VI. Системы и способы для промывания клеток

Промывание биологических клеток может иметь несколько целей. Например, промывание клеток может использоваться для замены жидкой среды, в которой биологические клетки суспендированы. В этом случае вторая жидкая среда добавляется для замены и/или разбавления исходной жидкой среды. Части исходной жидкой среды и замещающей жидкой среды отделяются от клеток. Дополнительные замещающие жидкие среды могут добавляться до тех пор, пока концентрация исходной жидкой среды не станет ниже определенной процентной величины. В дальнейшем клетки могут быть суспендированы, например, в замещающей среде.

Промывание клеток также может быть использовано для концентрирования или дополнительного концентрирования клеток в жидкой среде. Клетки, суспендированные в жидкой среде, промываются, в результате чего часть жидкой среды отделяется и удаляется из клеток.

Кроме того, промывание клеток может быть использовано для удаления нежелательных твердых частиц, таких как крупные твердые частицы, или нежелательного клеточного материала из взвеси клеток конкретного размера, или для “очистки” желаемой взвеси клеток или другой жидкости.

Способ, системы и устройство, описанные ниже, могут быть применены для промывания клеток по любой из описанных выше причин. В частности, но без ограничения, способы, системы и устройство, описанные ниже, могут быть применены для промывания клеток крови, таких как эритроциты, или белые клетки крови (лейкоциты), или тромбоциты.

В одном конкретном варианте осуществления взвесь, содержащая белые клетки крови в жидкой культуральной среде, может промываться с целью замены культуральной среды на другую среду, такую как физиологический раствор, до начала использования или дополнительной обработки. Взвесь клеток, содержащая белые клетки крови в жидкой культуральной среде, может доставляться и вводиться в сепаратор, такой как сепаратор с вращающейся мембраной. Сепаратор с вращающейся

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мембраной имеет мембранный фильтр с размером пор, меньшим, чем размер белых клеток крови. В одном из вариантов осуществления, жидкая среда для промывания, содержащая замещающую жидкую среду, такую как физиологический раствор, также добавляется в сепаратор для разбавления жидкой культуральной среды. Сепаратор функционирует таким образом, что жидкости проходят через поры мембраны и извлекаются как отходы. В данном варианте осуществления, при извлечении жидкости добавляется среда для промывания, в результате чего полученная взвесь клеток содержит белые клетки крови, суспендированные в замещающей жидкой среде (например, физиологическом растворе).

В другом варианте осуществления, взвесь клеток может подвергаться концентрированию (посредством удаления супернатанта) и сбора взвеси концентрированных клеток в контейнер набора обработки. Замещающая жидкость может быть введена в сепаратор, объединена с концентрированными клетками в контейнере, и затем клетки могут быть ресуспендированы в замещающей жидкости. При необходимости ресуспендированные клетки/замещающая жидкость могут быть введены в сепаратор для дальнейшего концентрирования клеток, удаления супернатанта и ресуспендирования концентрированных клеток в дополнительной замещающей жидкости. Данный цикл может быть повторен при необходимости.

Аналогичные процессы могут быть применены для промывания эритроцитов, суспендированных в жидкой среде хранения. Взвесь клеток, содержащая эритроциты, суспендированные в жидкой среде хранения, может промываться с целью замещения жидкой среды хранения на другую среду, такую как физиологический раствор, до начала использования или дополнительной обработки. Взвесь клеток доставляется и вводится в сепаратор, такой как сепаратор с вращающейся мембраной. Сепаратор с вращающейся мембраной имеет мембранный фильтр с размером пор, меньшим чем размер эритроцитов. В одном из вариантов осуществления, среда для промывания, то есть замещающая жидкая среда, такая как физиологический раствор, также может добавляться в сепаратор для разбавления жидкой среды хранения. Сепаратор функционирует таким образом, что жидкость проходит через поры мембраны и извлекается как отход. При извлечении жидкости добавляется среда для промывания, в результате чего полученная взвесь клеток содержит эритроциты, суспендированные в замещающей жидкой среде (то есть, физиологическом растворе). Жидкость для промывания и/или замещающая жидкость также может являться средой для хранения, которая содержит питательные вещества и другие компоненты, которые позволяют осуществлять долговременное хранение клеток. Альтернативно, в другом варианте осуществления, эритроциты могут сначала быть сконцентрированы и удалены в контейнер, как в общих чертах описано выше. Замещающая жидкость может затем быть объединена с эритроцитами в контейнере. Замещающая жидкость может быть введена в контейнер напрямую, или может быть введена в сепаратор и через сепаратор, и затем в контейнер.

Системы, способы и устройство для промывания клеток, описанные в настоящем документе, используют одноразовый набор, который включает в себя сепаратор, такой как сепаратор с вращающейся мембраной. Одноразовый набор с сепаратором с вращающейся мембраной устанавливается на компонент аппаратного обеспечения системы, то есть устройство разделения. Устройство разделения содержит фиксаторы, насосы, двигатели, датчики обнаружения воздуха, измерительные датчики давления, Hb-детекторы, весы, и управляющую логическую схему/микропроцессор, включенную в микропроцессор. Управляющая логическая схема/микропроцессор принимает входные

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данные и сигналы от оператора и/или различных датчиков, и управляет функционированием фиксаторов, насосов и двигателей.

Взвесь клеток, которая будет промываться, то есть клетки, суспендированные в среде, могут быть представлены в стерильном одноразовом исходном контейнере, который соединен, стерильным образом, с одноразовым набором. Среда для промывания, такая как физиологический раствор, или другая подходящая среда, также соединяется стерильным образом или предварительно прикрепляется к одноразовому набору. Управляющая логическая схема устройства управляет фиксаторами и насосами для передачи взвеси клеток через трубки одноразового набора на сепаратор (с вращающейся мембраной). Устройство разделения, через свою систему управления, также направляет раствор для промывания через трубки одноразового набора на сепаратор с вращающейся мембраной. Взвесь клеток и раствор для промывания могут быть смешаны внутри сепаратора с вращающейся мембраной, могут быть смешаны до введения в сепаратор с вращающейся мембраной, или могут быть объединены в контейнере, после того как взвесь клеток была сконцентрирована. Внутри сепаратора с вращающейся мембраной среда суспендирования отделяется от клеток, суспендированных в ней. Среда суспендирования и оставшаяся среда для промывания (если среда суспендирования и среда для промывания были объединены) выходит через канал для отходов, тогда как клетки проходят через отдельный выходной канал.

Если необходимо дальнейшее промывание и разбавление, то промытые клетки могут быть повторно пропущены через сепаратор с дополнительным объемом раствора для промывания. В одном из вариантов осуществления, клетки, которые должны промываться повторно, могут передаваться в один или более рабочих контейнеров, как будет описано ниже. Управляющая логическая схема устройства управляет фиксаторами и насосами для передачи взвеси клеток из рабочего контейнера через трубки на впуск сепаратора с вращающейся мембраной или на впуск второго сепаратора с вращающейся мембраной. Добавляется дополнительная среда для промывания, и процесс повторяется до тех пор, пока не будет достигнут приемлемый объем или концентрация клеток. Конечная взвесь клеток, содержащая клетки, предпочтительно, собирается в контейнере конечного продукта.

В соответствии с настоящим изложением, на фиг. 23-25 показаны примеры систем, подходящих для промывания биологических клеток, таких как эритроциты и белые клетки крови, но не ограничиваясь указанным. Как отмечалось выше, предполагается, что изложенные конкретные варианты осуществления являются примерами и не являются ограничивающими. Таким образом, в одном из вариантов осуществления, система, описанная в настоящем описании, содержит одноразовый набор 300 (фиг. 23 или 24) и компонент аппаратного обеспечения или устройство 400 (фиг. 25). Следует понимать, что одноразовые наборы 300 обработки, показанные на обеих фиг. 23 и 24, идентичны во многих отношениях, и общие цифровые обозначения используются на обеих фиг. 23 и 24 для идентификации идентичных или аналогичных элементов одноразовых наборов обработки. В той степени, в которой одноразовые наборы обработки различаются в структуре или в их использовании, такие различия обсуждаются ниже. Одноразовый набор 300 устанавливается на устройство 400 (фиг. 25), которое подробнее описывается ниже

Как показано на фиг. 23-24, сепаратор 301 является частью типового одноразового набора 300. Дополнительно, как будет подробнее описано ниже, одноразовый набор 300 содержит трубки, Y-соединители, рабочий(-е) пакет(-ы), мешок(-ки) с пробами, пакет(-ы) конечного продукта, пакет(-ы) с отходами и стерильный(-е) фильтр(-ы).

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Взвесь клеток, которая будет промываться, обычно представлена в исходном контейнере 302, показанном на фиг. 23 и 24 отсоединенным от одноразового набора. Как отмечалось выше, исходный контейнер 302 может быть прикреплен (стерильным образом) во время использования. Исходный контейнер 302 имеет один или более каналов 303, 305 приема, один из которых может быть приспособлен для приема гвоздевого соединителя 304 (фиг. 23) одноразового набора 300. Конкретнее, исходный контейнер 302 соединен с одноразовым набором 300 через гвоздевой соединитель 304, который может соединяться с каналом 303 доступа. Более предпочтительно, однако, чтобы исходные контейнеры (и жидкости в них) не имели гвоздевого соединителя (как показано на фиг. 24), и чтобы доступ к ним осуществлялся стерильным образом посредством использования стерильных стыковочных устройств, таких как BioWelder, поставляемое компанией Sartorius AG, или SCD IIB Tubing Welder, поставляемое компанией Terumo Medical Corporation. Также может быть представлен второй канал 305 доступа для извлечения жидкости из исходного пакета 302.

Как также показано на фиг. 23-24, сегмент 306 трубки может, необязательно, содержать подблок взятия проб в ответвительном соединителе 308. Одна из ветвей ответвительного соединителя 308 может содержать маршрут потока 310, приводящий к мешку или месту 312 с пробами. Мешок или место 312 с пробами позволяет осуществлять сбор проб из входящей исходной жидкости. Поток к мешку или месту 312 с пробами обычно контролируется фиксатором 314. Другая ветвь ответвительного соединителя 308 соединена с трубками 316. Трубки 316 соединены с еще одним расположенным по ходу потока ответвительным соединителем 318. Ответвительный соединитель 318 взаимодействует с трубками 316 и трубками 320, что обеспечивает маршрут потока жидкости из рабочего пакета 322, что подробнее описано ниже. Сегмент трубки 324 выходит из одного из каналов ответвительного соединителя 318 и соединяется с каналом еще одного расположенного по ходу потока ответвительного соединителя 326. Отдельный маршрут потока, задаваемый трубками 328, также соединен с каналом ответвительного соединителя 326. Трубки 328 могут содержать встроенный стерильный барьерный фильтр 330 для фильтрации любых частиц из жидкости, до того как она попадет в маршрут потока, приводящий ко второму ответвительному соединителю 326 и, в итоге, к сепаратору 301.

В соответствии с системой, изложенной в настоящем описании, раствор для промывания может быть прикреплен (или предварительно прикреплен) к набору 300. Как показано на фиг. 23 и 24, трубки 332 (определяющие маршрут потока), предпочтительно, содержат гвоздевой соединитель 334 на своем конце. Гвоздевой соединитель 334 представлен для установления взаимодействия потоков с контейнером жидкости для промывания, таким как одноразовый пакет, содержащий физиологический раствор или другой раствор (не показан). Среда или жидкость для промывания вытекает из источника жидкости для промывания через второй гвоздевой соединитель 334, через сегмент трубки 332, где она фильтруется посредством стерильного барьерного фильтра 330, описанного выше, и затем проходит через трубки 328 к выходу ответвительного соединителя 326, описанного выше.

Сегмент трубки 336 задает маршрут потока, соединенный с одного конца с каналом ответвительного соединителя 326 и с впускным каналом сепаратора 301.

Предпочтительно, в соответствии с настоящим изложением, сепаратор 301 представляет собой сепаратор с вращающейся мембраной описанного выше типа.

Как показано на фиг. 23, 24 и 25, сепаратор 301 с вращающейся мембраной имеет, по меньшей мере, два выпускных канала. Выпуск 646 сепаратора 301 принимает отходы

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от промывания (то есть, разбавленную среду взвеси), и соединен с трубками 338, который задают маршрут потока к контейнеру 340 для отходов. Контейнер для отходов содержит еще один соединительный канал 341 для получения проб или извлечения отходов из контейнера продукта.

Сепаратор 301, предпочтительно, содержит второй выпуск 648, который соединен с сегментом трубки 342. Другой конец сегмента трубки 342 соединен с ответвительным соединителем 344, который разветвляется и задает маршрут потока к одному или более рабочим контейнерам 322 и маршрут потока к контейнеру 350 конечного продукта. Контейнер 350 конечного продукта также может содержать мешок 352 с пробами (см. фиг. 23) и канал доступа или люэровский соединитель 354. Мешок 352 с пробами, показанный предварительно прикрепленным к держателю 352 трубок на фиг. 23, позволяет выполнять сбор проб конечного продукта. Контроль потока к мешку 352 с пробами, предпочтительно, осуществляется фиксатором 356. Маршрут потока через канал 354 доступа контролируется фиксатором 358.

Обратимся теперь к способу промывания с использованием набора 300 с фиг. 23 и 24; одноразовый набор 300 сначала устанавливается на панель 401 устройства разделения (то есть, аппаратного обеспечения) 400, показанную на фиг. 25. Устройство 400 содержит перистальтические насосы, фиксаторы и датчики, которые контролируют поток через одноразовый набор. Конкретнее, управление насосами, фиксаторами и т.п. обеспечивается программно-управляемым микропроцессором/контроллером устройства 400. Сегменты трубки 362, 366 и 368 (показанные на фиг. 23) избирательно стыкуются с перистальтическими насосами 402, 404 или 406 (показанными на фиг. 25). (Сегмент 368 насоса линии отходов может быть перемещен к линии 343 выпуска сепаратора, при необходимости). После того как одноразовый набор 300 устанавливается на панели 401 управления устройства 400, взвесь клеток в пакете 302 продукта прикрепляется, как было описано ранее, посредством гвоздевого соединителя 304 или посредством стерильного соединения. Среда для промывания, представленная в контейнере (не показана), прикрепляется аналогично. В соответствии с функционированием устройства 400, фиксатор 360 открывается и позволяет взвеси клеток протечь из контейнера 302 продукта.

Поток взвеси клеток продвигается посредством воздействия перистальтического насоса через трубки 324, определяемые сегментом насоса 362, в сепаратор 301 с вращающейся мембраной. Аналогично, среда для промывания продвигается посредством воздействия перистальтических насосов через длину трубки 328, определяемую сегментом насоса 366, с клапанами 362 и 364 в открытом положении. Среда для промывания протекает через трубки 332, стерильный барьерный фильтр 330, трубки 328, Y-соединитель 326 и в сепаратор 301 с вращающейся мембраной. Среда для промывания и взвесь клеток могут быть последовательно введены в сепаратор 301 с вращающейся мембраной, допуская возникновение смешивания взвеси и раствора для промывания в пределах камеры (зазора) сепаратора 301 или в рабочем контейнере 322, как описано ниже. Альтернативно, среда для промывания и взвесь клеток могут быть объединены до введения в сепаратор 301, (например), через второй ответвительный соединитель 326.

В еще одной альтернативе, взвесь клеток может быть сначала введена из исходного контейнера 302 в сепаратор 301, как в общих чертах описано выше. Взвесь клеток концентрируется внутри сепаратора 301, что позволяет супернатанту пройти через мембрану, через выпускной канал 382, в контейнер 340 для отходов. Концентрированные клетки выходят из сепаратора 301 через канал 384 и направляются в рабочий контейнер

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322.

После того как отделение концентрированных клеток от супенатанта взвеси клеток завершается, замещающая жидкость вводится из контейнера с замещающей жидкостью (не показан) в сепаратор 301 (для смывания всех оставшихся клеток) и аналогично направляется через канал 384 в рабочий контейнер 322. Концентрированные клетки ресуспендируются в замещающей жидкости внутри рабочего контейнера 322, как показано на фиг. 23. Если желательно или требуется дополнительное промывание, то система может быть предварительно запрограммирована или направлена другим способом на (повторное) введение ресуспендированных клеток/замещающей жидкости в сепаратор 301, в котором отделение концентрированных клеток от супернатанта повторяется. Конечный клеточный продукт собирается в контейнере 350 конечного продукта, где он может быть ресуспендирован с дополнительной замещающей жидкостью.

Независимо от последовательности введения взвеси клеток/раствора для промывания или используемого одноразового набора, вращательное воздействие устройства приводит к отделению клеток от оставшейся части жидкости, в который они были суспендированы, и/или от раствора для промывания. Предпочтительно, супернатант и раствор для промывания проходят через мембрану, тогда как искомые клетки концентрируются внутри камеры сепаратора. Отходы, возникающие при разделении и включающие среду для промывания и среду супернатанта, выходят из канала 382 и протекают через трубки 338 в контейнер 340 для отходов. Поток отходов управляется перистальтическим насосом через часть трубок 338, определяемую сегментом насоса 368, к пакету 340 с продуктами отходов.

Как описано выше, взвесь концентрированных и разделенных клеток выходит из второго выпуска 384 сепаратора 301 с вращающейся мембраной. Если дальнейшее промывание не требуется, то система управления закрывает фиксатор 370 и открывает фиксатор 372. Закрытие фиксатора 370 предотвращает протекание взвеси промытых клеток через трубки 346 и направляет ее через трубки 348 в пакет 350 конечного продукта. Контейнер 350 конечного продукта имеет вход для приема взвеси отделенных и промытых клеток. Контейнер 354 конечного продукта соединен с датчиком 374 веса. Устройство разделения измеряет вес 374 контейнера с целью определения того, находится ли объем собранных клеток в контейнере 350 конечного продукта в приемлемом диапазоне и, следовательно, закончен ли цикл промывания.

Если желательно или требуется дополнительное промывание взвеси разделенных клеток, то система управления устройства разделения закрывает фиксатор 372 и фиксатор 376, и открывает фиксатор 370. Закрытие фиксатора 372 предотвращает протекание взвеси клеток через трубки 348 и направляет ее через трубки 346 в рабочий пакет 322. Рабочий пакет 322 имеет впуск для приема взвеси разделенных клеток. Рабочий пакет 322 соединен с датчиком 378 веса. Система управления устройства разделения определяет вес, воспринимаемый датчиком веса, с целью определения того, достаточно ли взвеси разделенных клеток присутствует в рабочем пакете 322 для проведения еще одного цикла промывания. Если определено, что присутствует достаточно взвеси, и желательно дополнительное промывание, то система управления устройства разделения открывает фиксатор 376 с целью открытия и направления взвеси разбавленных и разделенных клеток через выход рабочего пакета 322, через трубки 320 в ответвительный соединитель 318, и через датчик 380 обнаружения воздуха. Датчик 380 обнаружения воздуха обнаруживает воздух во взвеси клеток, которая проходит через трубки 324. Устройство управления и эксплуатации измеряет показания датчика

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380 обнаружения воздуха и определяет, какие процессы должны быть выполнены далее.

Взвесь разделенных клеток, которая содержит клетки, суспендированные в разбавленной среде суспендирования, затем повторно проходит через процесс промывания, как описано выше. Процесс промывания может быть повторен столько раз, сколько необходимо, и, предпочтительно, до тех пор, пока взвесь разбавленных и разделенных клеток не будет иметь приемлемую остаточную концентрацию среды суспендирования. Конечная взвесь разбавленных и разделенных клеток собирается в пакете 350 конечного продукта.

Альтернативно, в отличие от повторения обработки жидкости через один рабочий контейнер, можно следовать процедуре обработки “пакетного типа” путем использования двух или более рабочих контейнеров 322 (в комбинации с контейнером 350 конечного продукта).

Одноразовый набор 300 обработки с фиг. 24, в частности, хорошо подходит для такой обработки “пакетного типа”. В соответствии с процедурой промывания клеток с использованием одноразового набора 300 с фиг. 24, клетки, первоначально выделенные из исходной среды суспендирования, удаляются из сепаратора 301 и вводятся в один из рабочих контейнеров 322a. Замещающая жидкость вводится в контейнер 322a, и клетки ресуспендируются. Ресуспендированные клетки в контейнере 322a могут затем быть введены в сепаратор 301, в котором они отделяются от супернатанта. Концентрированные клетки выходят через выпуск 648 в сепаратор 301 и вводятся в новый (второй) рабочий контейнер 322b. Дополнительная замещающая жидкость может быть введена в рабочий контейнер 322b, и процесс может быть повторен, при необходимости, с еще одним новым (третьим) рабочим контейнером (не показан). Конечный клеточный продукт затем собирается в контейнере 350 конечного продукта, как описано выше.

В соответствии с описанным выше способом промывания клеток “пакетного типа”, сегменты трубки 370a, 370b и 320a, 320b могут быть соединены с фиксаторами (не показаны) для управления потоком во множество рабочих контейнеров 322a и 322b и потоком из них. Таким образом, например, фиксатор на линии 370a будет открыт, тогда как фиксатор на линии 370b будет закрыт, с тем чтобы клетки, выходящие из сепаратора 301, направлялись в (первый) рабочий контейнер 322a.

С целью дополнительного промывания, клетки, ресуспендированные в свежей замещающей жидкости из контейнера 322a, вводятся в сепаратор 301, где клетки отделяются от супернатанта, как было описано ранее. Система управления устройства 400 закрывает фиксатор (не показан на фиг. 24) на сегменте трубки 370a и открывает фиксатор (не показан на фиг. 24) на сегменте трубки 370b, с тем чтобы обеспечить возможность потока клеток в новый (второй) рабочий контейнер 322b. После итогового промывания фиксаторы (не показаны) на сегментах 370a, 370b, и т.д. закрываются, и фиксатор 372 (как показано, например, на фиг. 23) открывается, обеспечивая возможность сбора конечного продукта в контейнере 350.

На фиг. 24 показана передняя панель 401 устройства 400 разделения; то есть аппаратное обеспечение, которое включает в себя перистальтические насосы 402, 404 и 406. Как описано выше, сегменты насоса 362, 364 и 368 из одноразового набора избирательно соединяются с перистальтическими насосами 402, 404 и 406. Перистальтические насосы сочленяются с жидкостным набором с фиг. 23 в сегментах насоса 362, 364 и 368, и продвигают взвесь клеток внутри одноразового набора, как будет понятно специалистам в данной области техники. Устройство 400 управления и эксплуатации также содержит фиксаторы 410, 412, 414. Фиксаторы 410, 412, 414 и 416

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используются для управления потоком взвеси клеток через различные сегменты одноразового набора, как описано выше.

Устройство 400 также содержит несколько датчиков для измерения различных условий. Выходные данные датчиков используются устройством 400 при выполнении цикла промывания. Один или более измерительных датчиков 426 давления могут быть представлены на устройстве 400 и могут быть соединены с одноразовым набором 300 в определенных точках для отслеживания давления во время процедуры. Измерительный датчик 426 давления может быть встроен в место контроля давления внутри линии (например, в сегмент трубки 336) для отслеживания давления внутри сепаратора 301. Датчик детектора 438 воздуха также может быть соединен с одноразовым набором 300, при необходимости. Детектор 438 воздуха является необязательным и может быть представлен для обнаружения положения поверхностей раздела жидкость/воздух.

Устройство 400 содержит весы 440, 442, 444 и 446, на которых могут быть рассчитаны и взвешены конечный пакет, рабочий пакет, пакет взвеси клеток и любой дополнительный пакет, соответственно. Веса пакетов отслеживаются датчиками веса и записываются в течение процедуры промывания. По измерениям датчиков веса устройство определяет, является ли каждый из пакетов пустым, частично заполненным или полным, и управляет компонентами устройства управления и эксплуатации 200, такими как перистальтические насосы и фиксаторы 410, 412, 414, 416, 418, 420, 422 и 424.

Устройство 400 содержит по меньшей мере один блок привода, или “вращатель” 448, который осуществляет непрямое управление сепаратором с вращающейся мембраной 301. Вращатель 448 может состоять из приводного двигателя, соединенного с устройством 400 и управляемого им, и подсоединенного для поворачивания кольцевого элемента магнитного привода, содержащего, по меньшей мере, пару постоянных магнитов. При вращении кольцевого элемента привода магнитное притяжение между соответствующими магнитами внутри корпуса сепаратора с вращающейся мембраной вызывает вращение вращателя внутри корпуса сепаратора с вращающейся мембраной.

На фиг. 26-28 в форме диаграмм излагается способ промывания клеток в соответствии с изложенным в настоящем описании. Этапы, описанные ниже, выполняются посредством программно-управляемого микропроцессорного блока устройства 400, при этом определенные этапы выполняются оператором, как было отмечено выше. Обратимся сначала к фиг. 26; устройство включается на этапе 500. Устройство проводит проверки автоматической калибровки 502, включающие в себя проверку перистальтических насосов, фиксаторов и датчиков. Затем устройство 400 запрашивает у пользователя ввод выбранных процедурных параметров (этап 504), таких как выполняемая процедура промывания, объем промываемой взвеси клеток, число промываний, которое должно быть выполнено, и т.д. Оператор может затем выбирать и вводить процедурные параметры для процедуры промывания (этап 506).

Устройство (через контроллер) подтверждает ввод параметров 506, и затем запрашивает у оператора загрузку (этап 510) одноразового набора. Оператор затем загружает одноразовый набор (этап 512) в панель устройства 400. После установки одноразового набора, устройство подтверждает установку, как показано (этап 514).

После того как одноразовый набор установлен, устройство автоматически проверяет правильность установки одноразового набора (этап 516). После того как устройство определяет, что одноразовый набор был установлен правильно, контроллер запрашивает у оператора подсоединение взвеси клеток и среды для промывания (этап 518). Затем оператор подсоединяет среду для промывания (такую как физиологический

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раствор, но не ограничиваясь им) (этап 520) к одноразовому набору через гвоздевой соединитель, как было описано ранее. Затем оператор подсоединяет взвесь клеток внутри пакета с продуктом (этап 522) к одноразовому набору через гвоздевой соединитель.

Как показано на фиг. 27, после того как взвесь клеток и среда для промывания были подсоединены к одноразовому набору, оператор подтверждает, что растворы были подсоединены (этап 524). Устройство запрашивает у оператора взятие образца взвеси клеток (этап 526). Затем оператор или устройство открывает фиксатор 528 мешка для сбора проб с целью введения жидкости в мешок для сбора проб (этап 546). После того как мешок для сбора проб был заполнен, он запечатывается и удаляется (542) из одноразового набора. Оператор подтверждает (этап 544), что образец был взят. После удаления мешка для сбора проб одноразовый набор заливается (этап 546) для процесса промывания.

Затем контроллер устройства разделения начинает процесс промывания. Взвесь клеток, предназначенная для промывания, передается из своего контейнера (например, 302 с фиг. 23) через одноразовый набор на сепаратор 301 с вращающейся мембраной. Аналогично, среда для промывания передается из своего источника через одноразовый набор на сепаратор 301 с вращающейся мембраной. В предпочтительном варианте осуществления, исходные клетки взвеси клеток концентрируются и/или собираются в рабочем пакете (для дальнейшей обработки) или собираются в пакете конечного продукта, который впоследствии удаляется из одноразового набора. Если необходимо (дополнительное) промывание или разбавление взвеси клеток, то взвесь клеток в рабочем пакете может промываться (второй раз) той же самой или другой средой для промывания в соответствии с процессом, кратко описанным выше. До завершения каждого цикла промывания, измеряется и записывается объем или вес взвеси клеток (этап 550). Когда концентрация клеток в среде для промывания достигает приемлемого уровня, заполняется пакет конечного продукта.

Как показано на фиг. 28, как только собран желаемый объем конечного продукта, устройство управления и эксплуатации запрашивает у оператора взятия пробы и запечатывания пакета конечного продукта (этап 552). Мешок для сбора проб прикрепляется к пакету конечного продукта. Оператор затем запечатывает и удаляет из одноразового набора взвесь промытых клеток в пакет с конечным продуктом (этап 552). Затем пакет с конечным продуктом взбалтывается (этап 556). Оператор открывает мешок для сбора образцов путем удаления фиксатора (этап 558). Допускается заполнение мешка для сбора образцов (этап 560). После того как пакет с образцами заполнен, фиксатор закрывается и мешок для сбора образцов запечатывается и удаляется (этап 562). Затем оператор запечатывает линии одноразового набора (этап 564) и подтверждает, что пакет продукта был запечатан и удален, мешок для взятия проб был заполнен и удален, и что линии одноразового набора были запечатаны (этап 566). Затем устройство управления и эксплуатации запрашивает у оператора удаление одноразового набора, как показано на этапе 568. Затем оператор удаляет и выбрасывает одноразовый набор, как показано на этапе 570.

Таким образом, изложен улучшенный сепаратор с вращающейся мембраной, а также способы и системы для применения такой вращающейся мембраны. Описание, представленное выше, приведено в целях иллюстрации, и не предполагается, что оно ограничивает объем изложения каким-либо конкретным способом, системой или установкой или устройством, описанными в настоящем описании.

