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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/608,183	09/01/2020	10758652	130670-08002	7286

86738 7590 08/12/2020

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

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

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 539 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 Application Information Retrieval (PAIR) WEB site (<http://pair.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 Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional applicants):

Michael Ragusa, Hingham, MA;
Haemonetics Corporation, Braintree, 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.

IR103 (Rev. 10/09)

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.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	-4644/G88- 130670-08002
		Application Number	15/608,183
Title of Invention	System and Method for Collecting Plasma		
<p>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.</p> <p>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.</p>			

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.)
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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	US	Country of Residence	MA	
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	92404 86738		
Email Address	usptomail@sunsteinlaw.com	docket@mccarter.com	Add Email Remove Email

Application Information:

Title of the Invention	System and Method for Collecting Plasma		
Attorney Docket Number	1644/G88 130670-08002	Small Entity Status Claimed ☐	
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	4	Suggested Figure for Publication (if any)	

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	1611/C80— 130670-08002
		Application Number	15/608,183
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	32404 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		Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the Add button.			
			Add

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	1611/C80 130670-08002
		Application Number	15/608,183
Title of Invention	System and Method for Collecting Plasma		

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)¹ 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).

Application Number	Country ¹	Filing Date (YYYY-MM-DD)	Access Code ¹ (if applicable)	Remove

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.

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.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	-1611/C80-- 130670-08002
		Application Number	15/608,183
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.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	-1614/G80- 130670-08002
		Application Number	15/608,183
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

Mailing Address Information For Applicant:

Address 1	100 Wood Road 125 Summer Street		
Address 2			
City	Braintree Boston	State/Province	MA
Country	US	Postal Code	02484 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.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	-1611/C80 130670-08002
		Application Number	15/608,183
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.				
				<input type="button" value="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		Postal Code		
Phone Number		Fax Number		
Email Address				
Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button.				<input type="button" value="Add"/>

Signature:

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). However, if this Application Data Sheet is submitted with the **INITIAL** filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	Jonathan C. Lovely, #60,821/		Date (YYYY-MM-DD)	2020-08-11
First Name	Jonathan C.	Last Name	Lovely	Registration Number 60,821
Additional Signature may be generated within this form by selecting the Add button.				<input type="button" value="Add"/>

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.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	-1611/C80---
		Application Number	130670-08002
Title of Invention	System and Method for Collecting Plasma		

This collection of information is required by 37 CFR 1.76. 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 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet 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.**

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 records.
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.

Electronic Acknowledgement Receipt	
EFS ID:	40249126
Application Number:	15608183
International Application Number:	
Confirmation Number:	7286
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:	130670-08002
Receipt Date:	11-AUG-2020
Filing Date:	30-MAY-2017
Time Stamp:	13:29:21
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Corrected Filing Receipt	Request_to_Update_the_Address_of_the_Applicant_and_Request_for_Corrected_Filing_Receipt_.pdf	22456 9af6cb8e651c53970fb04dfc7ed5ea42f8be45db	no	2

Warnings:

Information:					
2	Application Data Sheet	Corrected_ADS_.PDF	842917	no	8
			bbccc2d1537afd5dfc207bef5db1788c0c9b c089		
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
3	Miscellaneous Incoming Letter	Marked_Filing_Receipt_.PDF	354253	no	3
			de831121728f950d548206e6998b25e821d 00b48		
Warnings:					
Information:					
Total Files Size (in bytes):			1219626		
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

In re Utility Application of:
Haemonetics Corporation

Application No.: 15/608,183

Confirmation No.: 7286

Filed: May 30, 2017

Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING
PLASMA

Examiner: Deak, Leslie R.

REQUEST TO UPDATE THE ADDRESS OF THE APPLICANT AND
REQUEST FOR CORRECTED FILING RECEIPT

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

Dear Sir:

The Applicant hereby requests that the Applicant's address be updated and made of record and a corrected Filing Receipt be issued in the above-identified U.S. Utility Patent Application. The Application Data Sheet filed on May 30, 2017 and the Official Filing Receipt dated June 8, 2017, a copy of which is attached hereto, has an error in the Applicant(s) section.

Please correct the **address of the Applicant, Haemonetics Corporation** to read: **125 Summer Street, Boston, MA 02110** instead of 400 Wood Road, Braintree, MA 02184.

Applicant additionally requests that all pertinent U.S. Patent and Trademark Office records relating to the subject application be changed to reflect this correction.

Concurrent with the filing of this request, the following documents are submitted herewith:

- A Corrected Application Data Sheet (CADS) to correct the address of the Applicant as shown by underlining the correct address and removing the incorrect address as shown by a strikethrough; and

- A marked copy of the Official Filing Receipt to correct the city of the Applicant as shown by underlining the correct city and removing the incorrect city as shown by a strikethrough.

The Applicant believes no fee is due with this request. However, if a fee is due, please charge our Deposit Account No. 50-4876, under Order No. 130670-08002 from which the undersigned is authorized to draw.

Dated: August 11, 2010

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



UNITED STATES PATENT AND TRADEMARK OFFICE

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United States Patent and Trademark Office
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P.O. Box 1450
Alexandria, Virginia 22313-1450
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APPLICATION NUMBER	FILING or 371 (c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO.	TOT CLAIMS	IND CLAIMS
15/608,183	05/30/2017	3761	1740	1611/C80	20	2

130670-08002

CONFIRMATION NO. 7286

FILING RECEIPT



CC000000091875350

Date Mailed: 06/08/2017

2101-

~~Sunstein-Kann-Murphy & Timbers LLP~~

~~125 SUMMER STREET~~

~~BOSTON, MA 02110-1618~~

~~86738~~

~~MCCARTER & ENGLISH, LLP BOSTON~~

~~265 Franklin Street~~

~~Boston, MA 02110~~

Receipt is acknowledged of this non-provisional 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 APPLICANT, 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 Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections 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**

Inventor(s)

Michael Ragusa, Hingham, MA;

Applicant(s)

Haemonetics Corporation, ~~Braintree, MA;~~ Boston, MA;

Power of Attorney: The patent practitioners associated with Customer Number ~~92101~~ 86738

Domestic Applications for which benefit is claimed - None.

A proper domestic benefit claim must be provided in an Application Data Sheet in order to constitute a claim for domestic benefit. See 37 CFR 1.76 and 1.78.

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.

If Required, Foreign Filing License Granted: 06/06/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/608,183**

Projected Publication Date: 12/06/2018

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>.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/608,183	05/30/2017	Michael Ragusa	130670-08002	7286
86738	7590	07/28/2020		
MCCARTER & ENGLISH, LLP BOSTON			EXAMINER	
265 Franklin Street			DEAK, LESLIE R	
Boston, MA 02110				
			ART UNIT	PAPER NUMBER
			3799	
			NOTIFICATION DATE	DELIVERY MODE
			07/28/2020	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

Response to Rule 312 Communication	Application No. 15/608,183	Applicant(s) Ragusa, Michael	
	Examiner LESLIE R DEAK	Art Unit 3799	AIA (FITF) Status Yes
<p align="center">-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --</p> <p>1. ☒ The amendment filed on <u>15 July 2020</u> under 37 CFR 1.312 has been considered, and has been:</p> <p>a) ☒ entered.</p> <p>b) ☐ entered as directed to matters of form not affecting the scope of the invention.</p> <p>c) ☐ disapproved because the amendment was filed after the payment of the issue fee. Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue.</p> <p>d) ☐ disapproved. See explanation below.</p> <p>e) ☐ entered in part. See explanation below.</p> <p>_____</p>			
/LESLIE R DEAK/ Primary Examiner, Art Unit 3799			

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Haemonetics Corporation

Application No.: 15/608,183

Confirmation No.: 7286

Filed: May 30, 2017

Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING
PLASMA

Examiner: L. R. Deak

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

OK to enter.
/LRD/
22 July 2020

AMENDMENT AFTER ALLOWANCE UNDER 37 C.F.R. § 1.312

Prior to issuance of the patent, Applicant respectfully requests entry of this amendment under 37 C.F.R. § 1.312 for the above-captured patent application.

Amendments to the Claims may be found on page 2.

Remarks may be found on page 7.

Document Description: Issue Fee Payment (PTO-85B)

Issue Fee Transmittal Form

Application Number	Filing Date	First Named Inventor	Atty. Docket No.	Confirmation No.
15608183	30-May-2017	Michael Ragusa	130670-08002	7286

TITLE OF INVENTION :

System and Method for Collecting Plasma

Entity Status	Application Type	Art Unit	Class - Subclass	EXAMINER
Regular Undiscounted	Utility under 35 USC 111(a)	3799	006040	LESLIE DEAK
Issue Fee Due	Publication Due	Total Fee(s) Due	Date Due	Prev. Paid Fee
\$1000	\$0	\$1000	10-Aug-2020	\$0

1.Change of Correspondence Address and/or Indication Of Fee Address (37 CFR 1.33 & 1.363)

Current Correspondence Address:	Current Indicated Fee Address :
86738 MCCARTER & ENGLISH, LLP BOSTON 265 Franklin Street Boston MA 02110 UNITED STATES 617-449-6500 doctet@mccarter.com	
☐ Change of correspondence address requested, system generated AIA/122-EFS form attached	☐ Fee Address indication requested, system generated SB/47-EFS form attached

2.Entity Status**Change in Entity Status**

- Applicant certifying micro entity status; system generated Micro Entity certification form attached. See 37 CFR 1.29.
Note: Absent a valid certification of micro entity status, issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment. If this box is checked, you will be prompted to choose a micro entity status on the gross income basis (37 CFR 1.29(a)) or the institution of higher education basis (37 CFR 1.29(d)), and make the applicable certification online.
- ☐ 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.

Document Description: Issue Fee Payment (PTO-85B)

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4.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

1. McCarter & English LLP

2. Jonathan C. Lovely

3.

5.Assignee Name(s) and Residence Data To Be Printed

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Haemonetics Corporation	Boston	MASSACHUSETTS	united states	corporation

6.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 EFS-WEB on the date indicated below.

Signature	/Jonathan C. Lovely/	Date	07-15-2020
Name	Jonathan Lovely	Registration Number	60821

Electronic Patent Application Fee Transmittal				
Application Number:		15608183		
Filing Date:		30-May-2017		
Title of Invention:		System and Method for Collecting Plasma		
First Named Inventor/Applicant Name:		Michael Ragusa		
Filer:		Jonathan Lovely		
Attorney Docket Number:		130670-08002		
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 APPL ISSUE FEE	1501	1	1000	1000
PUBL. FEE- EARLY, VOLUNTARY, OR NORMAL	1504	1	0	0
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				1000

Electronic Acknowledgement Receipt	
EFS ID:	40002547
Application Number:	15608183
International Application Number:	
Confirmation Number:	7286
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:	130670-08002
Receipt Date:	15-JUL-2020
Filing Date:	30-MAY-2017
Time Stamp:	15:37:57
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$ 1000
RAM confirmation Number	E20207EF37551906
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Amendment after Notice of Allowance (Rule 312)	312_Amendment.pdf	35583	no	8
			4dfe59157e204bdf1029c018da7695aebfc724fc		
Warnings:					
Information:					
2	Issue Fee Payment (PTO-85B)	Web85b.pdf	46243	no	2
			09db84ac96131b4c42ef2f8ba050c751315362		
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	31764	no	2
			cc0f703c15ec2f577aaaa48e0f6be6042d4583a		
Warnings:					
Information:					
Total Files Size (in bytes):			113590		
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Haemonetics Corporation

Application No.: 15/608,183

Confirmation No.: 7286

Filed: May 30, 2017

Art Unit: 3799

For: SYSTEM AND METHOD FOR COLLECTING
PLASMA

Examiner: L. R. Deak

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

AMENDMENT AFTER ALLOWANCE UNDER 37 C.F.R. § 1.312

Prior to issuance of the patent, Applicant respectfully requests entry of this amendment under 37 C.F.R. § 1.312 for the above-captured patent application.

Amendments to the Claims may be found on page 2.

Remarks may be found on page 7.

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. (Previously Presented) A method for collecting plasma comprising:
 - (a) determining a weight of a donor;
 - (b) determining a hematocrit of the donor;
 - (c) inserting a venous-access device into the donor;
 - (d) withdrawing whole blood from the donor through the venous-access device and a draw line, the draw line connected to a blood component separation device;
 - (e) introducing anticoagulant into the withdrawn whole blood through an anticoagulant line;
 - (f) separating the withdrawn whole blood into a plasma component and at least a second blood component using the blood component separation device;
 - (g) collecting the plasma component from the blood component separation device and into a plasma collection container;
 - (h) calculating a volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma collection container;
 - (i) calculating a volume of pure plasma collected within the plasma collection container based, at least in part, on the calculated volume of anticoagulant in the collected plasma component; and
 - (j) continuing steps (d) through (i) until a target volume of pure plasma is collected within the plasma collection container.
2. (Currently Amended) A method according to claim 1, further comprising:
determining a change in volume within an anticoagulant container, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant container.

3. (Currently Amended) A method according to claim 1, further comprising:
determining a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the number of rotations of the anticoagulant pump.
4. (Currently Amended) A method according to claim 1, further comprising:
determining a volume of anticoagulant within the blood component separation device, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.
5. (Currently Amended) 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 container device based, at least in part, on the monitored volume of collected plasma component.
6. (Currently Amended) 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 container device based, at least in part, on the monitored weight of collected plasma component.
7. (Currently Amended) A method according to claim 1, wherein step (b) includes monitoring a volume of red blood cells collected within the blood component 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 component separation device and a volume of whole blood withdrawn from the donor.
8. (Original) A method according to claim 1, wherein the target volume of pure plasma is based, at least in part, on the weight of the donor.
9. (Previously Presented) A method according to claim 1, wherein the volume 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.

10. (Original) A method according to claim 1, further comprising:
returning, after collecting at least a portion of the target volume of pure plasma, the second blood component to the donor through a return line.
11. (Currently Amended) 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 blood draw line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw 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 blood component separation device and the blood draw pump, the controller configured to calculate (1) a volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma ~~collection~~ container, and (2) a volume of pure plasma collected within the plasma container based, at least in part, upon the volume of anticoagulant in the collected plasma component, the controller configured to stop the blood draw pump when a target volume of pure plasma is collected within the plasma container.
12. (Previously Presented) A system according to claim 11, wherein the volume 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.

13. (Currently Amended) A system according to claim 11, 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~~ source based on the measured weight of the anticoagulant source, the calculated volume of anticoagulant in the collected plasma component being based, at least in part, on the change in volume within the anticoagulant source.
14. (Currently Amended) A system according to claim 11, 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 volume of anticoagulant in the collected plasma component being based, at least in part, on the number of rotations of the anticoagulant pump.
15. (Currently Amended) A system according to claim 11, 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 volume of anticoagulant in the collected plasma component being based, at least in part, on the volume of anticoagulant within the blood component separation device.
16. (Currently Amended) A system according to claim 11, 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 container ~~collection device~~ based, at least in part, on the monitored volume of collected plasma component.
17. (Currently Amended) A system according to claim 11, 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 container ~~collection device~~ based, at least in part, on the monitored weight of collected plasma component.

18. (Currently Amended) A system according to claim 11, 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 component 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 component separation device and a volume of whole blood withdrawn from the ~~donor~~ subject.
19. (Currently Amended) A system according to claim 11, wherein the target volume of pure plasma is based, at least in part, on the weight of the ~~donor~~ subject.
20. (Previously Presented) A system according to claim 11, wherein the volume 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.

REMARKS

Applicant would like to thank the examiner for the Notice of Allowance dated May 8, 2020 and for finding claims 1-20 to be allowable. In the present paper, Applicant requests amendments to claims 2-7, 11 and 13-19 be entered. The amendments to the claims do not include new matter and the claims have not been amended for reasons related to patentability.

Amendments to the Claims

Claims 2-7, 11 and 13-19 have been amended herein for language consistency. In particular, the following amendments have been made:

- Claims 2-4 and 14-15 have been amended such that “collected plasma” now reads “collected plasma component”
- Claim 3 has also been amended to add “to” after “a method according...”
- Claims 5-6 have been amended such that “plasma collection device” now reads “plasma collection container”
- Claim 7 has been amended such that “blood separation device” now reads “blood component separation device”
- Claim 11 has been amended such that “plasma collection container” now reads “plasma container”
- Claim 13 has been amended such that “collected plasma” now reads “collected plasma component” and “anticoagulant container” now reads “anticoagulant source”
- Claims 16 and 17 have been amended such that “plasma collection device” now reads “plasma container”.
- Claim 18 has been amended such that “blood separation device” now reads “blood component separation device” and “donor” now reads “subject”

- Claim 19 has been amended such that “donor” now reads “subject”

Applicant respectfully requests that the Examiner enter the amendments presented herein pursuant to 37 C.F.R. § 1.312. The amendments to the claims merely correct obvious typographical errors and language inconsistency. The amendments do not change the scope of the claims and, therefore, are patentable for at least those reasons given in the Notice of Allowance. Applicant believes that the amended claims do not require additional search or examination. Applicant therefore respectfully requests that the amendments be approved and entered, and the application proceed to issuance.

CONCLUSION

It is believed that the application remains in order for allowance. This amendment is submitted with payment of the issue fee. The director is hereby authorized to charge any additional fees which may be required with respect to this communication or credit any overpayment to deposit account No. 50-4876, under order No. 130670-08002. Applicants also request that the examiner contact applicants’ attorney, Jonathan Lovely, if it will assist in processing this application through issuance.

Dated: July 15, 2020

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
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Attorney/Agent For Applicant



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NOTICE OF ALLOWANCE AND FEE(S) DUE

86738 7590 05/08/2020
MCCARTER & ENGLISH, LLP BOSTON
265 Franklin Street
Boston, MA 02110

EXAMINER

DEAK, LESLIE R

ART UNIT

PAPER NUMBER

3799

DATE MAILED: 05/08/2020

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/608,183	05/30/2017	Michael Ragusa	130670-08002	7286

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	\$1000	\$0.00	\$0.00	\$1000	08/10/2020

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.

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86738 7590 05/08/2020
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 EFS-Web 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.
15/608,183	05/30/2017	Michael Ragusa	130670-08002	7286

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	\$1000	\$0.00	\$0.00	\$1000	08/10/2020

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/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-09 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,

1 _____

(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.

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) ☐ Advance Order - # of Copies _____

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

☐ Electronic Payment via EFS-Web ☐ 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

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

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.

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.

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. _____



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
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/608,183	05/30/2017	Michael Ragusa	130670-08002	7286
86738	7590	05/08/2020	EXAMINER	
MCCARTER & ENGLISH, LLP BOSTON			DEAK, LESLIE R	
265 Franklin Street			ART UNIT	
Boston, MA 02110			PAPER NUMBER	
			3799	
DATE MAILED: 05/08/2020				

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.

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. 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 disclosure of these records is required by the Freedom of Information Act.
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 inspection 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.

Notice of Allowability	Application No. 15/608,183	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 AFCP filing submitted 1 May 2020.
☐ 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 1-20. 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)	5. ☐ Examiner's Amendment/Comment
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.	6. ☒ Examiner's Statement of Reasons for Allowance
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.	7. ☒ Other <u>AFCP form</u> .
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____.	

/LESLIE R DEAK/ Primary Examiner, Art Unit 3799	
--	--

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.

Allowable Subject Matter

2. Claims 1-20 are allowed.
3. 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.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

4. 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
5 May 2020**

Issue Classification 	Application/Control No. 15/608,183	Applicant(s)/Patent Under Reexamination Ragusa, Michael
	Examiner LESLIE R DEAK	Art Unit 3799

CPC						
Symbol					Type	Version
A61M	/	1	/	024	F	2013-01-01
A61M	/	1	/	029	I	2013-01-01
A61M	/	1	/	3672	I	2013-01-01
A61M	/	1	/	38	I	2013-01-01
G01N	/	15	/	05	A	2013-01-01
G01N	/	2015	/	055	A	2013-01-01
A61M	/	2230	/	207	A	2013-01-01
A61M	/	2202	/	0415	A	2013-01-01
A61M	/	1	/	3693	A	2013-01-01

CPC Combination Sets							
Symbol				Type	Set	Ranking	Version
	/		/				

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/LESLIE R DEAK/ Primary Examiner, Art Unit 3799 (Primary Examiner) _____ (Date) _____		O.G. Print Claim(s) 1	O.G. Print Figure 4

U.S. Patent and Trademark Office

Part of Paper No.: 20200505

Issue Classification 	Application/Control No. 15/608,183	Applicant(s)/Patent Under Reexamination Ragusa, Michael
	Examiner LESLIE R DEAK	Art Unit 3799

INTERNATIONAL CLASSIFICATION			
CLAIMED			
A61M1/02	/	1	02
A61M1/36	/	1	36
A61M1/38	/	1	38
NON-CLAIMED			
G01N15/05	/	15	05

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

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

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/LESLIE R DEAK/ Primary Examiner, Art Unit 3799 (Primary Examiner) _____ (Date) 05 May 2020		O.G. Print Claim(s) 1	O.G. Print Figure 4

U.S. Patent and Trademark Office

Part of Paper No.: 20200505

Issue Classification 	Application/Control No. 15/608,183	Applicant(s)/Patent Under Reexamination Ragusa, Michael
	Examiner LESLIE R DEAK	Art Unit 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

NONE (Assistant Examiner) _____ (Date) _____		Total Claims Allowed: 20	
/LESLIE R DEAK/ Primary Examiner, Art Unit 3799 (Primary Examiner) _____ (Date) 05 May 2020		O.G. Print Claim(s) 1	O.G. Print Figure 4

U.S. Patent and Trademark Office

Part of Paper No.: 20200505

AFCP 2.0 Decision

Application No.