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Формула изобретения

1. Устройство фильтрации крови, содержащее:

по существу, цилиндрический корпус, имеющий внутреннюю стенку;

внутренний элемент, установленный внутри корпуса и имеющий внешнюю поверхность;

одно из внутренней стенки корпуса и внешней поверхности внутреннего элемента, содержащей пористую мембрану, расположенную на расстоянии от указанной стенки корпуса или указанной поверхности внутреннего элемента с образованием кольцевого зазора между ними,

при этом корпус и внутренний элемент могут вращаться друг относительно друга;

впуск для направления цельной крови, содержащей плазму и эритроциты, в кольцевой зазор;

первый выпуск для направления плазмы, проходящей через мембрану, в контейнер для сбора; и

второй выпуск для направления из кольцевого зазора оставшихся компонентов крови,

при этом мембрана имеет площадь поверхности, достаточную для отделения плазмы с такой скоростью потока, что время нахождения эритроцитов в пределах кольцевого зазора является недостаточным для того, чтобы вызвать ненадлежащий гемолиз эритроцитов,

причем устройство дополнительно содержит область высокой перфузии, покрытую мембраной, и непроточную область, продолжающуюся за пределы мембраны, и содержит радиальный выступ, продолжающийся от одной из внутренней стенки корпуса и внешней поверхности внутреннего элемента, с тем чтобы уменьшить кольцевой зазор между ними, при этом радиальный выступ отделяет область высокой перфузии от непроточной области.

2. Устройство фильтрации крови по п. 1, в котором внутренний элемент имеет диаметр, превышающий 2,79 см (1,1 дюйм), и/или длину фильтрации, превышающую 7,62 см (3,0 дюйма).

3. Устройство фильтрации крови по любому из предыдущих пунктов, в котором внутренний элемент имеет диаметр вплоть до 5,59 см (2,2 дюйма) и длину фильтрации вплоть до 19,05 см (7,5 дюйма).

4. Устройство фильтрации крови по п. 1, в котором ротационный вращатель имеет диаметр около 1,65 дюйма и длину фильтрации около 5,52 дюйма.

5. Устройство фильтрации крови по п. 1, в котором радиальный выступ имеет осевой размер, не меньший размера кольцевого зазора.

6. Устройство фильтрации крови по п. 1, в котором радиальный выступ обеспечен на внешней поверхности внутреннего элемента.

7. Устройство фильтрации крови, содержащее:

по существу, цилиндрический корпус, имеющий внутреннюю стенку;

внутренний элемент, установленный внутри корпуса и имеющий внешнюю поверхность;

одно из внутренней стенки корпуса и внешней поверхности внутреннего элемента, содержащей мембрану фильтра, расположенную на расстоянии от передней стенки корпуса или поверхности внутреннего элемента с образованием кольцевого зазора между ними,

причем внешняя поверхность внутреннего элемента содержит область высокой

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перфузии, покрытую мембраной, и непроточную область, продолжающуюся за пределы мембраны,

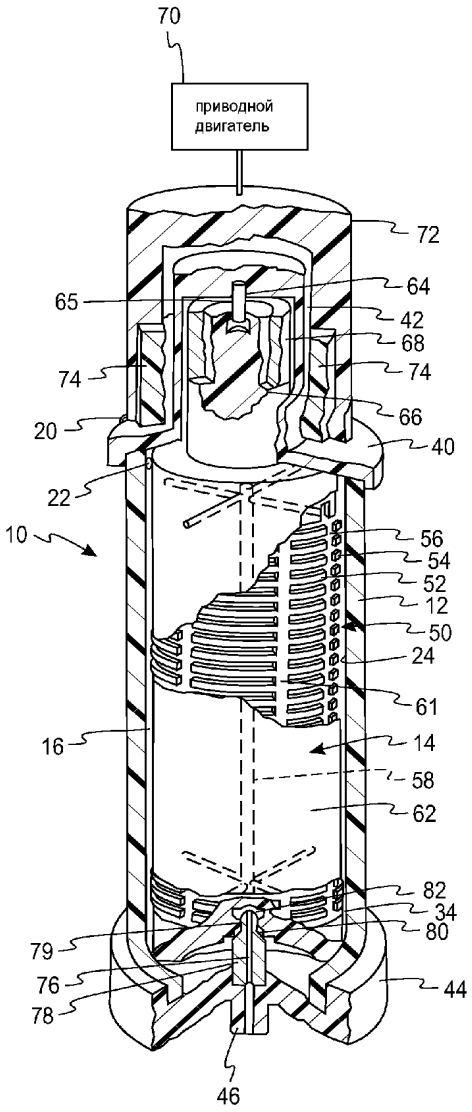
при этом корпус и внутренний элемент могут вращаться друг относительно друга;

радиальный выступ, продолжающийся от внутренней стенки корпуса или внешней поверхности внутреннего элемента, с тем чтобы уменьшить кольцевой зазор между ними, при этом радиальный выступ отделяет область высокой перфузии от непроточной области.

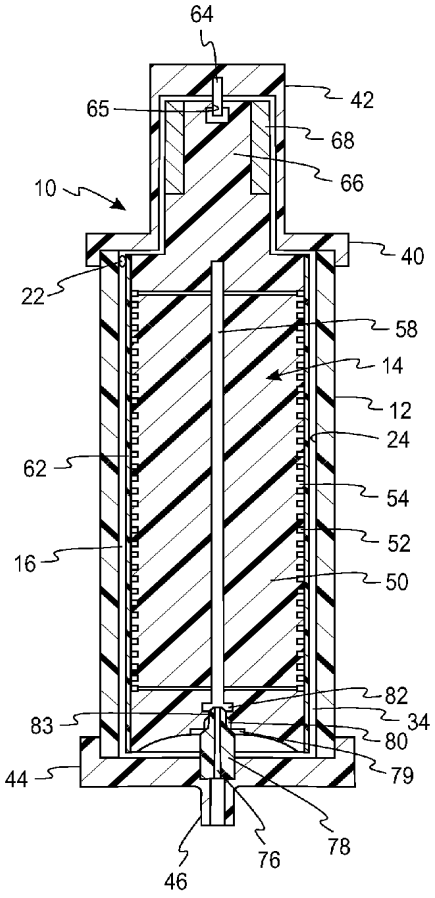
8. Устройство фильтрации крови по п. 7, в котором радиальный выступ имеет осевой размер, не меньший размера кольцевого зазора.

9. Устройство фильтрации крови по п. 7, в котором радиальный выступ обеспечен на внешней поверхности внутреннего элемента.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0415



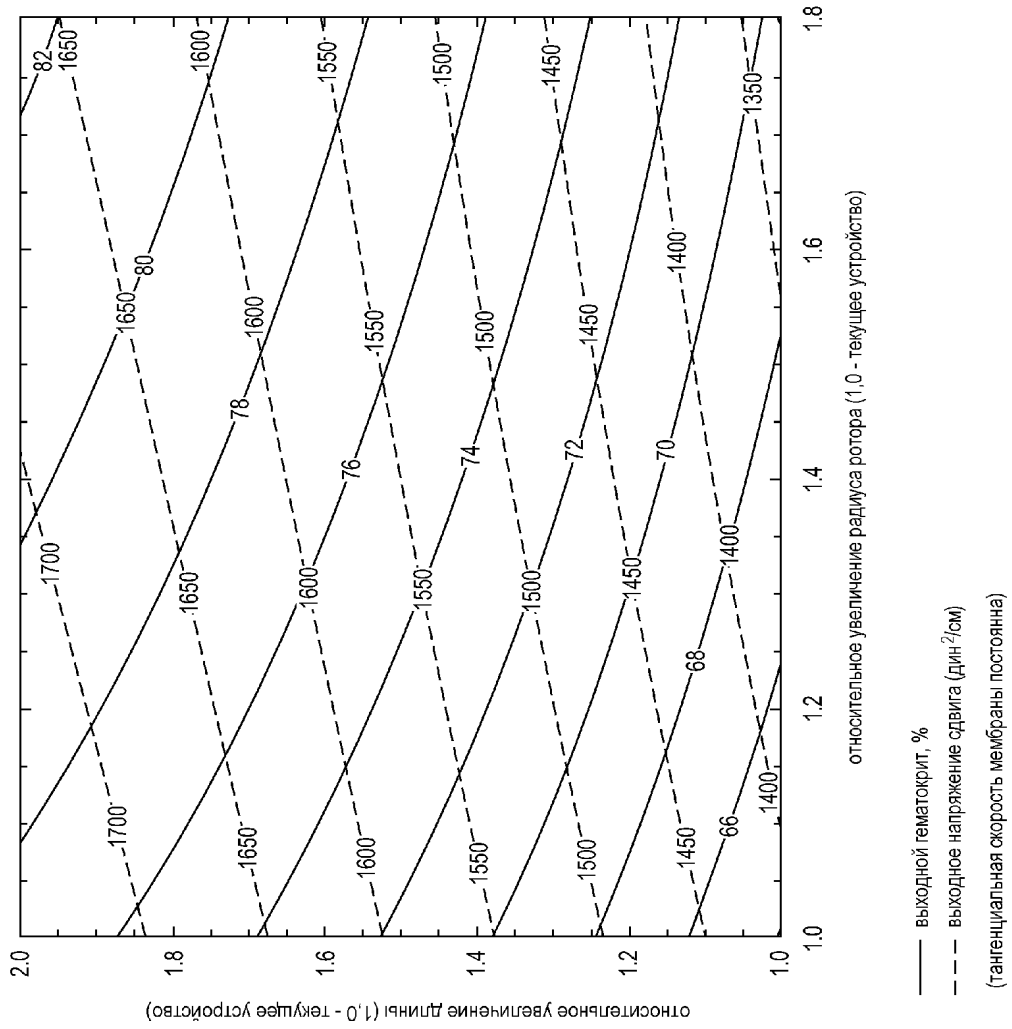
Фиг. 1



Фиг. 2

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0416

Фиг. 3



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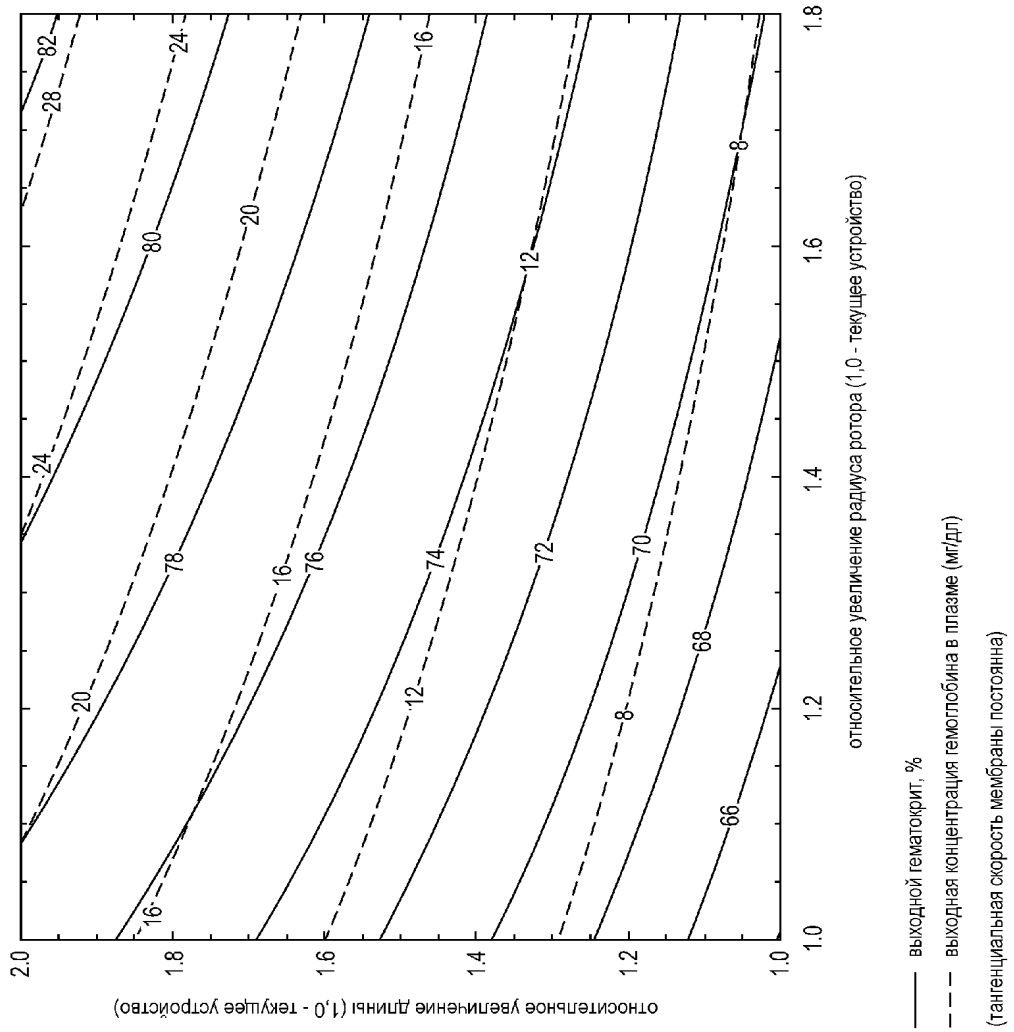
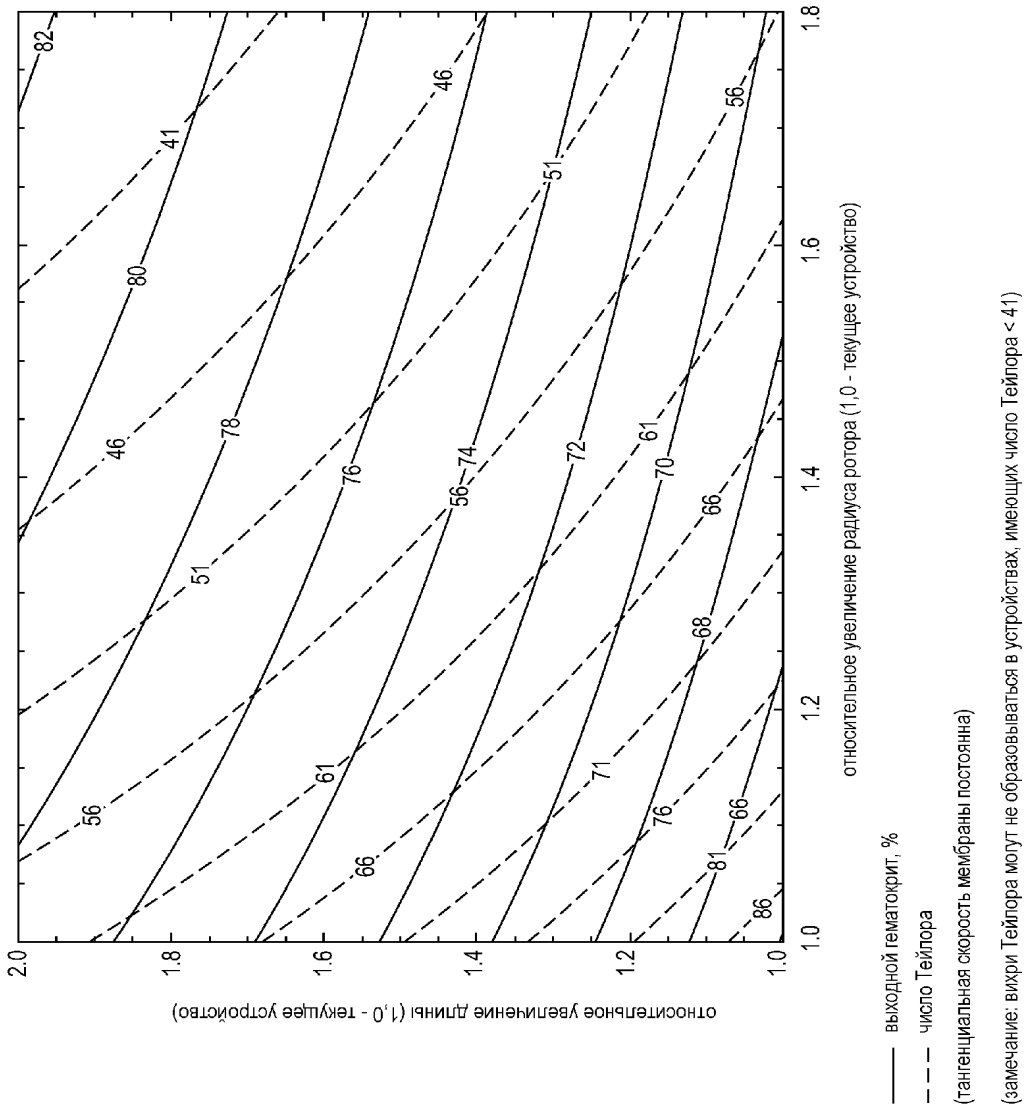
Petitioner Terumo Exhibit 1014-0417

Фиг. 4



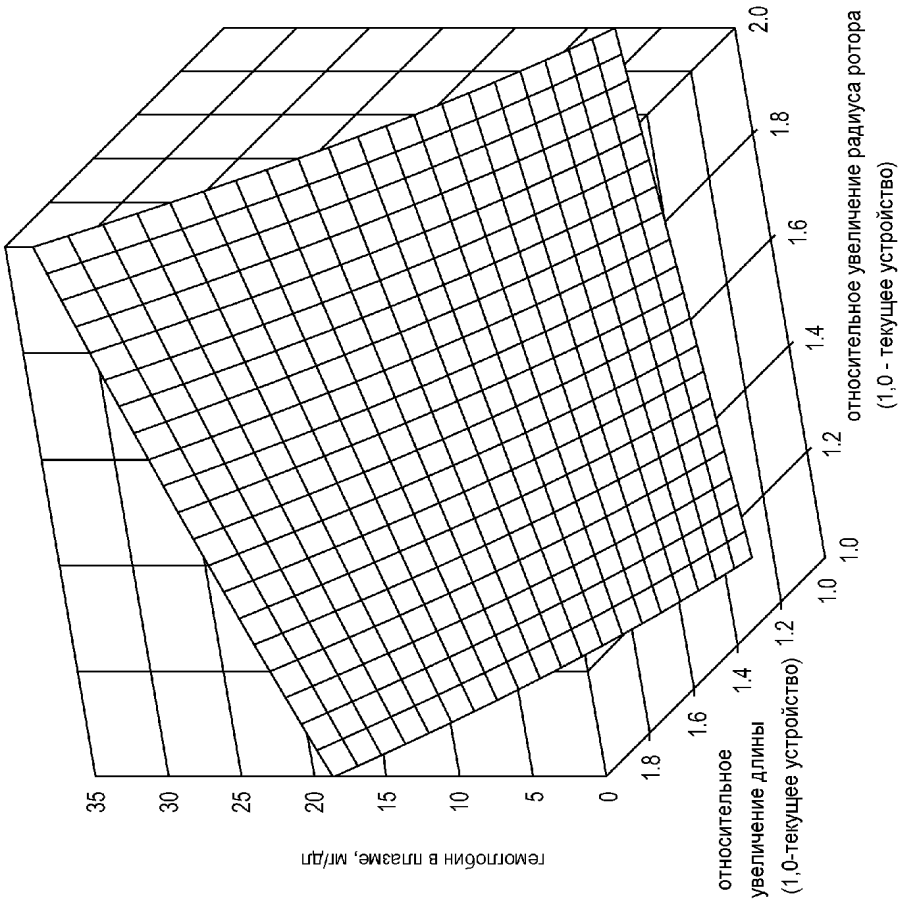
Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0418

Фиг. 5

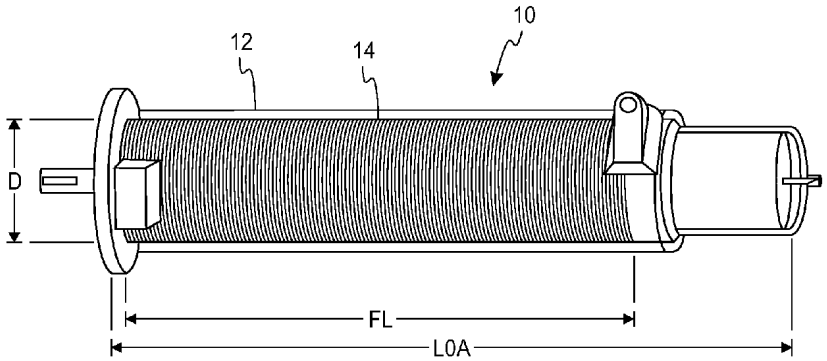


Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0419

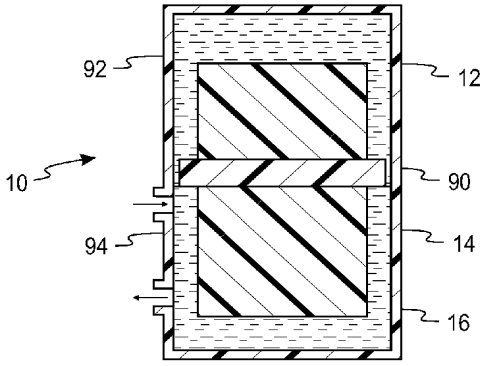
Фиг. 6



Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0420

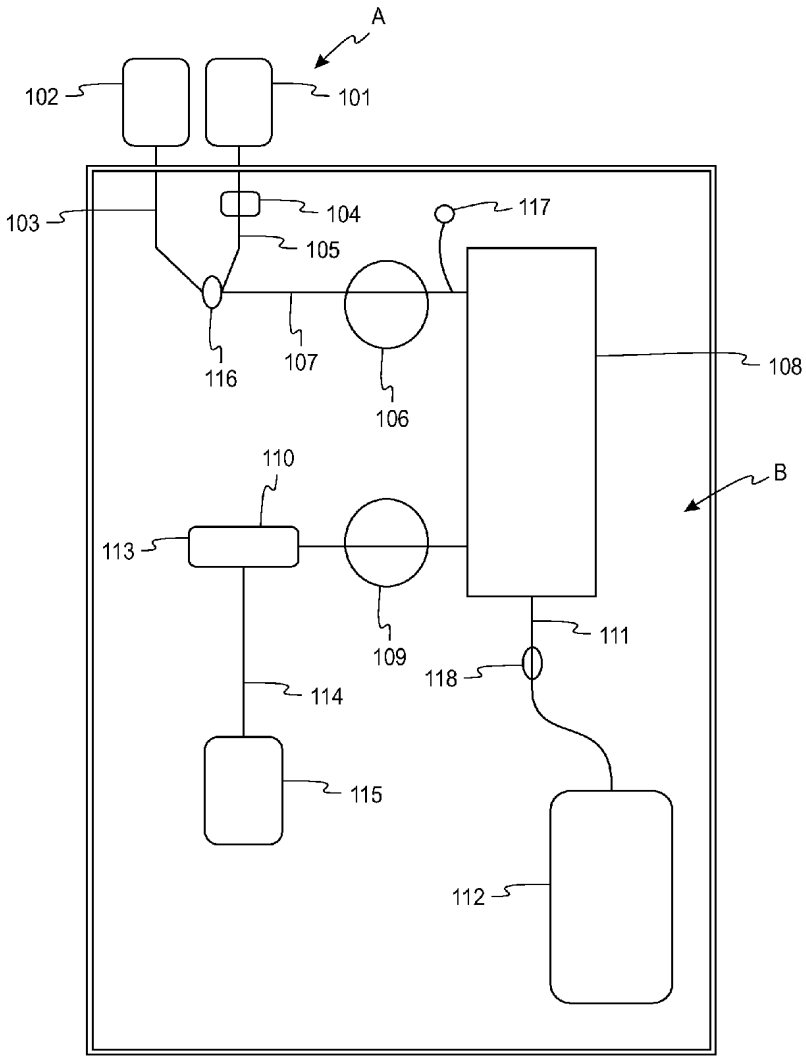


Фиг. 7



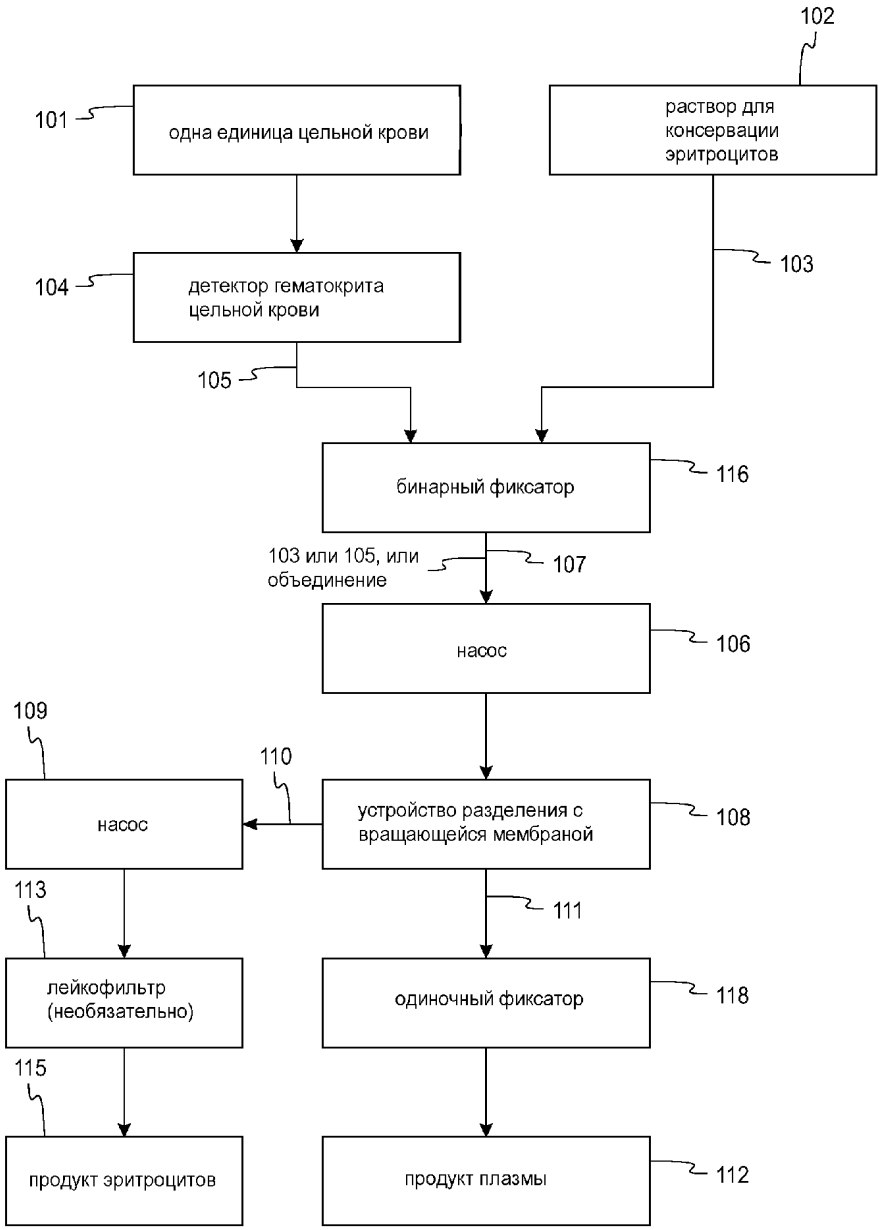
Фиг. 8

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0421



Фиг. 9

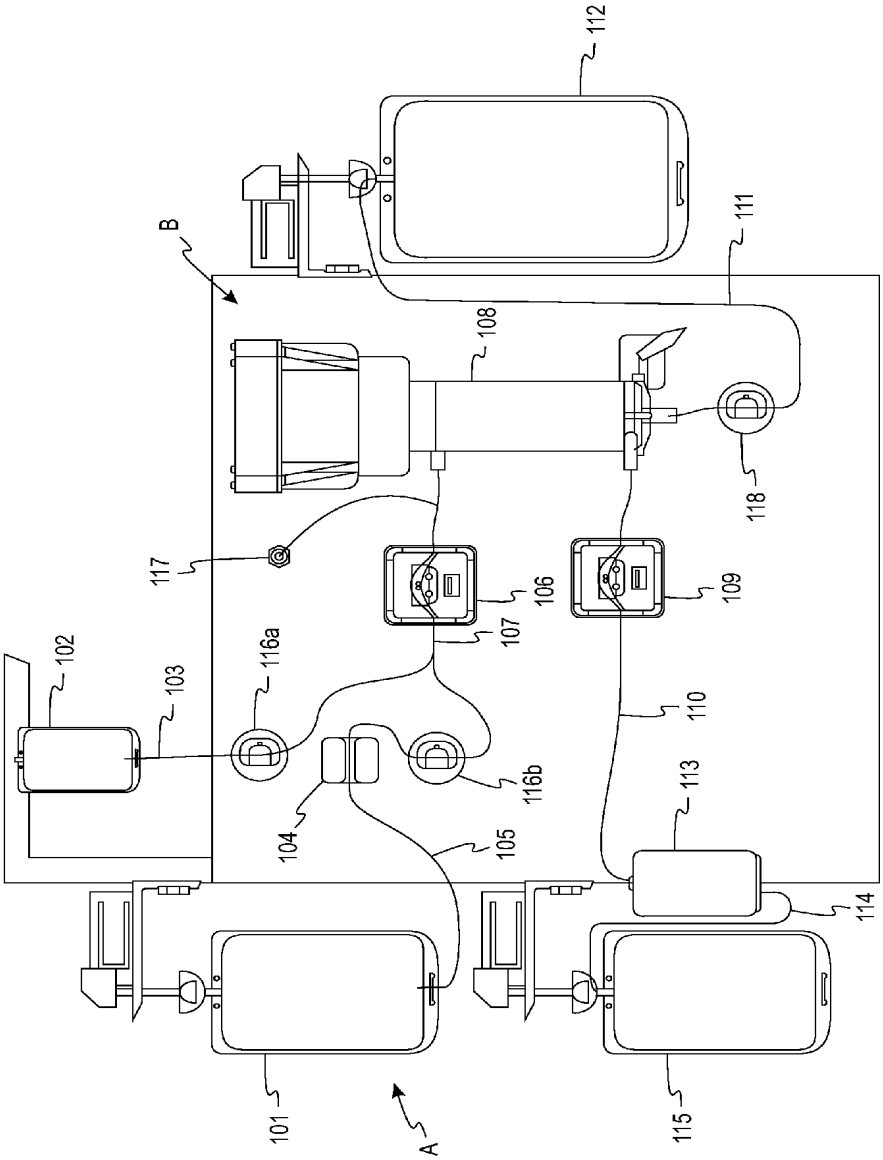
Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0422