15/608,183

Applicant(s)

Ragusa, Michael

Examiner

LESLIE R DEAK

Art Unit

3799

AIA (FITF) Status

Yes

This is in response to the After Final Consideration Pilot request filed 01 May 2020.

1. **Improper Request** – The AFCP 2.0 request is improper for the following reason(s) and the after final amendment submitted with the request will be treated under pre-pilot procedure.

- ☐ An AFCP 2.0 request form PTO/SB/434 (or equivalent document) was not submitted.
- ☐ A non-broadening amendment to at least one independent claim was not submitted.
- ☐ The request is not the first proper AFCP 2.0 request submitted in response to the most recent final rejection.
- ☐ Other: _____

2. **Proper Request**

- A. After final amendment submitted with the request will not be treated under AFCP 2.0.

The after final amendment cannot be reviewed and a search conducted within the guidelines of the pilot program.

- ☐ The after final amendment will be treated under pre-pilot procedure.

- B. Updated search and/or completed additional consideration.

The examiner performed an updated search and/or completed additional consideration of the after final amendment within the time authorized for the pilot program. The result(s) of the updated search and/or completed additional consideration are:

- ☒ 1. All of the rejections in the most recent final Office action are overcome and a Notice of Allowance is issued herewith.
- ☐ 2. The after final amendment would not overcome all of the rejections in the most recent final Office action. See attached interview summary for further details.
- ☐ 3. The after final amendment was reviewed, and it raises a new issue(s). See attached interview summary for further details.
- ☐ 4. The after final amendment raises new issues, but would overcome all of the rejections in the most recent final Office action. A decision on determining allowability could not be made within the guidelines of the pilot. See attached interview summary for further details, including any newly discovered prior art.
- ☐ 5. Other: _____

Examiner Note: Please attach an interview summary when necessary as described above.

Search Notes 	Application/Control No. 15/608,183	Applicant(s)/Patent Under Reexamination Ragusa, Michael
	Examiner LESLIE R DEAK	Art Unit 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

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

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

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Bibliographic Data

Application No: 15/608,183

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.
05/30/2017	604	3799	130670-08002
RULE			

APPLICANTS

Haemonetics Corporation, Braintree, MA, UNITED STATES

INVENTORS

Michael Ragusa Hingham, MA, UNITED STATES

CONTINUING DATA

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

06/06/2017

STATE OR COUNTRY

UNITED STATES

ADDRESS

MCCARTER & ENGLISH, LLP BOSTON

265 Franklin Street

Boston, MA 02110

UNITED STATES

FILING FEE RECEIVED

\$1,740

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3	"I15" and (hematocrit same anticoagulant)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2020/05/05 13:39
S1	2	("20180344910").PN.	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 11:36
S2	1	((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	2019/10/28 11:37
S3	1	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 11:37
S4	20	((A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 11:37
S5	3	"20120175313"	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:01
S6	2	"20030125881"	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:16
S7	27	2009/0215602	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:17

S8	3	"20090215602"	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:18
S9	2	S1 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	2019/10/28 12:25
S10	8637	((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	2019/10/28 12:25
S11	1805	S10 and hematocrit	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:26
S12	1	"I11" and (hematocrit with anticoagulant)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:26
S13	1	"I10" and (hematocrit with anticoagulant)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:30
S14	2	"I10" and (hematocrit same anticoagulant)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:30
S15	44	((("RAGUSA") near3 ("Michael"))).INV.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2019/10/28 12:31
S16	2	"I15" and (hematocrit same anticoagulant)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:31

S17	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" "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"	US-PGPUB; USPAT	OR	OFF	2019/10/28 12:37
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		"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.				
S18	2	("20180344910").PN.	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2020/02/27 09:46

EAST Search History (Interference)

<This search history is empty>

5/5/2020 1:51:45 PM

C:\Users\Ideak\Documents\EAST\Workspaces\15608183.wsp

Application No. 15/608,183
Amendment dated May 1, 2020
Reply to Final Office Action of March 3, 2020

Docket No.: 130670-08002

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 method for collecting plasma comprising:
 - (a) determining a weight of a donor;
 - (b) determining a hematocrit of the donor;
 - (c) inserting a venous-access device into the donor;
 - (d) withdrawing whole blood from the donor through the venous-access device and a draw line, the draw line connected to a blood component separation device;
 - (e) introducing anticoagulant into the withdrawn whole blood through an anticoagulant line;
 - (f) separating the withdrawn whole blood into a plasma component and at least a second blood component using the blood component separation device;
 - (g) collecting the plasma component from the blood component separation device and into a plasma collection container;
 - (h) calculating a percentage volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma collection container;
 - (i) calculating a volume of pure plasma collected within the plasma collection container based, at least in part, on the calculated percentage volume of anticoagulant in the collected plasma component; and
 - (j) continuing steps (d) through (i) until a target volume of pure plasma is collected within the plasma collection container.
2. (Currently Amended) A method according to claim 1, further comprising:
determining a change in volume within an anticoagulant container, the calculated volume percentage of anticoagulant in the collected plasma being based, at least in part, on the change in volume within the anticoagulant container.

3. (Currently Amended) A method according claim 1, further comprising:
determining a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump, the calculated volume percentage of anticoagulant in the collected plasma being based, at least in part, on the number of rotations of the anticoagulant pump.
4. (Currently Amended) A method according to claim 1, further comprising:
determining a volume of anticoagulant within the blood component separation device, the calculated volume percentage of anticoagulant in the collected plasma being based, at least in part, on the volume of anticoagulant within the blood component separation device.
5. (Original) 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.
6. (Original) 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.
7. (Currently Amended) A method according to claim 1, wherein step (b) includes monitoring a volume of red blood cells ~~collection~~ 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.
8. (Original) A method according to claim 1, wherein the target volume of pure plasma is based, at least in part, on the weight of the donor.
9. (Currently Amended) A method according to claim 1, wherein the volume 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.

10. (Original) A method according to claim 1, further comprising:
returning, after collecting at least a portion of the target volume of pure plasma, the second blood component to the donor through a return line.
11. (Currently Amended) 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 blood draw line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw 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~~ blood component separation device and the blood draw pump, the controller configured to calculate (1) a percentage volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma collection container, and (2) a volume of pure plasma collected within the plasma container based, at least in part, upon the percentage volume of anticoagulant in the collected plasma component, the controller configured to stop the blood draw pump when a target volume of pure plasma is collected within the plasma container.
12. (Currently Amended) A system according to claim 11, wherein the percentage volume 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.
13. (Currently Amended) A system according to claim 11, 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~~ volume of anticoagulant in the collected plasma being based, at least in part, on the change in volume within the anticoagulant source.

14. (Currently Amended) A system according to claim 11, 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~~ volume of anticoagulant in the collected plasma being based, at least in part, on the number of rotations of the anticoagulant pump.

15. (Currently Amended) A system according to claim 11, 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~~ volume of anticoagulant in the collected plasma being based, at least in part, on the volume of anticoagulant within the blood component separation device.

16. (Original) A system according to claim 11, 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.

17. (Original) A system according to claim 11, 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.

18. (Original) A system according to claim 11, 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

19. (Original) A system according to claim 11, wherein the target volume of pure plasma is based, at least in part, on the weight of the donor.

20. (Currently Amended) A system according to claim 11, wherein the ~~percentage~~ volume 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.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875				Application or Docket Number 15/608,183		Filing Date 05/30/2017		☐ To be Mailed	
ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO									
APPLICATION AS FILED - PART I									
		(Column 1)			(Column 2)				
FOR		NUMBER FILED		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), (l), 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 \$80 =			
INDEPENDENT CLAIMS (37 CFR 1.16(h))		minus 3 = *				x \$420 =			
☐ 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	05/01/2020	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE (\$)	ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(j))	* 20	Minus	** 20	= 0		x \$100 =	0	
	Independent (37 CFR 1.16(h))	* 2	Minus	*** 3	= 0		x \$460 =	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	
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE (\$)	ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(j))	*	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".							/LASHAWN R MORGAN/		
*** 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 number found in the appropriate box in column 1.									

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.

CERTIFICATION AND REQUEST FOR CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0		
Practitioner Docket No.: 130670-08002	Application No.: 15/608,183	Filing Date: May 30, 2017
First Named Inventor: Michael Ragusa	Title: SYSTEM AND METHOD FOR COLLECTING PLASMA	
<p>APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0 (AFCP 2.0) OF THE ACCOMPANYING RESPONSE UNDER 37 CFR 1.116.</p> <ol style="list-style-type: none"> 1. The above-identified application is (i) an original utility, plant, or design nonprovisional application filed under 35 U.S.C. 111(a) [a continuing application (<i>e.g.</i>, a continuation or divisional application) is filed under 35 U.S.C. 111(a) and is eligible under (i)], or (ii) an international application that has entered the national stage in compliance with 35 U.S.C. 371(c). 2. The above-identified application contains an outstanding final rejection. 3. Submitted herewith is a response under 37 CFR 1.116 to the outstanding final rejection. The response includes an amendment to at least one independent claim, and the amendment does not broaden the scope of the independent claim in any aspect. 4. This certification and request for consideration under AFCP 2.0 is the only AFCP 2.0 certification and request filed in response to the outstanding final rejection. 5. Applicant is willing and available to participate in any interview requested by the examiner concerning the present response. 6. This certification and request is being filed electronically using the Office's electronic filing system (EFS-Web). 7. Any fees that would be necessary consistent with current practice concerning responses after final rejection under 37 CFR 1.116, <i>e.g.</i>, extension of time fees, are being concurrently filed herewith. [There is no additional fee required to request consideration under AFCP 2.0.] 8. By filing this certification and request, applicant acknowledges the following: <ul style="list-style-type: none"> • Reissue applications and reexamination proceedings are not eligible to participate in AFCP 2.0. • The examiner will verify that the AFCP 2.0 submission is compliant, <i>i.e.</i>, that the requirements of the program have been met (see items 1 to 7 above). For compliant submissions: <ul style="list-style-type: none"> o The examiner will review the response under 37 CFR 1.116 to determine if additional search and/or consideration (i) is necessitated by the amendment and (ii) could be completed within the time allotted under AFCP 2.0. If additional search and/or consideration is required but cannot be completed within the allotted time, the examiner will process the submission consistent with current practice concerning responses after final rejection under 37 CFR 1.116, <i>e.g.</i>, by mailing an advisory action. o If the examiner determines that the amendment does not necessitate additional search and/or consideration, or if the examiner determines that additional search and/or consideration is required and could be completed within the allotted time, then the examiner will consider whether the amendment places the application in condition for allowance (after completing the additional search and/or consideration, if required). If the examiner determines that the amendment does not place the application in condition for allowance, then the examiner will contact the applicant and request an interview. <ul style="list-style-type: none"> ▪ The interview will be conducted by the examiner, and if the examiner does not have negotiation authority, a primary examiner and/or supervisory patent examiner will also participate. ▪ If the applicant declines the interview, or if the interview cannot be scheduled within ten (10) calendar days from the date that the examiner first contacts the applicant, then the examiner will proceed consistent with current practice concerning responses after final rejection under 37 CFR 1.116. 		
Signature	/Jonathan C. Lovely, Reg. No. 60,821/	Date May 1, 2020
Name (Print/Typed)	Jonathan C. Lovely	Practitioner Registration No. 60,821
<p>Note: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.</p>		
☐ * Total of <u>1</u> forms are submitted.		

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Haemonetics Corporation

Application No.: 15/608,183

Confirmation No.: 7286

Filed: May 30, 2017

Art Unit: 3799

For: **SYSTEM AND METHOD FOR COLLECTING
PLASMA**

Examiner: L. R. Deak

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

**RESPONSE UNDER 37 CFR 1.116 REQUESTING CONSIDERATION UNDER
THE AFTER FINAL CONSIDERATION PILOT PROGRAM (AFCP 2.0)**

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Final Office Action dated March 3, 2020, please amend the above-identified U.S. patent application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 7 of this paper.

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 method for collecting plasma comprising:
 - (a) determining a weight of a donor;
 - (b) determining a hematocrit of the donor;
 - (c) inserting a venous-access device into the donor;
 - (d) withdrawing whole blood from the donor through the venous-access device and a draw line, the draw line connected to a blood component separation device;
 - (e) introducing anticoagulant into the withdrawn whole blood through an anticoagulant line;
 - (f) separating the withdrawn whole blood into a plasma component and at least a second blood component using the blood component separation device;
 - (g) collecting the plasma component from the blood component separation device and into a plasma collection container;
 - (h) calculating a percentage volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma collection container;
 - (i) calculating a volume of pure plasma collected within the plasma collection container based, at least in part, on the calculated percentage volume of anticoagulant in the collected plasma component; and
 - (j) continuing steps (d) through (i) until a target volume of pure plasma is collected within the plasma collection container.
2. (Currently Amended) A method according to claim 1, further comprising:
 - determining a change in volume within an anticoagulant container, the calculated volume percentage of anticoagulant in the collected plasma being based, at least in part, on the change in volume within the anticoagulant container.

3. (Currently Amended) A method according claim 1, further comprising:
determining a volume of anticoagulant introduced into the whole blood based on a number of rotations of an anticoagulant pump, the calculated volume percentage of anticoagulant in the collected plasma being based, at least in part, on the number of rotations of the anticoagulant pump.
4. (Currently Amended) A method according to claim 1, further comprising:
determining a volume of anticoagulant within the blood component separation device, the calculated volume percentage of anticoagulant in the collected plasma being based, at least in part, on the volume of anticoagulant within the blood component separation device.
5. (Original) 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.
6. (Original) 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.
7. (Currently Amended) A method according to claim 1, wherein step (b) includes monitoring a volume of red blood cells ~~collection~~ 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.
8. (Original) A method according to claim 1, wherein the target volume of pure plasma is based, at least in part, on the weight of the donor.
9. (Currently Amended) A method according to claim 1, wherein the volume 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.

10. (Original) A method according to claim 1, further comprising:
returning, after collecting at least a portion of the target volume of pure plasma, the second blood component to the donor through a return line.
11. (Currently Amended) 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 blood draw line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw 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~~ blood component separation device and the blood draw pump, the controller configured to calculate (1) a percentage volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma collection container, and (2) a volume of pure plasma collected within the plasma container based, at least in part, upon the percentage volume of anticoagulant in the collected plasma component, the controller configured to stop the blood draw pump when a target volume of pure plasma is collected within the plasma container.
12. (Currently Amended) A system according to claim 11, wherein the percentage volume 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.
13. (Currently Amended) A system according to claim 11, 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~~ volume of anticoagulant in the collected plasma being based, at least in part, on the change in volume within the anticoagulant source.

14. (Currently Amended) A system according to claim 11, 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~~ volume of anticoagulant in the collected plasma being based, at least in part, on the number of rotations of the anticoagulant pump.

15. (Currently Amended) A system according to claim 11, 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~~ volume of anticoagulant in the collected plasma being based, at least in part, on the volume of anticoagulant within the blood component separation device.

16. (Original) A system according to claim 11, 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.

17. (Original) A system according to claim 11, 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.

18. (Original) A system according to claim 11, 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

19. (Original) A system according to claim 11, wherein the target volume of pure plasma is based, at least in part, on the weight of the donor.

20. (Currently Amended) A system according to claim 11, wherein the ~~percentage~~ volume 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.

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 1-4, 7, 9, 11-15 and 20 herewith. Claims 1-20 are currently pending in the application.

Examiner Interview Summary

Applicant would like to thank Examiner Deak for the telephone interview on March 25, 2020. During the interview, Examiner Deak, Applicant's counsel and Michael Ragusa (the inventor) discussed the pending claims, the Office Action dated March 3, 2020 and the cited prior art (e.g., U.S. Application No. 2003/012881 to Ryan, hereinafter "Ryan"). In particular, Applicant's counsel and Mr. Ragusa explained that Ryan does not calculate a volume of pure plasma and calculates the volume of anticoagulant in the plasma component in a different manner. Examiner Deak proposed adding a temporal component to the independent claims to specify when the volume of anticoagulant in the collected plasma component is calculated. To expedite prosecution, Applicant's counsel and Mr. Ragusa suggested the possibility of amending the claims to specify that the anticoagulant in the plasms component is calculated "as the plasma component is being collected in the plasma collection container." Examiner Deak indicated that such an amendment should overcome the cited prior art.

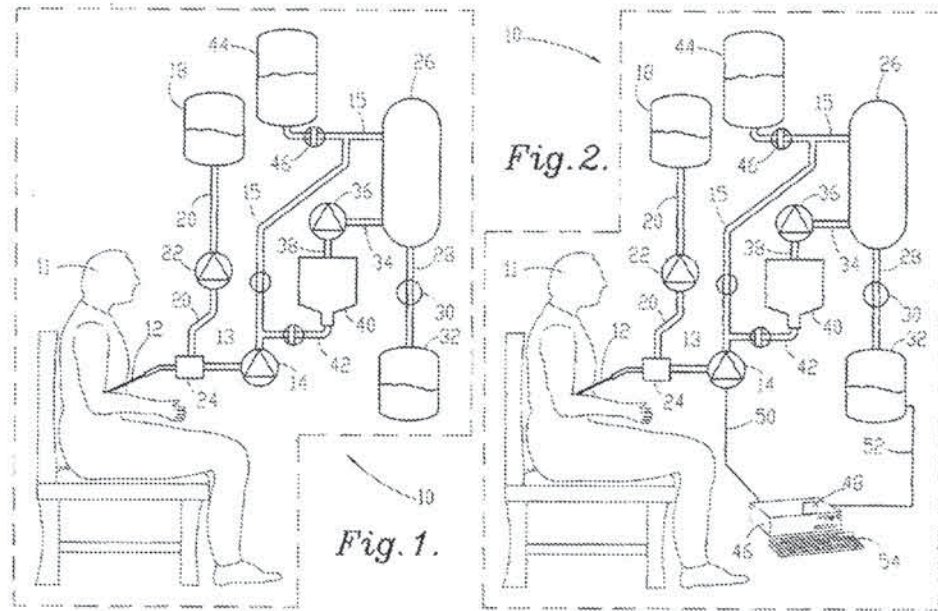
35 USC § 102

Claims 11, 12, 16, 17, 19 and 20 are rejected under 35 U.S.C. 102(a)(1) and (a)(2) as being anticipated by U.S. 2003/0125881 to Ryan.

Amended claim 11 defines, in relevant part, a system for collecting plasma that includes (1) a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and (2) 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. A blood draw line fluidly

connected to the venous-access device transports the drawn whole blood to the blood component separation device, and the flow through the blood draw line is controlled by a blood draw pump. An anticoagulant line is connected to an anticoagulant source and introduces anticoagulant into the drawn whole blood. The system also has a controller that controls the operation of the centrifuge bowl and the blood draw pump. The controller may calculate (1) a volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma collection container, and (2) a volume of pure plasma collected within the plasma container based, at least in part, upon the volume of anticoagulant in the collected plasma component. The controller may stop the blood draw pump when a target volume of pure plasma is collected within the plasma container.

Ryan fails to teach or suggest the claimed system. Rather, Ryan teaches a method and apparatus for collecting a plasma portion and that withdraws donor-weight specific plasma and blood volumes. Ryan's plasmapheresis system 10 includes a controller 46 that is in communicative control of a whole blood pump 14 as a function of either the volume of blood pumped by pump 14 or the volume of plasma contained in plasma reservoir 32 (e.g., as determined by the weight of the plasma reservoir 32 or by volume using optical sensors). The data from the scale or from the optical sensor is transmitted to the controller 46 and a processor 48 which monitor the amount of plasma collected. During operation, a donor 11 is weighed on a conventional scale, and the donor-specific body weight is obtained. Ryan then provides the processor 48 with the donor-specific body weight and the processor 48 calculates a particular plasma volume to be extracted from the donor based upon the donor-specific body weight and a selected standard of milliliters of plasma per pound of body weight. Ryan continues processing whole blood and collecting plasma until the calculated plasma volume is collected as determined by the number of revolutions of the pump 14 or the "actual" volume of plasma collected in the plasma reservoir 32 as measured by the weight of the reservoir 32 or the optical sensor. The "actual" volume of plasma is a combination of plasma and anticoagulant.



The office action suggests that Ryan's controller/processor 46/48 constitutes the claimed controller and that Ryan's controller/processor 46/48 calculate a percentage of anticoagulant in the collected plasma, a volume of plasma collected, and an appropriate time to stop the blood pump 14. As noted above, Applicant has amended claim 11 to specify that the controller calculates a volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma collection container. Ryan fails to teach or suggest such an anticoagulant calculation. Rather, at best, Ryan calculates a total collection volume (plasma and anticoagulant) prospectively prior to the start of the blood processing. In particular, as discussed within Ryan (e.g., see paragraphs [0024], [0025] and [0032] to [0036]), Ryan determines the donor's body weight and then multiplies the weight by a collection volume per pound (e.g., 5.8 milliliters per pound of donor body weight) to determine a volume of plasma and anticoagulant to collect. Ryan does not calculate the volume of anticoagulant in the collected plasma as the plasma component is collected in the container, as required by amended claim 11.

Furthermore, Ryan does not calculate a volume of pure plasma (plasma only without anticoagulant) collected within the plasma collection container and then stop the processing once a target of pure plasma is collected. Rather, as evidenced by the equation provided in paragraphs [0032] and [0033] of Ryan (e.g., " $V_{pac}=DW \times CV$ ") and the comparison in Table 3 of Ryan, Ryan calculates and stops based on a volume that includes both plasma and anticoagulant, not just pure plasma as required by amended claim 11. Additionally, Ryan specifically teaches using a scale to measure the weight of the bag 32 (the plasma collection container) or an optical sensor to measure the volume within the bag 32 and stopping when this measurement reaches the target. However, both the scale and the optical sensor measure the volume of the plasma and anticoagulant collected in the bag. Accordingly, Ryan does not teach or suggest calculating the volume of anticoagulant in the collected plasma component as the plasma component is collected and does not compensate for this volume of anticoagulant to obtain/calculate a volume of "pure plasma," as required by claim 11.

Therefore, claim 11 is allowable over Ryan. Moreover, claims 12, 16, 17, 19 and 20 which depend from claim 11 are also allowable over Ryan

35 USC § 103

Claims 1, 5, 6, 8-10 are rejected under 35 U.S.C. 103 as being unpatentable over U.S. 2003/0125881 to Ryan.

In a manner similar to claim 11, claim 1 defines, in relevant part, a method for collecting plasma that includes (1) determining the weight and hematocrit of a donor, (2) calculating a volume of anticoagulant in the collected plasma component as the plasma component is being collected in the plasma container, (3) calculating a volume of pure plasma collected within the plasma collection container, and (4) collecting plasma until a target volume of pure plasma is collected within the plasma collection container. Accordingly, claim 1 is allowable over Ryan for at least the same reasons as discussed above for claim 11. For example, as discussed above, Ryan fails to teach or suggest calculating the volume of anticoagulant in the collected plasma component as the plasma component is collected and does not compensate for this volume of anticoagulant to obtain/calculate a volume of "pure plasma" – Ryan sets a total volume of plasma and anticoagulant to collect prior

to the start of processing and looks at the volume of plasma and anticoagulant combined. Therefore, amended claim 1 is allowable over Ryan. Moreover, claims 5, 6, and 8-10 are allowable over Ryan for at least the same reasons.

Claims 2-4, 13 and 14 are rejected under 35 U.S.C. 103 as being unpatentable over U.S. 2003/0125881 to Ryan in view of U.S. 2012/0175313 to Barry et al.

As dependent claims of claims 1 and 11, claims 2-4 and 13-14 include all of the limitations of the base claim from which they depend. Therefore, claims 2-4 and 13-14 are allowable over the cited prior art for at least the reasons discussed above for claims 1 and 11.

Comments Regarding Claim Amendments

As discussed above, Applicant has amended the pending claims to specify that the volume of anticoagulant in the plasma component is calculated as the plasma component is being collected in the plasma collection container. Applicant would like to note that these amendments are being made to expedite prosecution and is not meant to be an agreement that the cited prior art teaches the claims as originally filed. Additionally, Applicant would like to note that other embodiments disclosed within the present application may calculate the anticoagulant within the plasma collection container in a different manner. For example, other disclosed embodiments may calculate the percentage of anticoagulant in the container and/or may calculate it at a different time (e.g., before blood processing begins). The amendments made herein are not intended to limit Applicant's ability to pursue such alternative embodiments in the future and are not intended to be a disclaimer of these alternative embodiments or any other subject matter supported by the disclosure of the present application, including the originally filed claims.

CONCLUSION

It is believed that the application is now in order for allowance and Applicants respectfully request that a notice of allowance be issued. Applicant believes no fee is due with this response. Applicants also request that the examiner contact applicants' attorney, Jonathan Lovely, if it will assist in processing this application through issuance.

Dated: May 1, 2020

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

Electronic Acknowledgement Receipt	
EFS ID:	39323624
Application Number:	15608183
International Application Number:	
Confirmation Number:	7286
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:	130670-08002
Receipt Date:	01-MAY-2020
Filing Date:	30-MAY-2017
Time Stamp:	15:20:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	After Final Consideration Program Request	After_Final_Consideration_Pilot_Program_Request_.pdf	34877 984da5c6f99984161b9e53d91b650619b325bffe	no	1

Warnings:

Information:				
2		Response_to_Final_Office_Action_.pdf	577219 8cf77d023f39b22711145f94b5d35b715baac6e2	yes 12
Multipart Description/PDF files in .zip description				
	Document Description	Start	End	
	Response After Final Action	1	1	
	Claims	2	6	
	Applicant Arguments/Remarks Made in an Amendment	7	12	
Warnings:				
Information:				
Total Files Size (in bytes):			612096	
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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/EQ/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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>				



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/608,183	05/30/2017	Michael Ragusa	130670-08002	7286
86738	7590	03/30/2020		
MCCARTER & ENGLISH, LLP BOSTON			EXAMINER	
265 Franklin Street			DEAK, LESLIE R	
Boston, MA 02110				
			ART UNIT	PAPER NUMBER
			3781	
			NOTIFICATION DATE	DELIVERY MODE
			03/30/2020	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

<i>Applicant-Initiated Interview Summary</i>	Application No. 15/608,183	Applicant(s) Ragusa, Michael	
	Examiner LESLIE R DEAK	Art Unit 3781	AIA (FITF) Status Yes

All participants (applicant, applicants representative, PTO personnel):

(1) LESLIE R. DEAK. (3) Michael Ragusa, Inventor.

(2) Jonathan Lovely, Counsel. (4) _____.

Date of Interview: 25 March 2020.

Type: ☒ Telephonic ☐ Video Conference
 ☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.
 If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☒102 ☒103 ☐Others
 (For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: 1 and 11.

Identification of prior art discussed: US 2003/0125881 to Ryan.

Substance of Interview
 (For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

See Continuation Sheet.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/LESLIE R DEAK/ Primary Examiner, Art Unit 3781	
--	--

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) 1.133 Interviews

Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiners responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicants correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,-
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicants record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiners version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, Interview Record OK on the paper recording the substance of the interview along with the date and the examiners initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: Steps h, i, j are the meat here. Prior art systems, when they collect plasma, FDA provides a nomogram based on weight of the patient, sets out how much volume you can pull out of each of the weight groups. Prior art systems collect plasma and AC, and base measurements off of the combined volume. In the instant case, if we tailor calculations to the donor, it's more accurate. Calculate the percentage of AC in the container, and from that, calculate the amount of pure plasma. Ryan doesn't follow FDA nomogram directly, but uses individual weights to figure out how much plasma to pull out. Ryan's calculations of collections are that of plasma and AC. AC percentage calculations done by Ryan are at the beginning of separation, and there's no teaching of how to calculate the AC in the actual collection bag.

How does this invention make the calculation of how much AC is in the collection bag? Fxn of donor hct and AC ratio. Based on weight or pump strokes.

Ryan calculates how much AC is going into the separator. Here, we're seeing how much AC is in the plasma after separation. Ryan lacks any ability to track how much AC is going to the product, and how much is being returned to the donor.

Examiner suggested adding "real-time" measurements of AC volume in steps h and i of the claimed method. Applicant will review the claim language and make formal amendments. Applicant's suggested claim language appears to overcome the Ryan reference.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/608,183	05/30/2017	Michael Ragusa	130670-08002	7286
86738	7590	03/03/2020		
MCCARTER & ENGLISH, LLP BOSTON			EXAMINER	
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Boston, MA 02110				
			ART UNIT	PAPER NUMBER
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			NOTIFICATION DATE	DELIVERY MODE
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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

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.

Response to Arguments

2. Applicant's arguments filed 31 January 2020 have been fully considered but they are not persuasive.
3. Applicant argues that Ryan fails to calculate a volume of "pure plasma" (plasma without anticoagulant) in the plasma container, the value of which is used to control the blood draw pump. Applicant alleges that Ryan calculates only the amount of fluid in the plasma container, which is a combination of pure plasma and anticoagulant. While Ryan focuses on total volume collection in Table 1, the following paragraphs go deeper. Ryan clearly discloses in paragraph 0022 that the apparatus and method can calculate a plasma volume of (such as 625mL) based on a total collection volume of plasma and anticoagulant (such as 690mL), and this information may be used to control the pumping of blood from the donor (see Table 2, ¶0022). As such, Ryan reasonably discloses the calculation of a pure plasma volume as claimed by Applicant.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale or otherwise available to the public before the effective filing date of the claimed invention.

(a)(2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was effectively filed before the effective filing date of the claimed invention.

5. Claims 11, 12, 16, 17, 19, and 20 are rejected under 35 U.S.C. 102(a)(1) and (a)(2) as being anticipated by US 2003/0125881 to Ryan.

In the specification and figures, Ryan teaches the apparatus as claimed by Applicant. With regard to claim 11, Ryan discloses a venous access device 12, a blood component separation device 26, plasma container 32, a blood draw line connected to venous access 12, a blood pump 14, an anticoagulant line 20, and a controller 46/48 that calculates a percentage of anticoagulant in the collected plasma, and a volume of plasma collected, and an appropriate time to stop blood pump 14 (see FIG 2, Table 2, ¶0022).

With regard to claims 12, 19, 20, Ryan teaches using a patient's weight, hematocrit, and amount of anticoagulant used to determine a target amount of collected plasma with a determined amount of anticoagulant (see ¶0014).

With regard to claims 15-17, Ryan discloses a plasma container weight sensor as well as an optical sensor (see ¶0031).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1, 5, 6, and 8-10 are rejected under 35 U.S.C. 103 as being unpatentable over US 2003/0125881 to Ryan.

In the specification and figures, Ryan teaches the method as claimed by Applicant. With regard to claims 1, 8, 9, Ryan teaches a method for collecting plasma comprising the steps of using donor weight, donor hematocrit and amount of anticoagulant used to determine a target amount of plasma that can be collected from a patient (see ¶0014). Once that determination is made, the method includes the steps of drawing blood from a patient, adding anticoagulant, separating the blood, collecting the plasma, and repeating those steps until a target plasma volume is reached (see ¶0011, 0012, 0022, 0023). Ryan does not teach that the steps of the method are performed in the same order as set forth by Applicant, but does teach using all of the same variables as those used by Applicant (donor weight, hematocrit, amount of anticoagulant) to generate the same result (target plasma volume), generally suggesting the claimed method to a person having ordinary skill in the art.

With regard to claims 5, 6, Ryan teaches that the volume of plasma collected is monitored throughout the procedure via weight or light transmission (see ¶0031, 0044).

With regard to claim 10, Ryan discloses that a second, cellular blood component may be returned to the patient (see ¶0012).

8. Claims 2-4, 7, 13, 14, and 18 are rejected under 35 U.S.C. 103 as being unpatentable over US 2003/0125881 to Ryan in view of US 2012/0175313 to Barry et al.

In the specification and figures, Ryan discloses the method and apparatus substantially as claimed by Applicant. With regard to claims 2-4, 13, 14, Ryan fails to disclose the step of determining a change in the volume of anticoagulant to determine the amount of anticoagulant in the system. However, Barry discloses monitoring pump strokes and, as a backup, weight of the anticoagulant container to determine the amount of anticoagulant in the extracorporeal system (see ¶0057). The monitoring of the pumps and weight sensor help ensure an accurate metering of anticoagulant within the separation circuit (see ¶0057). It would have been obvious to a person having ordinary skill in the art at the time of filing to add the monitoring system and steps disclosed by Barry to the apparatus and method disclosed by Ryan in order to provide accurate metering of anticoagulant within the separation circuit, as taught by Barry.

With regard to claims 7 and 18, Ryan is silent as to an optical hematocrit sensor. However, Barry discloses an apheresis apparatus and method that uses an optical hematocrit sensor to accurately set and monitor target collection volumes in order to more accurately control the collection procedure (see US 2009/0215602 ¶0327, incorporated by reference in '313. ¶0035, 0058, 0084). It would have been obvious to a person having ordinary skill in the art at the time of filing to add the optical monitoring system and steps disclosed by Barry to the apparatus and method disclosed by Ryan in order to provide accurate setting and monitoring of target collection values within the separation circuit, as taught by Barry.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. 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, Tatyana Zalukaeva can be reached on 571-272-1115. 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 <http://pair-direct.uspto.gov>. 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 3781
27 February 2020**

Search Notes 	Application/Control No. 15/608,183	Applicant(s)/Patent Under Reexamination Ragusa, Michael
	Examiner LESLIE R DEAK	Art Unit 3781

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

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

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 15/608,183

Confirmation No.: 7286

Filed: May 30, 2017

Art Unit: 3781

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 Sir:

INTRODUCTORY COMMENTS

In response to the Office Action dated November 1, 2019, please amend the above-identified U.S. patent application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 7 of this paper.

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. (Original) A method for collecting plasma comprising:
 - (a) determining a weight of a donor;
 - (b) determining a hematocrit of the donor;
 - (c) inserting a venous-access device into the donor;
 - (d) withdrawing whole blood from the donor through the venous-access device and a draw line, the draw line connected to a blood component separation device;
 - (e) introducing anticoagulant into the withdrawn whole blood through an anticoagulant line;
 - (f) separating the withdrawn whole blood into a plasma component and at least a second blood component using the blood component separation device;
 - (g) collecting the plasma component from the blood component separation device and into a plasma collection container;
 - (h) calculating a percentage of anticoagulant in the collected plasma component;
 - (i) calculating a volume of pure plasma collected within the plasma collection container based, at least in part, on the calculated percentage of anticoagulant in the collected plasma component; and
 - (j) continuing steps (d) through (i) until a target volume of pure plasma is collected within the plasma collection container.
2. (Original) A method according to claim 1, 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.

3. (Original) A method according claim 1, 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.
4. (Original) A method according to claim 1, 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.
5. (Original) 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.
6. (Original) 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.
7. (Original) A method according to claim 1, wherein step (b) includes monitoring a volume of red blood cells collection 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.
8. (Original) A method according to claim 1, wherein the target volume of pure plasma is based, at least in part, on the weight of the donor.
9. (Original) A method according to claim 1, 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.

10. (Original) A method according to claim 1, further comprising:
returning, after collecting at least a portion of the target volume of pure plasma, the second blood component to the donor through a return line.
11. (Original) 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 blood draw line fluidly connected to the venous-access device and configured to transport drawn whole blood to the blood component separation device, the flow through the blood draw line being controlled by a blood draw 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 blood draw pump, the controller configured to calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma container based, at least in part, upon the percentage of anticoagulant in the collected plasma component, the controller configured to stop the blood draw pump when a target volume of pure plasma is collected within the plasma container.
12. (Original) A system according to claim 11, 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.
13. (Original) A system according to claim 11, 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.

14. (Original) A system according to claim 11, 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.

15. (Original) A system according to claim 11, 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.

16. (Original) A system according to claim 11, 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.

17. (Original) A system according to claim 11, 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.

18. (Original) A system according to claim 11, 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

19. (Original) A system according to claim 11, wherein the target volume of pure plasma is based, at least in part, on the weight of the donor.

20. (Original) A system according to claim 11, 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.

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. Claims 1-20 are currently pending in the application.

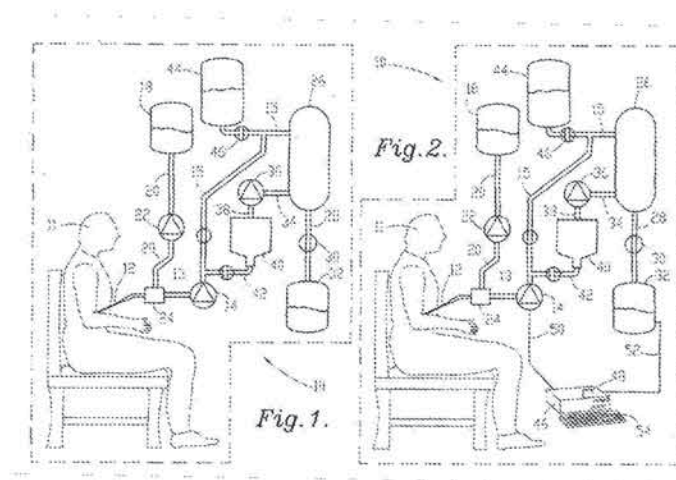
35 USC § 102

Claims 11, 12, 16, 17, 19 and 20 are rejected under 35 U.S.C. 102(a)(1) and (a)(2) as being anticipated by U.S. 2003/0125881 to Ryan.

Claim 11 defines, in relevant part, a system for collecting plasma that includes (1) a venous-access device for drawing whole blood from a subject and returning blood components to the subject, and (2) 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. A blood draw line fluidly connected to the venous-access device transports the drawn whole blood to the blood component separation device, and the flow through the blood draw line is controlled by a blood draw pump. An anticoagulant line is connected to an anticoagulant source and introduces anticoagulant into the drawn whole blood. The system also has a controller that controls the operation of the centrifuge bowl and the blood draw pump. The controller may calculate (1) a percentage of anticoagulant in the collected plasma component, and (2) a volume of pure plasma collected within the plasma container 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 is collected within the plasma container.

Ryan fails to teach or suggest the claimed system. Rather, Ryan teaches a method and apparatus for collecting the plasma portion and that withdraws donor-weight specific plasma and blood volumes. Ryan's plasmapheresis system 10 includes a controller 46 that is in communicative control of a whole blood pump 14 as a function of either the volume of blood pumped by pump 14 or the volume of plasma contained in plasma reservoir 32 (e.g., as determined by the weight of the

plasma reservoir 32 or by volume using optical sensors). The data from the scale or from the optical sensor is transmitted to the controller 46 and a processor 48 which monitor the amount of plasma collected. During operation, a donor 11 is weighed on a conventional scale, and the donor-specific body weight of the donor is obtained. Ryan then provides the processor 48 with the donor-specific body weight and the processor 48 calculates a particular plasma volume to be extracted from the donor based upon the donor-specific body weight and a selected standard of milliliters of plasma per pound of body weight. Ryan continues processing whole blood and collecting plasma until the calculated plasma volume is collected as determined by the number of revolutions of the pump 14 or the "actual" volume of plasma collected in the plasma reservoir 32 as measured by the weight of the reservoir 32 or the optical sensor.



The office action suggests that Ryan's controller/processor 46/48 constitutes the claimed controller and that Ryan's controller/processor 46/48 calculate a percentage of anticoagulant in the collected plasma and a volume of plasma collected, and an appropriate time to stop the blood pump 14. Applicant respectfully disagrees and would like to note that nowhere does Ryan teach or suggest calculating and/or collecting a volume of "pure plasma," as required by claim 11. As discussed within the present application, the volume of "pure plasma" is the volume of plasma only...it is not the volume of the plasma and anticoagulant mixed together (see paragraphs [0018] and [0035] of the present application. Additionally, as also discussed within the present application, the osmolarity

of the red blood cells prevents the added anticoagulant to remain with the red blood cells, and the anticoagulant mixes with the plasma component and is collected within the plasma collection container along with the plasma. Ryan does not calculate the volume of pure plasma collected within the plasma container and then stop when a target volume of pure plasma is collected in the container. Rather, as discussed above, Ryan either stops based on a volume of whole blood drawn from the subject (based on a number of pump rotations; see paragraph [0038] of Ryan) or the total volume of fluid (i.e., both plasma and anticoagulant) collected within the reservoir bag 32. For example, for embodiments that stop based on the fluid volume within the bag 32, Ryan may use a scale to measure the weight of the bag 32 or an optical sensor to measure the volume within the bag. However, both the scale and the optical sensor measure the volume of the plasma and anticoagulant collected in the bag...Ryan does not teach or suggest compensating for the volume of anticoagulant that is mixed with the plasma to obtain/calculate a volume of "pure plasma," as required by claim 11.

Applicant would also like to note that, although Ryan refers to the volume of plasma measured by the scale and/or optical sensor as the "actual volume of plasma," as discussed above this volume is actually a mixture of plasma and anticoagulant (e.g., because the added anticoagulant mixes with and is collected with the plasma). This is further evidenced by the equations provided within Ryan. In particular, Ryan provides the equation " $V_{pac}=DW \times CV$ " to determine the volume of plasma to collect. However, Ryan also specifically states that V_{pac} , which is the volume of plasma to be collected, is the "plasma and anticoagulant collection volume in milliliters" (emphasis added). Additionally, as shown in Table 3 of Ryan, Ryan is basing the amount of plasma on the FDA guidelines which specifically state that the values are "with anticoagulant." In other words, Ryan does not calculate a volume of pure plasma and/or stop based on a volume of pure plasma -- Ryan specifically teaches using a volume of plasma and anticoagulant.

Accordingly, claim 11 is allowable over Ryan. Moreover, claims 12, 16, 17, 19 and 20 which depend from claim 11 are also allowable over Ryan

35 USC § 103

Claims 1, 5, 6, 8-10 are rejected under 35 U.S.C. 103 as being unpatentable over U.S. 2003/0125881 to Ryan.

In a manner similar to claim 11, claim 1 defines, in relevant part, a method for collecting plasma that includes (1) determining the weight and hematocrit of a donor, (2) calculating a percentage of anticoagulant in the collected plasma component and a volume of pure plasma collected within the plasma collection container, and (3) collecting plasma until a target volume of pure plasma is collected within the plasma collection container. Accordingly, claim 1 is allowable over Ryan for at least the same reasons as discussed above for claim 11. For example, as discussed above, Ryan fails to teach or suggest calculating a volume of pure plasma and collecting plasma until a target volume of pure plasma is collected – Ryan looks at the volume of plasma and anticoagulant combined. Moreover, claims 5, 6, and 8-10 are allowable over Ryan for at least the same reasons.