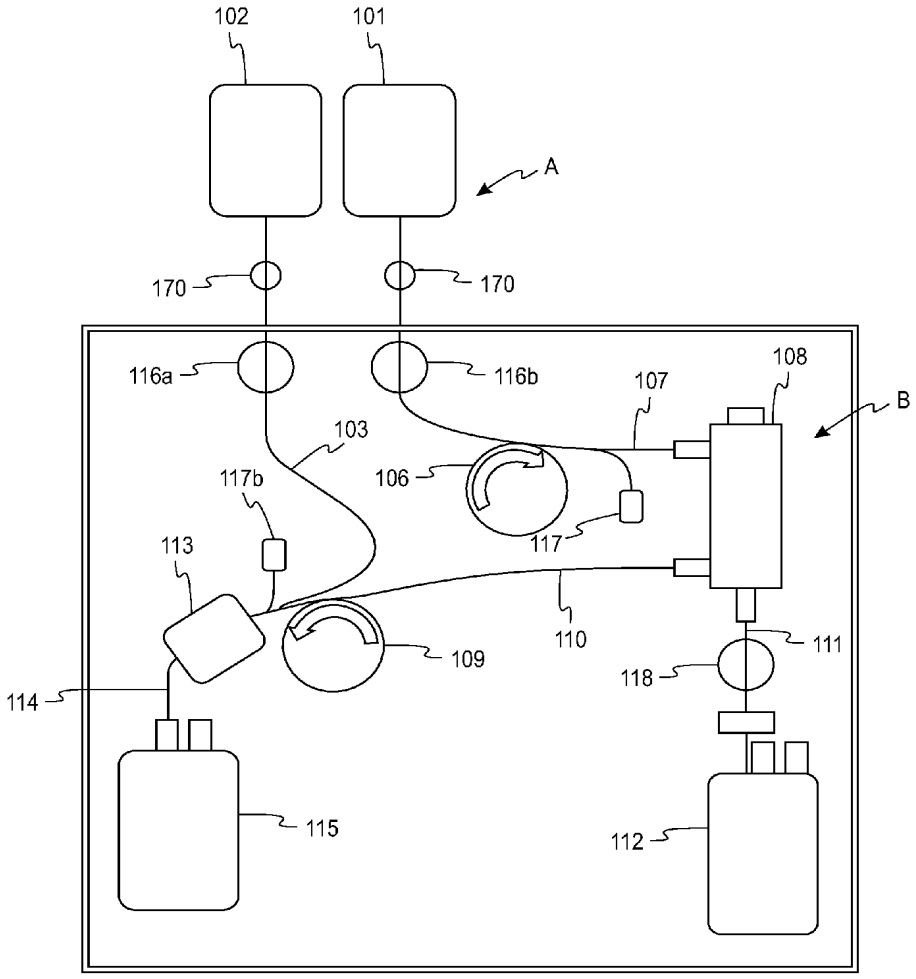
Фиг. 10

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0423

Фиг. 11

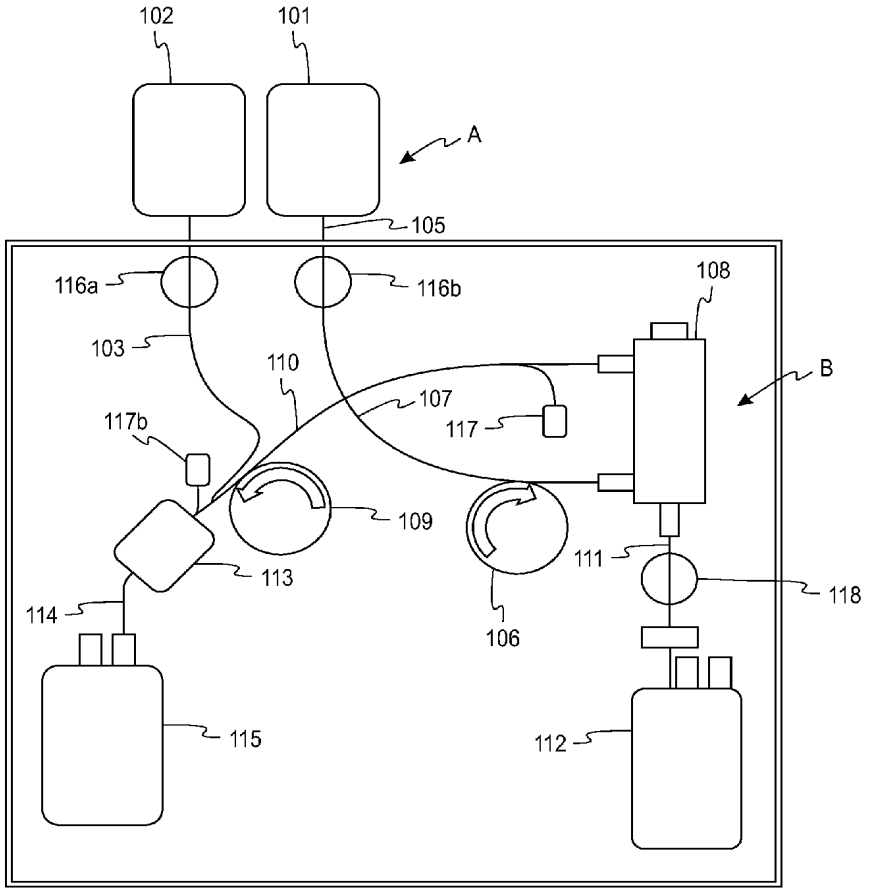


Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0424



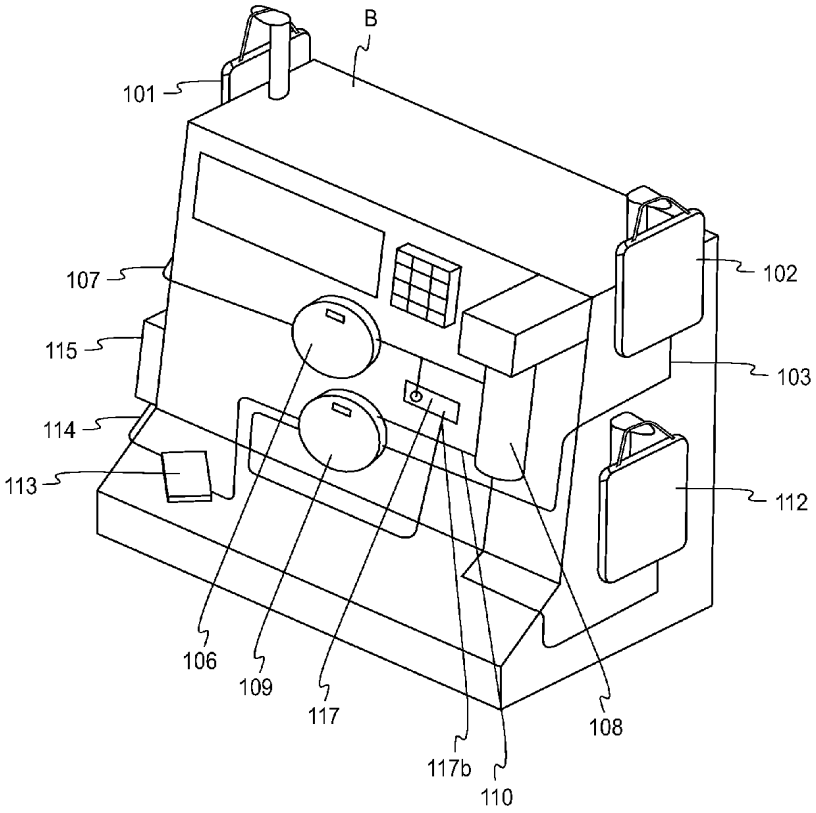
Фиг. 12

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0425



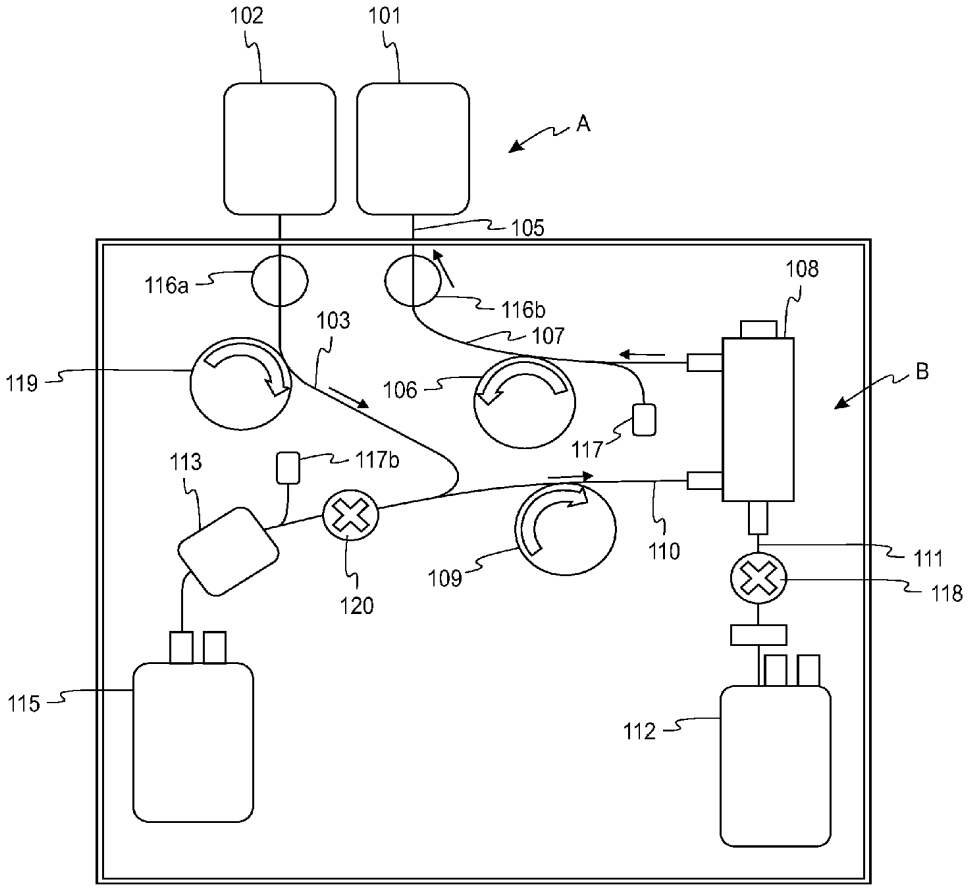
Фиг. 12a

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0426



Фиг. 13

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0427



Фиг. 14

Terumo v. Haemonetics - PGR2026-00006
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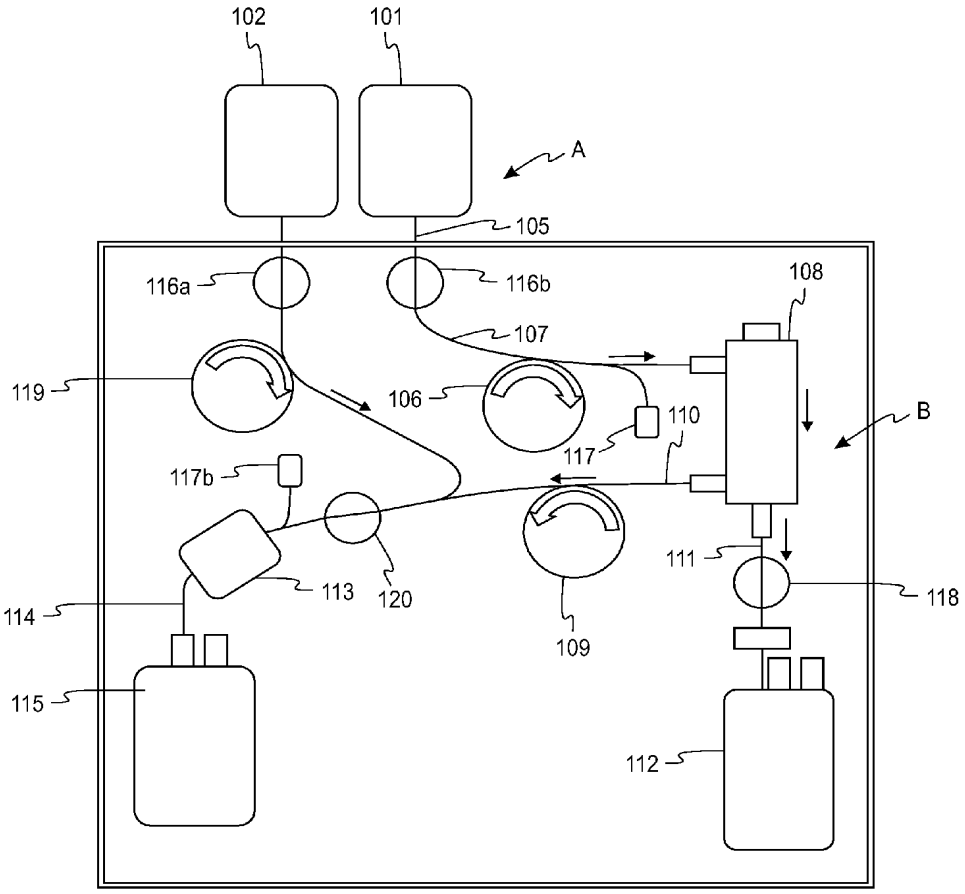
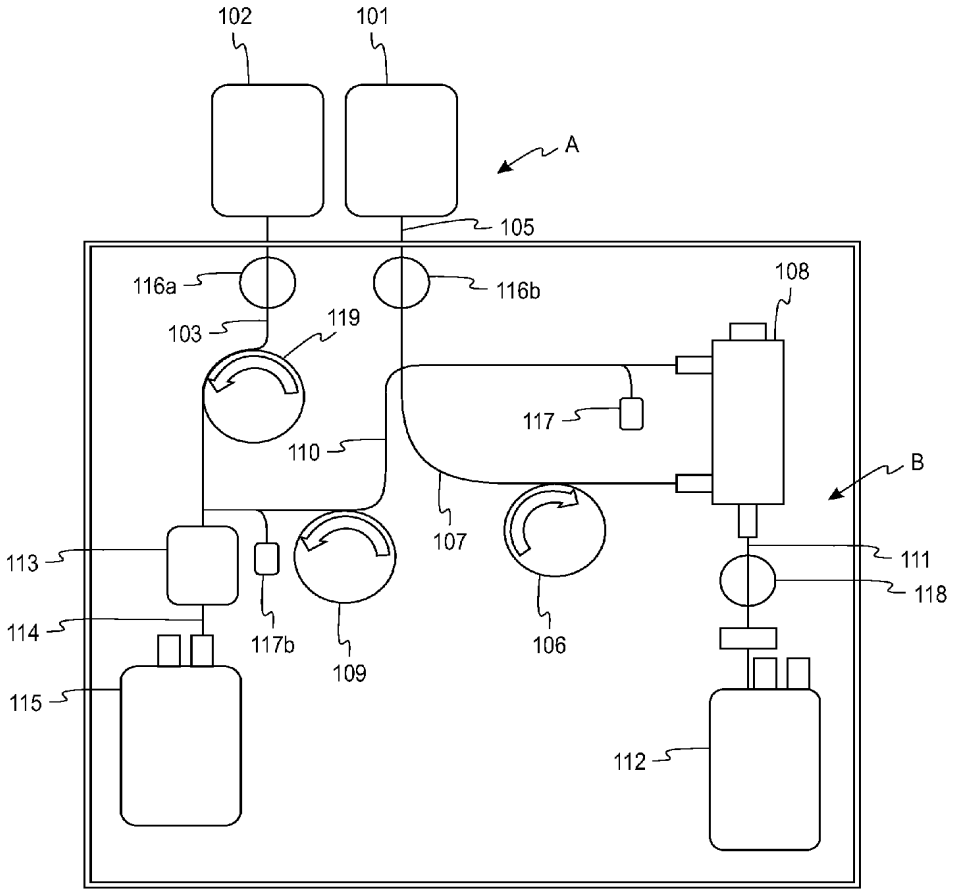