Claims 2-4, 13 and 14 are rejected under 35 U.S.C. 103 as being unpatentable over U.S. 2003/0125881 to Ryan in view of U.S. 2012/0175313 to Barry et al.

As dependent claims of claims 1 and 11, claims 2-4 and 13-14 include all of the limitations of the base claim from which they depend. Therefore, claims 2-4 and 13-14 are allowable over the cited prior art for at least the reasons discussed above for claims 1 and 11.

CONCLUSION

It is believed that the application is now in order for allowance and Applicants respectfully request that a notice of allowance be issued. Applicant believes no fee is due with this response. Applicants also request that the examiner contact applicants' attorney, Jonathan Lovely, if it will assist in processing this application through issuance.

Dated: January 31, 2020

Respectfully submitted,
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Electronic Acknowledgement Receipt	
EFS ID:	38456160
Application Number:	15608183
International Application Number:	
Confirmation Number:	7286
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:	130670-08002
Receipt Date:	31-JAN-2020
Filing Date:	30-MAY-2017
Time Stamp:	13:53:45
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		15608183_Response_to_Non-Final_OA.pdf	482877	yes	11
			9c20e8cfe0758f1fa605c6022a4c9793fecd efd		

	Multipart Description/PDF files in .zip description		
	Document Description	Start	End
	Amendment/Req. Reconsideration-After Non-Final Reject	1	1
	Claims	2	6
	Applicant Arguments/Remarks Made in an Amendment	7	11
Warnings:			
Information:			
Total Files Size (in bytes):		482877	
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>			

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875				Application or Docket Number 15/608,183		Filing Date 05/30/2017		☐ To be Mailed	
ENTITY: ☒ LARGE ☐ SMALL ☐ MICRO									
APPLICATION AS FILED - PART I									
		(Column 1)	(Column 2)						
FOR		NUMBER FILED	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), (l), 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 \$80 =			
INDEPENDENT CLAIMS (37 CFR 1.16(h))		minus 3 = *				x \$420 =			
☐ 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	01/31/2020	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(j))	* 20	Minus	** 20	= 0	x \$100 =		0	
	Independent (37 CFR 1.16(h))	* 2	Minus	*** 3	= 0	x \$460 =		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	
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(j))	*	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".						/MARCUS D MONROE/			
*** 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 number found in the appropriate box in column 1.									

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.**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/608,183	05/30/2017	Michael Ragusa	130670-08002	7286
86738	7590	11/01/2019		
MCCARTER & ENGLISH, LLP BOSTON			EXAMINER	
265 Franklin Street			DEAK, LESLIE R	
Boston, MA 02110				
			ART UNIT	PAPER NUMBER
			3781	
			NOTIFICATION DATE	DELIVERY MODE
			11/01/2019	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

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.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a)(1) the claimed invention was patented, described in a printed publication, or in public use, on sale or otherwise available to the public before the effective filing date of the claimed invention.

(a)(2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was effectively filed before the effective filing date of the claimed invention.

3. Claims 11, 12, 16, 17, 19, and 20 are rejected under 35 U.S.C. 102(a)(1) and (a)(2) as being anticipated by US 2003/0125881 to Ryan.

In the specification and figures, Ryan teaches the apparatus as claimed by Applicant. With regard to claim 11, Ryan discloses a venous access device 12, a blood component separation device 26, plasma container 32, a blood draw line connected to venous access 12, a blood pump 14, an anticoagulant line 20, and a controller 46/48 that calculates a percentage of anticoagulant in the collected plasma, and a volume of plasma collected, and an appropriate time to stop blood pump 14 (see FIG 2 and accompanying test).

With regard to claims 12, 19, 20, Ryan teaches using a patient's weight, hematocrit, and amount of anticoagulant used to determine a target amount of collected plasma with a determined amount of anticoagulant (see ¶0014).

With regard to claims 15-17, Ryan discloses a plasma container weight sensor as well as an optical sensor (see ¶0031).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1, 5, 6, 8-10 are rejected under 35 U.S.C. 103 as being unpatentable over US 2003/0125881 to Ryan.

In the specification and figures, Ryan teaches the method as claimed by Applicant. With regard to claims 1, 8, 9, Ryan teaches a method for collecting plasma comprising the steps of using donor weight, donor hematocrit and amount of anticoagulant used to determine a target amount of plasma that can be collected from a patient (see ¶0014). Once that determination is made, the method includes the steps of drawing blood from a patient, adding anticoagulant, separating the blood, collecting the plasma, and repeating those steps until a target plasma volume is reached (see ¶0011, 0012, 0023). Ryan does not teach that the steps of the method are performed in the same order as set forth by Applicant, but does teach using all of the same variables as

those used by Applicant (donor weight, hematocrit, amount of anticoagulant) to generate the same result (target plasma volume), generally suggesting the claimed method to a person having ordinary skill in the art.

With regard to claims 5, 6, Ryan teaches that the volume of plasma collected is monitored throughout the procedure via weight or light transmission (see ¶0031, 0044).

With regard to claim 10, Ryan discloses that a second, cellular blood component may be returned to the patient (see ¶0012).

6. Claims 1, 5, 6, 8-10 are rejected under 35 U.S.C. 103 as being unpatentable over US 2003/0125881 to Ryan in view of US 2012/0175313 to Barry et al.

In the specification and figures, Ryan discloses the method and apparatus substantially as claimed by Applicant. With regard to claims 2-4, 13, 14, Ryan fails to disclose the step of determining a change in the volume of anticoagulant to determine the amount of anticoagulant in the system. However, Barry discloses monitoring pump strokes and, as a backup, weight of the anticoagulant container to determine the amount of anticoagulant in the extracorporeal system (see ¶0057). The monitoring of the pumps and weight sensor help ensure an accurate metering of anticoagulant within the separation circuit (see ¶0057). It would have been obvious to a person having ordinary skill in the art at the time of filing to add the monitoring system and steps disclosed by Barry to the apparatus and method disclosed by Ryan in order to provide accurate metering of anticoagulant within the separation circuit, as taught by Barry.

With regard to claims 7 and 18, Ryan is silent as to an optical hematocrit sensor. However, Barry discloses an apheresis apparatus and method that uses an optical

hematocrit sensor to accurately set and monitor target collection volumes in order to more accurately control the collection procedure (see US 2009/0215602 ¶0327, incorporated by reference in '313. ¶0035, 0058, 0084). It would have been obvious to a person having ordinary skill in the art at the time of filing to add the optical monitoring system and steps disclosed by Barry to the apparatus and method disclosed by Ryan in order to provide accurate setting and monitoring of target collection values within the separation circuit, as taught by Barry.

Conclusion

7. 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, Tatyana Zalukaeva can be reached on 571-272-1115. 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 <http://pair-direct.uspto.gov>. 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 3781
28 October 2019**

Search Notes 	Application/Control No. 15/608,183	Applicant(s)/Patent Under Reexamination Ragusa, Michael
	Examiner LESLIE R DEAK	Art Unit 3781

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

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

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2	("20180344910").PN.	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 11:36
L2	1	((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	2019/10/28 11:37
L3	1	((A61M1/029 and A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 11:37
L4	20	((A61M1/3672 and A61M1/3693 and A61M1/38 and A61M2202/0415).CPC.)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 11:37
L5	3	"20120175313"	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:01
L6	2	"20030125881"	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:16
L7	27	2009/0215602	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:17
L8	3	"20090215602"	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:18
L9	2	1 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	2019/10/28 12:25
L10	8637	((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	2019/10/28 12:25
L11	1805	I10 and hematocrit	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:26
L12	1	"I11" and (hematocrit with anticoagulant)	US-PGPUB;	OR	OFF	2019/10/28

EAST Search History

			USPAT; USOCR; DERWENT			12:26
L13	1	"I10" and (hematocrit with anticoagulant)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:30
L14	2	"I10" and (hematocrit same anticoagulant)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:30
L15	44	((("RAGUSA") near3 ("Michael"))).INV.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2019/10/28 12:31
L16	2	"I15" and (hematocrit same anticoagulant)	US-PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:31

EAST Search History (Interference)

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10/ 28/ 2019 12:32:20 PM

C:\Users\Ideak\Documents\EAST\Workspaces\15608183.wsp

Used in Lieu of PTO/SB/08A/B
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Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Complete if Known	
				Application Number	15/608,183
				Filing Date	May 30, 2017
				First Named Inventor	Michael Ragusa
				Art Unit	3781
				Examiner Name	T. Zalukaeva
				Attorney Docket Number	130670-08002
Sheet	1	of	6		

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	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/ (10/28/2019)	Date Considered	10/28/2019
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				Art Unit	3781
				Examiner Name	T. Zalukaeva
				Attorney Docket Number	130670-08002
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	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.	
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	AP3	US-5,234,403	08-10-1993	Yoda et al.	

Examiner Signature	/LESLIE R DEAK/ (10/28/2019)	Date Considered	10/28/2019
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				First Named Inventor	Michael Ragusa
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				Examiner Name	T. Zalukaeva
				Attorney Docket Number	130670-08002
Sheet	3	of	6		

	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/ (10/28/2019)	Date Considered	10/28/2019
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				Art Unit	3781
				Examiner Name	T. Zalukaeva
				Attorney Docket Number	130670-08002
Sheet	4	of	6		

	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-20010027156-A1	10-04-2001	Egozy et al.	
	AI6	US-20020043492-A1	04-18-2002	Bischof	
	AJ6	US-20020120227-A1	08-29-2002	Childers et al.	
	AK6	US-20030055375-A1	03-20-2003	Holst et al.	
	AL6	US-20030066807-A1	04-10-2003	Suzuki	
	AM6	US-20030125881-A1	07-03-2003	Ryan	
	AN6	US-20030175150-A1	09-18-2003	Grimm	
	AO6	US-20040186409-A1	09-23-2004	Cavalcanti et al.	
	AP6	US-20050209522-A1	09-22-2005	Tadokoro et al.	
	AQ6	US-20050235733-A1	10-27-2005	Holst et al.	
	AR6	US-20060058167-A1	03-16-2006	Ragusa et al.	
	AS6	US-20060155236-A1	07-13-2006	Gara et al.	
	AT6	US-20070112289-A1	05-17-2007	Cavalcanti et al.	
	AU6	US-20080146993-A1	06-19-2008	Krishna	
	AV6	US-20120175313-A1	07-12-2012	Barry, JR. et al.	
	AW6	US-20140039373-A1	02-06-2014	Ragusa et al.	
	AX6	US-20140356851-A1	12-04-2014	Pages et al.	
	AY6	US-20180344921-A1	12-06-2018	Ragusa	

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				Examiner Name	T. Zalukaeva
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FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	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
		Country Code ² -Number ³ -Kind Code ⁵ (if known)				
	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-0578086-A1	01-12-1994	Terumo Corp		
	BF	EP-0654277-A1	05-24-1995	Cobe Laboratories, Inc		
	BG	EP-0885619-A1	12-23-1998	Terumo Corp		
	BH	EP-1057534-A1	12-06-2000	Haemonetics Corp		
	BI	EP-1295619-A2	03-26-2003	Terumo Corp		
	BJ	EP-1374927-A1	01-02-2004	Terumo Corp		
	BK	EP-257755-A1	03-02-1988	Haemonetics Corp		
	BL	EP-619145-A2	10-12-1994	Electromedics, Inc		
	BM	EP-664159-A1	07-26-1995	Haemonetics Corp		
	BN	EP-799645-A1	10-08-1997	Haemonetics Corp		
	BO	FR-2258898-A1	08-22-1975	Heraeus Christ GmbH,dt		
	BP	GB-2047110-A	11-26-1980	Hogman, C F		
	BQ	JP-H02-052665	02-22-1990	Nissho KK		√
	BR	JP-H03-131268	06-04-1991	Fresenius AG		√
	BS	JP-2002-291872-A	10-08-2002	Terumo Corp		√
	BT	JP-2008-506424-A	03-06-2008			√
	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-S59-006952	01-14-1984	Hitachi Koki KK		√
	BY	JP-S59-069166	04-19-1984	Nikkiso Co Ltd.		√
	BZ	SU-1146098-A1	03-23-1985	Sp K B Biofiz App		
	BA1	SU-660718-A1	05-05-1979	Sp K B Biofizicheskoy Apparatu		
	BB1	SU-762982-A1	09-15-1980	Sp K B Biofizicheskoy Apparatu		
	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		
	BJ1	WO-2007/041716-A1	04-12-2007	Gambro, Inc		
Examiner Signature	/LESLIE R DEAK/ (10/28/2019)			Date Considered	10/28/2019	

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				Examiner Name	T. Zalukaeva
Sheet	6	of	6	Attorney Docket Number	130670-08002

*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. 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.		

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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/ (10/28/2019)	Date Considered	10/28/2019
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ME1 28965507v.1

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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
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EAST Search History

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S13	1	"I10" and (hematocrit with anticoagulant)	US- PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:30
S14	2	"I10" and (hematocrit same anticoagulant)	US- PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:30
S15	44	((("RAGUSA") near3 ("Michael"))).INV.	US- PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2019/10/28 12:31
S16	2	"I15" and (hematocrit same anticoagulant)	US- PGPUB; USPAT; USOCR; DERWENT	OR	OFF	2019/10/28 12:31

EAST Search History (Interference)

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Doc code: IDS

Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (02-16)

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	15608183
	Filing Date	2017-05-30
	First Named Inventor	Michael Ragusa
	Art Unit	3781
	Examiner Name	T. Zalukaeva
	Attorney Docket Number	130670-08002

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	1	20010000185	A1	2001-04-05	Keller et al.	
	2	20020062100	A1	2002-05-23	Pierce et al.	

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Not for submission under 37 CFR 1.99)

Application Number	15608183
Filing Date	2017-05-30
First Named Inventor	Michael Ragusa
Art Unit	3781
Examiner Name	T. Zalukaeva
Attorney Docket Number	130670-08002

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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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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Art Unit	3781
Examiner Name	T. Zalukaeva
Attorney Docket Number	130670-08002

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)	2019-02-01
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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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.

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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.

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	15608183
	Filing Date	2017-05-30
	First Named Inventor	Michael Ragusa
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	Examiner Name	T. Zalukaeva
	Attorney Docket Number	130670-08002

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	15608183
	Filing Date	2017-05-30
	First Named Inventor	Michael Ragusa
	Art Unit	3781
	Examiner Name	T. Zalukaeva
Attorney Docket Number		130670-08002

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 Name	T. Zalukaeva
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OR

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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)	2019-02-01
Name/Print	Jonathan C. Lovely	Registration Number	60,821

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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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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: February 1, 2019
Electronic Signature for Jonathan C. Lovely: /Jonathan C. Lovely, Reg. No. 60,821/

Docket No.: 130670-08002
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 15/608,183

Confirmation No.: 7286

Filed: May 30, 2017

Art Unit: 3781

For: SYSTEM AND METHOD FOR COLLECTING
PLASMA

Examiner: T. Zalukaeva

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT (SIDS)

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 Supplemental 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).

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

ME1 29191322v.1

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 the 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: February 1, 2019

Respectfully submitted,
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Electronic Acknowledgement Receipt	
EFS ID:	35033193
Application Number:	15608183
International Application Number:	
Confirmation Number:	7286
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:	130670-08002
Receipt Date:	01-FEB-2019
Filing Date:	30-MAY-2017
Time Stamp:	14:24:25
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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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)	130670-08002_-_Information_Disclosure_Statement_Fillable_PDF.pdf	1034413 6eb7692e7e4ad2775b186449c2e4e9491868e7e9	no	4

Warnings:

Information:					
2	Transmittal Letter	IDS_Letter.pdf	23024	no	2
			7d8b61ccd002b7724875ff086967a02245bcb76f		
Warnings:					
Information:					
Total Files Size (in bytes):				1057437	
<p>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.</p> <p><u>New Applications Under 35 U.S.C. 111</u> 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.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> 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.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> 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.</p>					

Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Complete if Known	
				Application Number	15/608,183
				Filing Date	May 30, 2017
				First Named Inventor	Michael Ragusa
				Art Unit	3781
				Examiner Name	T. Zalukaeva
Sheet	1	of	6	Attorney Docket Number	130670-08002

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	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.	
	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		Date Considered	
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				Examiner Name	T. Zalukaeva
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	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.	
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	AI3	US-5,141,486	08-25-1992	Antwiler	
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Examiner Signature		Date Considered	
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				First Named Inventor	Michael Ragusa
				Art Unit	3781
				Examiner Name	T. Zalukaeva
Sheet	3	of	6	Attorney Docket Number	130670-08002

	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	
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	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	
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	AA5	US-5,728,060	03-17-1998	Kingsley et al.	
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	AD5	US-5,733,545	03-31-1998	Hood, III	
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	AI5	US-5,792,351	08-11-1998	Wehrle et al.	
	AJ5	US-5,849,203	12-15-1998	Brown et al.	
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	AL5	US-5,906,589	05-25-1999	Gordon et al.	
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Examiner Signature		Date Considered	
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Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>				Complete if Known	
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				Art Unit	3781
				Examiner Name	T. Zalukaeva
				Attorney Docket Number	130670-08002
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	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.	
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	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-20010027156-A1	10-04-2001	Egozy et al.	
	AI6	US-20020043492-A1	04-18-2002	Bischof	
	AJ6	US-20020120227-A1	08-29-2002	Childers et al.	
	AK6	US-20030055375-A1	03-20-2003	Holst et al.	
	AL6	US-20030066807-A1	04-10-2003	Suzuki	
	AM6	US-20030125881-A1	07-03-2003	Ryan	
	AN6	US-20030175150-A1	09-18-2003	Grimm	
	AO6	US-20040186409-A1	09-23-2004	Cavalcanti et al.	
	AP6	US-20050209522-A1	09-22-2005	Tadokoro et al.	
	AQ6	US-20050235733-A1	10-27-2005	Holst et al.	
	AR6	US-20060058167-A1	03-16-2006	Ragusa et al.	
	AS6	US-20060155236-A1	07-13-2006	Gara et al.	
	AT6	US-20070112289-A1	05-17-2007	Cavalcanti et al.	
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	AV6	US-20120175313-A1	07-12-2012	Barry, JR. et al.	
	AW6	US-20140039373-A1	02-06-2014	Ragusa et al.	
	AX6	US-20140356851-A1	12-04-2014	Pages et al.	
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FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	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
		Country Code ² -Number ³ -Kind Code ⁵ (if known)				
	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-0578086-A1	01-12-1994	Terumo Corp		
	BF	EP-0654277-A1	05-24-1995	Cobe Laboratories, Inc		
	BG	EP-0885619-A1	12-23-1998	Terumo Corp		
	BH	EP-1057534-A1	12-06-2000	Haemonetics Corp		
	BI	EP-1295619-A2	03-26-2003	Terumo Corp		
	BJ	EP-1374927-A1	01-02-2004	Terumo Corp		
	BK	EP-257755-A1	03-02-1988	Haemonetics Corp		
	BL	EP-619145-A2	10-12-1994	Electromedics, Inc		
	BM	EP-664159-A1	07-26-1995	Haemonetics Corp		
	BN	EP-799645-A1	10-08-1997	Haemonetics Corp		
	BO	FR-2258898-A1	08-22-1975	Heraeus Christ GmbH,dt		
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	BQ	JP-H02-052665	02-22-1990	Nissho KK		√
	BR	JP-H03-131268	06-04-1991	Fresenius AG		√
	BS	JP-2002-291872-A	10-08-2002	Terumo Corp		√
	BT	JP-2008-506424-A	03-06-2008			√
	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-S59-006952	01-14-1984	Hitachi Koki KK		√
	BY	JP-S59-069166	04-19-1984	Nikkiso Co Ltd.		√
	BZ	SU-1146098-A1	03-23-1985	Sp K B Biofiz App		
	BA1	SU-660718-A1	05-05-1979	Sp K B Biofizicheskoy Apparatu		
	BB1	SU-762982-A1	09-15-1980	Sp K B Biofizicheskoy Apparatu		
	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		
	BJ1	WO-2007/041716-A1	04-12-2007	Gambro, Inc		
Examiner Signature				Date Considered		

ME1 28965507v.1

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				Examiner Name	T. Zalukaeva
Sheet	6	of	6	Attorney Docket Number	130670-08002

*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. 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.		

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Examiner Signature		Date Considered	
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Utility Application of:
Michael Ragusa

Application No.: 15/608,183

Confirmation No.: 7286

Filed: May 30, 2017

Art Unit: 3781

For: SYSTEM AND METHOD FOR COLLECTING
PLASMA

Examiner: T. Zalukaeva

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 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 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.
15/793,339	October 25, 2017	2018-0344921	Published	130670-08003

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 the 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 10, 2019

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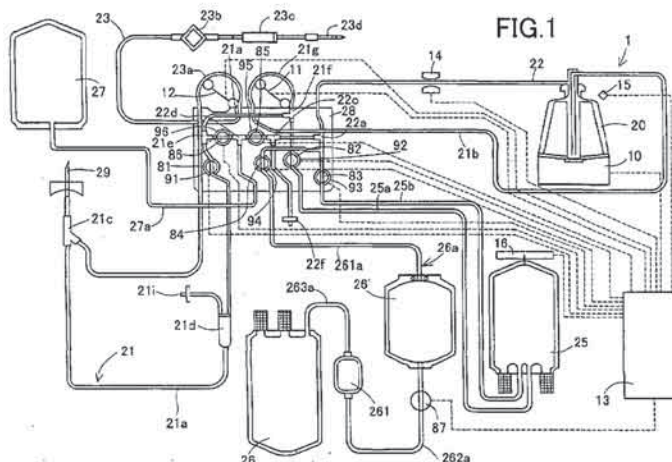
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(54) BLOOD COMPONENT COLLECTIG DEVICE

(57) An object is to provide a blood component collection system capable of collecting a desired blood component of high quality. A blood component collection system 1 comprises a centrifugal separator 20 centrifuging blood into a plurality of components, first line 21 for feeding the blood to the centrifugal separator 20, a second line 22 for releasing the blood component from the centrifugal separator 20, a temporary reservoir bag 26' for temporarily reserving the platelet concentrate, a leukoreduction filter 261 for separating and reducing

leukocyte from the platelet concentrate, and a platelet collection bag 26 for reserving the platelet concentrate having passed through the leukoreduction filter 261. The blood component collection system 1 is constructed to feed the platelet concentrate in the temporary reservoir bag 26' to the platelet collection bag 26 through the leukoreduction filter 261, and then, feed plasma and collect the platelet remaining in the leukoreduction filter 261 (platelet concentrate from which leukocyte have been reduced) together with the plasma into the platelet collection bag 26.



DescriptionTechnical Field

- 5 **[0001]** The present invention relates to a blood component collection system for separating blood into a plurality of components and collecting any of the separated components.

Background Art

- 10 **[0002]** To collect blood, currently, blood component collection is adopted for the purposes of effectively utilizing blood and alleviating a burden a donor must incur. Namely, the collected blood is separated into components through centrifugation or the like, only a component needed for a patient to be transfused is collected, and the other components are restored to a donor.

- 15 **[0003]** In the component collection, for preparing a platelet product, blood collected from a donor is routed to a blood component collection circuit. A centrifugal separator called a centrifugal bowl included in the blood component collection circuit is used to separate the blood into components, that is, plasma, a buffy coat, and red blood cells. Platelets are separated from the buffy coat and collected into a container, whereby a platelet product is prepared. The remaining plasma, white blood cells, and red blood cells are returned to the donor.

- 20 **[0004]** However, according to the above method, when a large number of platelets is needed, the number of leukocyte (white blood cells) mixed in a platelet product increases. This leads to an increase in the risk of an attack of fever, alloimmunization, virus infection, or the like.

- 25 **[0005]** In efforts to cope with the above problem, proposals have been made of a method according to which collected platelets are passed through a leukoreduction filter (leukocyte removal filter) in order to separate or reduce leukocyte, and the platelets separated from the leukocyte are collected in order to prepare a leukocyte reduced platelet product. In this case, platelets remain in the leukoreduction filter. In order to improve the yield of platelets, the leukoreduction filter is cleansed using a cleanser such as physiological saline or an anticoagulant.

- 30 **[0006]** However, according to the above method, the cleanser is mixed in the platelet product. This poses a problem that the quality of the platelet product is degraded.

Disclosure of Invention

- 35 **[0007]** An object of the present invention is to provide a blood component collection system capable of collecting a desired blood component of high quality.

- 40 **[0008]** To achieve the above object, the present invention provides a blood component collection system comprising: a centrifugal separator including a rotor having a blood reservoir space therein and an inlet and an outlet which communicate with the blood reservoir space, and centrifuging blood introduced through the inlet by rotation of the rotor, into a plurality of components in the blood reservoir space; a first container for temporarily reserving therein a first blood component; a cell separating filter for separating or reducing a predetermined kind of cells from the first blood component; and a second container for reserving the first blood component having passed through the cell separating filter, wherein the blood component collection system further comprises: channel open/close means for opening or closing a channel linking the first container and the cell separating filter; and control means for controlling action of the channel open/close means, the channel open/close means is used to carry the first blood component in the first container to the second container through the cell separating filter, then supply a second blood component, and collect the first blood component, from which the predetermined kind of cells remaining in the cell separating filter have been separated or reduced, together with the second blood component into the second container.

- 45 **[0009]** According to another aspect, the present invention provides a blood component collection system comprising: a centrifugal separator including a rotor having a blood reservoir space therein and an inlet and an outlet which communicate with the blood reservoir space, and centrifuging blood introduced through the inlet by rotation of the rotor, into a plurality of components in the blood reservoir space; a first container for temporarily reserving therein a first blood component; a cell separating filter connected to the first container through a feed tube, and used to separate or reduce a predetermined kind of cells from the first blood component fed through the feed tube; and a second container which is connected to the cell separating filter through a release tube and used for reserving therein the first blood component having passed through the cell separating filter, wherein the blood component collection system further comprises: channel open/close means for opening or closing a channel of the feed tube; and control means for controlling action of the channel open/close means, the channel open/close means is used to carry the first blood component in the first container to the second container through the feed tube, cell separating filter, and release tube in response to a command sent from the control means, thereafter, a second blood component is fed, and the first blood component that remains in the cell separating filter and the channel of the release tube and that has the predetermined

cells separated or reduced therefrom is collected together with the second blood component into the second container.

[0010] Preferably, in the blood component collection system according to the present invention, a full amount of a blood component to be collected into the second container is adjusted according to a fed amount of the second blood component. Specifically, the fed amount of the second blood component is determined based on a difference between a target full amount of the blood component to be collected into the second container and an amount of the first blood component to be carried to the second container.

[0011] More preferably, the blood component collection system according to the present invention further includes a third container for reserving the second blood component, wherein the second blood component is fed from the third container.

[0012] Preferably, in the blood component collection system according to the present invention, the second blood component is fed together with the first blood component which remains in the first container, to the cell separating filter.

[0013] More preferably, in the blood component collection system according to the present invention, the first blood component is plasma containing platelets, the second blood component is plasma, and the cell separating filter is a leukoreduction filter.

Brief Description of the Drawings

[0014]

Fig. 1 is a plan view showing the configuration of a blood component collection system according to the present invention;

Fig. 2 is a partly cutaway sectional view showing a state in which a centrifugal separator drive is mounted on a centrifugal separator included in the blood component collection system;

Fig. 3 is a timing chart for explaining the operation of the blood component collection system according to the present invention;

Fig. 4 is a flowchart describing the operation of the blood component collection system according to the present invention;

Fig. 5 is a flowchart describing the operation of the blood component collection system according to the present invention;

Fig. 6 is a flowchart describing the operation of the blood component collection system according to the present invention;

Fig. 7 is a flowchart describing the operation of the blood component collection system according to the present invention; and

Fig. 8 is a flowchart describing actions to be performed for cleansing a line in the blood component collection system according to the present invention.

Best Mode for Carrying Out the Invention

[0015] A blood component collection system according to the present invention will be detailed in conjunction with a preferred embodiment shown in the drawings below.

[0016] Fig. 1 is a plan view showing the configuration of the blood component collection system according to the present invention. Fig. 2 is a partly cutaway sectional view showing a state in which a centrifugal separator drive is mounted on a centrifugal separator included in the blood component collection system. Fig. 3 is a timing chart for explaining the operation of the blood component collection system according to the present invention. Furthermore, Fig. 4 to Fig. 7 are flowcharts describing the operation of the blood component collection system according to the present invention. Fig. 8 is a flowchart describing the actions the blood component collection system according to the present invention performs for cleansing a line.

[0017] The blood component collection system 1 shown in Fig. 1 is a system for separating blood into a plurality of components and collecting any of the separated components (especially platelets). The blood component collection system 1 comprises a centrifugal separator 20 and a blood component collection circuit 2. The centrifugal separator 20 includes a rotor 142 having a blood reservoir space 146 therein and an inlet 143 and an outlet 144 which communicate with the blood reservoir space 146, and centrifuges the blood, which is introduced through the inlet 143 by rotation of the rotor 142, within the blood reservoir space 146. The blood component collection circuit 2 comprises: a first line 21 that links a blood collection needle 29 and the inlet 143 of the centrifugal separator 20; a second line 22 joined to the outlet 144 of the centrifugal separator 20; a third line 23 joined to the first line 21; a plasma collection bag 25 having a first tube 25a joined to the first line 21 and having a second tube 25b joined to the second line 22; a platelet collection bag 26 having a third tube 26a joined to the second line 22; and a buffy coat collection bag 27 having a fourth tube 27a joined to the second line 22.

5 [0018] Furthermore, the blood component collection system 1 comprises: a centrifugal separator drive 10 which rotates the rotor 142 included in the centrifugal separator 20; a first fluid feeder pump 11 for the first line 21; a second fluid feeder pump 12 for the third line 23; a plurality of pieces of channel open/close means 81, 82, 83, 84, 85, 86, and 87 that is used to open or close the middle points of channels defined by the blood component collection circuit 2; a control unit (control means) 13 which controls the centrifugal separator drive 10, first fluid feeder pump 11, second fluid feeder pump 12, and plurality of pieces of channel open/close means 81 to 87; a turbidity sensor 14; an optical sensor 15; and a weight sensor 16.

[0019] To begin with, the blood component collection circuit 2 will be described below.

10 [0020] The blood component collection circuit 2 comprises: the first line (blood collection/return line) 21 that links the blood collection needle (blood collecting means) 29 used to collect blood and the inlet 143 of the centrifugal separator 20, and that includes a first pump tube 21g; the second line 22 that links the outlet 144 of the centrifugal separator 20 and the first line 21; the third line (anticoagulant injection line) 23 that is located near the blood collection needle 29 included in the first line 21 and that includes a second pump tube 23a; the plasma collection bag 25 that has the first tube 25a connected on the side of the blood component collection circuit 2 near the blood collection needle 29 beyond the pump tube 21g included in the first line 21, and has the second tube 25b joined to the second line 22; the platelet collection bag 26 that has the third tube 26a joined to the second line 22; and the buffy coat collection bag 27 that has a fourth tube 27a joined to the second line 22.

[0021] Incidentally, the blood collecting means is not limited to the blood collection needle 29. Alternatively, a connector (for example, a metallic or synthetic resin needle) coupled to a blood bag or any other blood pool will do.

20 [0022] As the blood collection needle 29, for example, a known metallic needle is adopted.

[0023] The first line 21 includes a first blood collection needle-side line 21a joined to the blood collection needle 29 and a first centrifugal separator-side line 21b joined to the inlet 143 of the centrifugal separator 20.

25 [0024] The first blood collection needle-side line 21a has a plurality of soft resin tubes concatenated. The first blood collection needle-side line 21a includes: orderly from the side thereof near the centrifugal separator 20, a branch connector 21c that joins the first blood collection needle-side line 21a and the third line 23; a chamber 21d used to remove bubbles or micro-aggregates; a branch connector 21e that joins the first blood collection needle-side line 21a and the second line 22; and a branch connector 21f that joins the first blood collection needle-side line 21a and the first tube 25a extending from the plasma collection bag 25.

[0025] Moreover, an air-permeable and bacteria-impermeable filter 21i is connected to the chamber 21d.

30 [0026] On the other hand, the first centrifugal separator-side line 21b is coupled to the branch connector 21f that joins the first blood collection needle-side line 21a and the first tube 25a, and includes the first pump tube 21g located near the connector.

35 [0027] The second line 22 that links the outlet 144 of the centrifugal separator 20 and the first line 21 has one end thereof coupled to the outlet 144 of the centrifugal separator 20 and the other end thereof coupled to the branch connector 21e of the first line 21.

[0028] The second line 22 includes: a branch connector 22a that joins the second line 22, the second tube 25b extending from the plasma collection bag 25, and the third tube 26a extending from the platelet collection bag 26; a branch connector 22c that joins the second line 22 and a tube including a bubble removing filter 22f; and a branch connector 22d that joins the second line 22 and the fourth tube 27a extending from the buffy coat collection bag 27.

40 [0029] The third line 23 has one end thereof coupled to the branch connector 21c included in the first line 21.

[0030] The third line 23 includes, orderly from the side thereof coupled to the branch connector 21c, the second pump tube 23a, a bacteria removal filter 23b, a bubble removing chamber 23c, and an anticoagulant container joint needle 23d.

45 [0031] The plasma collection bag (third container) 25 is a container into which plasma (second blood component) is collected (reserved). The plasma collection bag 25 has the first tube 25a coupled to the branch connector 21f which is located on the side of the blood component collection circuit near the blood collection needle 29 beyond the pump tube 21g included in the first line 21. The plasma collection bag 25 also has the second tube 25b coupled to the branch connector 22a included in the second line 22. Namely, the plasma collection bag 25 and second tube 25b constitute a plasma collection branch line used to collect plasma.

50 [0032] The platelet collection bag (second container) 26 is a container into which plasma containing platelets (first blood component) and having passed through a leukoreduction filter 261 that will be described later. The platelet collection bag 26 has the third tube 26a coupled to the branch connector 22a included in the second line 22. Hereinafter, plasma containing platelets (first blood component) shall be called "platelet concentrate (PC)", and the platelet concentrate (PC) collected (reserved) into the platelet collection bag 26 shall be called "a platelet product".

55 [0033] Moreover, a temporary reservoir bag (first container) 26' in which the platelet concentrate (first blood component) is temporarily reserved, and the leukoreduction filter (cell separating filter) 261 that separates or reduce leukocyte (predetermined kind of cells) from the platelet concentrate are inserted into the third tube 26a.

[0034] In short, the third tube 26a is composed of three tubes 261a, 262a, and 263a. The tube 261a links the branch

connector 22a and the temporary reservoir bag 26'. The tube 262a links the temporary reservoir bag 26' and leukoreduction filter 261. The tube 263a links the leukoreduction filter 261 and the platelet (platelet product) collection bag 26.

[0035] The tube 262a serves as a feed tube that feeds platelet concentrate from the temporary reservoir bag 26' to the leukoreduction filter. The tube 263a serves as a release tube that releases the platelet concentrate, which has leukocyte reduced therefrom, from the leukoreduction filter 261 (feeds the platelet concentrate to the platelet collection bag 26).

[0036] In other words, the third tube 26 (composed of the tubes 261a, 262a, and 263a), temporary reservoir bag 26', leukoreduction filter 261, and platelet collection bag 26 constitute a platelet collection branch line that collects platelets (platelet product).

[0037] Moreover, the temporary reservoir bag 26', leukoreduction filter 261, and platelet collection bag 26 are positioned with the blood component collection system 1 constructed so that the leukoreduction filter 261 will be located at a lower position than the temporary reservoir bag 26' is and the platelet collection bag 26 will be located at a lower position than the leukoreduction filter 261 is.

[0038] Moreover, what is used as the leukoreduction filter 261 is, for example, a filter formed by inserting a filtration member into a casing having an inlet and an outlet formed at both ends thereof. The filtration member has one or two layers of a porous substance such as woven cloth, non-woven cloth, mesh, or foam made of a synthetic resin such as polypropylene, polyester, polyurethane, or polyamide.

[0039] The buffy coat collection bag 27 is a container into which a buffy coat is collected. The buffy coat bag 27 has the fourth tube 27a coupled to the branch connector 22d included in the second line 22. Namely, the buffy coat collection bag 27 and fourth tube 27a constitute a buffy coat collection branch line that collects buffy coat.

[0040] Preferably, the tubes used to form the first to third lines 21 to 23, pump tubes 21g and 23a, and the tubes 25a, 25b, 26a (composed of the tubes 261a, 262a, and 263a), and 27a coupled to the bags 25 to 27 are made of polyvinyl chloride.

[0041] When the tubes are made of polyvinyl chloride, satisfactory flexibility and softness are ensured. The tubes are therefore easy to handle. Moreover, the tubes can be readily blocked using a clamp or the like.

[0042] Moreover, the same material as the material made into the tubes can be adopted as the material to be made into the branch connectors 21c, 21e, 21f, 22a, 22c, and 22d.

[0043] What are used as the pump tubes 21g and 23a are tubes that are strong enough to remain undamaged even when pressurized by the fluid feeder pumps 11 and 12 (for example, roller pumps) to be described later.

[0044] What are used as the plasma collection bag 25, platelet collection bag 26, temporary reservoir bag 26', and buffy coat collection bag 27 are made by layering a flexible resin sheet material and fusing the margins of the layers (through heat fusion, high-frequency fusion, or ultrasonic fusion) in the form of a sac or bonding them using an adhesive in the form thereof.

[0045] The material to be made into the bags 25 to 27 and 26' is, for example, soft polyvinyl chloride.

[0046] Preferably, the sheet material used to make the platelet collection bag 26 is a material superb in gas permeability in terms of improvement of the ability to reserve platelets in good condition.

[0047] Preferably, the sheet material is made of, for example, polyolefin or DnDP flexible polyvinyl chloride. Otherwise, the above resin flexible sheet material may be adopted and made relatively thin (for example, the thickness ranges from about 0.1 mm to about 0.5 mm, or more particularly, from about 0.1 mm to about 0.3 mm).

[0048] Moreover, a platelet preservative, for example, GAC, PAS, or PSM-1 may be poured into the plasma collection bag 26 in advance.

[0049] The major elements of the blood component collection circuit 2 are, as shown in Fig. 1, provided as cassettes. Namely, the blood component collection circuit 2 has the lines (first line 21, second line 22, and third line 23) and the tubes (first tube 25a, second tube 25b, third tube 26a, and fourth tube 27a) partly stored and preserved, or in other words, partly locked in a cassette housing 28.

[0050] Both the ends of the first pump tube 21g and both the ends of the second pump tube 23a are locked in the cassette housing 28. The pump tubes 21g and 23a are projected from the cassette housing 28 in the form of a loop in line with the shape of the fluid feeder pumps (for example, roller pumps) 11 and 12. Consequently, the first and second pump tubes 21g and 23a can be easily attached to the fluid feeder pumps 11 and 12 respectively.

[0051] Furthermore, the cassette housing 28 has a plurality of openings 91 to 96 formed therein.

[0052] The centrifugal separator 20 included in the blood component collection circuit 2 is generally called a centrifugal bowl, and designed to separate blood into a plurality of components by utilizing centrifugal force.

[0053] The centrifugal separator 20 comprises, as shown in Fig. 2, a pipe 141 extending vertically and having the inlet 143 formed at the upper end thereof, and a hollow rotor 142 that rotates about the pipe 141 and is sealed off from an upper part 145 in a fluid-tight manner.

[0054] The rotor 142 has the annular blood reservoir space 146 formed along the internal surface of the circumferential wall thereof. The blood reservoir space 146 is shaped (tapered) so that the inner and outer diameters thereof will gradually diminish from the lower part thereof shown in Fig. 2 to the upper part thereof. The lower part of the blood

reservoir space 146 communicates with the lower-end opening of the pipe 141 by way of a substantially disk-like channel formed on the bottom of the rotor 142. The upper part of the blood reservoir space 146 communicates with the outlet 144. Moreover, the volume of the blood reservoir space 146 included in the rotor 142 ranges, for example, from about 100 mL to about 350 mL. The maximum inner diameter (maximum radius) of the blood reservoir space with the axis of rotation of the rotor 142 as a center ranges, for example, from about 55 mm to about 65 mm.

[0055] The rotor 142 is rotated under predetermined conditions for centrifugation (rotating speed and rotation time) predetermined by the centrifugal separator drive 10 included in the blood component collection system 1. Under the conditions for centrifugation, a blood separation pattern (for example, the number of blood components to be separated) can be determined for blood introduced into the rotor 142.

[0056] According to the present embodiment, the conditions for centrifugation are determined so that blood will be, as shown in Fig. 2, separated into, orderly from the innermost layer, a layer of plasma 131, a buffy coat layer 132, and a layer of red blood cells 133.

[0057] Next, the overall configuration of the blood component collection system 1 shown in Fig. 1 will be described below.

[0058] The blood component collection system 1 comprises: the centrifugal separator drive 10 that rotates the rotor 142 included in the centrifugal separator 20; the first fluid feeder pump 11 located in the middle of the first line 21; the second fluid feeder pump 12 located in the middle of the third line 23; the plurality of pieces of channel open/close means 81, 82, 83, 84, 85, 86, and 87 that can open or close the middles of the channels defined by (the first line 21, second line 22, first tube 25a, second tube 25b, and third tube 26a included in) the blood component collection circuit 2; and the control unit (control means) 13 that controls the centrifugal separator drive 10, first fluid feeder pump 11, second fluid feeder pump 12, and plurality of pieces of channel open/close means 81 to 87.

[0059] Furthermore, the blood component collection system 1 comprises: the turbidity sensor 14 attached to (included in) the second line 22 on the side of the second line near the centrifugal separator 20 (upstream) beyond the connector 22a that joins the second line 22 and the second tube 25b; the optical sensor 15 located near the centrifugal separator 20; and the weight sensor 16 that measures the weight of plasma together with the weight of the plasma collection bag 25.

[0060] The control unit 13 includes two pump controllers (not shown) that control the first fluid feeder pump 11 and second fluid feeder pump 12 respectively. The control unit 13 is electrically connected to the first fluid feeder pump 11 and second fluid feeder pump 12 via the respective pump controllers.

[0061] A driving controller (not shown) included in the centrifugal separator drive 10 is electrically connected to the control unit 13.

[0062] The pieces of channel open/close means 81 to 87 are electrically connected to the control unit 13.

[0063] The turbidity sensor 14, optical sensor 15, and weight sensor 16 are electrically connected to the control unit 13.

[0064] The control unit 13 is formed with, for example, a microcomputer, and receives detection signals from the turbidity sensor 14, optical sensor 15, and weight sensor 16 respectively at any time.