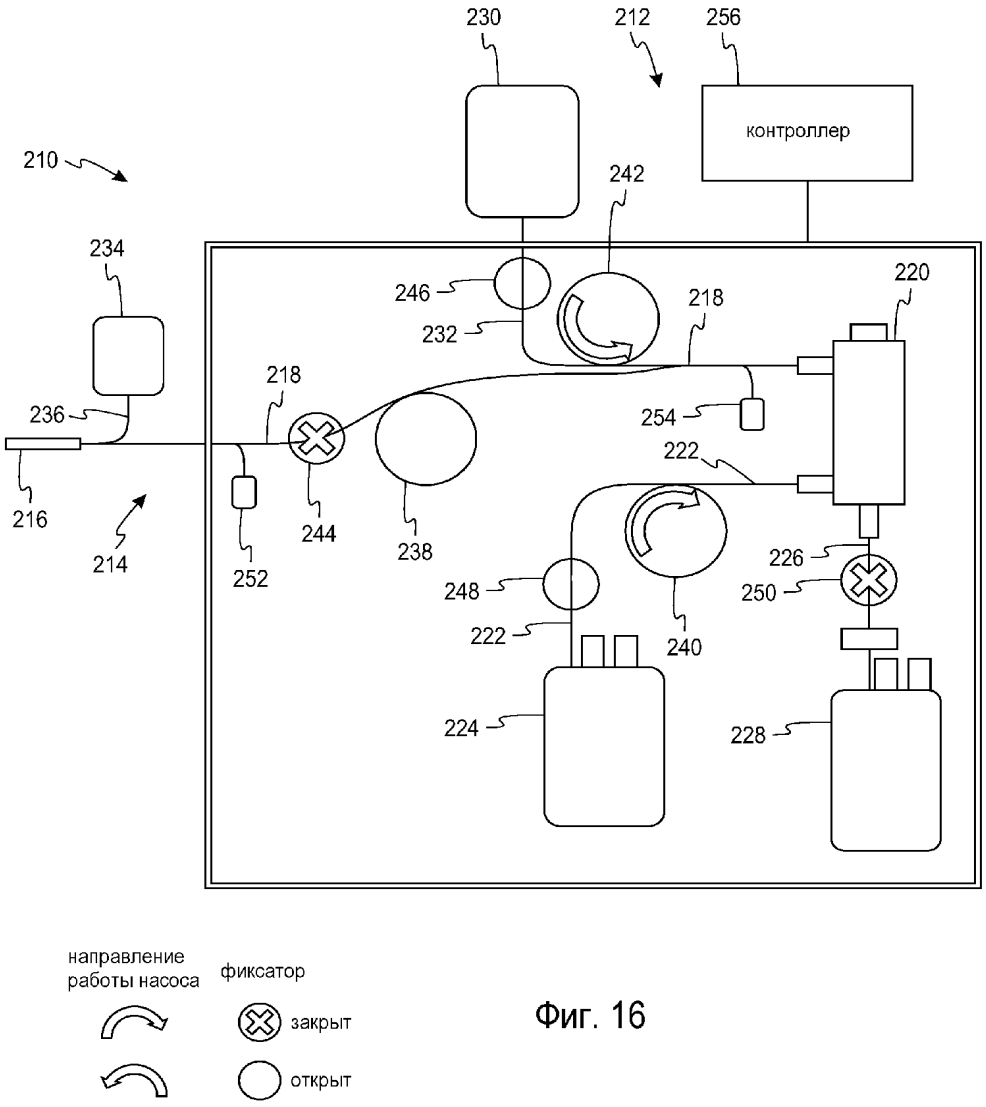
Фиг. 15

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0429



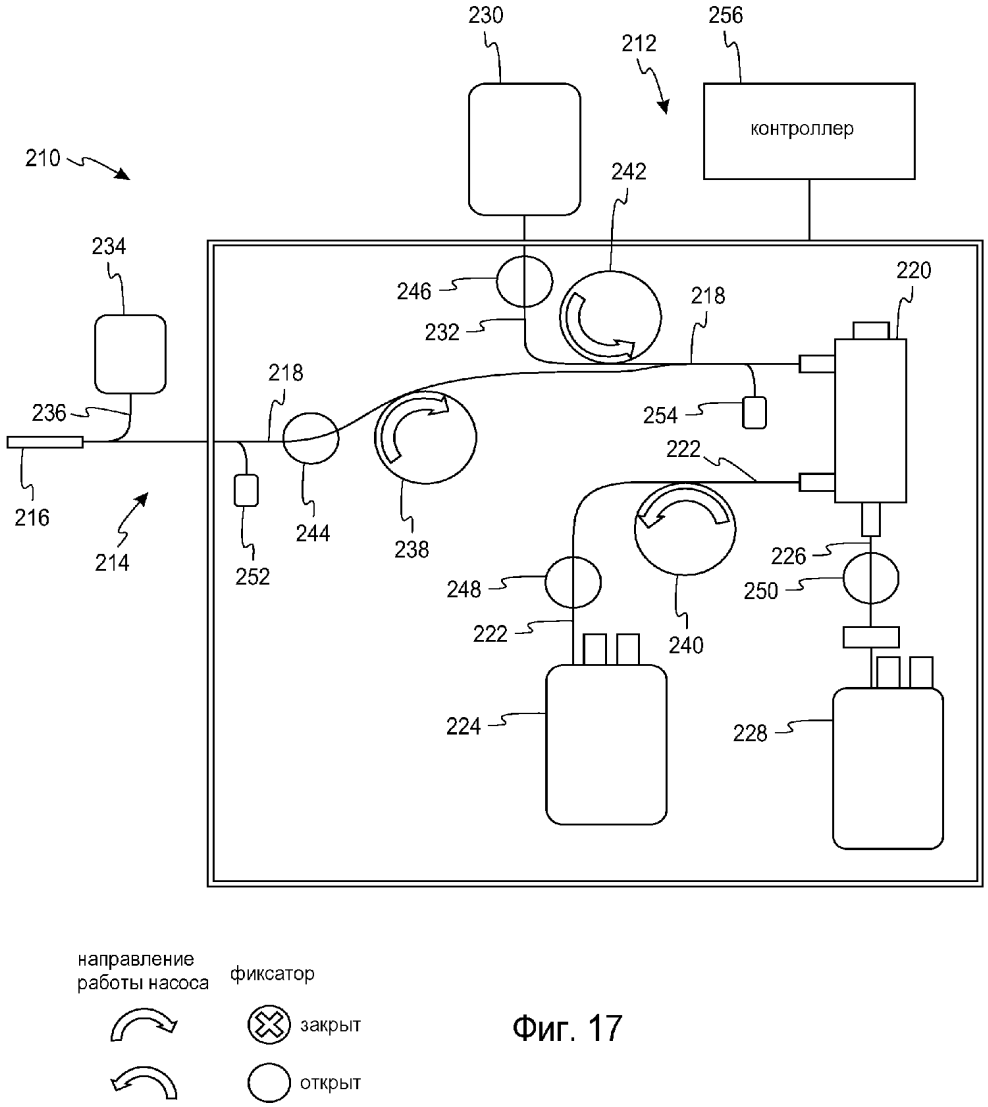
Фиг. 15a

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0430



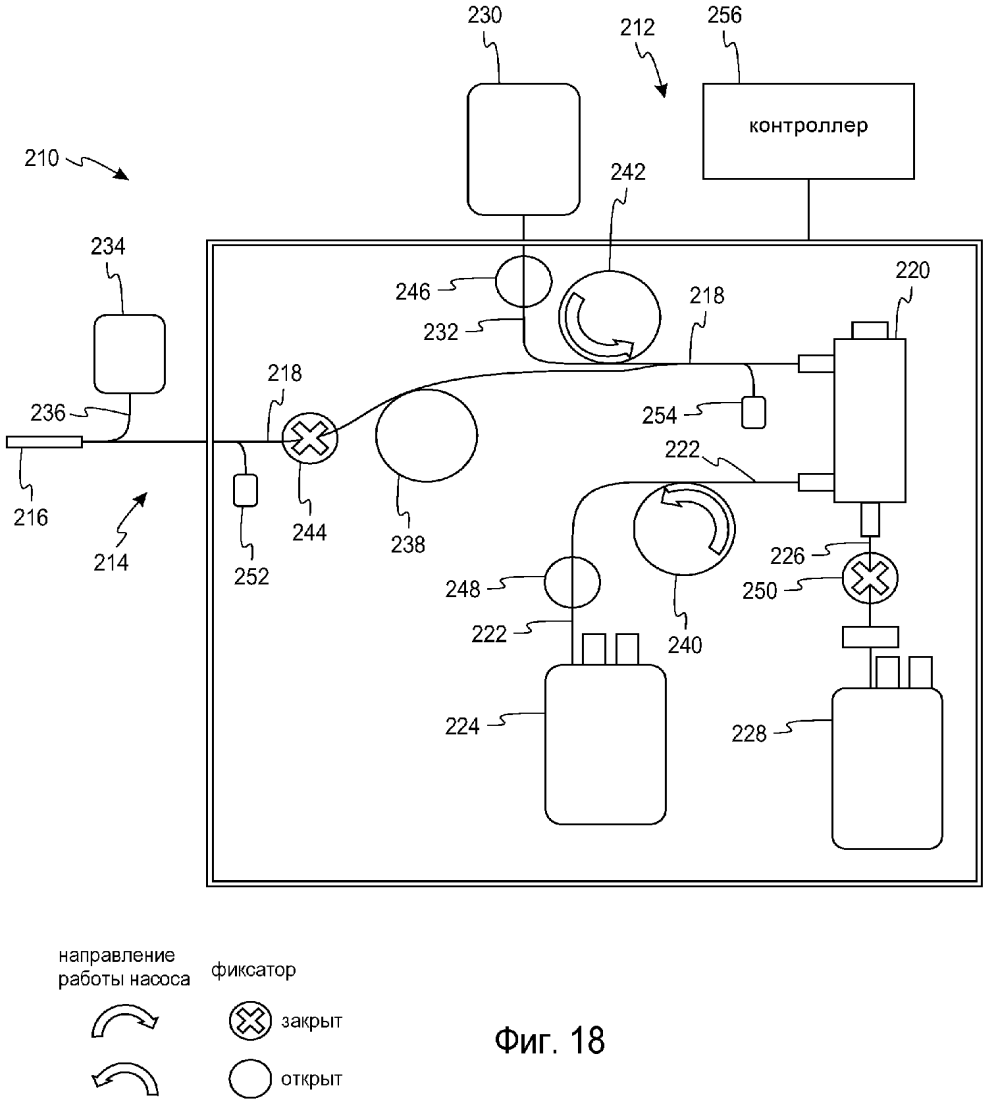
Фиг. 16

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0431



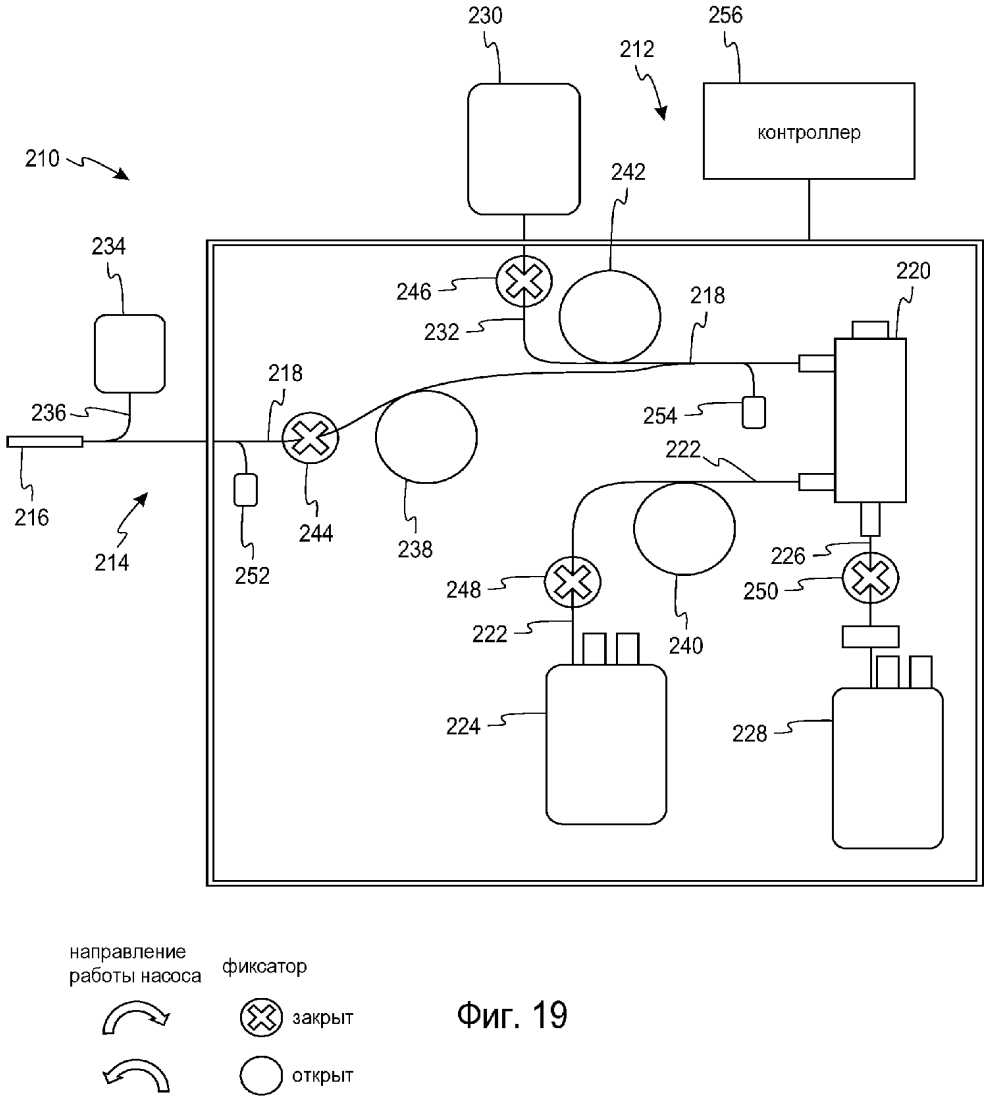
Фиг. 17

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0432



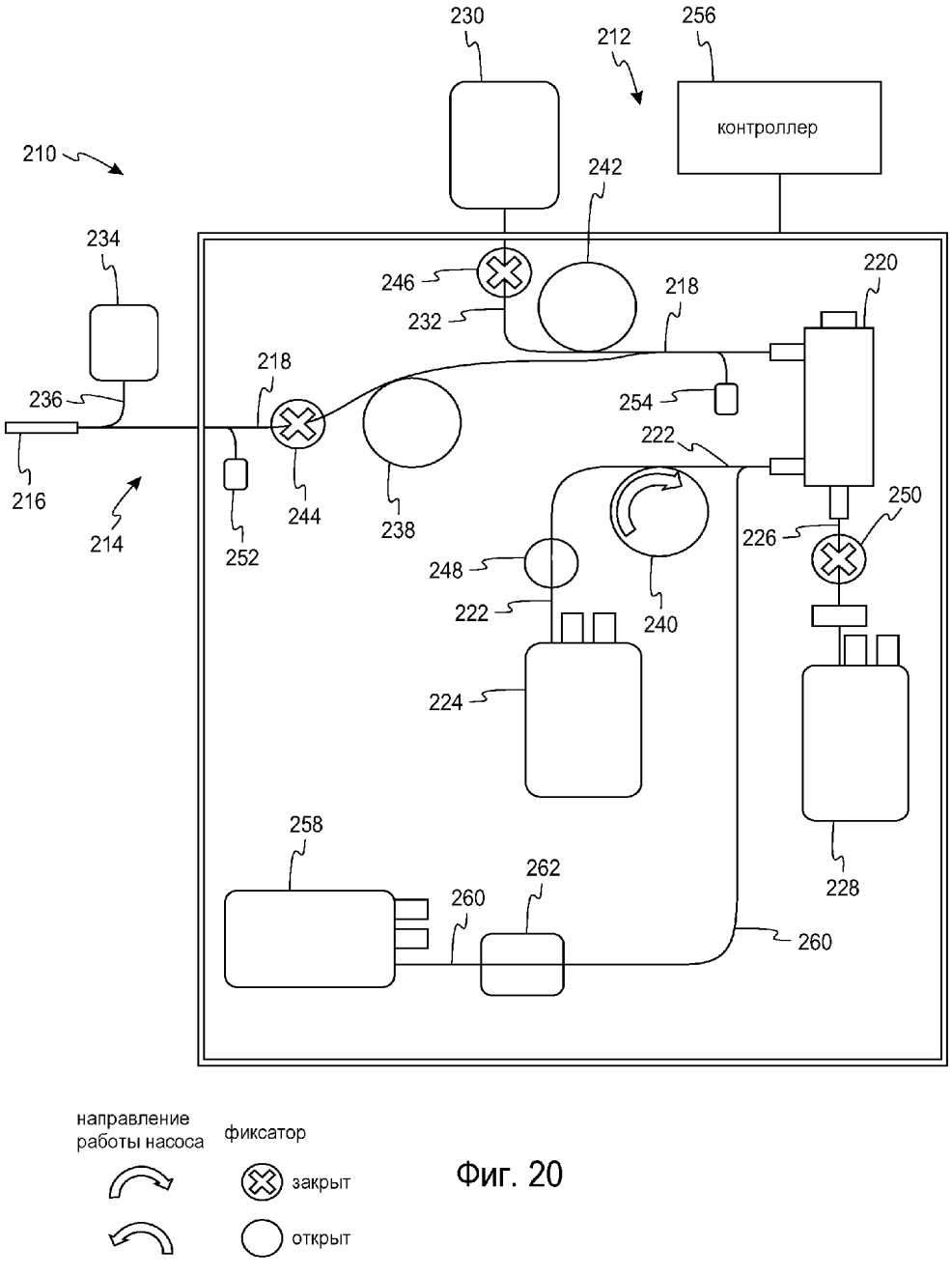
Фиг. 18

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0433



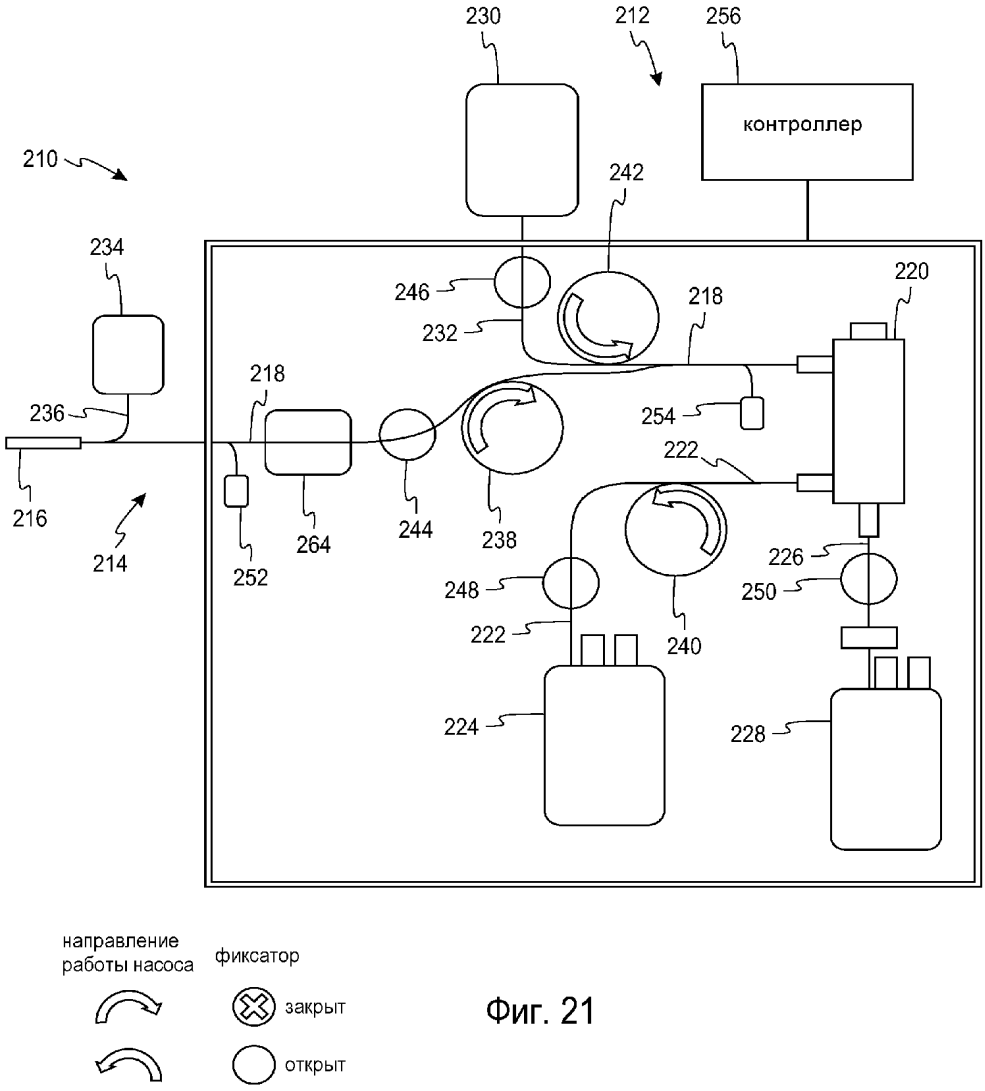
Фиг. 19

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0434



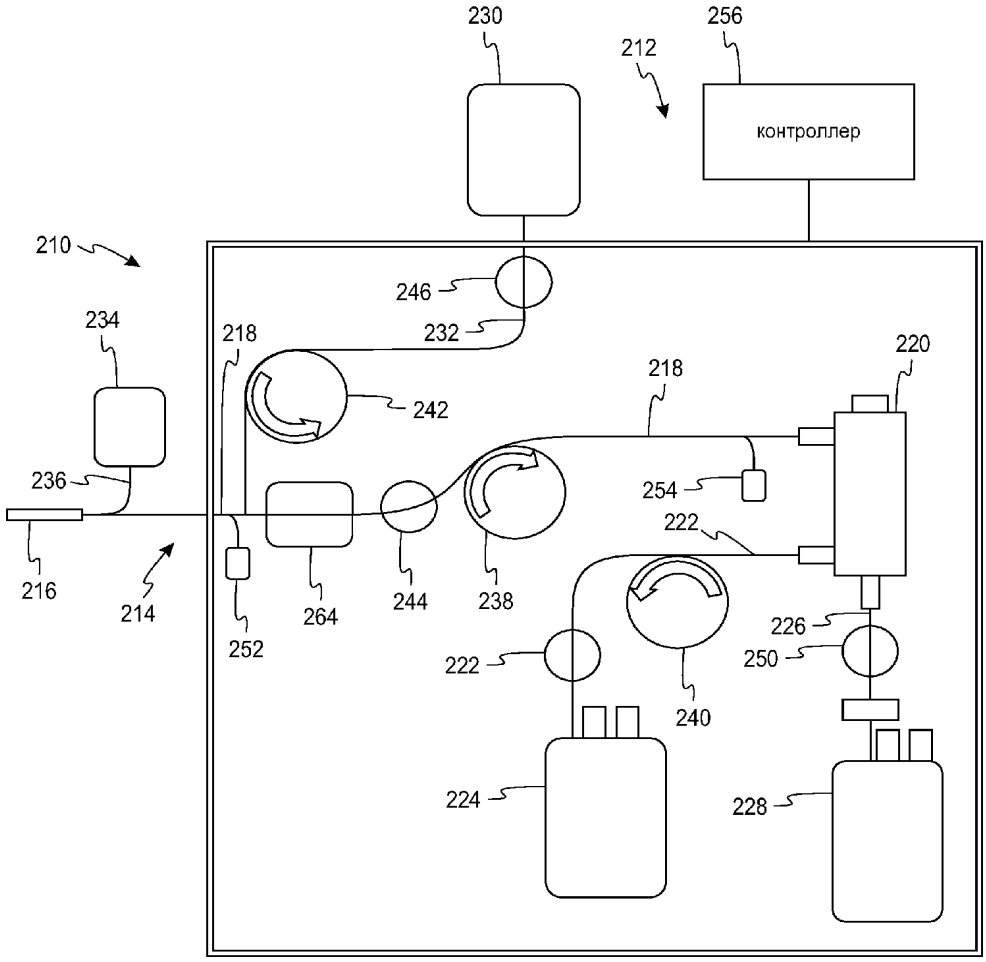
Фиг. 20

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0435



Фиг. 21

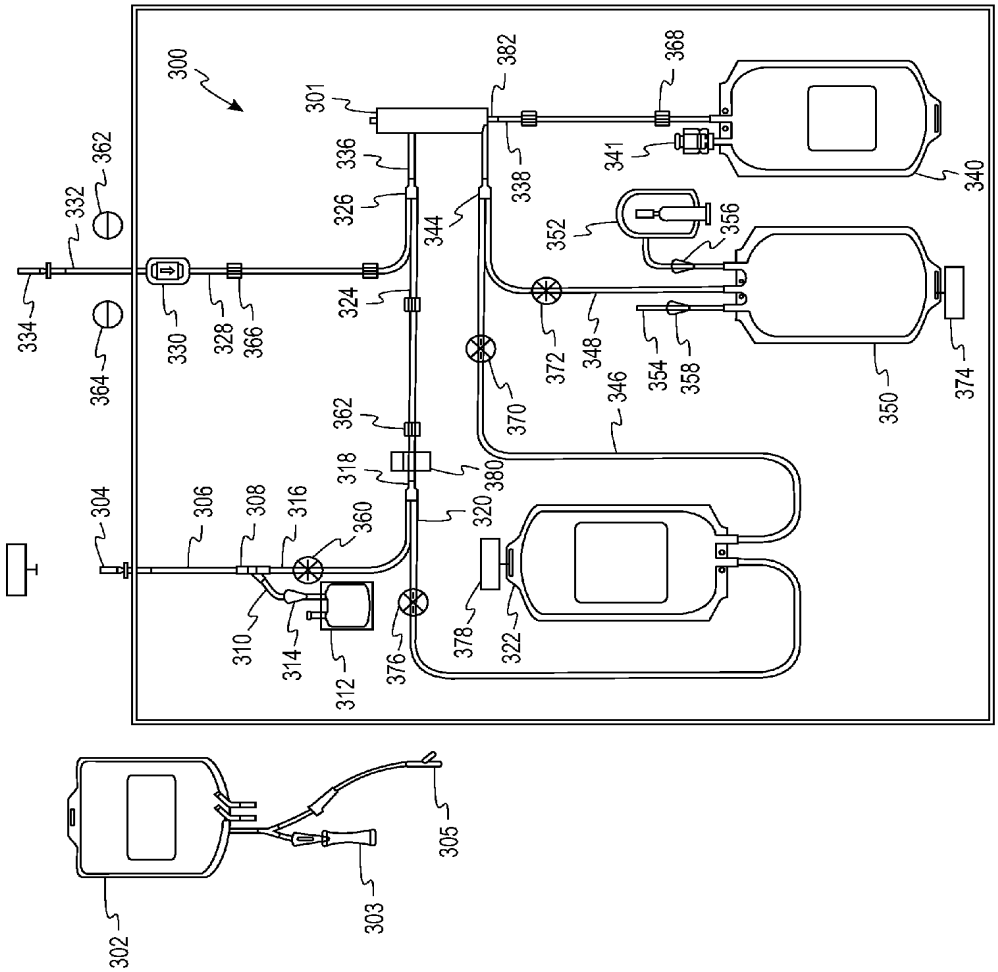
Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0436



Фиг. 22

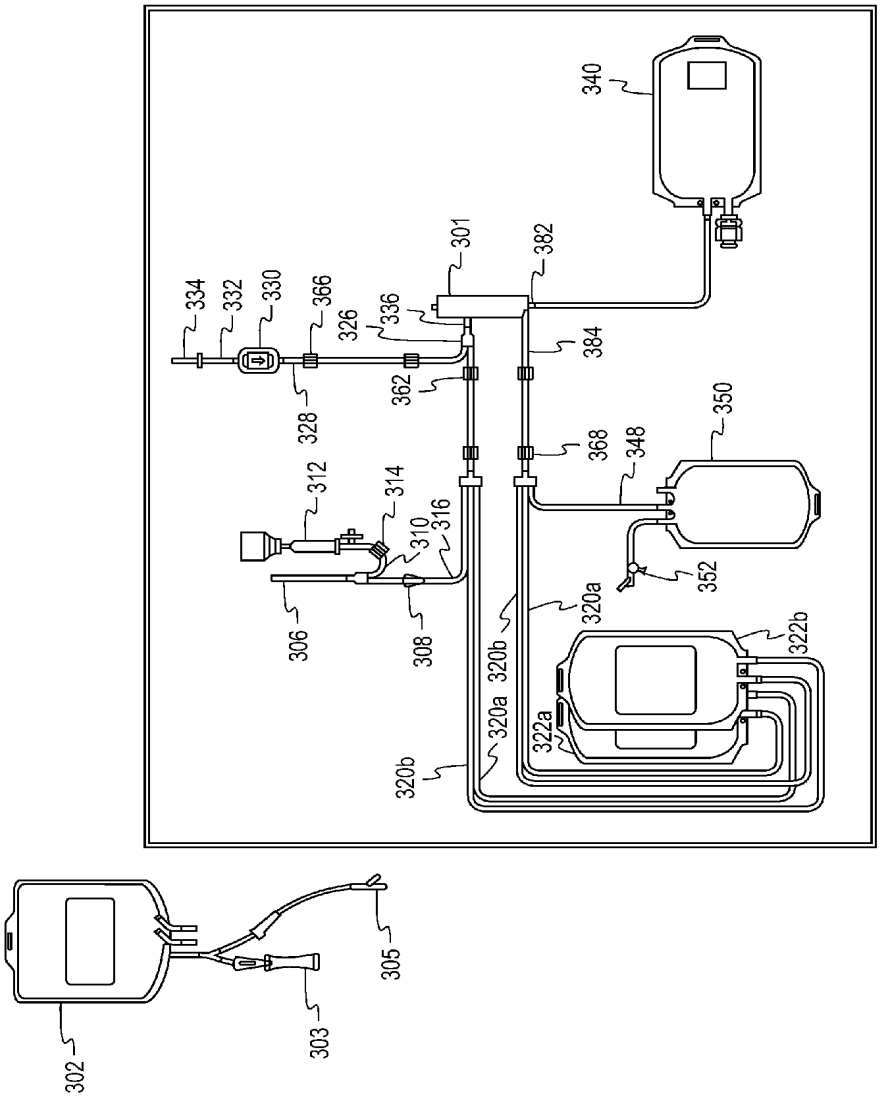
Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0437

Фиг. 23



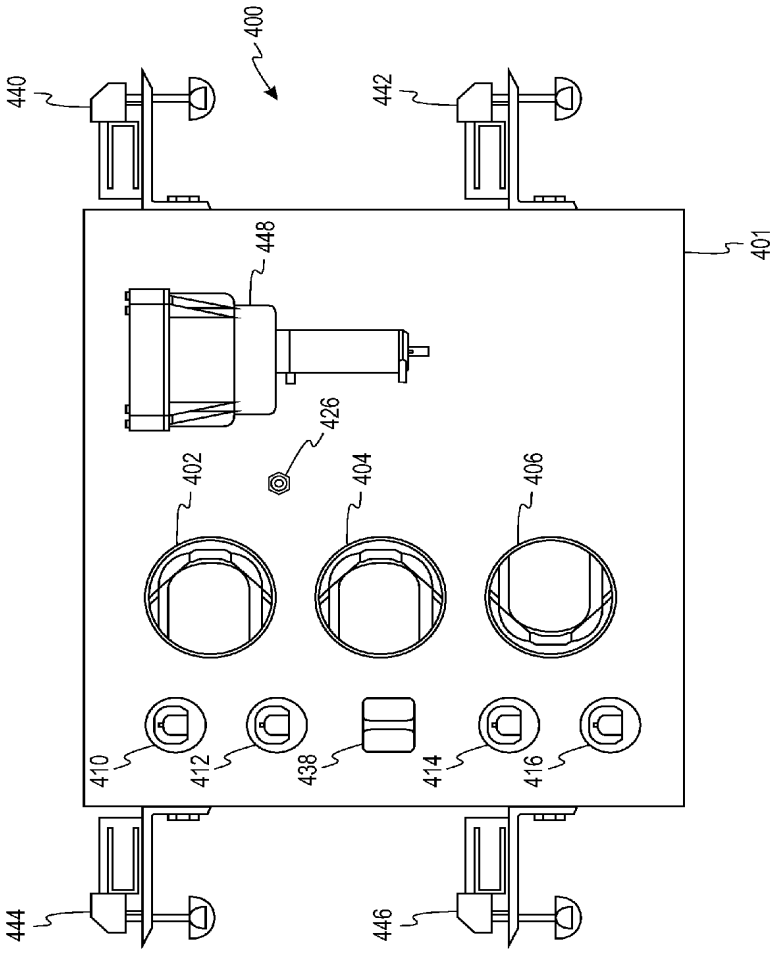
Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0438

Фиг. 24

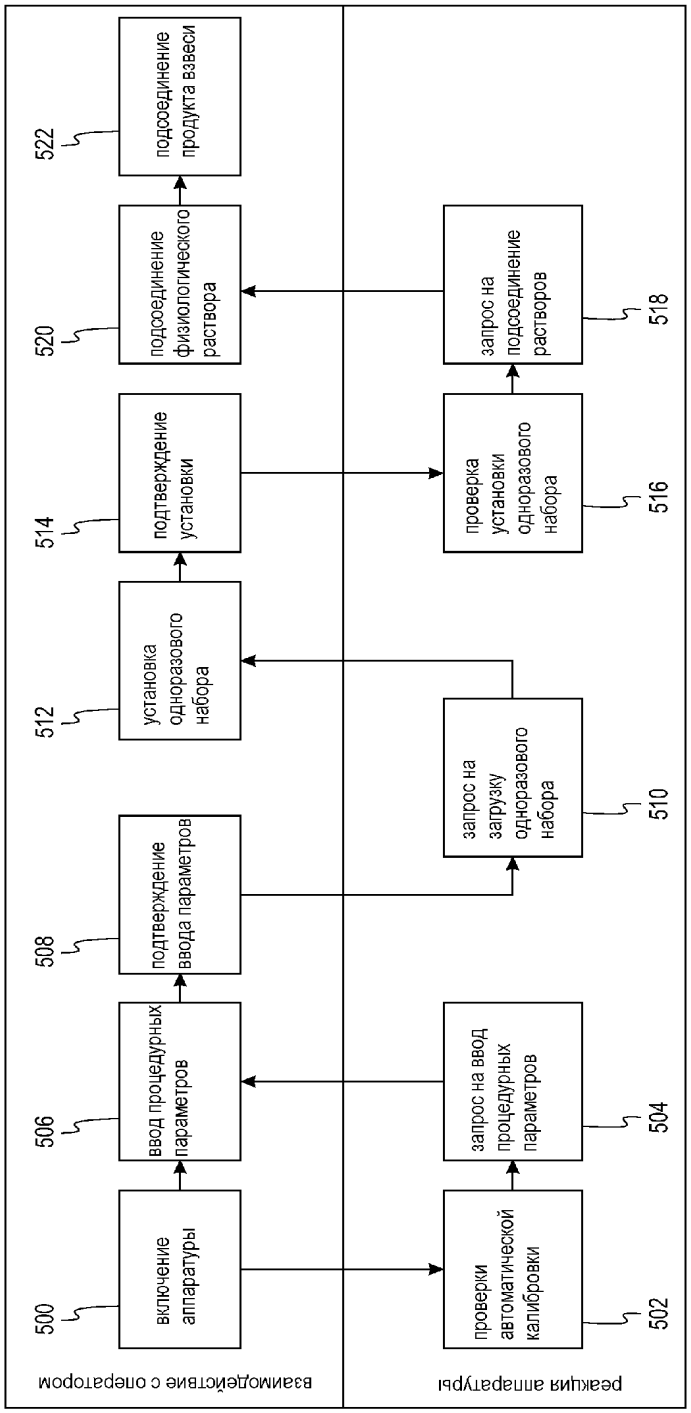


Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0439

Фиг. 25



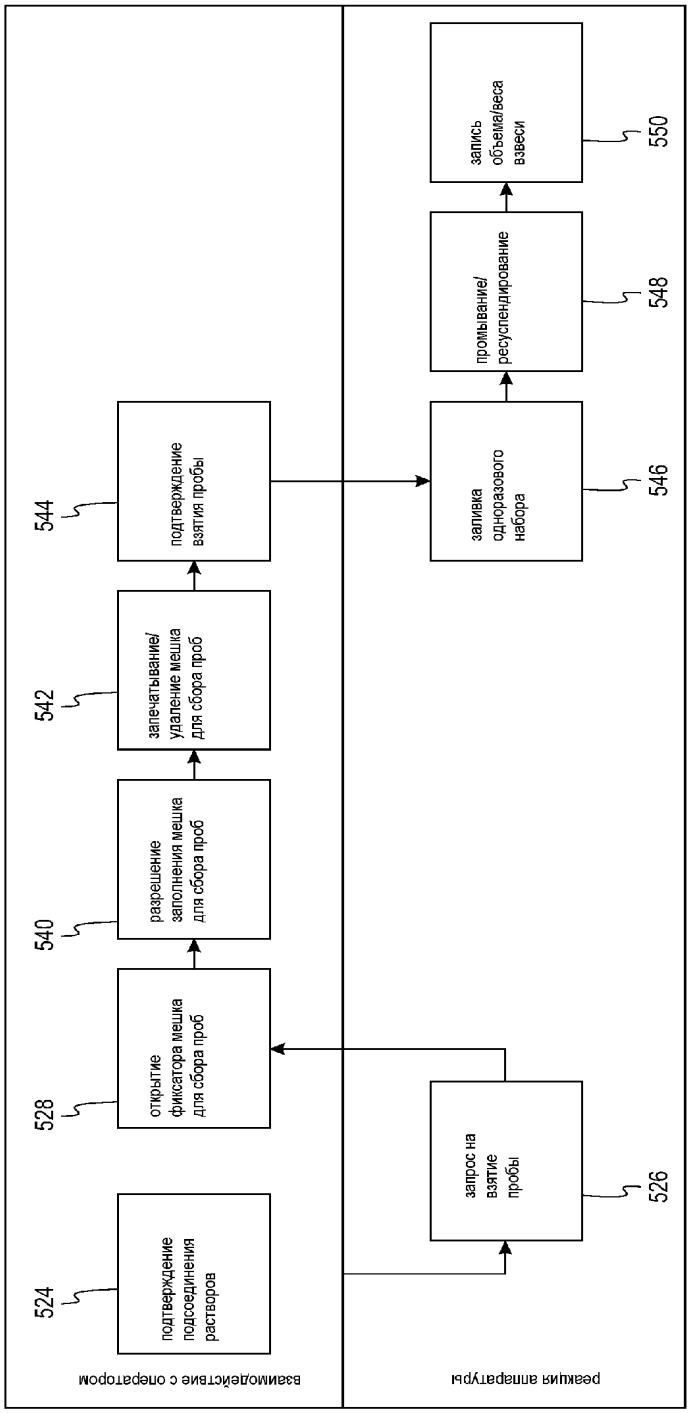
Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0440