[0065] Based on the detection signals received from the turbidity sensor 14, optical sensor 15, and weight sensor 16 respectively, the control unit 13 activates the components of the blood component collection system 1 according to a pre-installed program. Specifically, the control unit 13 controls the start or stop of the rotations of the fluid feeder pumps 11 and 12, and the direction of rotation (forward rotation or reverse rotation). Moreover, if necessary, the control unit 13 controls the open or close of the pieces of channel open/close means 81 to 87 and the activation of the centrifugal separator drive 10.

[0066] The first channel open/close means 81 opens or closes the first line 21 while being located on the side of the blood component collection circuit near the blood collection needle 29 beyond the first pump tube 21g.

[0067] The second channel open/close means 82 opens or closes the first tube 25a extending from the plasma collection bag 25.

[0068] The third channel open/close means 83 opens or closes the second tube 25b extending from the plasma collection bag 25.

[0069] The fourth channel open/close means 84 opens or closes the third tube 26a (tube 261a) extending from the platelet collection bag 26.

[0070] The fifth channel open/close means 85 opens or closes the second line 22 while being located on the side (upstream) of the blood component collection circuit near the centrifugal separator 20 beyond the connector (branch connector 22d) that joins the second line 22 and the fourth tube 27a extending from the buffy coat collection bag 27.

[0071] The sixth channel open/close means 86 opens or closes the second line 22 while being interposed between the connector (branch connector 21e) that joins the first line 21 and second line 22, and the connector (branch connector 22d) that joins the second line 22 and the fourth tube 27a (downstream the connector that joins the second line 22 and fourth tube 27a).

[0072] Moreover, the seventh channel open/close means 87 opens or closes the third tube 26a (tube 262a).

[0073] The pieces of channel open/close means 81 to 87 each have an insertion member into which the first line 21, second line 22, first tube 25a, second tube 25b, or third tube 26a (tube 261a or 262a) can be inserted. The insertion member includes a clamp that is actuated by a driving source, for example, a solenoid, an electric motor, or a (hydraulic or pneumatic) cylinder. More particularly, an electromagnetic clamp to be actuated by a solenoid is preferred.

5 [0074] The pieces of channel open/close means (clamps) 81 to 87 are actuated based on a signal sent from the control unit 13.

[0075] The centrifugal separator drive 10 comprises, as shown in Fig. 2, a housing 201 in which the centrifugal separator 20 is stored, legs 202, a motor 203 that is a driving source, and a disk-like locking base 205 that bears the centrifugal separator 20.

10 [0076] The housing 201 is placed on and fixed to the tops of the legs 202. Moreover, the motor 203 is fixed to the bottom of the housing 201 using a bolt 206 with a spacer 207 between them.

[0077] The locking base 205 is engaged with the distal part of a rotation shaft 204 of the motor 203 so that the locking base 205 will be rotated concentrically and together with the rotation shaft 204. A concave part in which the bottom of the rotor 142 is fitted is formed in the upper surface of the locking base 25.

15 [0078] Moreover, the upper part 145 of the centrifugal separator 20 is fixed to the housing 201 using a fixing member that is not shown.

[0079] In the centrifugal separator drive 10 having the foregoing components, when the motor 23 is driven, the locking base 205 and the rotor 142 fixed to the locking base 205 are rotated at, for example, a rotational frequency ranging from about 3000 rpm to about 6000 rpm.

20 [0080] The optical sensor 15 is located on the side (left side in Fig. 2) of the housing 201.

[0081] The optical sensor 15 is designed to irradiate light to the blood reservoir space 146 and receive light reflected therefrom.

[0082] In the optical sensor 15, light (for example, laser light) is irradiated from a floodlight 151. A light receiver 152 receives light reflected from the reflecting surface 147 of the rotor 142. The light receiver 152 converts the received light into an electric signal whose level is proportional to the amount of received light.

25 [0083] At this time, the irradiated light and reflected light pass through the blood components in the blood reservoir space 146. However, the abundance ratio of each blood component varies depending on the position of the interface between the blood component and an adjoining blood component (in the present embodiment, the interface B between the layer of plasma 131 and the buffy coat layer 132) through which the irradiated light or reflected light passes. For this reason, the transmittance of each blood component varies depending on the position. Accordingly, the amount of light received by the light receiver 152 varies (changes). The variation is detected as a change in output voltage sent from the light receiver 152.

[0084] In short, the optical sensor 15 can detect the position of the interface between adjoining blood components according to a change in the amount of light received by the light receiver 152.

35 [0085] The interface between adjoining blood components whose position is detected by the optical sensor 15 is not limited to the interface B but may be the interface between, for example, the buffy coat layer 132 and the layer of red blood cells 133.

[0086] Now, the layers 131 to 133 in the blood reservoir space 146 are different from one another in terms of color because of the difference among the blood components. In particular, the layer of red blood cells 133 is reddish because red blood cells are red. Consequently, from the viewpoint of improvement in precision to be offered by the optical sensor 15, light serving as irradiated light should preferably have a spectrum ranging, for example, from about 600 nm to about 900 nm, or more preferably, from about 750 nm to about 800 nm, though it is not limited to the range.

40 [0087] The turbidity sensor 14 senses the turbidity of a fluid flowing through the second line 22 and transmits a voltage inversely proportional to a degree of turbidity. Specifically, when the degree of turbidity is high, the turbidity sensor 14 transmits a low voltage. When the degree of turbidity is low, the turbidity sensor 14 transmits a high voltage.

[0088] Owing to the turbidity sensor 14, for example, a change of a fluid flowing through the second line 22 from air to plasma, a change in the concentration of platelets in plasma, or mixture of red blood cells in plasma can be detected.

45 [0089] As the first fluid feeder pump 11 to which the first pump tube 21g is attached and the second fluid feeder pump 12 to which the second pump tube 23a is attached, a non-blood contact pump, for example, a roller pump is adopted preferably.

[0090] Moreover, as the first fluid feeder pump (blood pump) 11, a pump capable of feeding blood in either directions is adopted. Specifically, a roller pump capable of rotating forward and reversely is adopted.

50 [0091] Next, referring to Fig. 1, Fig. 3, and Fig. 4 to Fig. 8 that are flowcharts, blood component collection to be performed using the blood component collection system 1 will be described by taking for instance a case where platelets are collected. Fig. 3 is a timing chart outlining a first cycle of blood component collection to be performed using the blood component collection system 1.

55 [0092] The blood component collection system 1 acts to execute platelet collection composed of, as shown in Fig. 3, a first plasma collection process (A), a constant-speed plasma circulation process (B), a second plasma collection

process (C), an accelerated plasma circulation process (D), a third plasma collection process (E), a platelet collection step (F), and a blood return step.

[0093] Moreover, according to the present embodiment, the platelet collection is repeated three times (first cycle to third cycle). Furthermore, a buffy coat collection process (G) is executed prior to the blood return process after the completion of the platelet collection process (F) within each cycle other than the final (third) cycle. A buffy coat return process is executed prior to the first plasma collection process (A) within the next platelet collection.

[0094] According to the present invention, in the blood component collection system 1, concurrently with the final cycle of platelet collection, platelet concentrate temporarily collected (reserved) in the temporary reservoir bag 26' is fed to the leukoreduction filter 261, and filtered to have leukocyte separated or reduced therefrom (see S401 in Fig. 8). From the viewpoint of shortening the binding time during which a donor is bound, the filtration should preferably be started concurrently with the final cycle of platelet collection (in particular, in an early process within platelet collection). In the blood component collection system 1 of the present embodiment, the filtration is started nearly concurrently with the second plasma collection process (C) within the final cycle of platelet collection.

[0095] [0] First, the third line 23 and blood collection needle 29 are primed with an anticoagulant. Thereafter, a donor's vessel is punctured with the blood collection needle 29.

[1] First cycle of platelet collection (see Fig. 4 and Fig. 5)

[0096] [11] First, the blood component collection system 1 executes the first plasma collection (first PPP collection) process (A). In the first plasma collection process (A), blood is routed to the blood reservoir space 146 of the rotor 142, and centrifuged. Consequently, separated plasma (PPP) is collected into the plasma collection bag 25.

[0097] In the first plasma collection process (A), first, the control unit 13 executes plasma (second blood component) collection (step S101 in Fig. 4).

[0098] Specifically, the first channel open/close means 81 and fourth channel open/close means 84 are unblocked under the control of the control unit 13, but the other pieces of channel open/close means are left blocked. In this state, the first fluid feeder pump 11 is actuated (rotated forward) at a predetermined rotating speed (preferably, about 250 mL/min or less, or more preferably, from about 40 mL/min to about 150 mL/min, and in the present embodiment, 60 mL/min). Thus, blood is collected from the donor.

[0099] Concurrently with the blood collection, the second fluid feeder pump 12 is actuated under the control of the control unit 13. An anticoagulant, for example, an ACD-A solution is fed through the third line 23, and mixed in the collected blood.

[0100] At this time, the control unit 13 controls the rotating speed of the second fluid feeder pump 12 so that the anticoagulant will be mixed in the collected blood at a predetermined ratio (preferably, about 1/20 to about 1/6, for example, 1/10).

[0101] Consequently, the blood (anticoagulant-inclusive blood) is carried through the first line 21. The blood then enters the inlet 143 of the centrifugal separator 20, passes through the pipe 141, and is thus routed to the blood reservoir space 146 of the rotor 142.

[0102] At this time, the air (sterilized air) in the centrifugal separator 20 is fed to the temporary reservoir bag 26' by way of the second line 22 and third tube 26a.

[0103] Concurrently with the blood collection, or before or after the blood collection, the control unit 13 actuates the centrifugal separator drive 10 and rotates the rotor 142 at a predetermined rotational frequency.

[0104] With the rotation of the rotor 142, the blood introduced into the blood reservoir space 146 is separated into the layer of plasma (PPP) 131, buffy coat layer (BC) 132, and layer of red blood cells (CRC) 133 in that order from the innermost layer.

[0105] The rotational frequency of the rotor 142 ranges, preferably, from about 3000 rpm to about 6000 rpm, or more preferably, from about 4200 rpm to about 5800 rpm. Moreover, in the processes described below, the control unit 13 does not change the rotational frequency of the rotor 142 unless otherwise described.

[0106] Furthermore, the blood collection and the feed of an anticoagulant are continued. When an amount of blood (approx. 270 mL) exceeding the capacity of the blood reservoir space 146 is routed to the blood reservoir space 146, the blood reservoir space 146 is filled with blood, and plasma (PPP) overflows through the outlet 144 of the centrifugal separator 20.

[0107] At this time, the turbidity sensor 14 attached to the second line 22 detects that a fluid flowing through the second line 22 has changed from air to plasma. Based on the detection signal sent from the turbidity sensor 14, the control unit 13 blocks the fourth channel open/close means 84 and unblocks the third channel open/close means 83.

[0108] Consequently, plasma is routed or collected into the plasma collection bag (third container) 25 by way of the second line 22 and second tube 25b.

[0109] The weight sensor 16 measures the weight of the plasma collection bag 25. A weight signal representing the measured weight is transferred to the control unit 13.

- [0110] Thereafter, the control unit 13 judges from the information (weight signal) sent from the weight sensor 16 whether a predetermined amount of plasma has been collected into the plasma collection bag 25 (step S102 in Fig. 4).
- [0111] The (predetermined) collected amount of plasma ranges, preferably, from about 10 g to about 150 g, or more preferably, from about 20 g to about 40 g.
- 5 [0112] If it is found at step S102 that the predetermined amount of plasma has not been collected into the plasma collection bag 25, the control unit 13 returns to step S101, and repeats step S101 and subsequent steps.
- [0113] If it is found at step S102 that the predetermined amount of plasma has been collected into the plasma collection bag 25, the control unit 13 terminates the process [11] (first plasma collection process (A)), and proceeds to the constant-speed plasma circulation process (B).
- 10 [0114] [12] Thereafter, the blood component collection system 1 executes the constant-speed plasma circulation (constant-speed PPP circulation) process (B). In the constant-speed plasma circulation process (B), the plasma in the plasma collection bag 25 is circulated through the blood reservoir space 146 at a constant speed.
- [0115] In the constant-speed plasma circulation process (B), first, the control unit 13 executes plasma circulation (step S103 in Fig. 4).
- 15 [0116] Specifically, under the control of the control unit 13, the first channel open/close means 81 is blocked and the second channel open/close means 82 is unblocked. Moreover, the second fluid feeder pump 12 is inactivated, and the first fluid feeder pump 11 is actuated (rotated forward) at a predetermined rotating speed (preferably, from about 60 mL/min to about 250 mL/min, and in the present embodiment, 200 mL/min).
- 20 [0117] Consequently, blood collection is suspended. The plasma in the plasma collection bag 25 is routed to the blood reservoir space 146 by way of the first tube 25a and first line 21 at a constant speed. Plasma flowing out of the outlet 144 of the centrifugal separator 20 is collected into the plasma collection bag 25 by way of the second line 22 and second tube 25b. In short, the plasma in the plasma collection bag 25 is circulated through the blood reservoir space 146 at the constant speed.
- [0118] Thereafter, the control unit 13 judges whether a predetermined time (preferably, from about 10 sec to about 90 sec, for example, 30 sec) has elapsed since the start of the constant-speed plasma circulation (step S104 in Fig. 4).
- 25 [0119] If it is found at step S104 that the predetermined time has not elapsed since the start of the constant-speed plasma circulation, the control unit 13 returns to step S103, and repeats step S103 and subsequent steps.
- [0120] If it is found at step S 104 that the predetermined time has elapsed since the start of the constant-speed plasma circulation, the control unit 13 terminates the process [12] (constant-speed plasma circulation process (B)), and proceeds to the second plasma collection process (C).
- 30 [0121] [13] Thereafter, the blood component collection system 1 executes the second plasma (PPP) collection process (C). In the second plasma collection process (C), blood is routed to the blood reservoir space 146 of the rotor 142 and centrifuged. Separated plasma is then collected into the plasma collection bag 25.
- [0122] In the second plasma collection process (C), the same steps as those included in the process [11] (first plasma collection process (A)) are executed except the step of measuring a collected amount of plasma using the weight sensor 16. Instead of the step, the position of the interface between the layer of plasma 131 and the buffy coat layer 132 is detected.
- 35 [0123] In the second plasma collection process (C), first, the control unit 13 collects plasma (step S105 in Fig. 4).
- [0124] At this time, the control unit 13 blocks the second channel open/close means 82 and unblocks the first channel open/close means 81.
- 40 [0125] Consequently, the number of red blood cells in the blood reservoir space 146 increases, that is, the thickness of the layer of red blood cells 133 increases. Accordingly, the interface B rises gradually (moves towards the axis of rotation of the rotor 142).
- [0126] Thereafter, the control unit 13 judges from the detection signal sent from the optical sensor 15 (information of the detected interface position) whether the interface B has reached a predetermined level (first position) (step S106 in Fig. 4).
- 45 [0127] Incidentally, the first position of the interface B is a position at which the detection signal sent from the first optical sensor 15 (an output voltage sent from the light receiver 152) ranges, preferably, from about 1 V to about 2 V.
- [0128] If it is found at step S106 that the interface B has not reached the first position, the control unit 13 returns to step S105, and repeats step S105 and subsequent steps.
- 50 [0129] Moreover, if it is found at step S 105 that the interface B has reached the first position, the control unit 13 terminates the present process [13] (second plasma collection process (C)) and proceeds to the accelerated plasma circulation process (D).
- [0130] [14] Thereafter, the blood component collection system 1 executes the accelerated plasma (PPP) circulation process (D). In the accelerated plasma (PPP) circulation process (D), the plasma in the plasma collection bag 25 is circulated through the blood reservoir space 146 while being accelerated.
- 55 [0131] In the accelerated plasma (PPP) circulation process (D), first, the control unit 13 executes plasma circulation (step S107 in Fig. 4).

- [0132] Specifically, the first channel open/close means 81 is blocked under the control of the control unit 13, and the second channel open/close means 82 is unblocked thereunder. Moreover, the second fluid feeder pump 12 is inactivated, and the first fluid feeder pump 11 is activated (rotated forward) so that the rotating speed thereof will increase at a rate corresponding to a constant acceleration.
- 5 [0133] Consequently, blood collection is suspended. Moreover, the plasma in the plasma collection bag 25 is routed to the blood reservoir space 146 by way of the first tube 25a and first line 21 while being accelerated. Plasma flowing out of the outlet 144 of the centrifugal separator 20 is collected into the plasma collection bag 25 by way of the second line 22 and second tube 25b. In short, the plasma in the plasma collection bag 25 is circulated through the blood reservoir space 146 while being accelerated.
- 10 [0134] At this time, the control unit 13 extends control so that the rotating speed of the first fluid feeder pump 11 will increase at a rate corresponding to a constant acceleration from a speed lower than the speed attained during the constant-speed plasma circulation (initial speed is, in the present embodiment, 60 mL/min).
- [0135] The condition for acceleration (acceleration) ranges, preferably, from about 1 mL/min/sec to 10 mL/min/sec, or more preferably, from about 3 mL/min/sec to about 6 mL/min/sec. In the present embodiment, the acceleration is set to a fixed value. Alternatively, the acceleration may be varied stepwise or continuously within the above range.
- 15 [0136] Thereafter, the control unit 13 judges whether the circulating speed at which plasma circulates through the blood reservoir space 146 has reached the maximum speed, that is, whether the rotating speed of the first fluid feeder pump 11 has reached the maximum speed (preferably, from about 130 mL/min to 250 mL/min, and in the present embodiment, 170 mL/min) (step S108 in Fig. 4).
- 20 [0137] The step S108 is continued until the circulating speed at which plasma circulates through the blood reservoir space 146 reaches the maximum speed.
- [0138] If it is found at step S108 that the circulating speed at which plasma circulates through the blood reservoir space 146 has reached the maximum speed, the control unit 13 terminates the present process [14] (accelerated plasma circulation process (D)) and proceeds to the third plasma collection process (E).
- 25 [0139] [15] Thereafter, the blood component collection system 1 executes the third plasma (PPP) collection process (E). In the third plasma collection process (E), blood is routed to the blood reservoir space 146 of the rotor 142 and centrifuged. Separated plasma is collected into the plasma collection bag 25.
- [0140] In the third plasma collection process (E), first, the control unit 13 executes plasma collection (step S109 in Fig. 4).
- 30 [0141] Thereafter, the control unit 13 judges from the information (weight signal) sent from the weight sensor 16 whether a predetermined amount of plasma has been collected into the plasma collection bag 25 (step S110 in Fig. 4).
- [0142] The (predetermined) collected amount of plasma ranges, preferably, from about 2 g to about 30 g, or more preferably, from about 5 g to about 15 g.
- 35 [0143] If it is found at step S110 that the predetermined amount of plasma has been collected into the plasma collection bag 25, the control unit 13 terminates the present process [15] (third plasma collection process (E)) and proceeds to the plasma collection process (F) (① in Fig. 5).
- [0144] [16] Thereafter, the blood component collection system 1 executes the platelet (PC) collection process (F). In the platelet collection process (F), the plasma in the plasma collection bag 25 is circulated through the blood reservoir space 146 while being accelerated at a first acceleration. Thereafter, the first acceleration is changed to a second acceleration that is higher than the first acceleration. The plasma is circulated while being accelerated at the second acceleration. This causes platelets to flow out of the blood reservoir space 146. Consequently, platelet concentrate is collected (reserved) into the temporary reservoir bag 26'.
- 40 [0145] In the platelet collection process, first, the control unit 13 executes plasma (PPP) circulation at the first acceleration (first acceleration step in Fig. 3, step S111 in Fig. 5).
- 45 [0146] Specifically, the first channel open/close means 81 is blocked under the control of the control unit 13, and the second channel open/close means 82 is unblocked thereunder. The second fluid feeder pump 12 is inactivated, and the first fluid feeder pump 11 is activated (rotated forward) so that the rotating speed thereof will increase at a rate corresponding to the first acceleration.
- [0147] Consequently, blood collection is suspended. Moreover, the plasma in the plasma collection bag 25 is routed to the blood reservoir space 146 by way of the first tube 25a and first line 21 while being accelerated at the first acceleration. Plasma flowing out of the outlet 144 of the centrifugal separator 20 is collected into the plasma collection bag 25 by way of the second line 22 and second tube 25b. In short, the plasma in the plasma collection bag 25 is circulated through the blood reservoir space 146 while being accelerated at the first acceleration.
- 50 [0148] At this time, when plasma is circulated through the blood reservoir space 146 while being accelerated at the first acceleration, the thickness of the layer of red blood cells 133 increases. Consequently, the interface B rises gradually (moves toward the axis of rotation of the rotor 142).
- 55 [0149] The first acceleration ranges, preferably, from about 0.5 mL/min/sec to about 10 mL/min/sec, or more preferably, from about 1.5 mL/min/sec to about 2.5 mL/min/sec. In the present embodiment, the first acceleration is set to

a fixed value. Alternatively, the first acceleration may be varied stepwise or continuously within the above range.

[0150] Moreover, the initial rotating speed of the first fluid feeder pump 11 for circulating plasma at the first acceleration ranges, preferably, from about 40 mL/min to about 150 mL/min, or more preferably, from about 50 mL/min to about 80 mL/min. In the present embodiment, the initial rotating speed of the first fluid feeder pump 11 is set to 60 mL/min.

[0151] Thereafter, the control unit 13 continues step S111 until the circulating speed at which plasma circulates through the blood reservoir space 146 reaches a predetermined speed (step S112 in Fig. 5).

[0152] Incidentally, the circulating speed of plasma, that is, the rotating speed of the first fluid feeder pump 11 ranges, preferably, from about 100 mL/min to about 180 mL/min, or more preferably, from about 140 mL/min to about 160 mL/min. In the present embodiment, the rotating speed of the first fluid feeder pump 11 is set to 150 mL/min.

[0153] If it is found at step S112 that the circulating speed at which plasma circulates through the blood reservoir space 146 has reached the predetermined speed, the control unit 13 executes plasma (PPP) circulation at a second acceleration speed (first acceleration step in Fig. 3, step S113 in Fig. 5).

[0154] Specifically, the acceleration of the first fluid feeder pump 11 is changed from the first acceleration to the second acceleration under the control of the control unit 13. Moreover, the first fluid feeder pump 11 is activated (rotated forward) so that the rotating speed thereof will increase at a rate corresponding to the second acceleration. Consequently, the plasma in the plasma collection bag 25 is circulated through the blood reservoir space 146 while being accelerated at the second acceleration.

[0155] When the plasma is circulated through the blood reservoir space 146 while being accelerated at the second acceleration, the thickness of the layer of red blood cells 133 increases, and the interface B rises gradually (moves toward the axis of rotation of the rotor 142). Moreover, the platelets (PC) contained in the buffy coat layer 132 floats (goes up) against centrifugal force, and moves toward the outlet 144 of the rotor 142.

[0156] The second acceleration is determined to be higher than the first acceleration, and ranges, preferably, from about 3 mL/min/sec to about 20 mL/min/sec, or more preferably, from about 5 mL/min/sec to about 10 mL/min/sec. In the present embodiment, the second acceleration is set to a fixed value. Alternatively, the second acceleration may be varied stepwise or continuously within the range.

[0157] Thereafter, the control unit 13 judges whether the circulating speed at which plasma circulates through the blood reservoir space 146 has reached the maximum speed, that is, whether the rotating speed of the first fluid feeder pump 11 has reached the maximum speed (preferably, from about 120 mL/min to 300 mL/min, and in the present embodiment, 200 mL/min) (step S114 in Fig. 5).

[0158] If it is found at step S114 that the circulating speed at which plasma circulates through the blood reservoir space 146 has not reached the maximum speed, the control unit 13 returns to step S113, and repeats step S113 and subsequent steps.

[0159] If it is found at step S114 that the circulating speed at which plasma circulates through the blood reservoir space 146 has reached the maximum speed, the control unit 13 continues plasma (PPP) circulation (step S115 in Fig. 5).

[0160] Specifically, the control unit 13 extends control so that the rotating speed of the first fluid feeder pump 11 will be retained (held) at the maximum speed attained at step S115. Consequently, the circulating speed at which plasma circulates through the blood reservoir space 146 ranges, preferably, from about 120 mL/min to about 300 mL/min. In the present embodiment, the circulating speed is set to 200 mL/min.

[0161] Thereafter, the control unit 13 judges whether a predetermined time (preferably, from about 5 sec to about 15 sec, for example, 10 sec) has elapsed since the continuation of plasma circulation is determined (step S116 in Fig. 5).

[0162] If it is found at step S116 that the predetermined time has not elapsed since the continuation of plasma circulation is determined, the control unit 13 judges whether the output voltage (PC concentration voltage) sent from the turbidity sensor 14 had dropped to a predetermined value (preferably, from about 2.5 V to about 3.5 V, for example, 3.0 V) or less (step S117 in Fig. 5).

[0163] If it is found at step S117 that the output voltage sent from the turbidity sensor 14 has not dropped to the predetermined value or less, the control unit 13 returns to step S115 and repeats step S115 and subsequent steps.

[0164] While steps S115 to S117 are repeated, if it is found at step S116 that the predetermined time has elapsed since the continuation of plasma circulation is determined, the control unit 13 terminates the present process [16] (platelet collection process (F)) and proceeds to the buffy coat collection process (G).

[0165] If it is found at step S117 that the output voltage sent from the turbidity sensor 14 has dropped to the predetermined value or less, that is, if the concentration of platelets contained in plasma which flows through the second line 22 along with the outflow of platelets from the outlet 144 of the rotor 142 has reached a predetermined value or more, the control unit 13 executes platelet (PC) collection (step S118 in Fig. 5).

[0166] Specifically, based on the detection signal sent from the turbidity sensor 14, the control unit 13 blocks the third channel open/close means 83 and unblocks the fourth channel open/close means 84.

[0167] Consequently, platelet concentrate is routed to the temporary reservoir bag 26' by way of the second line 22 and third tube 26a (tube 261a), and collected (reserved). At this time, since the seventh channel open/close means 87 is blocked, the platelet concentrate does not flow out of the temporary reservoir bag 26'.

[0168] Moreover, the control unit 13 calculates the concentration of platelets (concentration of cumulative platelets) in the temporary reservoir bag 26' according to the output voltage (detection signal) sent from the turbidity sensor 14. The concentration of platelets keeps rising after the start of platelet collection. Once the concentration of platelets reaches the maximum value, it decreases.

5 **[0169]** Thereafter, the control unit 13 judges whether a predetermined time (preferably, from about 10 sec to about 25 sec, for example, 15 sec) has elapsed since the start of PC collection (step S119 in Fig. 5).

[0170] If it is found at step S119 that the predetermined time has not elapsed since the start of platelet collection, the control unit 13 judges whether the output voltage sent from the turbidity sensor 14 (platelet (PC) concentration voltage) has reached a predetermined value or less (step S 120 in Fig. 5).

10 **[0171]** The predetermined value of the output voltage sent from the turbidity sensor 14 is a value near the value of the output voltage transmitted when red blood cells (CRC) are mixed in plasma flowing through the second line 22, or preferably, about 0.5 V or less.

[0172] If it is found at step S120 that the output voltage sent from the turbidity sensor 14 has not reached the predetermined value or less, the control unit 13 judges whether the amount of platelet concentrate in the temporary reservoir bag 26' has reached a predetermined amount (step S121 in Fig. 5).

15 **[0173]** Incidentally, the collected (predetermined) amount of platelet concentrate ranges, preferably, about 20 mL to about 100 mL, or more preferably, from about 40 mL to about 70 mL.

[0174] If it is found at step S121 that the platelet concentrate in the temporary reservoir bag 26' has not reached the predetermined amount, the control unit 13 returns to step S118 and repeats step S118 and subsequent steps.

20 **[0175]** While steps S118 to S121 are repeated, if it is found at step S119 that the predetermined time has elapsed since the start of platelet collection, or if it is found at step S120 that the output voltage sent from the turbidity sensor 14 has reached the predetermined value or less, the control unit 13 terminates the present process [16] (platelet collection process (F)) and proceeds to the buffy coat collection process (G).

[0176] If it is found at step S121 that the platelet concentrate in the temporary reservoir bag 26' has reached the predetermined amount, the control unit 13 terminates the present process [16] (platelet collection process (F)) and proceeds to the buffy coat collection process (G).

25 **[0177]** [17] Thereafter, the blood component collection system 1 executes the buffy coat (BC) collection process (G). In the buffy coat (BC) collection process (G), a buffy coat is caused to flow out of the blood reservoir space 146 of the rotor 142 and collected.

30 **[0178]** In the buffy coat collection process (G), first, the control unit 13 executes buffy coat collection (step S122 in Fig. 5).

[0179] Specifically, the fourth channel open/close means 84 is blocked under the control of the control unit 13, and the fifth channel open/close means 85 is unblocked thereunder. The first fluid feeder pump 11 is activated (rotated forward) at the predetermined rotating speed (preferably, from about 60 mL/min to about 300 mL/min, and in the present embodiment, 200 mL/min).

35 **[0180]** Consequently, the plasma in the plasma collection bag 25 is routed to the blood reservoir space 146 at the predetermined speed by way of the first tube 25a and first line 21. The buffy coat flowing out of the outlet 144 of the rotor 142 is routed and collected into the buffy coat collection bag 27 by way of the second line 22 and fourth tube 27a.

[0181] In the buffy coat collection process (G), the control unit 13 changes the rotational frequency of the rotor 142.

40 **[0182]** The rotational frequency of the rotor 142 is set to be lower than the rotational frequency thereof set in the aforesaid processes [11] to [16] by, for example, a value ranging from about 100 rpm to about 300 rpm. Specifically, the rotational frequency ranging from about 4500 rpm to about 4600 rpm is preferred.

[0183] Thereafter, the control unit 13 judges whether a predetermined amount of a buffy coat has been collected into the buffy coat collection bag 27 (step S123 in Fig. 5).

45 **[0184]** Specifically, the control unit 13 calculates a collected (predetermined) amount of a buffy coat according to an amount of collected blood, a donor's hematocrit, and the number of platelets collected in the platelet collection process. The control unit 13 then determines the number of rotations, by which the first fluid feeder pump 11 should be rotated, on the basis of the calculated acquired amount. The control unit 13 then judges whether the first fluid feeder pump 11 has been rotated by the number of rotations required to collect the calculated collected amount.

50 **[0185]** If it is found at step S123 that the predetermined amount of a buffy coat has not been collected into the buffy coat collection bag 27, that is, if the first fluid feeder pump 11 has not been rotated by the required number of rotations, the control unit 13 returns to step S122 and repeats step S122 and subsequent steps.

[0186] Moreover, if it is found at step S123 that the predetermined amount of a buffy coat has been collected into the buffy coat collection bag 27, that is, if the first fluid feeder pump 11 has been rotated by the required number of rotations, the control unit 13 blocks all the channel open/close means 81 to 87, inactivates the first fluid feeder pump 11, and terminates the present process [17] (buffy coat collection process (G)).

55 **[0187]** [18] Thereafter, the blood component collection system 1 executes a process of inactivating the centrifugal separator 20.

[0188] In this process, first, the control unit 13 decelerates the centrifugal separator 20 (step S124 in Fig. 5).

[0189] Specifically, the rotational frequency of the centrifugal separator drive 10 is decreased under the control of the control unit 13. The rotor 142 is thus decelerated.

[0190] Furthermore, the control unit 13 inactivates the centrifugal separator 20 (step S125 in Fig. 5).

5 [0191] Specifically, the rotation of the centrifugal separator drive 10 is stopped in order to inactivate the rotor 142 under the control of the control unit 13.

[0192] [19] Thereafter, the blood component collection system 1 executes a blood return process. In the blood return process, the blood components in the blood reservoir space 146 of the rotor 142 are returned.

[0193] In the blood return process, the control unit 13 executes blood return (step S126 in Fig. 5).

10 [0194] Specifically, the first channel open/close means 81 is unblocked under the control of the control unit 13. Moreover, the first fluid feeder pump 11 is activated (rotated reversely) at a predetermined rotating speed (preferably, from about 20 mL/min to about 120 mL/min, for example, 90 mL/min).

[0195] Consequently, the blood components (mainly red blood cells) remaining in the blood reservoir space 146 of the rotor 142 are released from the outlet 144 of the centrifugal separator 20, and returned (restored) to the donor by
15 way of the first line 21.

[0196] Incidentally, the full amount of the blood components (amount of returned blood) is calculated based on the amount of collected blood, the collected amount of plasma, and the collected amount of platelet concentrate.

[0197] The first fluid feeder pump 11 is rotated by the number of rotations required to restore the full amount of blood components (amount of returned blood) to the donor under the control of the control unit 13. Thereafter, the first channel
20 open/close means 81 is blocked, the first fluid feeder pump 11 is inactivated, and the present process [19] (blood return process) is terminated.

[0198] Thus, the first cycle of platelet collection is completed.

[2] Second cycle of platelet collection (see Fig. 6 and Fig. 5)

25 [0199] Thereafter, the second cycle of platelet collection is executed.
[0200] The second cycle of platelet collection comprises the same processes as the first cycle of platelet collection except that a buffy coat restoration process precedes the first plasma collection process.

[0201] [20] First, the blood component collection system 1 executes the buffy coat (BC) restoration process. In the buffy coat restoration process, a collected buffy coat is restored to the blood reservoir space 146 of the rotor 142.
30 [0202] In the buffy coat restoration process, first, the control unit 13 executes buffy coat restoration (step S20X in Fig. 6).

[0203] Specifically, the fourth channel open/close means 84 and sixth channel open/close means 86 are unblocked under the control of the control unit 13. The other channel open/close means are left blocked. In this state, the first
35 fluid feeder pump 11 is activated (rotated forward) at a predetermined rotating speed (preferably, from about 60 mL/min to about 250 mL/min, for example, 100 mL/min). Moreover, the centrifugal separator drive 10 is activated at a predetermined rotational frequency (for example, 4800 rpm).

[0204] Consequently, the buffy coat in the buffy coat collection bag 27 is fed to the pipe 141 through the inlet 143 of the centrifugal separator 20 by way of the fourth tube 27a and first line 21, and routed to the blood reservoir space 146
40 of the rotor 142. At this time, the air in the centrifugal separator 20 is fed to the temporary reservoir bag 26' through the second line 22.

[0205] Thereafter, the control unit 13 judges whether the buffy coat collection bag 27 has run out of a buffy coat to be restored (step S20Y in Fig. 6).

[0206] Specifically, the control unit 13 determines the number of rotations, by which the first fluid feeder pump 11
45 should be rotated, on the basis of the collected amount of a buffy coat. The control unit 13 then judges whether the first fluid feeder pump 11 has rotated by the number of rotations required to restore the buffy coat.

[0207] If it is found at step S20Y that the buffy coat to be restored is left, that is, if the first fluid feeder pump 11 has not rotated by the required number of rotations, the control unit 13 returns to step S20X and repeats the step S20X
50 and subsequent steps.

[0208] If it is found at step S20Y that the buffy coat to be restored has run out, that is, the first fluid feeder pump 11 has rotated by the required number of rotations, the control unit 13 terminates the present process [20] (buffy coat restoration process) and proceeds to the first plasma collection process.

[0209] [21] to [29] The same processes as the processes [11] to [19] are executed.

55 [0210] Consequently, the second cycle of platelet collection is completed.

[3] Third (final) cycle of platelet collection (see Fig. 6 and Fig. 7).

[0211] Successively, the third cycle of platelet collection is executed.

[0212] In the third cycle of platelet collection, the same processes as those included in the second cycle of platelet collection are executed except that the buffy coat collection process is not executed and that a line cleansing process is executed for cleansing the platelet collection branch line with plasma.

[0213] [30] to [32] The same processes as the processes [20] to [22] are executed.

5 [0214] [33] The same process as the process [23] is executed.

[0215] Nearly concurrently with the process [33] (second plasma collection process), the control unit 13 feeds platelet concentrate, which is collected (reserved) temporarily in the temporary reservoir bag 26', to the leukoreduction filter 261. Thus, the platelet concentrate is filtered, that is, leukocyte contained in the platelet concentrate are separated or reduced.

10 [0216] Specifically, the seventh channel open/close means 87 is unblocked under the control of the control unit 13. Consequently, the platelet concentrate in the temporary reservoir bag 26' passes through the tube 262a, leukoreduction filter 261, and tube 263a owing to a fall (own weight). The platelet concentrate is thus carried to the platelet collection bag 26. At this time, the platelet concentrate almost entirely passes through the filtration member of the leukoreduction filter 261. However, the filtration member catches leukocyte. Consequently, the leukocyte contained in a platelet product are highly efficiently reduced.

[0217] In order to carry platelet concentrate from the temporary reservoir bag 26' to the platelet collection bag 26, a pump may be employed.

[0218] Moreover, instead of the means to be activated under the control of the control unit 13, the seventh channel open/close means 87 may be a clamp capable of manually opening or closing the middle of a channel of the tube 262a.

20 [0219] [34] and [35] The same processes as the processes [24] and [25] are executed.

[0220] [36] The same process as the process [26] is executed.

[0221] In the present process [36], the platelet concentrate collected into the temporary reservoir bag 26' is fed to the leukoreduction filter 261 and filtered.

25 [0222] [3A] Thereafter, the blood component collection system 1 executes a line cleansing process. In the line cleansing process, plasma is fed from the plasma collection bag 25 to the platelet collection branch line, and the platelet collection branch line is cleansed.

[0223] The line cleansing process that is a constituent feature of the present invention will be described with reference to the flowchart of Fig. 8. First, under the control of the control unit 13, the blood component collection system 1 feeds platelet concentrate, which is temporarily collected (reserved) in the temporary reservoir bag 26', to the leukoreduction filter 261, and then executes filtration for separating or reducing leukocyte from the platelet concentrate (S401). The filtration is started substantially concurrently with the start of the second plasma collection process in the final cycle of platelet collection. Thus, the binding time during which a donor is bound is shortened.

30 [0224] The filtration is carried out according to a procedure described below. Specifically, the seventh channel open/close means 87 is unblocked under the control of the control unit 13. This causes the platelet concentrate in the temporary reservoir bag 26' to pass through the tube 262a, leukoreduction filter 261, and tube 263a due to a fall (own weight). The platelet concentrate is thus carried to the platelet collection bag 26. At this time, the platelet concentrate almost entirely passes through the filtration member of the leukoreduction filter 261. However, the filtration member catches leukocyte. Thus, the leukocyte contained in the platelet concentrate are separated or reduced. Eventually, the leukocyte mixed in the platelet product are minimized.

40 [0225] Nearly concurrently with the filtration, the second plasma collection process included in the final cycle of platelet collection is started (S402). At this time, the seventh channel open/close means 87 located downstream the temporary reservoir bag 26' is unblocked. Consequently, platelet concentrate collected in the second plasma collection process in the final cycle is fed to the leukoreduction filter 261 and filtered.

45 [0226] Thereafter, the control unit 13 calculates a fed amount of plasma (PPP) according to an expression below (S403).

$$\text{Fed amount of plasma} = \frac{\text{Full amount of a target platelet product} -$$

$$\text{Collected amount of platelet concentrate}}$$

$$(\text{PC})$$

55 [0227] Herein, the full amount of a target platelet product is normally determined prior to blood collection and depends on the specification and unit adopted for a platelet product. Moreover, the collected amount of platelet concentrate (PC) depends on the total number of rotations by which the first fluid feeder pump 11 is rotated with the fourth channel open/close means 84 unblocked.

[0228] After the control unit 13 calculates the fed amount of plasma, the control unit 13 feeds plasma to the platelet

collection branch line (executes plasma feed) (S404, step S327 in Fig. 7). Specifically, while the second channel open/close means 82 and fourth channel open/close means 84 are left unblocked, the rotating speed of the first fluid feeder pump 11 and the rotational frequency of the rotor 142 are changed under the control of the control unit 13.

[0229] The rotating speed of the second fluid feeder pump 11 is, preferably, about 250 mL/min or less, or more preferably, ranges from about 40 mL/min to about 250 mL/min.

[0230] Moreover, the rotational frequency of the rotor 142 is set to be larger than the rotational frequency of the rotor 142 adopted in the processes [30] to [36] by, for example, a value ranging from about 300 rpm to about 800 rpm. Preferably, the rotational frequency ranges from about 5000 rpm to about 5500 rpm.

[0231] Consequently, the plasma in the plasma collection bag 25 is routed (fed) to the platelet collection bag 26 by way of the first tube 25a, first line 21, rotor 142 (centrifugal separator 20), second line 22, and tube 261a. That is, the plasma is routed (fed) from the upstream of the temporary reservoir bag (first container) 26' through the temporary reservoir bag 26', tube 262a, leukoreduction filter 261, and tube 263a to the platelet collection bag 26.

[0232] At this time, the platelets (platelet concentrate having leukocyte separated or reduced) remaining in the leukoreduction filter 261 and the channel defined by the tube 263a are collected together with the plasma into the platelet collection bag 26. This results in a high yield of platelets in a platelet product.

[0233] Moreover, since plasma is fed from the upstream of the temporary reservoir bag 26', the plasma is routed together with the platelet concentrate (first blood component), which remains in the temporary reservoir bag 26' and the channel of the tube 262a, to the leukoreduction filter 261. The yield of platelets in a platelet product can be improved.

[0234] As mentioned above, in the cleansing process, the full amount of a platelet product (a blood component in the platelet collection bag 26) is adjusted based on a fed amount of plasma. Consequently, another process for adjusting the full amount of a platelet product can be omitted. Moreover, since the adjustment can be performed in the blood component collection circuit 2 (closed state), a sterile state can be maintained.

[0235] The fed amount of plasma ranges, preferably, from about 5 mL to about 200 mL, or more preferably, from about 12 mL to about 150 mL.

[0236] The fed amount of plasma is detected as a change (decrease) in the weight of the plasma collection bag 25 by the weight sensor 16.

[0237] The control unit 13 then judges from the detection signal sent from the weight sensor 16 whether plasma has been fed to the temporary reservoir bag 26' by the fed (set) amount calculated at step S403 (S405). At this time, if the amount of plasma has not reached the set amount (S405: No), plasma is kept fed (S404). If the amount of plasma has reached the set amount (S405: Yes), the control unit 13 extends control to block the channel open/close means 81 to 84 and 86 and to inactivate the first fluid feeder pump 11. Thereafter, a platelet product is collected (S406). The present process [3A] (line cleansing process) is then terminated.

[0238] Prior to the present process [3A], the control unit 13 may extend control to suspend the first fluid feeder pump 11 with the rotor 142 kept rotated. Consequently, in the process [36] (platelet collection process), the buffy coat layer 132 and the layer of red blood cells 133 which are diffused in the blood reservoir space 146 of the rotor 142 (whose thicknesses are increased) can be compressed (the thicknesses can be decreased). Therefore, in the process [3A] (line cleansing process), the buffy coat or red blood cells can be reliably prevented from being mixed in plasma flowing out of the outlet 144 of the rotor 142.