Фиг. 26

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0441

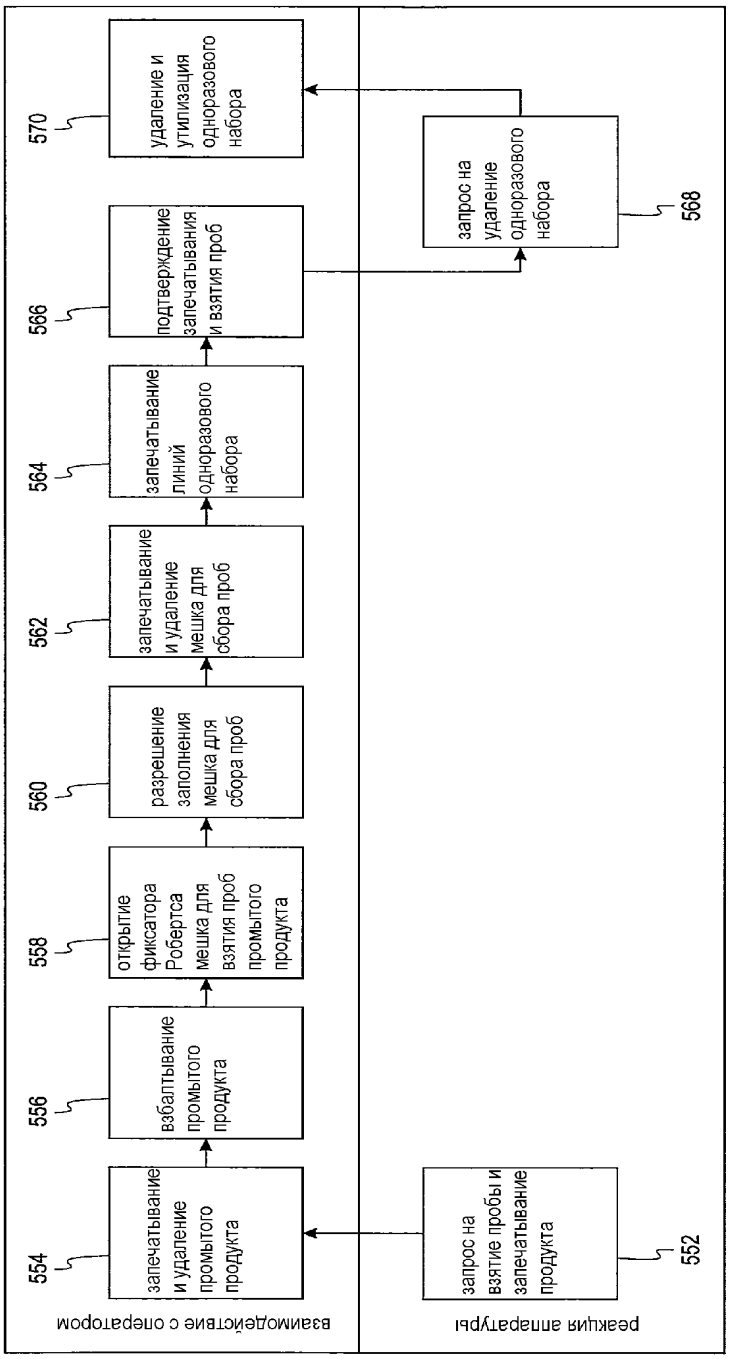
27/30



Фиг. 27

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0442

Фиг. 28



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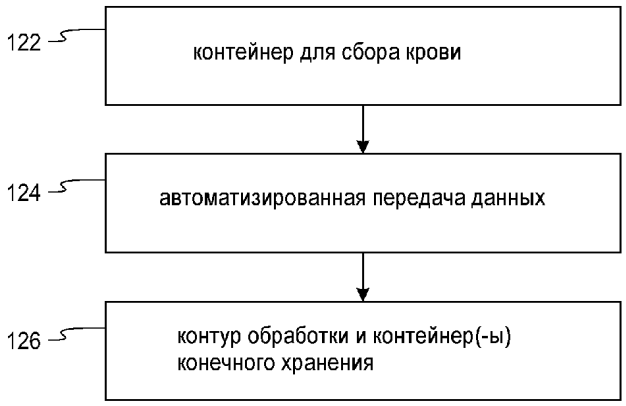
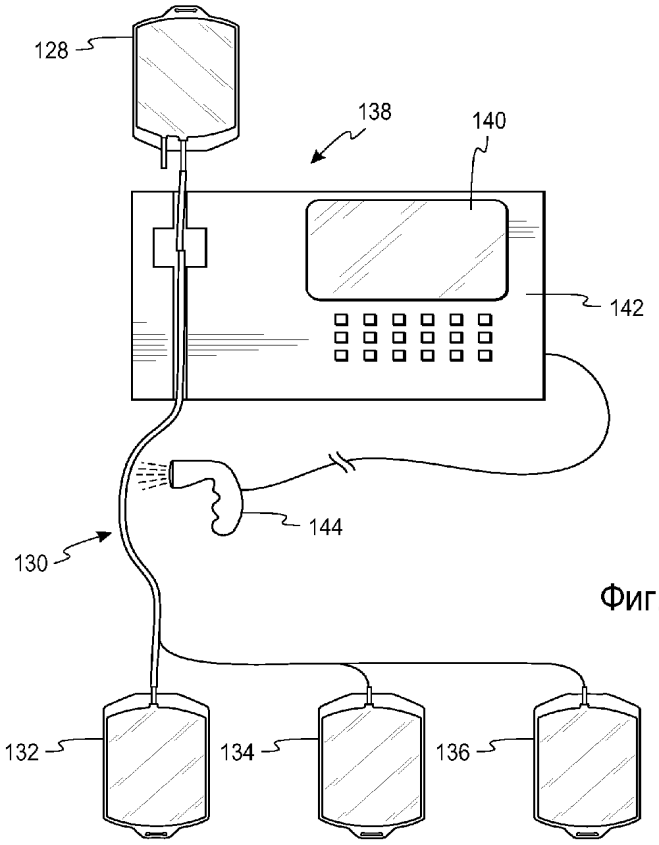
Petitioner Terumo Exhibit 1014-0443

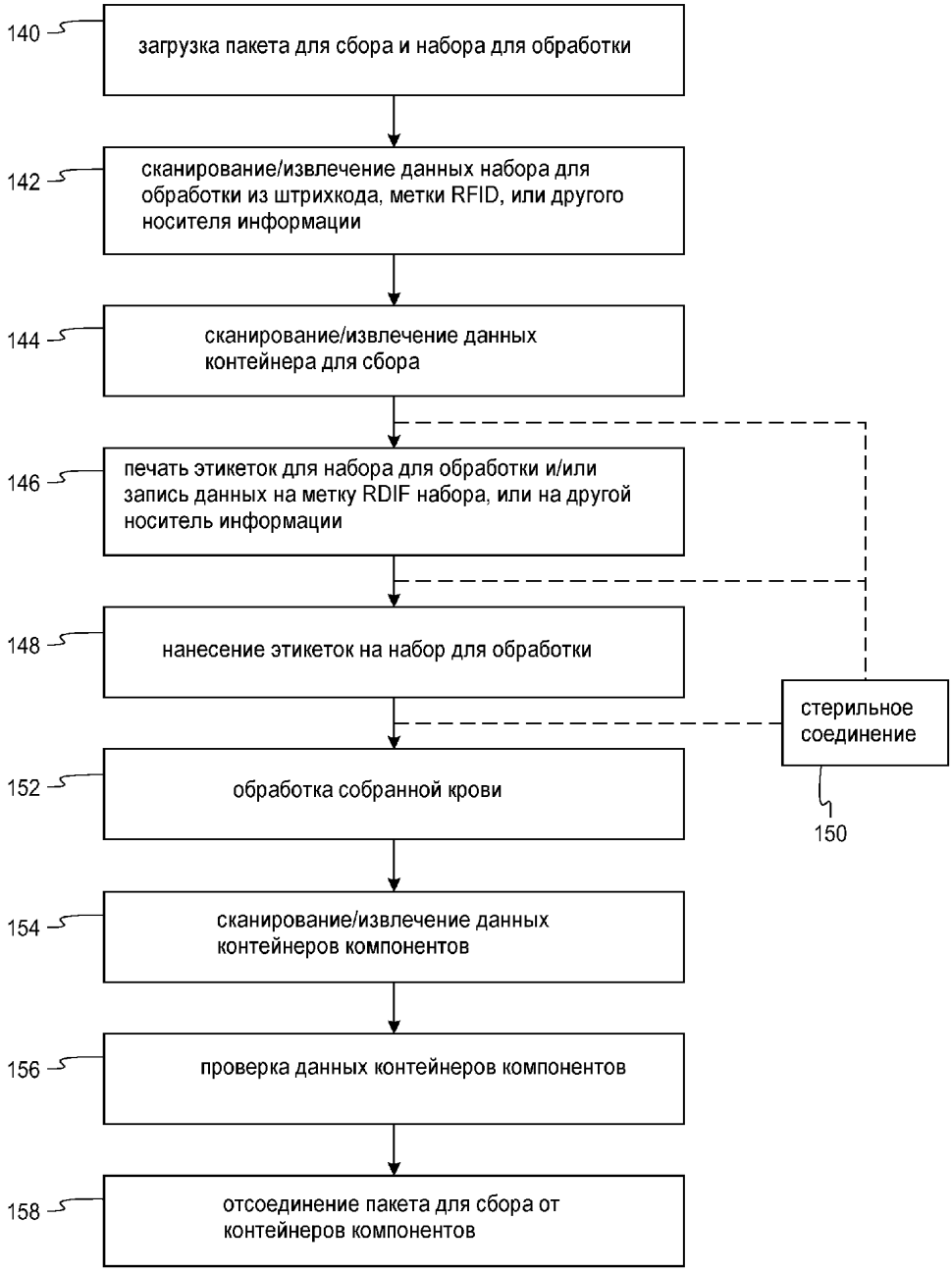


Фиг. 29



Фиг. 30

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0444



Фиг. 31

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0445

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-18)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	3799
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

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	2	20210205509	A1	2021-07-08	Ragusa	

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Petitioner Terumo Exhibit 1014-0446

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	3799
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
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Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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Petitioner Terumo Exhibit 1014-0447

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17205400
Filing Date	2021-03-18
First Named Inventor	Michael Ragusa
Art Unit	3799
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (YYYY-MM-DD)	2021-07-14
Name/Print	Jonathan C. Lovely	Registration Number	60,821

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0448

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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Petitioner Terumo Exhibit 1014-0449

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 14, 2021
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 | Confirmation No.: 4686

Filed: March 18, 2021 | Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING PLASMA | Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR 1.97, Applicant hereby makes of record the following additional documents. A PTO Form SB/08 and a full copy of each of the documents required under 37 CFR 1.98(a)(2) accompany this statement.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned (37 C.F.R. § 1.97(b)(3)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patent applications. Applicant submits herewith a copy of the cited foreign patent in accordance with 37 C.F.R. § 1.98(a)(2).

The Examiner is advised that the following co-pending applications contain subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	10,980,926	Issued	130670-08005
17/205,374	March 18, 2021	2021-0205509	Published	130670-08006
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	10,980,934	Issued	130670-80103

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Applicant believes no fee is due with this response.

Dated: July 14, 2021

Respectfully submitted,
Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0451

Electronic Acknowledgement Receipt

EFS ID:	43247534
Application Number:	17205400
International Application Number:	
Confirmation Number:	4686
Title of Invention:	SYSTEM AND METHOD FOR COLLECTING PLASMA
First Named Inventor/Applicant Name:	Michael Ragusa
Customer Number:	86738
Filer:	Jonathan Lovely
Filer Authorized By:	
Attorney Docket Number:	130670-80104
Receipt Date:	14-JUL-2021
Filing Date:	18-MAR-2021
Time Stamp:	15:08:19
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	130670-80104_-_EP1128887A1.pdf	134969 773b639750f77406c9770a79f45dbdce90c2da12	no	3

Warnings:

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0452

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	130670-80104_-_Information_Disclosure_Statement_Fillable_PDF.pdf	1034219 3f4b7b0f20dcca2c14a4b88a84e6d09c4e02d079	no	4
Warnings:					
Information:					
3	Transmittal Letter	Information_Disclosure_Statement.pdf	25174 4a6fe18aa25f7e7b6014e11b017c65cb4a69788c	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	1194362	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Espacenet

Bibliographic data: EP1128887 (A1) — 2001-09-05

BLOOD PROCESSING SYSTEMS AND METHODS WITH SENSORS TO DETECT CONTAMINATION

Inventor(s): VISHNOI ROHIT [US]; WESTBERG TOM [US]; MULLER MATTHEW R [US]; SMITH KELLY B [US]; JOIE MICHEL L F [BE]; VANDLIK MARK R [US] ± (VISHNOI, ROHIT, ; WESTBERG, TOM, ; MULLER, MATTHEW, R, ; SMITH, KELLY, B, ; JOIE, MICHEL, L., F, ; VANDLIK, MARK, R)

Applicant(s): BAXTER INT [US] ± (BAXTER INTERNATIONAL INC)

Classification: **- international:** ***A61M1/02; A61M1/34; A61M1/36; B01D17/02; B01D21/24; B04B5/00; G01N21/27; G01N21/35; G01N33/48; G01N33/483; G01N33/49;*** (IPC1-7): A61M1/36; B04B5/04

- cooperative: **A61M1/0236 (EP); A61M1/3496 (EP); A61M1/3646 (EP); A61M1/3693 (EP); A61M1/3696 (EP); B01D17/0217 (EP); B01D21/2444 (EP); B01D21/245 (EP); B01D21/26 (EP); B01D21/262 (EP); B01D21/302 (EP); B01D21/34 (EP);** A61M2202/0415 (EP); A61M2202/0429 (EP); A61M2205/125 (EP); A61M2205/128 (EP); A61M2205/331 (EP); A61M2205/3393 (EP); B01D2221/08 (EP); B01D2221/10 (EP)

Application number: EP20000961406 20000829 Global Dossier

Priority number(s): WO2000US23697 20000829 ; US19990390492 19990903

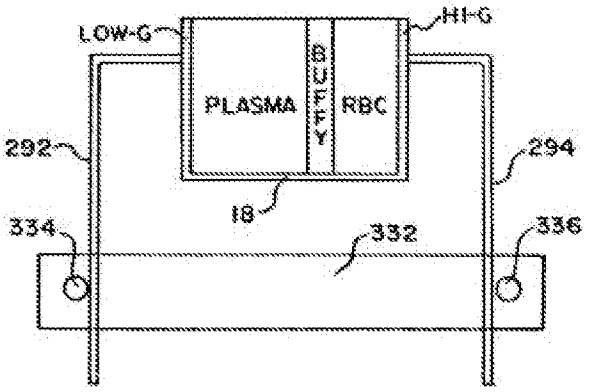
Also published as: EP1128887 (A4) EP1128887 (B1) AT334708 (T) AT381359 (T) AU7336200 (A) more

Abstract not available for EP1128887 (A1)
Abstract of corresponding document: WO0117652 (A1)

Blood processing systems and methods employ two sensors (334, 336), one (334) to detect a condition of plasma exiting a separation device (18) and another sensor (336) to detect a condition of a cellular component exiting the separation device (18). The first sensor (334) detects, e.g., contamination of the plasma due to the presence of

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0454

unwanted cellular components. The second sensor (336) detects, e.g., dilution of the cellular component due to presence of plasma. Blood processing parameters are carried out based, at least in part, by conditions detected by one or both of the sensors (334, 336).



Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0455

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Veröffentlichungsnummer:
(11) Publication number:
(11) Numéro de publication:

EP 1 128 887 A0

Internationale Anmeldung veröffentlicht durch die Weltorganisation für geistiges Eigentum unter der Nummer:

WO 01/17652 (art. 158 des EPÜ).

International application published by the World Intellectual Property Organisation under number:

WO 01/17652 (art. 158 of the EPC).

Demande internationale publiée par l'Organisation Mondiale de la Propriété sous le numéro:

WO 01/17652 (art. 158 de la CBE).

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0456

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
17/205,400	03/18/2021	Michael Ragusa	130670-80104

CONFIRMATION NO. 4686

86738
MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

PUBLICATION NOTICE

Title:SYSTEM AND METHOD FOR COLLECTING PLASMA

Publication No.US-2021-0205526-A1
Publication Date:07/08/2021

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently https://portal.uspto.gov/pair/PublicPair. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

Terumo v. Haemonetics - PGR2026-00006
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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
17/205,400	03/18/2021	3781	3000	130670-80104	27	4

CONFIRMATION NO. 4686

86738
MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

FILING RECEIPT

OC000000124437681

Date Mailed: 03/30/2021

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Michael Ragusa, Hingham, MA;

Applicant(s)

Haemonetics Corporation, Boston, MA;

Power of Attorney: The patent practitioners associated with Customer Number 86738

Domestic Priority data as claimed by applicant

This application is a CON of 16/931,333 07/16/2020
which is a CON of 15/793,339 10/25/2017 PAT 10792416
which is a CIP of 15/608,183 05/30/2017 PAT 10758652

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0458

If Required, Foreign Filing License Granted: 03/29/2021

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 17/205,400**

Projected Publication Date: 07/08/2021

Non-Publication Request: No

Early Publication Request: No

Title

SYSTEM AND METHOD FOR COLLECTING PLASMA

Preliminary Class

604

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0459

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0460

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 17/205,400

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	320
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	700
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	800
TOTAL CLAIMS (37 CFR 1.16(i))	27 minus 20 =	* 7			OR	x 100 =	700
INDEPENDENT CLAIMS (37 CFR 1.16(h))	4 minus 3 =	* 1				x 480 =	480
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	3000

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)		RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0461

Used in Lieu of PTO/SB/08A/B
(Based on PTO 10-07 version)

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Not Yet Assigned
				Filing Date	Concurrently Herewith
				First Named Inventor	Michael Ragusa
				Art Unit	3781
(Use as many sheets as necessary)				Examiner Name	Not Yet Assigned
Sheet	1	of	6	Attorney Docket Number	130670-80104

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	AA	US-1,025,059	04-30-1912	Hatton et al.	
	AB	US-1,611,725	12-21-1926	Degerth et al.	
	AC	US-2,087,778	07-20-1937	Nelin	
	AD	US-2,661,150	12-01-1953	Abbott, Jr.	
	AE	US-2,750,107	06-12-1956	More	
	AF	US-2,792,172	05-14-1957	Tait	
	AG	US-3,096,283	07-02-1963	Hein	
	AH	US-3,145,713	08-25-1964	Latham, Jr.	
	AI	US-3,239,136	03-08-1966	Hein	
	AJ	US-3,244,362	04-05-1966	Hein	
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	AL	US-3,409,213	11-05-1968	Latham, Jr.	
	AM	US-3,456,875	07-22-1969	Hein	
	AN	US-3,489,145	01-13-1970	Judson et al.	
	AO	US-3,565,330	02-23-1971	Latham, Jr.	
	AP	US-3,655,058	04-11-1972	Novak	
	AQ	US-3,737,096	06-05-1973	Jones et al.	
	AR	US-3,774,840	11-27-1973	Boatright	
	AS	US-3,987,961	10-26-1976	Sinn et al.	
	AT	US-4,007,871	02-15-1977	Jones et al.	
	AU	US-4,010,894	03-08-1977	Kellogg et al.	
	AV	US-4,014,497	03-29-1977	Spiewok et al.	
	AW	US-4,040,965	08-09-1977	Kohlheb	
	AX	US-4,056,224	11-01-1977	Lolachi	
	AY	US-4,082,217	04-04-1978	Westberg	
	AZ	US-4,086,924	05-02-1978	Latham, Jr.	
	AA1	US-4,140,268	02-20-1979	Lacour	
	AB1	US-4,142,670	03-06-1979	Ishimaru et al.	
	AC1	US-4,151,844	05-01-1979	Cullis et al.	
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	AH1	US-4,321,921	03-30-1982	Laszczower	
	AI1	US-4,387,848	06-14-1983	Kellogg et al.	
	AJ1	US-4,425,114	01-10-1984	Schoendorfer et al.	
	AK1	US-4,430,072	02-07-1984	Kellogg et al.	
	AL1	US-4,447,221	05-08-1984	Mulzet	
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	AS1	US-4,534,863	08-13-1985	Bacon et al.	

Examiner Signature		Date Considered	

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0462

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Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Not Yet Assigned
				Filing Date	Concurrently Herewith
				First Named Inventor	Michael Ragusa
				Art Unit	3781
(Use as many sheets as necessary)				Examiner Name	Not Yet Assigned
Sheet	2	of	6	Attorney Docket Number	130670-80104

	AT1	US-4,643,714	02-17-1987	Brose	
	AU1	US-4,647,279	03-03-1987	Mulzet et al.	
	AV1	US-4,655,742	04-07-1987	Vantard	
	AW1	US-4,680,025	07-14-1987	Kruger et al.	
	AX1	US-4,684,361	08-04-1987	Feldman et al.	
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	AA2	US-4,713,176	12-15-1987	Schoendorfer et al.	
	AB2	US-4,734,089	03-29-1988	Cullis	
	AC2	US-4,740,202	04-26-1988	Stacey et al.	
	AD2	US-4,740,313	04-26-1988	Schoendorfer et al.	
	AE2	US-4,755,300	07-05-1988	Fischel et al.	
	AF2	US-4,767,396	08-30-1988	Powers	
	AG2	US-4,795,419	01-03-1989	Yawn et al.	
	AH2	US-4,795,448	01-03-1989	Stacey et al.	
	AI2	US-4,806,247	02-21-1989	Schoendorfer et al.	
	AJ2	US-4,806,252	02-21-1989	Brown et al.	
	AK2	US-4,808,307	02-28-1989	Fischel et al.	
	AL2	US-4,850,995	07-25-1989	Tie et al.	
	AM2	US-4,869,812	09-26-1989	Schoendorfer et al.	
	AN2	US-4,871,462	10-03-1989	Fischel et al.	
	AO2	US-4,876,013	10-24-1989	Shmidt et al.	
	AP2	US-4,889,524	12-26-1989	Fell et al.	
	AQ2	US-4,911,833	03-27-1990	Schoendorfer et al.	
	AR2	US-4,934,995	06-19-1990	Cullis	
	AS2	US-4,940,543	07-10-1990	Brown et al.	
	AT2	US-4,943,273	07-24-1990	Pages	
	AU2	US-4,968,295	11-06-1990	Neumann	
	AV2	US-4,983,156	01-08-1991	Knelson	
	AW2	US-4,983,158	01-08-1991	Headley	
	AX2	US-4,985,153	01-15-1991	Kuroda et al.	
	AY2	US-4,994,188	02-19-1991	Prince	
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	AB3	US-5,098,372	03-24-1992	Jonsson	
	AC3	US-5,098,373	03-24-1992	Polaschegg	
	AD3	US-5,100,372	03-31-1992	Headley	
	AE3	US-5,100,564	03-31-1992	Pall et al.	
	AF3	US-5,112,298	05-12-1992	Prince et al.	
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	AH3	US-5,135,667	08-04-1992	Schoendorfer	
	AI3	US-5,141,486	08-25-1992	Antwiler	
	AJ3	US-5,147,290	09-15-1992	Jonsson	
	AK3	US-5,154,716	10-13-1992	Bauman et al.	
	AL3	US-5,174,894	12-29-1992	Ohsawa et al.	
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Examiner Signature		Date Considered	

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0463

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Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Not Yet Assigned
				Filing Date	Concurrently Herewith
				First Named Inventor	Michael Ragusa
(Use as many sheets as necessary)				Art Unit	3781
				Examiner Name	Not Yet Assigned
Sheet	3	of	6	Attorney Docket Number	130670-80104

	AQ3	US-5,254,248	10-19-1993	Nakamura	
	AR3	US-5,273,517	12-28-1993	Barone et al.	
	AS3	US-5,277,701	01-11-1994	Christie et al.	
	AT3	US-5,298,016	03-29-1994	Gordon	
	AU3	US-5,298,171	03-29-1994	Biesel	
	AV3	US-5,300,060	04-05-1994	Nelson	
	AW3	US-5,316,540	05-31-1994	McMannis et al.	
	AX3	US-5,318,511	06-07-1994	Riquier et al.	
	AY3	US-5,318,512	06-07-1994	Neumann	
	AZ3	US-5,348,533	09-20-1994	Papillon et al.	
	AA4	US-5,368,542	11-29-1994	McMannis et al.	
	AB4	US-5,368,555	11-29-1994	Sussman et al.	
	AC4	US-5,386,734	02-07-1995	Pusinelli	
	AD4	US-5,387,174	02-07-1995	Rochat	
	AE4	US-5,387,187	02-07-1995	Fell et al.	
	AF4	US-5,403,272	04-04-1995	Deniega et al.	
	AG4	US-5,405,308	04-11-1995	Headley et al.	
	AH4	US-5,417,650	05-23-1995	Gordon	
	AI4	US-5,431,814	07-11-1995	Jorgensen	
	AJ4	US-5,437,598	08-01-1995	Antwiler	
	AK4	US-5,437,624	08-01-1995	Langley	
	AL4	US-5,462,667	10-31-1995	Wollinsky et al.	
	AM4	US-5,470,483	11-28-1995	Bene et al.	
	AN4	US-5,484,396	01-16-1996	Naficy	
	AO4	US-5,494,592	02-27-1996	Latham, Jr. et al.	
	AP4	US-5,505,685	04-09-1996	Antwiler	
	AQ4	US-5,514,070	05-07-1996	Pages	
	AR4	US-5,543,062	08-06-1996	Nishimura	
	AS4	US-5,551,941	09-03-1996	Howell	
	AT4	US-5,585,007	12-17-1996	Antanavich et al.	
	AU4	US-5,607,579	03-04-1997	Latham, Jr. et al.	
	AV4	US-5,649,903	07-22-1997	Deniega et al.	
	AW4	US-5,651,766	07-29-1997	Kingsley et al.	
	AX4	US-5,656,163	08-12-1997	Brown	
	AY4	US-5,665,061	09-09-1997	Antwiler	
	AZ4	US-5,712,798	01-27-1998	Langley et al.	
	AA5	US-5,728,060	03-17-1998	Kingsley et al.	
	AB5	US-5,733,253	03-31-1998	Headley et al.	
	AC5	US-5,733,446	03-31-1998	Holm	
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	AE5	US-5,738,792	04-14-1998	Schoendorfer	
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	AK5	US-5,882,289	03-16-1999	Sakota et al.	
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Examiner Signature		Date Considered	

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0464

Substitute for form 1449/PTO				*Complete if Known*	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				**Application Number**	Not Yet Assigned
				Filing Date	Concurrently Herewith
				First Named Inventor	Michael Ragusa
				Art Unit	3781
(Use as many sheets as necessary)				Examiner Name	Not Yet Assigned
Sheet	4	of	6	Attorney Docket Number	130670-80104

	AN5	US-5,964,724	10-12-1999	Rivera et al.	
	AO5	US-5,970,432	10-19-1999	Ishimoto et al.	
	AP5	US-5,980,760	11-09-1999	Min et al.	
	AQ5	US-6,007,725	12-28-1999	Brown	
	AR5	US-6,059,979	05-09-2000	Brown	
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	AT5	US-6,234,989-B1	05-22-2001	Brierton et al.	
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	AV5	US-6,464,624-B2	10-15-2002	Pages	
	AW5	US-6,497,676-B1	12-24-2002	Childers et al.	
	AX5	US-6,558,307-B2	05-06-2003	Headley	
	AY5	US-6,623,443-B1	09-23-2003	Polaschegg	
	AZ5	US-6,743,192-B1	06-01-2004	Sakota et al.	
	AA6	US-7,115,205-B2	10-03-2006	Robinson et al.	
	AB6	US-7,186,231-B2	03-06-2007	Takagi et al.	
	AC6	US-7,270,645-B2	09-18-2007	Langley et al.	
	AD6	US-7,704,454-B1	04-27-2010	Langley et al.	
	AE6	US-8,628,489-B2	01-14-2014	Pages et al.	
	AF6	US-8,702,637-B2	04-22-2014	Pages et al.	
	AG6	US-8,759,094-B2	06-24-2014	Ranby	
	AH6	US-9,283,316-B2	03-15-2016	Flexman	
	AI6	US-10,758,652-B2	09-01-2020	Ragusa	
	AJ6	US-10,792,416-B2	10-06-2020	Ragusa	
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	AL6	US-20010027156-A1	10-04-2001	Egozy et al.	
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	AO6	US-20020120227-A1	08-29-2002	Childers et al.	
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	AT6	US-20040186409-A1	09-23-2004	Cavalcanti et al.	
	AU6	US-20050209522-A1	09-22-2005	Tadokoro et al.	
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Examiner Signature		Date Considered	

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0465

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 5 of 6

Complete if Known	
Application Number	Not Yet Assigned
Filing Date	Concurrently Herewith
First Named Inventor	Michael Ragusa
Art Unit	3781
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

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Examiner Initials*	Cite No.[1]	Foreign Patent Document Country Code[3]-Number[4]-Kind Code[5] *(if known)*	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T[6]
	BA**	CN-2735985-Y	10-26-2005	Shanghai Dahua Medical Apparatus Co., Ltd		√
	BB**	EP-0128683-A2	12-19-1984	Baxter Travenol Laboratories, Inc		
	BC**	EP-0171749-A1	02-19-1986	Terumo Corp		
	BD**	EP-0208061-A1	01-14-1987	Biotest Pharma GmbH		
	BE**	EP-257755-A1	03-02-1988	Haemonetics Corp		
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	BG**	EP-619145-A2	10-12-1994	Electromedics, Inc		
	BH**	EP-0654277-A1	05-24-1995	Cobe Laboratories, Inc		
	BI**	EP-664159-A1	07-26-1995	Haemonetics Corp		
	BJ**	EP-799645-A1	10-08-1997	Haemonetics Corp		
	BK**	EP-0885619-A1	12-23-1998	Terumo Corp		
	BL**	EP-1057534-A1	12-06-2000	Haemonetics Corp		
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	BN**	EP-1374927-A1	01-02-2004	Terumo Corp		
	BO**	FR-2258898-A1	08-22-1975	Heraeus Christ Gmbh,dt		
	BP**	GB-2047110-A	11-26-1980	Hogman, C F		
	BQ**	JP-S59-006952	01-14-1984	Hitachi Koki KK		√
	BR**	JP-S59-069166	04-19-1984	Nikkiso Co Ltd.		√
	BS**	JP-H02-052665	02-22-1990	Nissho KK		√
	BT**	JP-H03-131268	06-04-1991	Fresenius AG		√
	BU**	JP-H07-075746	03-20-1995	Electromedics Inc.		√
	BV**	JP-H08-131539	05-28-1996	Terumo Corp.		√
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	BY**	JP-2008-506424-A	03-06-2008			√
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	BA1**	SU-762982-A1	09-15-1980	Sp K B Biofizicheskoj Apparatu		
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	BC1**	WO-1985/02561-A1	06-20-1985	Baxter Travenol Laboratories, Inc		
	BD1**	WO-1990/00059-A1	01-11-1990	Sirchia, Girolamo		
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	BG1**	WO-1996/11747-A2	04-25-1996	Transfusion, Technologies Corporation		
	BH1**	WO-1996/33023-A1	10-24-1996	Cobe Laboratories, Inc		
	BI1**	WO-2002/05059-A2	01-17-2002	Baxter Int		

Examiner Signature		Date Considered	

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0466

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Substitute for form 1449/PTO **INFORMATION DISCLOSURE STATEMENT BY APPLICANT** *(Use as many sheets as necessary)*				***Complete if Known***	
				Application Number	Not Yet Assigned
				Filing Date	Concurrently Herewith
				First Named Inventor	Michael Ragusa
				Art Unit	3781
				Examiner Name	Not Yet Assigned
Sheet	6	of	6	Attorney Docket Number	130670-80104

	BJ1**	WO-2007/041716-A1	04-12-2007	Gambro, Inc		☐

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NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	CA**	Haemonetics Nomogram - Male, 2 pages, May 1990.	
	CB**	LEMMENS et al., Estimating blood volume in obese and morbidly obese patients. Obes Surg. 2006 Jun;16(6):773-6.	
	CC**	NADLER et al., Prediction of blood volume in normal human adults. Surgery. 1962 Feb;51(2):224-32.	
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Jonathan C. Lovely	(617) 449-6556
Typed or printed name	Telephone number

Note: Each paper must have its own certificate of mailing or transmission, or this certificate must identify each submitted paper:

IDS (Citation) by Applicant (230 References) (6 pages)

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0468

Electronic Acknowledgement Receipt

EFS ID:	42238441
Application Number:	17205400
International Application Number:	
Confirmation Number:	4686
Title of Invention:	SYSTEM AND METHOD FOR COLLECTING PLASMA
First Named Inventor/Applicant Name:	Michael Ragusa
Customer Number:	86738
Filer:	Jonathan Lovely
Filer Authorized By:	
Attorney Docket Number:	130670-80104
Receipt Date:	22-MAR-2021
Filing Date:	
Time Stamp:	13:33:14
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	130670-80104_IDS_Transmittal_Letter.PDF	27092 b0ab9214737ab517b00c569c498105bc6e9c5b86	no	3

Warnings:

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0469

Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	130670-80104_IDS_SB08.PDF	93518 c06f59691db6661e97ce45abdd1308c414c5694f	no	7

Warnings:
Information:
This is not an USPTO supplied IDS fillable form

Total Files Size (in bytes):	120610

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: March 22, 2021
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-80104
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 17/205,400 | Confirmation No.: N/A

Filed: March 18, 2021 | Art Unit: 3781

For: SYSTEM AND METHOD FOR COLLECTING PLASMA | Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. §§ 1.56, 1.97, and 1.98, the attention of the United States Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of the above-identified application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed within three months of the U.S. filing date (37 C.F.R. § 1.97(b)(1)).

In accordance with 37 C.F.R. § 1.98(a)(2)(ii), Applicant has not submitted copies of U.S. patents and U.S. patent applications.

In accordance with 37 C.F.R. § 1.98(d)(1) and as noted by a double-asterisk next to the Cite No. on the attached PTO/SB/08, the cited references are not supplied because they were previously

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cited by or submitted to the Office in prior application numbers 16/931333 filed July 16, 2020, 15/793339 filed October 25, 2017, and 15/608183 filed May 30, 2017 and relied on in the above-identified application for an earlier effective filing date under 35 U.S.C. § 120.

The Examiner is advised that the following co-pending application contains subject matter that may be related to the present application:

U.S. Application	Filing Date	Publication No. / Patent No.	Status	Atty. Docket No.
15/608,183	May 30, 2017	10,758,652	Issued	130670-08002
16/866,078	May 4, 2020	2020-0261630	Allowed	130670-08005
17/205,374	March 18, 2021		Pending	130670-08006
15/793,339	October 25, 2017	10,792,416	Issued	130670-80102
16/931,333	July 16, 2020	2020-0345924	Allowed	130670-80103

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made. In accordance with 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in this Information Disclosure Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

It is submitted that the Information Disclosure Statement is in compliance with 37 C.F.R. § 1.98, and the Examiner is respectfully requested to consider the listed references.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0472

Applicant believes no fee is due with this response.

Dated: March 22, 2021

Respectfully submitted,

Electronic signature: /Jonathan C. Lovely, Reg. No. 60,821/
Jonathan C. Lovely
Registration No.: 60,821
MCCARTER & ENGLISH, LLP
265 Franklin Street
Boston, Massachusetts 02110
(617) 449-6556
(617) 607-9200 (Fax)
Attorney/Agent For Applicant

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0473

Doc Code: PA..
Document Description: Power of Attorney

PTO/AIA/82A (07-13)
Approved for use through 03/31/2021. OMB 0651-0035
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMITTAL FOR POWER OF ATTORNEY TO ONE OR MORE REGISTERED PRACTITIONERS

NOTE: This form is to be submitted with the Power of Attorney by Applicant form (PTO/AIA/82B) to identify the application to which the Power of Attorney is directed, in accordance with 37 CFR 1.5, unless the application number and filing date are identified in the Power of Attorney by Applicant form. If neither form PTO/AIA/82A nor form PTO/AIA82B identifies the application to which the Power of Attorney is directed, the Power of Attorney will not be recognized in the application.

Application Number	Not Yet Assigned
Filing Date	Concurrently Herewith
First Named Inventor	Michael Ragusa
Title	SYSTEM AND METHOD FOR COLLECTING PLASMA
Art Unit	N/A
Examiner Name	Not Yet Assigned
Attorney Docket Number	130670-80104

SIGNATURE of Applicant or Patent Practitioner

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date (Optional)	March 18, 2021
Name	Jonathan C. Lovely	Registration Number	60,821
Title (if Applicant is a juristic entity)			
Applicant Name (if Applicant is a juristic entity)			

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ *Total of 1 forms are submitted.

Doc Code: PA..
Document Description: Power of Attorney

PTO/AIA/82B (07-13)
Approved for use through 01/31/2018. OMB 0651-0035
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POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

☑ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above: 86738

OR

☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

Please recognize or change the correspondence address for the application identified in the attached transmittal letter or the boxes above to:

☑ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

☐ Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

Haemonetics Corporation

☐ Inventor or Joint Inventor (title not required below)

☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☑ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature	/John F. Perullo/	Date (Optional)	8/23/18
Name	John F. Perullo		
Title	Vice President, Associate General Counsel and Chief Intellectual Property Officer, Haemonetics Corporation		

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ Total of forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0475

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA

As the below named inventor, I hereby declare that:

This declaration is directed to:

- [ ] The attached application, or
- [x] United States application or PCT international application number 15/793,339 filed on 10/25/2017.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby state that I have reviewed and understand the contents of the above identified specification,

I acknowledge the duty to disclose all information known to me that is material to patentability in accordance with Title 37, Code of Federal Regulations § 1.56.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Michael Ragusa Date (Optional): Oct 25, 2018

Signature: Michael J. Ragusa

Note: An application data sheet (PTO/AIA/14 or equivalent), including naming the entire inventive entity, must accompany this form. Use an additional PTO/SB/AIA/01 form for each additional inventor.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0476

PTO/AIA/14 (02-18)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	130670-80104
	Application Number	
Title of Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Michael		Ragusa	

Residence Information (Select One) ● US Residency Non US Residency Active US Military Service

City	Hingham	State/Province	MA	Country of Residence	US

Mailing Address of Inventor:

Address 1	4 Willow Circle
Address 2	

City	Hingham	State/Province	MA
Postal Code	02043	**Country**	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

Customer Number	86738		
Email Address	docket@mccarter.com	Add Email	Remove Email

Application Information:

Title of the Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA		
Attorney Docket Number	130670-80104	**Small Entity Status Claimed**	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	5	**Suggested Figure for Publication (if any)**	

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0477

PTO/AIA/14 (02-18)
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	130670-80104
	Application Number	
Title of Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	● Customer Number	US Patent Practitioner	◯ Limited Recognition (37 CFR 11.9)
Customer Number	86738		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	16/931333	2020-07-16

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0478

PTO/AIA/14 (02-18)
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	130670-80104
	Application Number	
Title of Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA	

Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
16/931333	Continuation of	15/793339	2017-10-25	10792416	2020-10-06
Prior Application Status	Patented				Remove
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
15/793339	Continuation in part of	15/608183	2017-05-30	10758652	2020-09-01
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button.					Add

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove

Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button. Add

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0479

PTO/AIA/14 (02-18)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	130670-80104
	Application Number	
Title of Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA	

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0480

PTO/AIA/14 (02-18)
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	130670-80104
	Application Number	
Title of Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA	

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1 — Remove

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

Clear

● Assignee	Legal Representative under 35 U.S.C. 117	Joint Inventor
Person to whom the inventor is obligated to assign.	Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	Haemonetics Corporation		
Mailing Address Information For Applicant:			
Address 1	125 Summer Street		
Address 2			
City	Boston	**State/Province**	MA
Country	US	Postal Code	02110
Phone Number		Fax Number	
Email Address			

Additional Applicant Data may be generated within this form by selecting the Add button. Add

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Terumo v. Haemonetics - PGR2026-00006
Petitioner Terumo Exhibit 1014-0481

PTO/AIA/14 (02-18)
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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	130670-80104
	Application Number	
Title of Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA	

Assignee 1

Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

Remove

If the Assignee or Non-Applicant Assignee is an Organization check here. ☐

Prefix	**Given Name**	Middle Name	**Family Name**	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1			
Address 2			
City		**State/Province**	
Country i		Postal Code	
Phone Number		Fax Number	
Email Address			

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	Application Number	
Title of Invention	SYSTEM AND METHOD FOR COLLECTING PLASMA	

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SYSTEM AND METHOD FOR COLLECTING PLASMA

Priority

[0001] This application is a continuation of and claims priority from co-pending U.S. Application No. 16/931,333, entitled "System and Method for Collecting Plasma," filed July 16, 2020, attorney docket number 130670-80103, and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

[0002] U.S. Application No. 16/931,33, in turn, is a continuation of and claims priority from U.S. Application No. 15/793,339, entitled "System and Method for Collecting Plasma," filed October 25, 2017, now U.S. Patent No. 10,792,416, attorney docket number 130670-80102 (formerly 1611/C86), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

[0003] U.S. Application No. 15/793,339 is a continuation-in-part of and claims priority to U.S. Patent Application No. 15/608,183, entitled "System and Method for Collecting Plasma," filed May 30, 2017, now U.S. Patent No. 10,758,652, attorney docket number 130670-08002 (formerly 1611/C80), and naming Michael Ragusa as inventor, the disclosure of which is incorporated herein, in its entirety, by reference.

Technical Field

[0004] The present invention relates to systems and methods for blood apheresis, and more particularly system and methods for collecting a plasma product.

Background Art

[0005] Apheresis is a procedure in which individual blood components can be separated and collected from whole blood temporarily withdrawn from a subject. Typically, whole blood is withdrawn through a needle inserted into a vein of the subjects arm and into a cell separator, such as a centrifugal bowl. Once the whole blood is separated into its various components, one or more of the components (e.g., plasma) can be removed from the centrifugal bowl. The remaining components can be returned to the subject along with optional compensation fluid to make up for the volume of the removed component. The

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process of drawing and returning continues until the quantity of the desired component has been collected, at which point the process is stopped. A central feature of apheresis systems is that the processed but unwanted components are returned to the donor. Separated blood components may include, for example, a high density component such as red blood cells, an intermediate density component such as platelets or white blood cells, and a lower density component such as plasma.

[0006] Many jurisdictions have regulations regarding the amount of whole blood and/or blood components that can be removed from a donor. For example, the U.S. Food and Drug Administration ("the FDA") sets both an upper limit on the volume of plasma that may be collected (e.g., 800 ml for an adult weighing more than 175 pounds) as well as an upper limit on the total collection volume (e.g., 880 ml for an adult weighing more than 175 pounds). Prior art plasma collection systems are unable to determine the total volume of plasma that has been collected (e.g., because the product collected is a mixture of plasma and anticoagulant) and, therefore collect based on the total collection volume, even if the total volume of plasma that has been collected is below the limit prescribed by the FDA. Additionally, prior art collection systems do not tailor the amount of plasma collected to the individual (e.g., other than what weight group they fall into) and, therefore, the percentage of the patient's plasma that is collected varies widely from patient to patient (e.g., only 23% percent of the plasma is collected for some patients and 29% - or greater – of the plasma is collected for others).

Summary of the Invention

[0007] In accordance with some embodiments of the present invention, a method for collecting plasma includes determining the weight and hematocrit of a donor, and inserting a venous-access device into the donor. Once the venous access device is inserted, the method may withdraw whole blood from the donor through the venous-access device and a draw line that is connected to a blood component separation device. The method may then introduce anticoagulant into the withdrawn whole blood through an anticoagulant line and separate, using the blood component separation device, the withdrawn whole blood into a plasma component and at least a second blood component. Once separated, the plasma component

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may be collected from the blood component separation device and into a plasma collection container. During processing, the method may calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma collection container. The volume of pure plasma may be based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component. The method may continue the process (e.g., withdrawing whole blood, introducing anticoagulant into the whole blood, separating the blood, collecting the plasma, and calculating the percentage of anticoagulant and volume of pure plasma) until a target volume of pure plasma is collected within the plasma collection container.

[0008] In some embodiments, the method may determine a change in volume within an anticoagulant container, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant container. Additionally or alternatively, the method may determine a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump. The method may also determine a volume of anticoagulant within the blood component separation device, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the volume of anticoagulant within the blood component separation device.

[0009] In further embodiments, the method may monitor the volume and/or weight of the plasma component collected within the plasma collection container (e.g., using a weight sensor), and the calculated volume of pure plasma collected within the plasma collection device may be based, at least in part, on the monitored volume and/or weight of the collected plasma component. Additionally or alternatively, determining the hematocrit of the donor may include monitoring a volume of red blood cells collection within the blood separation device. In such embodiments, the determined hematocrit of the donor may be based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor.

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[0010] The target volume of pure plasma may be based, at least in part, on the weight of the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant that is added to the system during a priming step. After collecting at least a portion of the target volume of pure plasma, the method may return the second blood component to the donor through a return line.

[0011] In accordance with additional embodiments, a system for collecting plasma includes a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and a blood component separation device for separating the drawn blood into a plasma component and a second blood component. The blood component separation device has an outlet and is configured to send the plasma component to a plasma container. The system may also include a blood draw line fluidly connected to the venous-access device and an anticoagulant line connected to an anticoagulant source. The blood draw line transports drawn whole blood to the blood component separation device, and the flow through the blood draw line may be controlled by a blood draw pump. The anticoagulant line may introduce anticoagulant into the drawn whole blood.

[0012] Additionally, the system may include a controller that controls the operation of the centrifuge bowl. The controller may also calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma container. The volume of pure plasma may be based, at least in part, upon the percentage of anticoagulant in the collected plasma component. The controller may stop the blood draw pump when a target volume of pure plasma (e.g., based, at least in part, on the weight of the donor) is collected within the plasma container. In some embodiments, the percentage of anticoagulant in the collected plasma component may be based, at least in part, on the volume of anticoagulant added to the drawn whole blood and the subject's hematocrit.

[0013] The system may also include an anticoagulant source weight sensor that measures the weight of the anticoagulant source. The controller may monitor the change in volume within the anticoagulant container based on the measured weight of the anticoagulant source, and the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant source. Additionally or

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alternatively, the controller may monitor the number of rotations of an anticoagulant pump to determine a volume of anticoagulant introduced into the whole blood. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump.

[0014] In some embodiments, the system may include an optical sensor located on the blood component separation device. The optical sensor may monitor the contents of the blood component separation device and determine if a volume of anticoagulant remains within the blood component separation device. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the volume of anticoagulant within the blood component separation device.

[0015] In additional embodiments, the system may also include a plasma container weight sensor that monitors a volume and/or weight of the plasma component collected within the plasma collection container. The calculated volume of pure plasma collected within the plasma collection container may be based, at least in part, on the monitored volume and/or weight of collected plasma component. The system may also have an optical sensor located on the blood component separation device. The optical sensor may monitor the volume of red blood cells collected within the blood separation device. The controller may then determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added to the system during a priming step.

[0016] In accordance with additional embodiments, a method for collecting plasma determines the weight, height, and hematocrit of a donor, and calculates a donor plasma volume based, at least in part, on the weight, height and hematocrit of the donor. The method then calculates a target plasma collection volume based, at least in part, on the calculated donor plasma volume and a target percentage of plasma (e.g., between 26.5 and 29.5 percent of the donor's plasma volume), and withdraws whole blood from the donor through the venous-access device and a first line that is connected to a blood component separation

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device. As the whole blood is withdrawn, the method may introduce anticoagulant into the withdrawn whole blood through an anticoagulant line.

[0017] The blood component separation device separates the withdrawn whole blood into a plasma component and at least a second blood component, and the method may collect the plasma component from the blood component separation device and into a plasma collection container. During processing, the method may calculate a volume of pure plasma collected within the plasma collection container. The method continues the withdrawing, introduction of anticoagulant, separating, collecting, and calculating steps until the volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

[0018] In some embodiments, after collecting at least a portion of the target plasma collection volume, the method may return the contents of the blood component separation device to the donor through the first line. Additionally or alternatively, the method may calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and the volume of the contents of the blood component separation device that are returned to the donor. The method may also return a volume of saline to the donor to obtain a target intravascular deficit. The target intravascular deficit may be between -250 and 500 milliliters (e.g., it may be 0 milliliters or 250 milliliters).The donor plasma volume may be calculated based, at least in part, on the donor's body mass index that, in turn, is calculated based on the donor's weight and height.

[0019] In further embodiments, the method may include calculating a percentage of anticoagulant in the collected plasma component. In such embodiments, the volume of pure plasma may be based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on a change in volume within the anticoagulant container, the number of rotations of the anticoagulant pump, and/or the volume of anticoagulant within the blood component separation device. The method may determine the change in volume within the anticoagulant container, the volume of anticoagulant introduced into the whole blood, and/or the volume of anticoagulant within the blood component separation device. The percentage of anticoagulant in the collected plasma component may

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include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

[0020] In some embodiments, the method may include monitoring a volume or and/or weight of the plasma component collected within the plasma collection container. In such embodiments, the calculated volume of pure plasma collected within the plasma collection device may be based, at least in part, on the monitored volume and/or weight of collected plasma component. To determine the donor's hematocrit, the method may monitor the volume of red blood cells collected within the blood separation device. The hematocrit of the donor may be based, at least in part, on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor.

[0021] In accordance with still further embodiments, a system for collecting plasma includes a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and a blood component separation device for separating the drawn blood into a plasma component and a second blood component. The blood component separation device may have an outlet and may send the plasma component to a plasma container. The system may also have a first line and an anticoagulant line. The first line may be fluidly connected to the venous-access device and may (1) transport drawn whole blood to the blood component separation device and (2) return fluid within the blood component separation device to the subject. The flow through the first line may be controlled by a first pump. The anticoagulant line may be connected to an anticoagulant source and may introduce anticoagulant into the drawn whole blood.

[0022] The system may also include a controller that controls the operation of the centrifuge bowl and the first pump. The controller may calculate (1) a donor plasma volume, (2) a target plasma collection volume, and (3) a volume of pure plasma collected within the plasma container. The donor plasma volume may be based, at least in part, on a weight and height of the donor and a hematocrit of the donor. The target plasma collection volume may be based, at least in part, on the calculated donor plasma volume and a target percentage of plasma. The volume of pure plasma collected within the plasma container may be based, at least in part, upon a percentage of anticoagulant in the collected plasma component. The

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controller may stop the first pump when the calculated volume of pure plasma collected within the plasma collection container equals the target plasma collection volume.

[0023] In further embodiments, the controller may return, after collecting at least a portion of the target plasma collection volume, fluid remaining within the blood component separation device via the first line. Additionally or alternatively, the controller may calculate an intravascular deficit based, at least in part on, the volume of pure plasma collected and the volume of the contents of the blood component separation device returned to the donor. The system may also include a saline line that fluidly connects to a saline source and the blood component separation device. The controller may return a volume of saline to the donor to obtain a target intravascular deficit (e.g., between -250 and 500 milliliters).

[0024] The controller may calculate the donor's body mass index based, at least in part, on the weight and height of the donor. The donor plasma volume may, in turn, be calculated based, at least in part, on the donor's body mass index. The target percentage of plasma may be between 26.5 and 29.5 percent (e.g., 28.5 percent) of the donor's plasma volume.

[0025] In additional embodiments, the controller may calculate the percentage of anticoagulant in the collected plasma component, for example, based on the volume of anticoagulant added to the drawn whole blood, and the subject's hematocrit. The system may also include an anticoagulant source weight sensor that measures the weight of the anticoagulant source. The controller may then monitor a change in volume within the anticoagulant container based on the measured weight of the anticoagulant source. The calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the change in volume within the anticoagulant source. Additionally or alternatively the controller may monitor a number of rotations of the anticoagulant pump to determine the volume of anticoagulant introduced into the whole blood. In such embodiments, the calculated percentage of anticoagulant in the collected plasma may be based, at least in part, on the number of rotations of the anticoagulant pump.

[0026] The system may also include an optical sensor and/or a plasma container weight sensor. The optical sensor may be located on the blood component separation device and may monitor the contents of the blood component separation device to determine if a

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volume of anticoagulant remains within the blood component separation device. The calculated percentage of anticoagulant in the collected plasma may then be based, at least in part, on the volume of anticoagulant within the blood component separation device. The plasma container weight sensor may monitor a volume and/or weight of the plasma component collected within the plasma container. The calculated volume of pure plasma collected within the plasma collection device may then be based, at least in part, on the monitored volume and/or weight of collected plasma component. The optical sensor may also monitor the volume of red blood cells collected within the blood separation device, and the controller may determine the subject's hematocrit based, at least in part, upon on the monitored volume of red blood cells collected within the blood separation device and the volume of whole blood withdrawn from the donor. The percentage of anticoagulant in the collected plasma component may include at least a portion of the anticoagulant introduced into the withdrawn blood and at least a portion of a volume of anticoagulant added during a priming step.

Brief Description of the Drawings

[0027] The foregoing features of the invention will be more readily understood by reference to the following detailed description, taken with reference to the accompanying drawings, in which:

[0028] Fig. 1 schematically shows a perspective view of a blood processing system in accordance with some embodiments of the present invention.

[0029] Fig. 2 schematically shows a top view of the blood processing system of Figure 1, in accordance with some embodiments of the present invention;

[0030] Fig. 3 schematically shows a disposable set installed within the blood processing system of Figure 1, in accordance with some embodiments of the present invention.

[0031] Fig. 4 is a flowchart depicting a method of collecting plasma, in accordance with embodiments of the present invention.

[0032] Fig. 5 is a flowchart depicting an alternative method of collecting plasma, in accordance with further embodiments of the present invention.

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Detailed Description of Specific Embodiments

[0033] Illustrative embodiments of the present invention provide blood processing systems and methods for collecting a target volume of pure plasma. The system and method calculate a percentage of anticoagulant collected within a plasma collection container (e.g., in addition to the plasma that is collected within the container) based on the amount of anticoagulant added to the system and the hematocrit of the donor. The system/method may then calculate the volume of pure plasma (e.g., plasma without anticoagulant) that has been collected within the container. Further embodiments may tailor the volume of plasma collected based on the donor's plasma volume and a target percentage of plasma to collect. Details of the illustrative embodiments are discussed below.

[0034] As shown in Figures 1 and 2, the blood processing system 100 includes a cabinet 110 that houses the main components of the system 100 (e.g., the non-disposable components). Within the cabinet 110, the system 100 may include a first/blood pump 232 that draws whole blood from a subject, and a second/anticoagulant pump 234 that pumps anticoagulant through the system 100 and into the drawn whole blood. Additionally, the system 100 may include a number of valves that may be opened and/or closed to control the fluid flow through the system 100. For example, the system 100 may include a donor valve 120 that may open and close to selectively prevent and allow fluid flow through a donor line 218 (e.g., an inlet line; Fig. 3), and a plasma valve 130 that selectively prevents and allows fluid flow through an outlet/plasma line 222 (Fig. 3). Some embodiments may also include a saline valve 135 that selectively prevents and allows saline to flow through a saline line 223.

[0035] To facilitate the connection and installation of a disposable set and to support the corresponding fluid containers, the system 100 may include an anticoagulant pole 150 on which the anticoagulant solution container 210 (Fig. 3) may be hung, and a saline pole 160 on which a saline solution container 217 (Fig. 3) may be hung (e.g., if the procedure being performed requires the use of saline). Additionally, in some applications, it may be necessary and/or desirable to filter the whole blood drawn from the subject for processing. To that end, the system 100 may include blood filter holder 170 in which the blood filter (located on the disposable set) may be placed.

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[0036] As discussed in greater detail below, apheresis systems 100 in accordance with embodiments of the present invention withdraw whole blood from a subject through a venous access device 206 (Fig. 3) using the blood pump 232. As the system 100 withdraws the whole blood from the subject, the whole blood enters a blood component separation device 214, such as a Latham type centrifuge (other type of separation chambers and devices may be used, such as, without limitation, an integral blow-molded centrifuge bowl, as described in U.S. Patent Nos. 4,983,158 and 4,943,273, which are hereby incorporated by reference). The blood component separation device 214 separates the whole blood into its constituent components (e.g., red blood cells, white blood cell, plasma, and platelets). Accordingly, to facilitate operation of the separation device 214, the system 100 may also include a well 180 in which the separation device 214 may be placed and in which the separation device 214 rotates (e.g., to generate the centrifugal forces required to separate the whole blood).

[0037] To allow the user/technician to monitor the system operation and control/set the various parameters of the procedure, the system 100 may include a user interface 190 (e.g., a touch screen device) that displays the operation parameters, any alarm messages, and buttons which the user/technician may depress to control the various parameters. Additional components of the blood processing system 100 are discussed in greater detail below (e.g., in relation to the system operation).

[0038] FIG. 3 is a schematic block diagram of the blood processing system 100 and a disposable collection set 200 (with an inlet disposable set 200A and an outlet disposable set 200B) that may be loaded onto/into the blood processing system 100, in accordance with the present invention. The collection set 200 includes a venous access device 206 (e.g., a phlebotomy needle) for withdrawing blood from a donor's arm 208, a container of anti-coagulant 210, a centrifugation bowl 214 (e.g., a blood component separation device), a saline container 217, and a final plasma collection bag 216. The blood/inlet line 218 couples the venous access device 206 to an inlet port 220 of the bowl 214, the plasma/outlet line 222 couples an outlet port 224 of the bowl 214 to the plasma collection bag 216, and a saline line 223 connects the outlet port 224 of the bowl 214 to the saline container 217. An anticoagulant line 225 connects the anti-coagulant container 210 to the inlet line 218. In

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addition to the components mentioned above and as shown in Figure 3, the blood processing system 100 includes a controller 226, a motor 228, and a centrifuge chuck 230. The controller 226 is operably coupled to the two pumps 232 and 234, and to the motor 228, which, in turn, drives the chuck 230. The controller 226 may be operably coupled to and in communication with the user interface 190.

[0039] In operation, the disposable collection set 200 (e.g., the inlet disposable set 200A and the outlet disposable set 200B) may be loaded onto/into the blood processing system 100 prior to blood processing. In particular, the blood/inlet line 218 is routed through the blood/first pump 232 and the anticoagulant line 225 from the anti-coagulant container 210 is routed through the anticoagulant/second pump 234. The centrifugation bowl 214 may then be securely loaded into the chuck 230. Once the bowl 214 is secured in place, the technician may install the outlet disposable set 200B. For example the technician may connect a bowl connector 300 to the outlet 224 of the bowl 214, install the plasma container 216 into the weight senor 195, run the saline line 223 through valve 135, and run the plasma/outlet line 222 through valve 130 and the line sensor 185. Once the disposable set 200 is installed and the anticoagulant and saline containers 210/217 are connected, the system 100 is ready to begin blood processing.

[0040] Figure 4 is a flowchart depicting an exemplary method of collecting plasma in accordance with various embodiments of the present invention. Prior to connecting the donor to the blood processing device 100, it is beneficial (and perhaps necessary in some instances) to obtain/determine some information regarding the donor, namely, the donor's weight (Step 410) and hematocrit (Step 415). Not only does this information help determine if the individual is a viable donor and the volumes of blood components that may be withdrawn/collected (e.g., per the FDA guidelines), the hematocrit may be used during processing to help collect a target volume of plasma. The technician may obtain/determine the donor's weight by weighing the donor (e.g., on a scale). To obtain/determine the donor's hematocrit, the technician may draw a blood sample from the donor and test the sample of blood. Additionally or alternatively, as discussed in greater detail below, the system may determine the hematocrit during blood processing. For example, the blood processing device 100 may include a hematocrit sensor (not shown) that determines the hematocrit of the blood

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flowing into the blood processing device 100 and/or the system 100 may determine the hematocrit based on a volume of red blood cells collected within the bowl 214.

[0041] Once the lines 222/223 are in place and the technician has determined the donor's weight and/or hematocrit (if needed), the user/technician may insert the venous access device 206 into the donor's arm 208 (Step 420). Next, the controller 226 activates the two pumps 232, 234 and the motor 228. Operation of the two pumps 232, 234 causes whole blood to be drawn from the donor (step 425), anticoagulant from container 210 to be introduced into the drawn whole blood (step 430), and the now anticoagulated whole blood to be delivered to the inlet port 220 of the bowl 214.

[0042] It should be noted that the anticoagulant line 225 may also include a bacteria filter (not shown) that prevents any bacteria in the anticoagulant source 210, the anticoagulant, or the anticoagulant line 225 from entering the system 100 and/or the subject. Additionally, the anticoagulant line 225 may include an air detector 140 that detects the presence of air within the anticoagulant. The presence of air bubbles within any of the system 100 lines can be problematic for the operation the system 100 and may also be harmful to the subject if the air bubbles enter the blood stream. Therefore, the air detector may be connected to an interlock that stops the flow within the anticoagulant line 225 in the event that an air bubble is detected (e.g., by stopping the anticoagulant pump 234), thereby preventing the air bubbles from entering the subject.

[0043] As the anti-coagulated whole blood is withdrawn from the subject and contained within the blood component separation device 214, the blood component separation device 214 separates the whole blood into several blood components (Step 435). For example, the blood component separation device 214 may separate the whole blood into a first, second, third, and, perhaps, fourth blood component. More specifically, the blood component separation device 214 (and the centrifugal forces created by rotation of the separation device 214) can separate the whole blood into plasma, platelets, red blood cells ("RBC"), and, perhaps, white blood cells ("WBC"). The higher density component, i.e., RBC, is forced to the outer wall of the bowl 214 while the lower density plasma lies nearer the core. A buffy coat is formed between the plasma and the RBC. The buffy coat is made up of an inner layer of platelets, a transitional layer of platelets and WBC and an outer layer

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of WBC. The plasma is the component closest to the outlet port and is the first fluid component displaced from the bowl 214 via the outlet port 224 as additional anticoagulated whole blood enters the bowl 214 through the inlet port 220.

[0044] As shown in Figure 3, the system 100 may also include an optical sensor 213 that may be applied to a shoulder portion of the bowl 214. The optical sensor monitors each layer of the blood components as they gradually and coaxially advance toward the core from the outer wall of the bowl 214. The optical sensor 213 may be mounted in a position (e.g., within the well 180) at which it can detect the buffy coat and/or the red blood cells reaching a particular radius, and the steps of drawing the whole blood from the subject/donor and introducing the whole blood into the bowl 12 may be altered and/or terminated in response to the detection.

[0045] Additionally, in some embodiments, the optical sensor 213 may be used to determine the hematocrit of the donor during processing. For example, as the bowl 214 fills with red blood cells and the optical sensor 213 detects the layer of red blood cells, the system 100 (e.g., the controller) can determine the volume of red blood cells within bowl 214 based on the location of the red blood cell layer and the fixed/known bowl volume. The system 100 may then calculate the donor hematocrit based on the volume of red blood cells within the bowl and the volume of whole blood that has been processed to that point.

[0046] Once the blood component separation device 214 has separated the blood into the various components, one or more of the components can be removed from the blood component separation device 214. For instance, the plasma may be removed to a plasma container 216 (e.g., a plasma bottle) through line 222 (Step 440). As noted above, some embodiments of the system 100 may include a weight sensor 195 (Fig. 1) that measures the amount of plasma collected. The plasma collection process may continue until a target volume of pure plasma (discussed in greater detail below) is collected within the plasma collection container 216. Although not shown, if the blood processing system 100 and/or the disposable set 200 include platelet, red blood cell, and/or white blood cell bags, each of the bags/containers may include similar weight sensors (e.g., load cells).

[0047] In some embodiments, the system 100 may also include a line sensor 185 (mentioned above) that can determine the type of fluid (e.g., plasma, platelets, red blood cells

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etc.) exiting the blood component separation device 214. In particular, the line sensor 185 consists of an LED which emits light through the blood components leaving the bowl 214 and a photo detector which receives the light after it passes through the components. The amount of light received by the photo detector is correlated to the density of the fluid passing through the line. For example, if plasma is exiting the bowl 214, the line sensor 185 will be able to detect when the plasma exiting the bowl 214 becomes cloudy with platelets (e.g., the fluid existing the bowl 214 is changing from plasma to platelets). The system 100 may then use this information to either stop the removal of blood components from the bowl 214, stop drawing whole blood from the subject, or redirect the flow by, for example, closing one valve an opening another.

[0048] It is important to note that during processing, the osmolarity of the red blood cells prevents the anticoagulant introduced into the whole blood from entering/remaining with the red blood cells (e.g., within the bowl 214). Rather, the anticoagulant mixes with the plasma component. Therefore, the anticoagulant exits the bowl 214 with the plasma and is collected within collection container 216 along with the plasma. In other words, the weight of the product measured by the weight senor 195 is the weight of the plasma, as well as any anticoagulant that is mixed with the plasma – the weight provided by the weight sensor 195 is not the weight of pure plasma.

[0049] Additionally, whole blood contains a variable amount of plasma, as determined by the donor's hematocrit. The hematocrit for typical donors can vary from 38% to 54%, which means that for 100 ml of whole blood, the volume of plasma can vary from 36 to 62 ml. Furthermore, the amount of anticoagulant added to the withdrawn whole blood is fixed (e.g., it does not depend on the hematocrit of the donor), meaning that the percentage of anticoagulant in the collected plasma may vary from 9.7% to 12.7% for donor hematocrits between 38% to 54%, respectively. Therefore, not only does the volume measured by the weight sensor 195 include the volume of anticoagulant, that volume of anticoagulant may vary from donor to donor based on the hematocrit.

[0050] As mentioned above, some embodiments of the present invention continue the blood processing/separation procedure until a target volume of pure plasma (e.g., plasma only – without the volume of any anticoagulant mixed with the plasma included in the target

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volume) is collected within the plasma collection container 216. To that end, some embodiments of the present invention may calculate the volume of pure plasma within the plasma collection container 216. For example, the technician or the system 100 (e.g., the controller) may calculate the percentage of anticoagulant within the collected plasma (Step 455) (e.g., the plasma contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor. The technician and/or system can calculate the percentage of anticoagulant according to the following equation, where AC is the amount of anticoagulant added to the system 100. As noted above, because the osmolarity of the red blood cells prevents the anticoagulant from mixing with it, essentially all of the anticoagulant exits the bowl 214 and is collected within the plasma collection container 216 along with the plasma.

$$\%\boldsymbol{AC} = \frac{\mathbf{1}}{\mathbf{1} + (\boldsymbol{AC} - \mathbf{1})(\mathbf{1} - \boldsymbol{Hct_D})}$$

[0051] The amount of anticoagulant that is added to the system 100 can be determined in a number of ways. For example, the system 100 can base the amount of anticoagulant (e.g., the value of "AC" in the above equation) on the predetermined ratio of anticoagulant per unit of anticoagulated whole blood. In some embodiments, the value of "AC" may be the inverse of the predetermined ratio (e.g., "AC" would be 16 if the ratio of anticoagulant to anticoagulated whole blood was 1:16). Additionally or alternatively, the technician/system 100 can monitor the volume of anticoagulant added to the system. In such embodiments, the technician/system can monitor the volume of anticoagulant added to the system 100 based on the number of rotations of the anticoagulant pump (e.g., each rotation of the anticoagulant pump introduces a set volume of anticoagulant into the system 100) and/or based on the change in weight of the anticoagulant container 210 as measured by a weight sensor (discussed in greater detail below).

[0052] Once the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 465). For example, the technician/system 100 may determine the volume of

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anticoagulant within the container (based on the percentage of anticoagulant within the container 216) and subtract this volume from the total volume of fluid within the container 216 as measured by the weight sensor 195. The system 100 may continue to monitor the volume of pure plasma collected within the container 216 and continue processing whole blood (e.g., continue performing Steps 425, 430, 435, 440, 455, 460 and 465) until a target volume of pure plasma is collected within the plasma collection container 216 (Step 470) (e.g., 800 mL for an adult donor weighing more than 175 pounds or other limit prescribed by the FDA or similar governing body).

[0053] Once the system 100 has collected the target volume of pure plasma within the plasma collection container 216, the system 100 can return the remaining components (e.g., the components remaining within the bowl 214) to the subject (Step 475). For example, when all the plasma has been removed and the bowl 214 is full of RBCs (and any other blood component not collected), the controller 226 stops the draw of whole blood from the subject and reverses the direction of the blood/first pump 232 to draw the RBCs (and other components) from the bowl 214 directly back to the subject. Alternatively, if the system 100 is so equipped, the system may return the components to the subject via a dedicated return line.

[0054] In addition to the non-collected blood components (e.g., the components remaining in the bowl 214), the system 100 may also return saline to the patient/subject. The saline may be used as a compensation fluid to make up for the volume of the blood component (e.g., plasma) that was removed and collected, and is not being returned to the patient. To that end, during the return step (e.g., Step 475), the saline valve 135 may be opened to allow saline from the saline container 217 to flow through the saline line 223 and into the bowl 214 (via outlet 224), where it can be returned to the patient/donor with or after the remaining blood components.

[0055] It should be noted that some embodiments may perform some additional and optional steps to help determine the volume of pure plasma within the plasma collection container 216. For example, as mentioned above, some embodiments may monitor the change in weight of the anticoagulant container 210 (e.g., as measured by a weight sensor/load cell on the anticoagulant container 210) (step 445). This measurement provides

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an indication of the volume of anticoagulant that has been added to the system 100, and may be used help determine the percentage of anticoagulant within the plasma collection container 216. Additionally or alternatively, some embodiments may similarly, monitor the change in weight and/or volume of the plasma and anticoagulant collected within the plasma collection container 216 (e.g., via weight sensor 195) (step 450). This measurement may be used to calculate of the total volume of pure plasma collected within the plasma collection container 216 (e.g., to obtain the total weight from which to subtract the calculated volume of anticoagulant).

[0056] Some embodiments may also (optionally) monitor the volume of anticoagulant remaining in the bowl 214 (step 460) (e.g., anticoagulant that did not mix with the plasma and/or otherwise remained in the bowl). For example, the system 100 may utilize the optical sensor on the bowl 214 to determine whether any anticoagulant remains within the bowl 214. If it does, the method 400/system 100 may modify the calculation of the amount of pure plasma collected within the plasma collection container (e.g., either increase the calculated amount or decreased the calculated amount), based on the volume of anticoagulant remaining within the bowl 214.

[0057] The various embodiment of the present invention described above provide numerous benefits over prior art plasma collection systems. In particular, as noted above, prior art plasmapheresis devices end plasma collection based on a total volume of anticoagulated plasma (e.g., pure plasma plus the added anticoagulant). Although this is the easiest method because it requires only that the product collection container be weighed, the amount of true product – the pure plasma – is dependent on the donor's hematocrit. In other words, prior art systems will collect more plasma from low hematocrit donors than from high hematocrit donors because of the variation of the percentage of anticoagulant in the product. Various embodiments of the present invention address the issues of prior art systems by collecting a standard volume (e.g., a target volume) of pure plasma from each donor. As noted above, embodiments of the present invention accomplish this by using knowledge of the donor's hematocrit and the amount of anticoagulant collected within the plasma collection container 216 (e.g., by counting pump rotations and/or using scale/weight sensors, etc.) to determine the percentage of anticoagulant in the product. Additionally, by stopping

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the plasma collection process based on a volume of pure plasma collected, embodiments of the present invention are able to collect a greater volume of plasma as compared to prior art systems that stop based on a plasma/anticoagulant mixture.

[0058] Figure 5 shows an alternative method for collecting plasma, using the system (or similar system) shown within Figures 1-3, that bases the total volume of plasma to collect on the individual donor (e.g., based on their height, weight, hematocrit, blood volume and/or plasma volume). In a manner similar to that described above for the method shown in Figure 4, prior to connecting the donor to the blood processing device 100, the system/method may obtain/determine some information regarding the donor, namely, the donor's weight and height (Step 505) and hematocrit (Step 510). For example, the technician may obtain/determine the donor's weight by weighing the donor (e.g., on a scale) and the donor's height by measuring the donor. To obtain/determine the donor's hematocrit (e.g., in a manner similar to that described above), the technician may test a blood sample or the system may determine the hematocrit during blood processing using a hematocrit sensor and/or based on the volume of red blood cells collected within the bowl 214.

[0059] Using the donor height and weight, and the hematocrit, the system 100/method 500 may calculate the donor's plasma volume (e.g., the volume of plasma within the donor's blood) (Step 515). For example, the system 100/method 500 may calculate the donor/subject's body mass index ("BMI") using the donor's height and weight (e.g., BMI = weight/height^2), and then the total blood volume within the donor/subject using the calculated BMI (e.g., see Lemmens et al., *Estimating Blood Volume in Obese and Morbidly Obese Patients*, Obesity Surgery, 2006:16, 773-776, the subject matter incorporated herein by reference). The total blood volume may be calculated using the following equation:

[0060] $$InBV = \frac{70}{\sqrt{BMIp/22}}$$

[0061] In the above equation, InBV is the indexed blood volume (e.g., the donor's total blood volume), BMIp is the patient's BMI (e.g., kg/ m^2), 22 is the BMI value (e.g., also in kg/m^2) for an ideal body weight (IBW), and 70 is the total blood volume (in mL/kg) for a donor at their ideal weight (BMI = 22 kg/ m^2). Once the system 100 has calculated the total

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blood volume within the donor/subject, the system 100 (e.g., the controller) may then determine/calculate the volume of plasma within the donor's blood (Step 515) based, for example, on the donor's hematocrit.

[0062] As mentioned above, the embodiment shown in Figure 5 bases the volume of plasma to collect on the individual donor. To that end, once the system 100/method 500 has determined the donor's plasma volume, the system 100/method 500 may then calculate the target volume of plasma to collect (Step 520). For example, the system 100/method 500 may multiply the total plasma volume within the patient by a target percentage of plasma to collect to obtain the target plasma volume to collect (e.g., if the total plasma volume is 2700 ml and the target percentage to collect is 28.5%, then the target plasma volume to collect is 769.5 ml). The target percentage of plasma to collect may depend on the application and/or the donor, and may be input directly into the system 100 (e.g., using the user interface 190) or may be preset from the factory. In some embodiments, the target percentage may be between 26.5 and 30%, and preferably may be 28.5%. However, in other embodiments, the target percentage may be below 26.5% or above 30%.

[0063] Once the lines 222/223 are in place and the system 100/method 500 has calculated the target plasma volume, the user/technician may insert the venous access device 206 into the donor's arm 208 (Step 525). Next, in a manner similar to that described above for the method shown in Figure 4, the controller 226 activates the two pumps 232, 234 and the motor 228. Operation of the two pumps 232, 234 causes whole blood to be drawn from the donor (step 530), anticoagulant from container 210 to be introduced into the drawn whole blood (step 535), and the now anticoagulated whole blood to be delivered to the inlet port 220 of the bowl 214.

[0064] As the anti-coagulated whole blood is withdrawn from the subject and introduced into the blood component separation device 214, the blood component separation device 214 separates the whole blood into the respective blood components (e.g., into plasma, platelets, RBC, and, perhaps, WBC) (Step 540). As discussed above, the higher density component, i.e., RBC, is forced to the outer wall of the bowl 214 and the plasma is the component closest to the outlet port and, therefore, is the first fluid component displaced from the bowl 214 via the outlet port 224 as additional anticoagulated whole blood enters the

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bowl 214 through the inlet port 220. During separation and processing, the optical sensor 213 monitors each layer of the blood components as they gradually and coaxially advance toward the core from the outer wall of the bowl 214, and the steps of drawing the whole blood from the subject/donor and introducing the whole blood into the bowl 12 may be altered and/or terminated in response to the detection. Additionally, as discussed above, the optical sensor 213 may be used to determine the hematocrit of the donor during processing (e.g., if it is not known and/or determined prior to the start of processing).

[0065] Once the blood component separation device 214 has separated the blood into the various components, the plasma may be removed to a plasma container 216 (e.g., a plasma bottle) through line 222 (Step 545). As noted above, some embodiments of the system 100 may include a weight sensor 195 (Fig. 1) that measures the amount of plasma collected. The plasma collection process may continue until the target plasma collection volume (discussed in greater detail below) is collected within the plasma collection container 216. If equipped with the line sensor 185, the system 100 may then use the information from the sensor 185 to either stop the removal of blood components from the bowl 214, stop drawing whole blood from the subject, or redirect the flow by, for example, closing one valve an opening another.

[0066] As mentioned above, some embodiments of the present invention continue the blood processing/separation procedure until a target plasma collection volume is collected. In order to ensure that this volume does not include the volume of any anticoagulant collected within the container 216, the target plasma collection volume should only include the volume of pure plasma (e.g., plasma only – without the volume of any anticoagulant mixed with the plasma included in the target volume). To that end and in a manner similar to that described above, some embodiments of the present invention may calculate the volume of pure plasma within the plasma collection container 216. To determine the volume of pure plasma, the technician or the system 100 (e.g., the controller) may calculate the percentage of anticoagulant within the collected plasma (Step 560) (e.g., the plasma contained within the plasma collection container 216) based on the amount of anticoagulant added/metered into the whole blood and the hematocrit of the donor (see equation provided above). The amount of anticoagulant that is added to the system 100 can be determined in any of the ways

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mentioned above (e.g., based on the predetermined ratio of anticoagulant per unit of anticoagulated whole blood, by monitoring the volume of anticoagulant added to the system, etc.).

[0067] Once the technician/system 100 has calculated the percentage of anticoagulant within the plasma collection container 216, the technician/system 100 may then use this information to calculate the volume of pure plasma within the plasma collection container 216 (Step 570). For example, as discussed above, the technician/system 100 may determine the volume of anticoagulant within the container (based on the percentage of anticoagulant within the container 216) and subtract this volume from the total volume of fluid within the container 216 as measured by the weight sensor 195. The system 100 may continue to monitor the volume of pure plasma collected within the container 216 and continue processing whole blood (e.g., continue performing Steps 530, 535, 540, 545, 560, 570 and, possibly, steps 550, 555 and 565) until the volume of pure plasma collected within the plasma collection container 216 reaches the target plasma volume (Step 575) (e.g., as calculated based on the individual plasma volume of the donor and the target percentage of plasma to collect).

[0068] Once the system 100 has collected the target plasma volume within the plasma collection container 216, the system 100 can return the remaining components (e.g., the components remaining within the bowl 214) to the subject (Step 580) by stopping the draw of whole blood from the subject and reversing the direction of the blood/first pump 232 to draw the RBCs (and other components) from the bowl 214 and back to the subject (e.g., directly via the blood/inlet line 218 or, if so equipped, via a dedicated return line.

[0069] It is important to note that, because the system 100/method 500 collect and do not return some of the blood components (e.g., the plasma), the volume of fluid that is returned to the donor/subject is less than the volume that was removed. This, in turn, creates an intravascular deficit that is equal to the amount of plasma collected (e.g., the volume of whole blood removed from the donor minus the volume of plasma collected/not returned). In instances in which the intravascular deficit is too large, the donor is at risk of fainting when the procedure is complete and they get up to leave the facility. To reduce the intravascular deficit (and the risk of donor injury), as noted above, some embodiments of the present

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invention return saline to the patient/subject (Step 585). The saline may be used as a compensation fluid to make up for the volume of the blood component (e.g., plasma) removed. To that end, during the return step (e.g., Step 580), the controller 226 (or the technician) may open the saline valve to allow saline from the saline container 217 to flow through the saline line 223 and into the bowl 214 (via outlet 224), where it can be returned to the patient/donor with or after the remaining blood components.

[0070] As mentioned above, the volume of plasma that is collected from the donor varies from donor to donor (e.g., because it is based on the donor's height, weight, hematocrit, and blood volume). Therefore, the volume of saline that is returned to the donor to reduce the intravascular deficit may similarly be dependent on the donor. To that end, when returning the contents of the separation device and the saline (Steps 580 and 585) to the donor, the system 100/method 500 may calculate the intravascular deficit (Step 590) based on the total volume of whole blood removed from the donor and the volume of blood components and saline that has been returned (or based on the volume of plasma collected and the volume of blood components and saline that have been returned). The system 100/method 500 may continue returning saline until the donor's intravascular deficit reaches a target intravascular deficit (Step 595).

[0071] The target intravascular deficit may be any intravascular deficit that reduces the donor's risk for fainting and may be the same for each donor. For example, the target intravascular deficit may be set to 0 mL or 250 mL for each donor. Alternatively, like the target plasma volume to collect, the target intravascular deficit may be different for each donor. In other words, the target intravascular deficit may be set to 0 mL for some donors and 250 mL for others. It should be noted that 0 and 250 mL are provided as examples only and other embodiments may have target intravascular deficits between 0 and 250, or greater than 250 mL. Additionally, in some instances, it may be beneficial to return more fluid to the donor than was removed/collected. In such instances, the target intravascular deficit may be set less than zero (e.g., -1 to -250 mL) so that the donor has more fluid/volume after the procedure than they did before the procedure.

[0072] Like the method 400 shown in Figure 4, the method 500 may similarly perform some additional and optional steps to help determine the volume of pure plasma

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within the plasma collection container 216. For example, some embodiments may monitor the change in weight of the anticoagulant container 210 (e.g., as measured by a weight sensor/load cell on the anticoagulant container 210) (step 550). This measurement provides an indication of the volume of anticoagulant that has been added to the system 100, and may be used help determine the percentage of anticoagulant within the plasma collection container 216. Additionally or alternatively, some embodiments may similarly, monitor the change in weight and/or volume of the plasma and anticoagulant collected within the plasma collection container 216 (e.g., via weight sensor 195) (step 555). This measurement may be used to calculate of the total volume of pure plasma collected within the plasma collection container 216 (e.g., to obtain the total weight from which to subtract the calculated volume of anticoagulant). Also, some embodiments may also monitor the volume of anticoagulant remaining in the bowl 214 (step 565) (e.g., anticoagulant that did not mix with the plasma and/or otherwise remained in the bowl) using the optical sensor on the bowl 214 to determine whether any anticoagulant remains within the bowl 214 and modify the calculation of the amount of pure plasma collected within the plasma collection container (e.g., either increase the calculated amount or decreased the calculated amount), based on the volume of anticoagulant remaining within the bowl 214.

[0073] As noted above, prior art systems that follow the current FDA nomogram for plasma collection collect a volume of plasma product (e.g., anticoagulant and plasma mixed together) based solely on the weight of the donor – the same volume is collected from every donor at the same weight. However, the total blood volume and plasma volume for two donors may vary greatly. For example, when comparing two donors in the same weight grouping according to the FDA nomogram – one obese and one not obese – the obese donor will effectively have a lower blood volume that the non-obese donor. Furthermore, with respect to the total plasma volume, donors with high hematocrit will have lower plasma volumes. In other words, because the total blood volume and total plasma volume vary from donor to donor (even among donors that weight the same), the percentage of the donor's plasma that is ultimately collected may vary widely from donor to donor. By tailoring the plasma collection to the donor (e.g., based on the donor's height, weight, BMI, hematocrit, total blood volume, and/or total plasma volume) and collecting a predetermined percent of

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plasma from each donor, embodiments of the preset invention are able to collect a greater volume of plasma (e.g., pure plasma) from some donors but less plasma from more vulnerable donors (e.g., smaller donors with high hematocrit, donors with lower plasma volume, etc.), as compared to systems that do not base the collection volume on the individual donor.

[0074] Similarly, current systems do not tailor the saline return volume to the patient (e.g., each donor at a given level receives the same volume of saline, for example, if the target plasma product volume is 800 mL, the donor will receive 500 mL of saline). However, because prior art systems collect based on the volume of the plasma product (which includes both plasma and anticoagulant) and the volume of pure plasma that is actually collected (and therefore, the volume removed from the donor) varies based on the donor hematocrit, the intravascular deficit for each donor will vary. In other words, the volume of saline returned to the donor may be sufficient for some, but insufficient for others. By tailoring the saline return to the individual donor, embodiments of the present invention are able to ensure that each donor has the same intravascular deficit (if any) once the procedure is complete. This, in turn, allows embodiments of the present invention to achieve isovolemia for each donor and greatly reduce any adverse reactions that the donor may experience (e.g., falling, fainting, light-headedness, vasovagal reactions, etc.).

[0075] It is also important to note that, although the various embodiments discussed above are in relation to a blood processing system that collects plasma, the features discussed herein may be applied to any type of blood processing system. For example, the features described herein may be implemented on blood processing systems that collect and/or process red blood cells, platelets and/or white blood cells.

[0076] The embodiments of the invention described above are intended to be merely exemplary; numerous variations and modifications will be apparent to those skilled in the art. All such variations and modifications are intended to be within the scope of the present invention as defined in any appended claims.

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What is claimed is:

1. A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight and hematocrit, to determine a target volume for plasma product and/or raw plasma, to control the system to operate a draw and return cycle to withdraw the whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor, to establish a current value of the hematocrit of the donor and a new target volume for plasma product and/or raw plasma, and to control the system to operate a subsequent draw and return cycle, whereby the donor's changing hematocrit is taken into account in calculating the new target volume for plasma product and/or raw plasma.

2. The system of claim 1, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma before a start of a first draw and return cycle.

3. The system of claim 2, wherein the controller is programmed to repeat draw and return phases until the target volume of plasma product and/or raw plasma is collected, wherein the

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target volume for plasma product and/or raw plasma is redetermined prior to the start of each draw phase.

4. The system of claim 3, wherein the controller is programmed to perform the draw and return phases at least three times.

5. The system of claim 1, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based on the donor's total blood volume and the donor's plasma volume.

6. The system of claim 1, wherein the controller is programmed to initiate a final return of the second blood component when (1) a measured volume of plasma product in the plasma collection container reaches the target volume for plasma product and/or (2) a volume of raw plasma in the plasma collection container reaches the target volume for raw plasma.

7. A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height, sex and

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hematocrit, to determine a target volume for plasma product and/or raw plasma based at least in part on the weight, height, sex and hematocrit, to control the system to operate draw and return phases to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

8. The system of claim 7, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separately from the plasma product.

9. The system of claim 8, wherein the controller is further programmed to account for anticoagulant introduced into the plasma collection container separate from the plasma product attributable to a priming or other pre-processing step.

10. A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the blood separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive at least a donor's weight, height and hematocrit and to determine a target volume for plasma product comprising raw plasma and

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anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on an anticoagulant ratio, the donor's weight, height and the donor's hematocrit, the controller programmed to then control the system to operate a plurality of draw and return cycles to withdraw whole blood from the donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

11. The system of claim 10, wherein the controller is programmed to determine the target volume for plasma product based on the donor's total blood volume and the donor's plasma volume.

12. The system of claim 11, wherein the controller is programmed to determine the donor's total blood volume based on multiple parameters selected from the group consisting of the weight, height, sex, age, and morphology of the donor.

13. The system of claim 10, wherein the controller is configured to receive the donor's weight and hematocrit electronically.

14. The system of claim 10, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until the plasma product in the plasma product collection container reaches the determined target volume.

15. The system of claim 10, wherein the controller is programmed to perform the draw and return cycles at least three times and the controller is programmed to determine a volume of whole blood to be drawn in a final draw phase which is different than a volume drawn in a prior draw phase.

16. A system for collecting plasma, comprising:

a venipuncture needle configured to draw whole blood from a donor;

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a blood separator configured to separate the whole blood into a plasma product and a second blood component comprising red blood cells, the blood separator having a plasma output port coupled to a plasma line configured to send the plasma product to a plasma product collection container;

a donor line fluidly coupled to the venipuncture needle configured to introduce the whole blood from the donor to the separator, flow through the donor line being controlled by a first pump;

an anticoagulant line coupled to an anticoagulant source, the anticoagulant line configured to combine anticoagulant with the whole blood from the donor, flow through the anticoagulant line being controlled by a second pump;

a touchscreen configured to receive input from an operator; and

a controller programmed to control operation of the system, the controller coupled to the touchscreen and programmed to receive donor parameters electronically, to determine a target volume for plasma product and/or raw plasma based at least in part on the donor parameters and to control the system to operate draw and return phases to withdraw whole blood from a donor and separate the whole blood into the plasma product and the second blood component and to return the second blood component to the donor.

17. The system of claim 16, wherein the controller is programmed to control the system to collect the plasma product in the plasma product collection container until a collected volume of plasma product reaches the target volume for plasma product and/or raw plasma.

18. The system of claim 16, further comprising a control system, wherein the control system is in electronic communication with the controller.

19. The system of claim 18, wherein the control system is programmed to calculate the target volume for plasma product and/or raw plasma and the controller is programmed to determine a target volume for plasma product and/or raw plasma by receiving the target volume for plasma product and/or raw plasma from the control system.

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20. The system of claim 16, wherein the controller determines the target volume for plasma product and/or raw plasma by calculating the target volume for plasma product and/or raw plasma and wherein the controller is local to and coupled to the blood separator.

21. The system of claim 16, wherein the donor parameters received electronically comprise a donor weight, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor weight.

22. The system of claim 21, wherein the donor parameters received electronically comprise a donor hematocrit, wherein the controller is programmed to determine the target volume for plasma product and/or raw plasma based at least in part on the donor hematocrit.

23. The system of claim 22, wherein the controller is programmed to determine a target volume for plasma product based on the donor's total blood volume and the donor's plasma volume.

24. The system of claim 23, wherein the controller is programmed to determine the donor's total blood volume based on the weight and height of the donor.

25. The system of claim 24, wherein the controller is programmed to determine the donor's total blood volume before whole blood is withdrawn from the donor during a donation.

26. The system of claim 25, wherein the controller is programmed to determine the target volume for plasma product comprising raw plasma and anticoagulant, wherein the target volume for plasma product is determined prior to withdrawing the whole blood from the donor based at least in part on an anticoagulant ratio, the donor's weight and the donor's hematocrit.

27. The system of claim 16, further comprising a reservoir separate from the blood separator for receiving concentrated red blood cells.

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Abstract

A method for collecting plasma includes determining the weight, height, and hematocrit of a donor, and calculating a donor plasma volume and a target plasma collection volume. The target plasma collection volume is based on the donor plasma volume and a target percentage of plasma. The method then withdraws blood from the donor through a line connected to a blood component separation device, and introduces anticoagulant into the withdrawn blood. The blood component separation device separates the blood into a plasma component and a second blood component, and the plasma component is collected from the blood component separation device and into a plasma collection container. The method may then calculate the volume of pure plasma collected within the plasma collection container, and continue processing/collecting until the calculated volume of pure plasma equals the target plasma collection volume.

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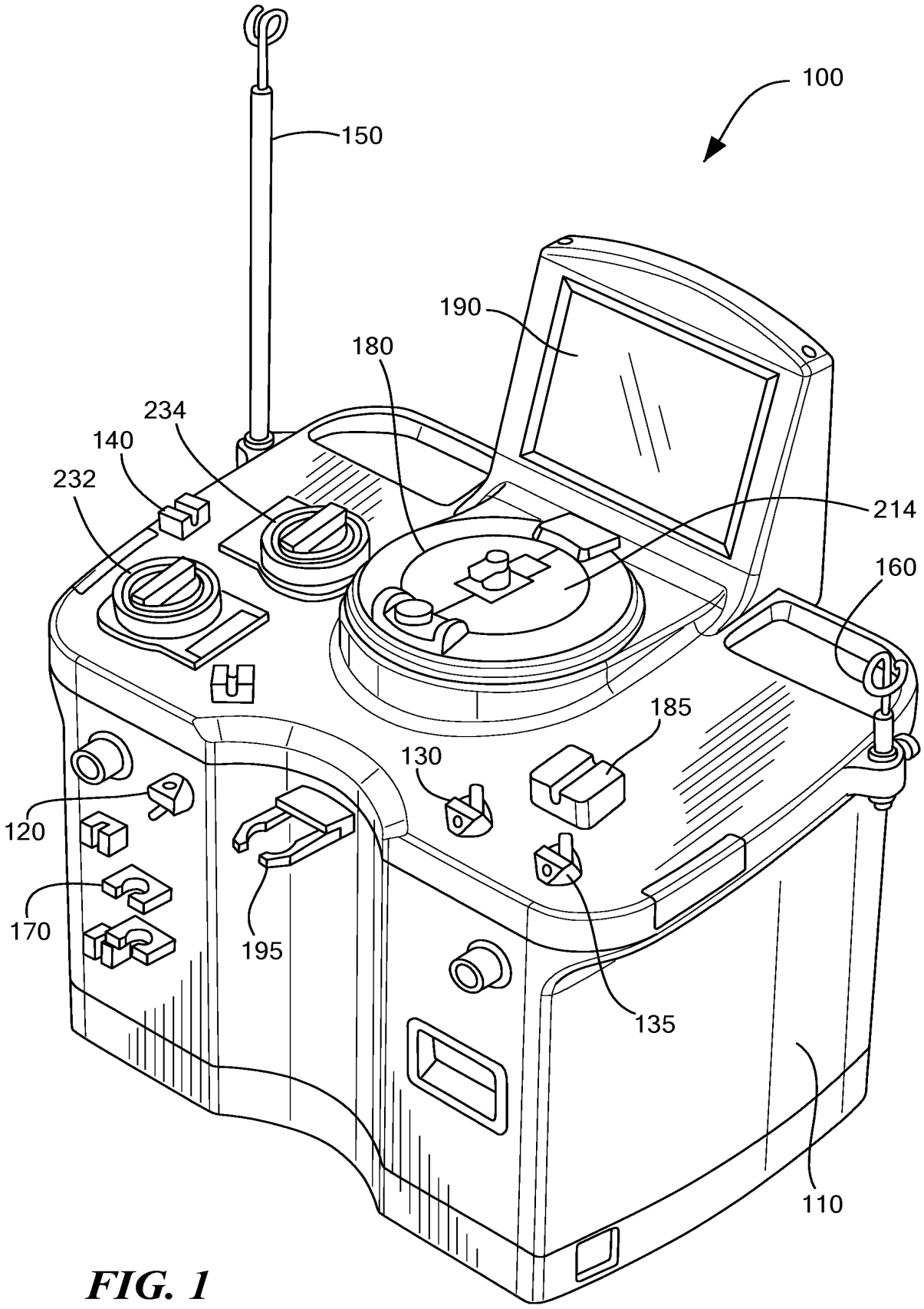

FIG. 1

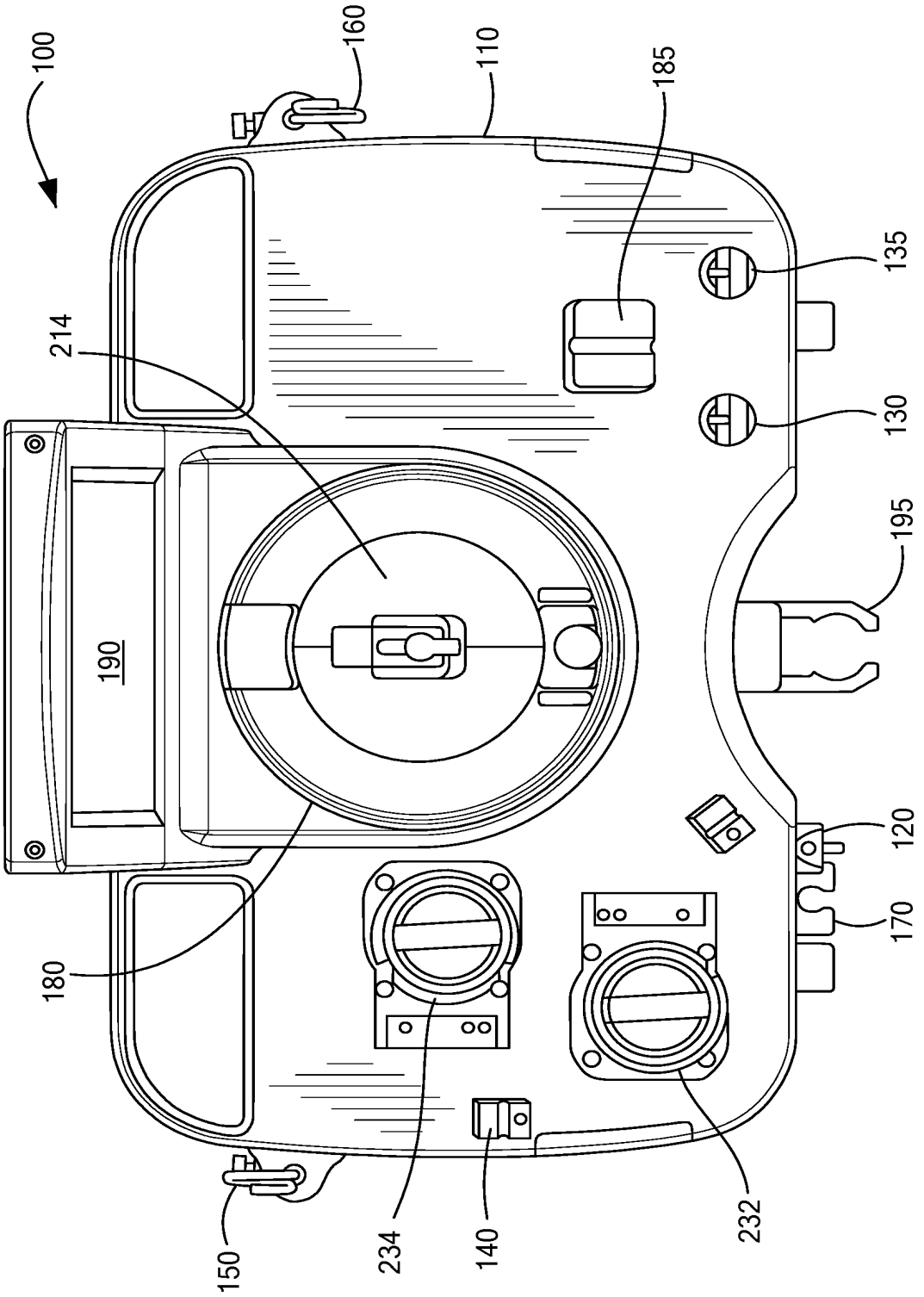

FIG. 2

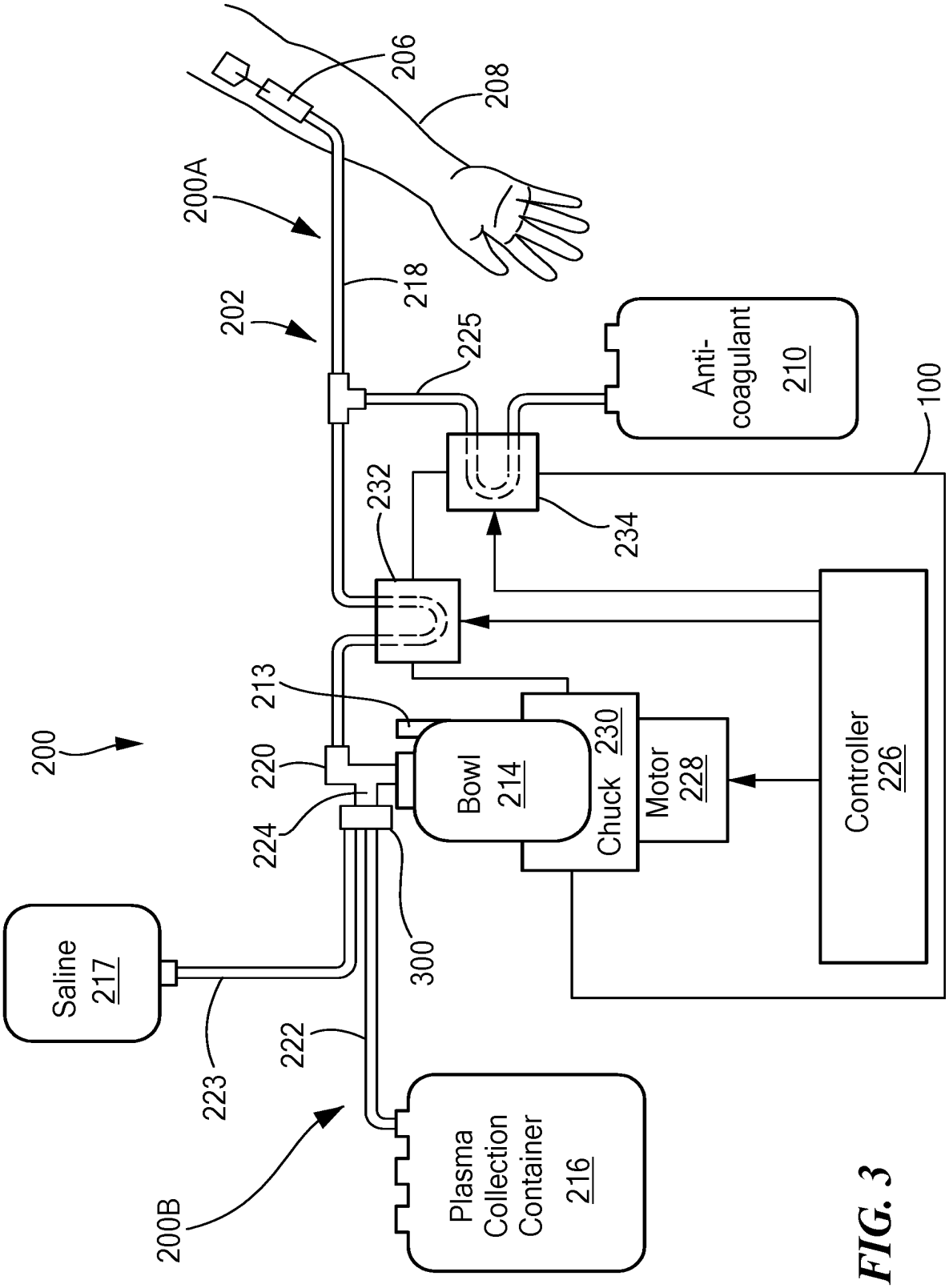
206
208
200A
218
202
225
Anti-coagulant 210
100
232
234
213
200
220
Bowl 214
Chuck 230
Motor 228
Controller 226
224
300
Saline 217
223
222
Plasma Collection Container 216
200B

FIG. 3

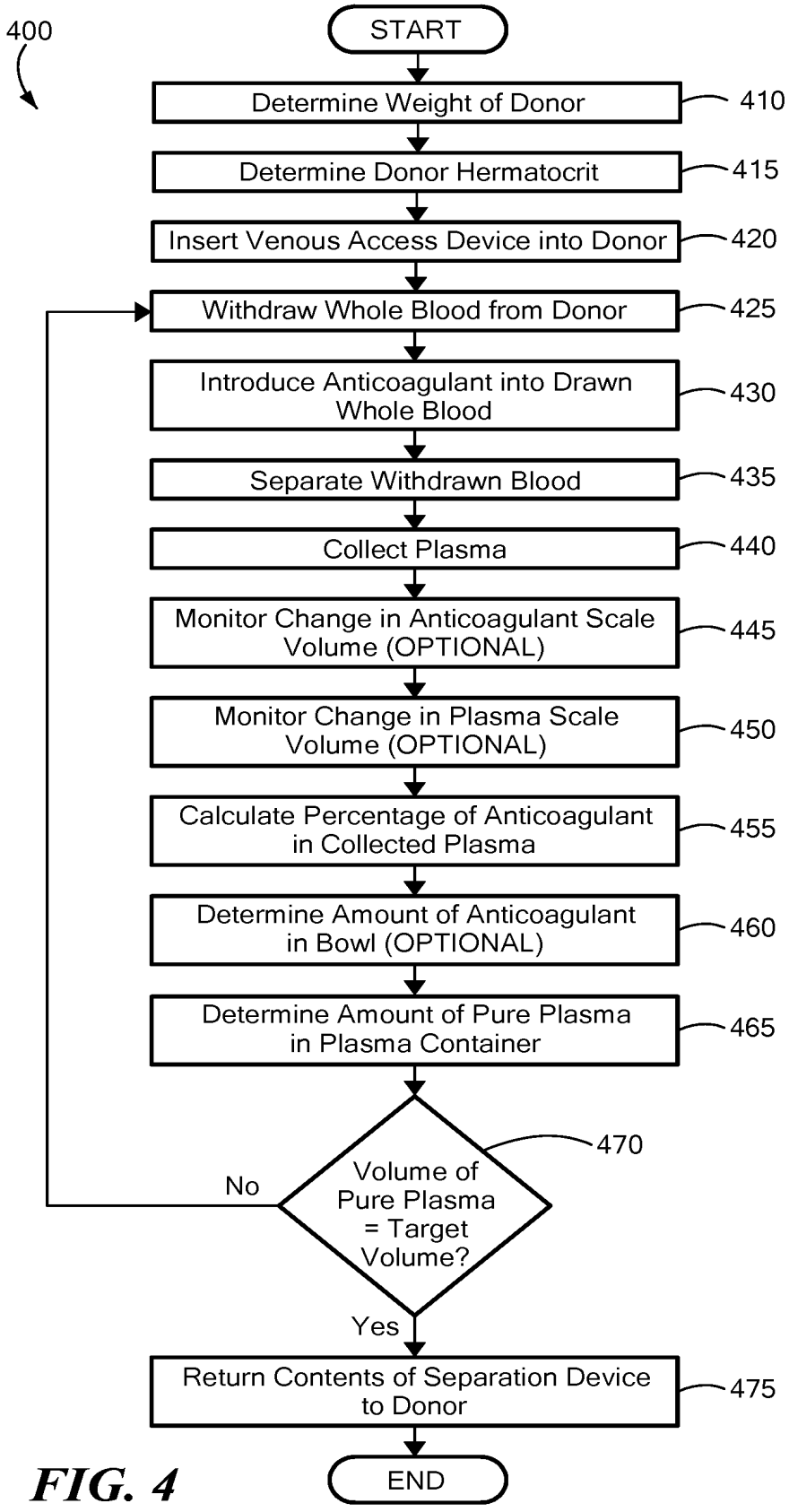
400
START
Determine Weight of Donor
410
Determine Donor Hermatocrit
415
Insert Venous Access Device into Donor
420
Withdraw Whole Blood from Donor
425
Introduce Anticoagulant into Drawn Whole Blood
430
Separate Withdrawn Blood
435
Collect Plasma
440
Monitor Change in Anticoagulant Scale Volume (OPTIONAL)
445
Monitor Change in Plasma Scale Volume (OPTIONAL)
450
Calculate Percentage of Anticoagulant in Collected Plasma
455
Determine Amount of Anticoagulant in Bowl (OPTIONAL)
460
Determine Amount of Pure Plasma in Plasma Container
465
Volume of Pure Plasma = Target Volume?
470
No
Yes
Return Contents of Separation Device to Donor
475
END

FIG. 4

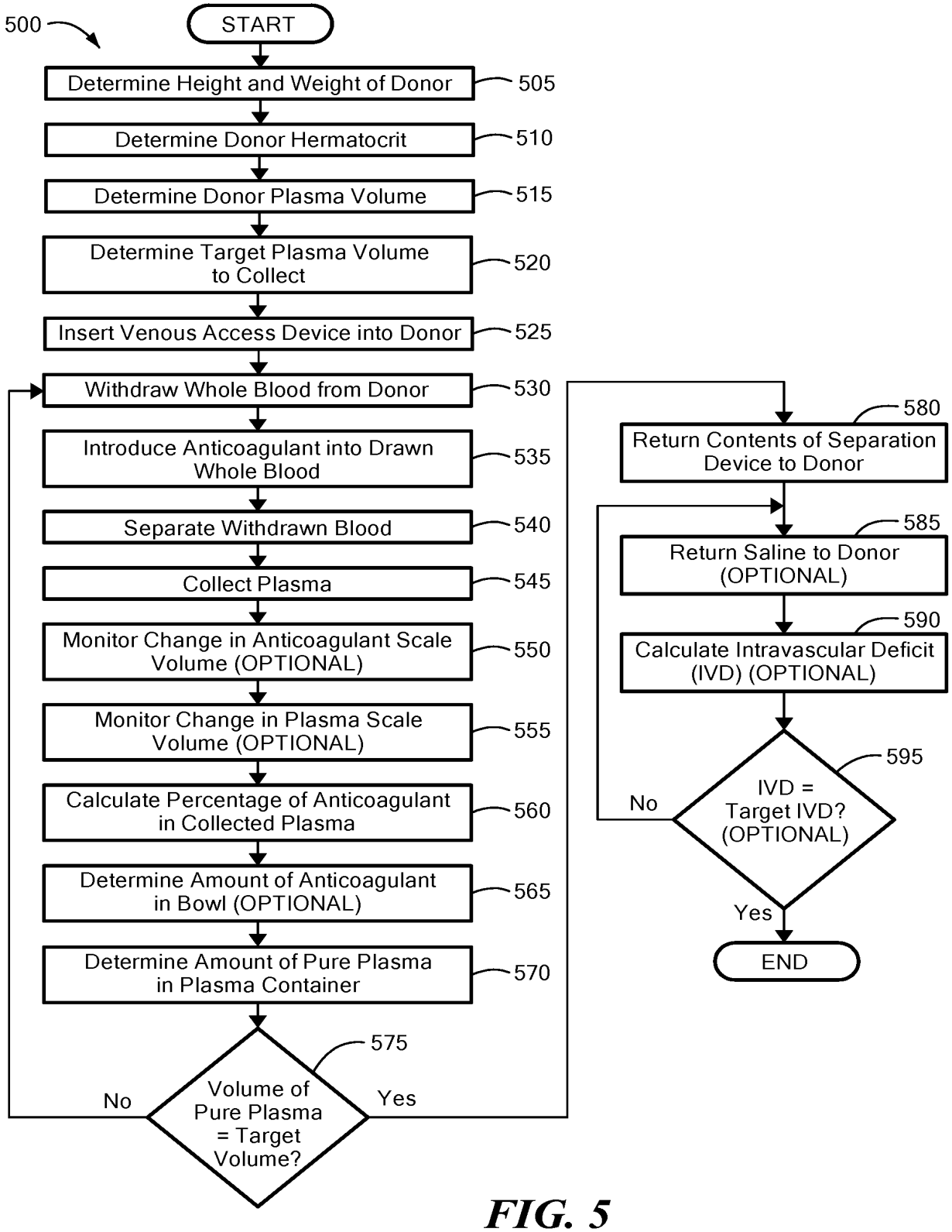
500
START
Determine Height and Weight of Donor
505
Determine Donor Hermatocrit
510
Determine Donor Plasma Volume
515
Determine Target Plasma Volume to Collect
520
Insert Venous Access Device into Donor
525
Withdraw Whole Blood from Donor
530
Introduce Anticoagulant into Drawn Whole Blood
535
Separate Withdrawn Blood
540
Collect Plasma
545
Monitor Change in Anticoagulant Scale Volume (OPTIONAL)
550
Monitor Change in Plasma Scale Volume (OPTIONAL)
555
Calculate Percentage of Anticoagulant in Collected Plasma
560
Determine Amount of Anticoagulant in Bowl (OPTIONAL)
565
Determine Amount of Pure Plasma in Plasma Container
570
575
Volume of Pure Plasma = Target Volume?
No
Yes
580
Return Contents of Separation Device to Donor
585
Return Saline to Donor (OPTIONAL)
590
Calculate Intravascular Deficit (IVD) (OPTIONAL)
595
IVD = Target IVD? (OPTIONAL)
No
Yes
END

FIG. 5

Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	SYSTEM AND METHOD FOR COLLECTING PLASMA
First Named Inventor/Applicant Name:	Michael Ragusa
Filer:	Jonathan Lovely/Tricia Troup
Attorney Docket Number:	130670-80104

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
UTILITY APPLICATION FILING	1011	1	320	320
UTILITY SEARCH FEE	1111	1	700	700
UTILITY EXAMINATION FEE	1311	1	800	800
Pages:				
Claims:				
CLAIMS IN EXCESS OF 20	1202	7	100	700
INDEPENDENT CLAIMS IN EXCESS OF 3	1201	1	480	480
Miscellaneous-Filing:				

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Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**3000**

Electronic Acknowledgement Receipt

EFS ID:	42217530
Application Number:	17205400
International Application Number:	
Confirmation Number:	4686
Title of Invention:	SYSTEM AND METHOD FOR COLLECTING PLASMA
First Named Inventor/Applicant Name:	Michael Ragusa
Customer Number:	86738
Filer:	Jonathan Lovely
Filer Authorized By:	
Attorney Docket Number:	130670-80104
Receipt Date:	18-MAR-2021
Filing Date:	
Time Stamp:	14:30:20
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	$3000
RAM confirmation Number	E20213HE30521724
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

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Petitioner Terumo Exhibit 1014-0524

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal of New Application	Utility_Patent_Application_Transmittal.pdf	31981 58b42fad3de4f1add55d1740029e81f9fea63dbf	no	1
Warnings:					
Information:					
2	Power of Attorney	Haemonetics_Corporation_GPOA.pdf	169121 09ee38ef68619178cdfdd9414ff838c961ad68ff	no	2
Warnings:					
The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing					
Information:					
3	Oath or Declaration filed	Executed_Declaration_-_Michael_Ragusa_15_793339.PDF	99922 f914d7ceee82b879229fe014d8c786c9b07b56bd	no	1
Warnings:					
Information:					
4	Application Data Sheet	130670-80104_-_Application_Data_Sheet_Fillable_PDF.pdf	1255635 ee615962ab710a7ee4ccda32d9d17e4e25bbcb6b	no	8
Warnings:					
Information:					
5		Application.pdf	118192 fbed5c8693772fec657a6ad04d5c72b586bbaaa5	yes	32

Multipart Description/PDF files in .zip description

Document Description	Start	End
Specification	1	25
Claims	26	31

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	Abstract		32	32	
Warnings:					
Information:					
6	Drawings-only black and white line drawings	Figures.PDF	140972 417f9009a2bdf6044427fd31c78e93c58890f348	no	5
Warnings:					
Information:					
7	Fee Worksheet (SB06)	fee-info.pdf	37802 35e5c61904466ae3e4b6468c8412f9a950a0e1db	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	1853625		

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/AIA/15 (10-17)
Approved for use through 11/30/2020. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	130670-80104
First Named Inventor	Michael Ragusa
Title	SYSTEM AND METHOD FOR COLLECTING PLASMA
Priority Mail Express® Label No.	

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

1. [ ] **Fee Transmittal Form** (PTO/SB/17 or equivalent)
2. [ ] **Applicant asserts small entity status.** See 37 CFR 1.27
3. [ ] **Applicant certifies micro entity status.** See 37 CFR 1.29. Applicant must attach form PTO/SB/15A or B or equivalent.
4. [X] **Specification** [*Total Pages* 32] Both the claims and abstract must start on a new page. *(See MPEP § 608.01(a) for information on the preferred arrangement)*
5. [X] **Drawing(s)** (35 U.S.C. 113) [*Total Sheets* 5]
6. **Inventor's Oath or Declaration** [*Total Pages* 1] *(including substitute statements under 37 CFR 1.64 and assignments serving as an oath or declaration under 37 CFR 1.63(e))*
   a. [ ] Newly executed (original or copy)
   b. [X] A copy from a prior application (37 CFR 1.63(d))
7. [X] **Application Data Sheet** ** See note below.* See 37 CFR 1.76 (PTO/AIA/14 or equivalent)
8. **CD-ROM or CD-R** in duplicate, large table, or Computer Program (*Appendix*)
   [ ] Landscape Table on CD
9. **Nucleotide and/or Amino Acid Sequence Submission** (*if applicable, items a. – c. are required*)
   a. [ ] Computer Readable Form (CRF)
   b. [ ] Specification Sequence Listing on:
      i. [ ] CD-ROM or CD-R (2 copies); or
      ii. [ ] Paper
   c. [ ] Statements verifying identity of above copies

ADDRESS TO: **Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450**

ACCOMPANYING APPLICATION PAPERS

10. [ ] **Assignment Papers** (cover sheet & document(s))
    Name of Assignee
11. [ ] **37 CFR 3.73(c) Statement** (*when there is an assignee*) [X] **Power of Attorney**
12. [ ] **English Translation Document** (*if applicable*)
13. [ ] **Information Disclosure Statement** (PTO/SB/08 or PTO-1449)
    [ ] Copies of citations attached
14. [ ] **Preliminary Amendment**
15. [ ] **Return Receipt Postcard** (*MPEP § 503*) (*Should be specifically itemized*)
16. [ ] **Certified Copy of Priority Document(s)** (*if foreign priority is claimed*)
17. [ ] **Nonpublication Request** Under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35 or equivalent.
18. [ ] **Other:**

***Note:** (1) Benefit claims under 37 CFR 1.78 and foreign priority claims under 1.55 **must** be included in an Application Data Sheet (ADS).
(2) For applications filed under 35 U.S.C. 111, the application must contain an ADS specifying the applicant if the applicant is an assignee, person to whom the inventor is under an obligation to assign, or person who otherwise shows sufficient proprietary interest in the matter. See 37 CFR 1.46(b).

19. CORRESPONDENCE ADDRESS

[X] The address associated with Customer Number: 86738 **OR** [ ] Correspondence address below

Name					
Address					
City		State		Zip Code	
Country		Telephone		Email	

Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date	March 18, 2021
Name (Print/Type)	Jonathan C. Lovely	Registration No. (Attorney/Agent)	60,821

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