[0239] Moreover, the process [3A] may be started after the completion of release of platelet concentrate from the temporary reservoir bag 26'. This can be realized by disposing a bubble sensor or the like, which can detect the presence of bubbles in a channel, in the tube 262a near the temporary reservoir bag 26'.

[0240] [38] and [39] The same processes as the processes [28] and [29] are executed. Incidentally, the same process as the process [27] is omitted.

[0241] Consequently, the third cycle of platelet collection is completed.

[0242] The number of times by which platelet collection is performed is not limited to three. If necessary, the platelet collection may be performed twice or four or more times.

[0243] In the foregoing blood component collection system 1, the leukoreduction filter 261 is used to separate or reduce leukocyte from platelet concentrate separated or collected from blood. Therefore, a platelet product having the least number of leukocyte mixed therein can be prepared.

[0244] Moreover, platelets remaining in the leukoreduction filter 261 and tube 263a are washed away with plasma and collected into the platelet collection bag 26. Consequently, a platelet product containing platelets at a very high yield can be prepared.

[0245] Moreover, platelets are collected (washed away) using plasma (blood component). Therefore, compared with when physiological saline or an anticoagulant is employed, a higher-quality platelet product can be prepared.

[0246] Moreover, the configuration of the blood component collection circuit 2 included in the blood component collection system 1 can be determined appropriately but not limited to the illustrated one.

[0247] For example, a tube (line) linking the plasma collection bag 25 and platelet collection branch line may be included. In this case, a method for feeding (carrying) plasma from the plasma collection bag 25 to the platelet collection

branch line may be a method utilizing a fall or a method employing a pump. Even in this case, the plasma collection bag 25 is, preferably, disposed upstream the temporary reservoir bag 26'.

[0248] Moreover, for example, a second plasma collection bag different from the plasma collection bag 25 may be included. Plasma to be fed to the platelet collection branch line during the line cleansing process may be reserved in the second plasma collection bag.

[0249] Furthermore, in the blood component collection system 1, conditions can be set for each of processes constituting platelet collection (blood component collection). Moreover, if necessary, any process can be added or omitted.

[0250] The blood component collection system according to the present invention has been described in conjunction with the illustrated embodiment. The present invention is not limited to the embodiment. The components of the blood component collection system may be replaced with others that can exhibit the same abilities.

[0251] For example, the present invention is not limited to the illustrated optical sensor. Alternatively, for example, a line sensor will do.

[0252] The blood component collection system of the present invention is not limited to a case where a platelet product is prepared. Alternatively, for example, the blood component collection system may be adapted to a case where a plasma product, an albumin product, a red blood cell product, or the like is prepared. Moreover, a kind of cells to be separated or reduced using the cell separating filter is not limited to leukocyte.

[0253] Next, a concrete example of the present invention will be described.

(Example)

[0254] A blood component collection circuit (Terumo Leukoreductive Apheresis set (with a leukoreduction filter) manufactured by Terumo Corp.), and a blood component collection system (Terumo Apheresis machine AC-550 manufactured by Terumo Corp.) were remodeled in order to construct the blood component collection system shown in Fig. 1. The system was used to perform platelet collection (four times) by executing the aforesaid processes.

[0255] Moreover, the conditions for each of the processes to be executed in order to achieve platelet collection will be listed below. The interface between blood components to be detected was the interface between a layer of plasma and a buffy coat layer.

[First plasma collection process]	
Rotor: rotational frequency	4800 rpm
First fluid feeder pump	rotating speed: 60 mL/min
Condition for terminating the process	A collected amount should reach 30 g.

[Constant-speed plasma circulation process]	
Rotor: rotational frequency	4800 rpm
First fluid feeder pump: rotating speed	200 mL/min
Condition for terminating the process	30 sec should elapse.

[Second plasma collection process]	
Rotor: rotational frequency	4800 rpm
First fluid feeder pump	rotating speed: 60 mL/min
Condition for terminating the process	The output voltage of the first optical sensor should become 1.8 V.

[Accelerated plasma circulation process]	
Rotor: rotational frequency	4800 rpm
First fluid feeder pump: rotating speed	60 mL/min (initial speed), 5.0 mL/min/sec (acceleration)
Condition for terminating the process	The rotating speed of the first fluid feeder pump should be 170 mL/min.

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5	[Third plasma collection process]	
	Rotor: rotational frequency	4800 rpm
	First fluid feeder pump	rotating speed: 60 mL/min
	Condition for terminating the process	A collected amount should reach 10 g.
10	[Platelet collection process]	
	Rotor: rotational frequency	4800 rpm
	First fluid feeder pump: rotating speed	60 mL/min (initial speed), 2 mL/min/sec (first acceleration)
		When the rotating speed becomes 150 mL/min, the acceleration is changed. 10 mL/min/sec (second acceleration)
	Condition for terminating the process	200 mL/min (maximum speed) A collected amount of platelet concentrate should reach 50 mL.
20	[Buffy coat collection process]	
	Rotor: rotational frequency	4600 rpm
	First fluid feeder pump	rotating speed: 205 mL/min
	Condition for terminating the process	A calculated amount of a buffy coat should have been collected
30	[Blood return process]	
	First fluid feeder pump	rotating speed: 90 mL/min
	Condition for terminating the process	A calculated amount of blood to be returned should have been returned.
35	[Buffy coat restoration process]	
	Rotor: rotational frequency	4800 rpm
	First fluid feeder pump	rotating speed: 100 mL/min
	Condition for terminating the process	A calculated amount of a buffy coat should have been restored.
40	[Line cleansing process]	
	Rotor: rotational frequency:	5200 rpm
	First fluid feeder pump:	rotating speed: 60 mL/min
	Condition for terminating the process:	15 mL of plasma should have been fed.

(Comparative example)

[0256] A blood component collection circuit (Terumo Leukoreductive Apheresis set (with a leukoreduction filter) manufactured by Terumo Corp.) and a blood component collection system (Terumo Apheresis machine AC-550 manufactured by Terumo Corp.) were remodeled in order to construct the blood component collection system shown in Fig. 1. Using the system, platelet collection was performed (four times) in the same manner as in the above example except that the line cleansing process was omitted.

[0257] Incidentally, the platelet collection in the comparative example was performed on the same donor as the one in the example and was executed two weeks after the platelet collection.

(Evaluation)

[0258] In both the example and comparative example, the collected amount of platelet concentrate in the temporary reservoir bag and the collected amount of a platelet product in the platelet collection bag were measured.

[0259] Moreover, the platelet concentrate in the temporary reservoir bag and the platelet product in the platelet collection bag were sampled in order to measure the number of contained platelets and the number of contained leukocyte. For the measurement, a cytometer (Sysmex® SE-9000 manufactured by Sysmex Corp.) was employed. The lower limit of the number of leukocyte measurable by the Sysmex SE-9000 is calculated as 0.1×10^2 cells/ μ L. The number of leukocyte contained in a sample and falling below the lower limit is measured according to a Nageotte [1:9] method.

[0260] The results of the measurement are listed in Table 1.

[Table 1]

		In temporary reservoir bag (platelet concentrate)	In platelet collection bag (platelet product)	Yield (%)
Example	collected amount [ml]	200	200	96.35
	the number of platelets [cells/bag]	2.19×10^{11}	2.11×10^{11}	
	the number of leukocyte [cells/bag]	3.0×10^7	1.0×10^4	
Comparative Ex.	collected amount [ml]	200	200	92.37
	the number of platelets [cells/bag]	2.36×10^{11}	2.18×10^{11}	
	the number of leukocyte [cells/bag]	5.6×10^7	1.0×10^4	

[0261] As seen from Table 1, since the line cleansing process is included in the example, a loss of platelets occurring over the platelet collection branch line can be reduced more successfully than it can in the comparative example. Consequentially, the yield of platelets in a platelet product can be improved more successfully.

[0262] Specifically, the yield of platelets in the example was 96.35 %, while the yield of platelets in the comparative example was 92.37 %. Thus, the yield of platelets in a platelet product could be improved approximately 4 %. Herein, the yield is calculated as follows: the number of platelets in the platelet collection bag / the number of platelets in the temporary reservoir bag $\times 100$ (%).

[0263] Incidentally, in both the example and comparative example, leukocyte were successfully reduced from a platelet product.

Industrial Applicability

[0264] As described so far, in a blood component collection system according to the present invention, a cell separating filter is used to separate or reduce a predetermined kind of cells. In order to prepare a blood product, for example, a platelet product, leukocyte (especially, lymphocytes) can be reduced from the platelet product (blood product) at a high removable rate. The risk of an attack of fever, isoantigen sensitization, virus infection, or the like can be lowered. High safety can be guaranteed.

[0265] Moreover, in a blood component collection system according to the present invention, when a blood product, for example, a platelet product is prepared, platelets remaining in a cell separating filter are collected using, for example, plasma (blood component) as a medium. This results in a high yield of platelets in a platelet product. Moreover, since platelets are collected using the blood component, a high-quality platelet product (blood product) can be prepared.

Claims

1. A blood component collection system comprising: a centrifugal separator including a rotor having a blood reservoir space therein and an inlet and an outlet which communicate with the blood reservoir space, and centrifuging blood

introduced through the inlet with the rotation of the rotor, into a plurality of components in the blood reservoir space; a first container for temporarily reserving therein a first blood component; a cell separating filter for separating or reducing a predetermined kind of cells from the first blood component; and a second container for reserving the first blood component having passed through the cell separating filter,

5 wherein the blood component collection system further comprises:

channel open/close means for opening or closing a channel linking the first container and the cell separating filter; and

10 control means for controlling action of the channel open/close means,

the channel open/close means is used to carry the first blood component in the first container to the second container through the cell separating filter, then supply a second blood component, and collect the first blood component, from which the predetermined kind of cells remaining in the cell separating filter have been separated or reduced, together with the second blood component into the second container.

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2. A blood component collection system comprising: a centrifugal separator including a rotor having a blood reservoir space therein and an inlet and an outlet which communicate with the blood reservoir space, and centrifuging blood introduced through the inlet by rotation of the rotor, into a plurality of components in the blood reservoir space; a first container for temporarily reserving therein a first blood component; a cell separating filter connected to the first container through a feed tube, and used to separate or reduce a predetermined kind of cells from the first blood component fed through the feed tube; and a second container which is connected to the cell separating filter through a release tube and used for reserving therein the first blood component having passed through the cell separating filter,

25 wherein the blood component collection system further comprises:

channel open/close means for opening or closing a channel of the feed tube; and
control means for controlling action of the channel open/close means,

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the channel open/close means is used to carry the first blood component in the first container to the second container through the feed tube, cell separating filter, and release tube in response to a command sent from the control means,

thereafter, a second blood component is fed, and the first blood component that remains in the cell separating filter and the channel of the release tube and that has the predetermined cells separated or reduced therefrom is collected together with the second blood component into the second container.

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3. The blood component collection system according to claim 1 or 2, wherein a full amount of a blood component to be collected into the second container is adjusted according to a fed amount of the second blood component.
4. The blood component collection system according to any one of claims 1 through 3, wherein the fed amount of the second blood component is determined based on a difference between a target full amount of the blood component to be collected into the second container and an amount of the first blood component to be carried to the second container.
- 40 5. The blood component collection system according to any one of claims 1 through 4, further including a third container for reserving the second blood component, wherein the second blood component is fed from the third container.
- 45 6. The blood component collection system according to any one of claims 1 through 5, wherein the second blood component is fed together with the first blood component which remains in the first container, to the cell separating filter.
- 50 7. The blood component collection system according to any one of claims 1 through 6, wherein the first blood component is plasma containing platelets.
- 55 8. The blood component collection system according to any one of claims 1 through 7, wherein the second blood component is plasma.
9. The blood component collection system according to any one of claims 1 through 8, wherein the cell separating

filter is a leukoreduction filter.

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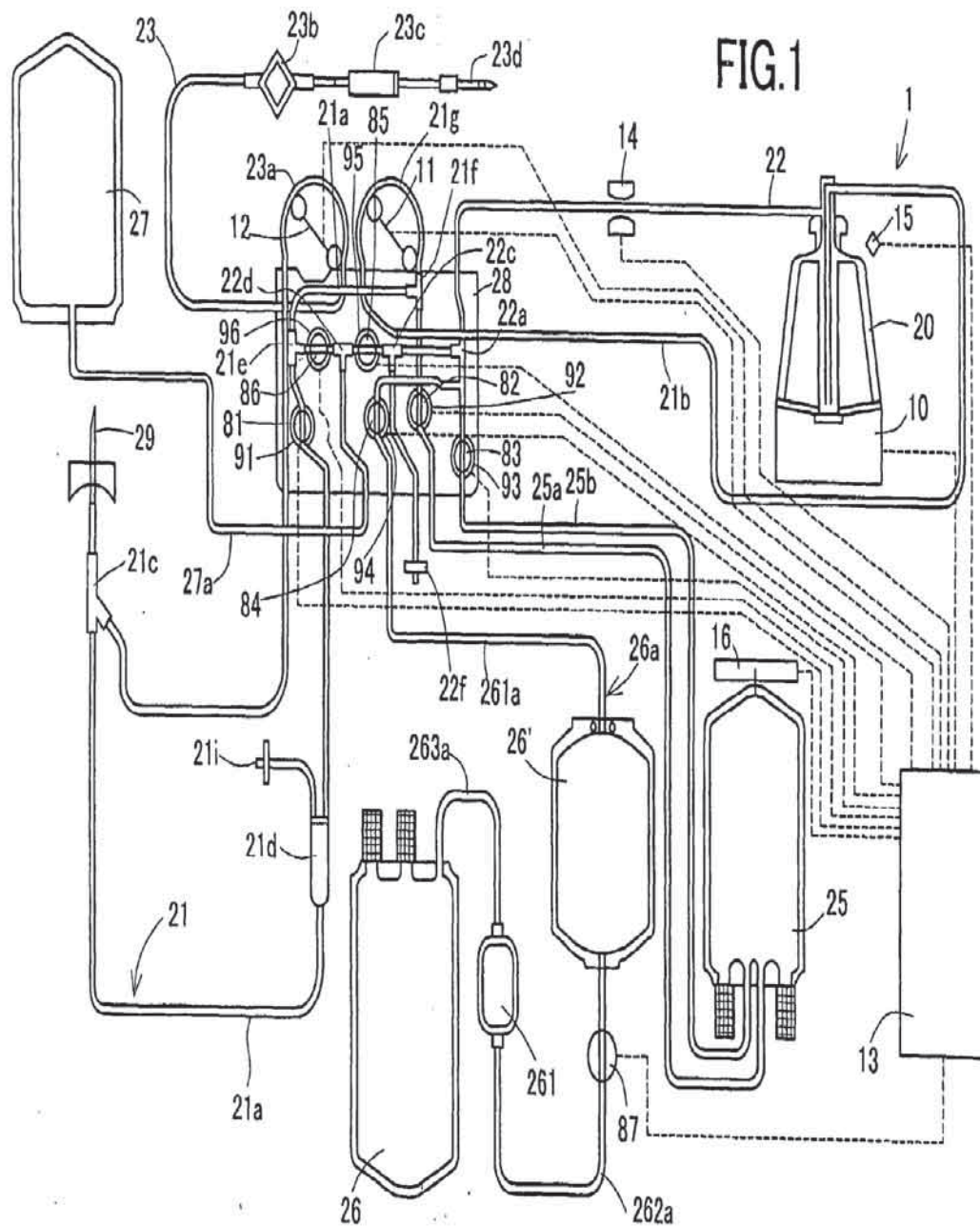
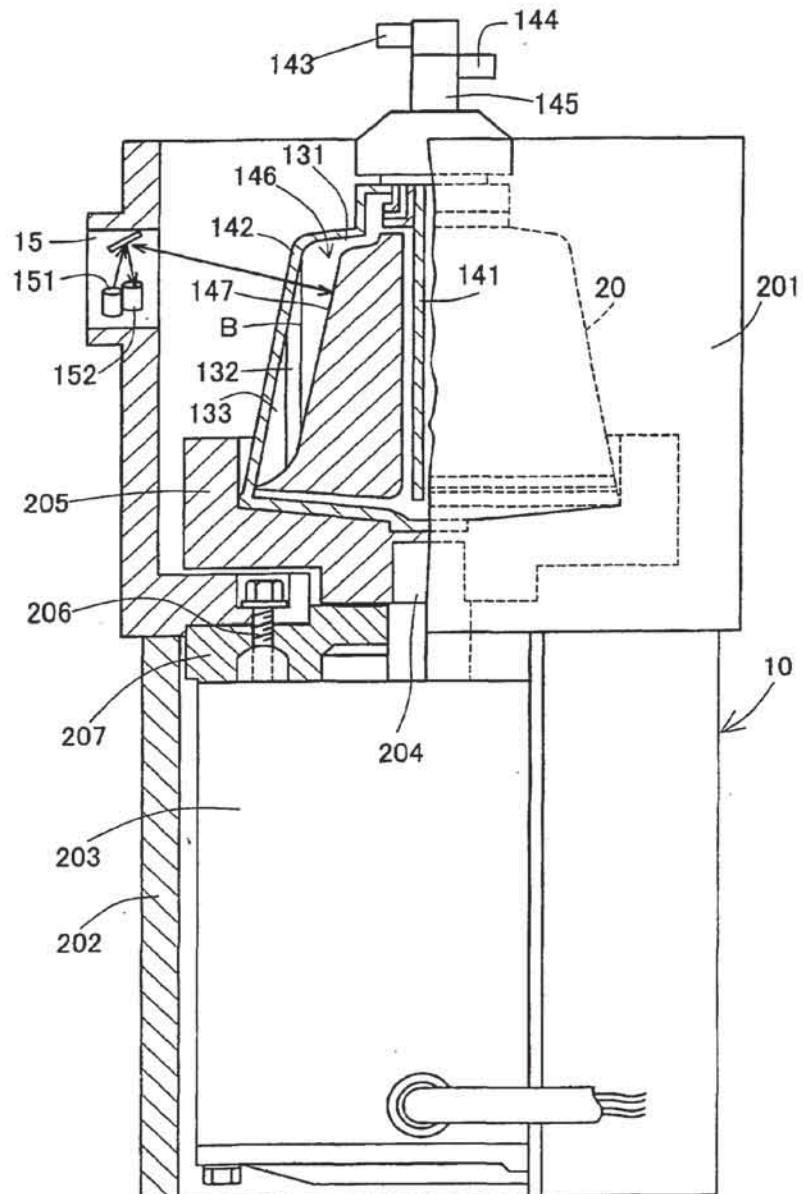
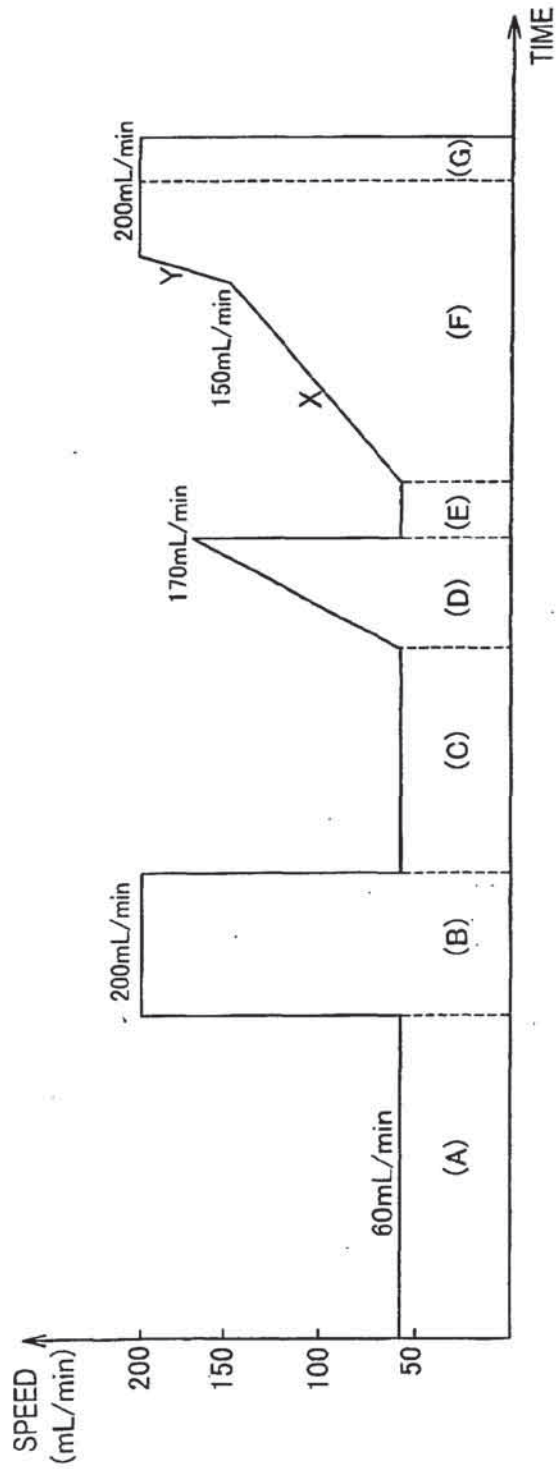


FIG. 1

FIG.2





X: FIRST ACCELERATION
Y: SECOND ACCELERATION

FIG.4

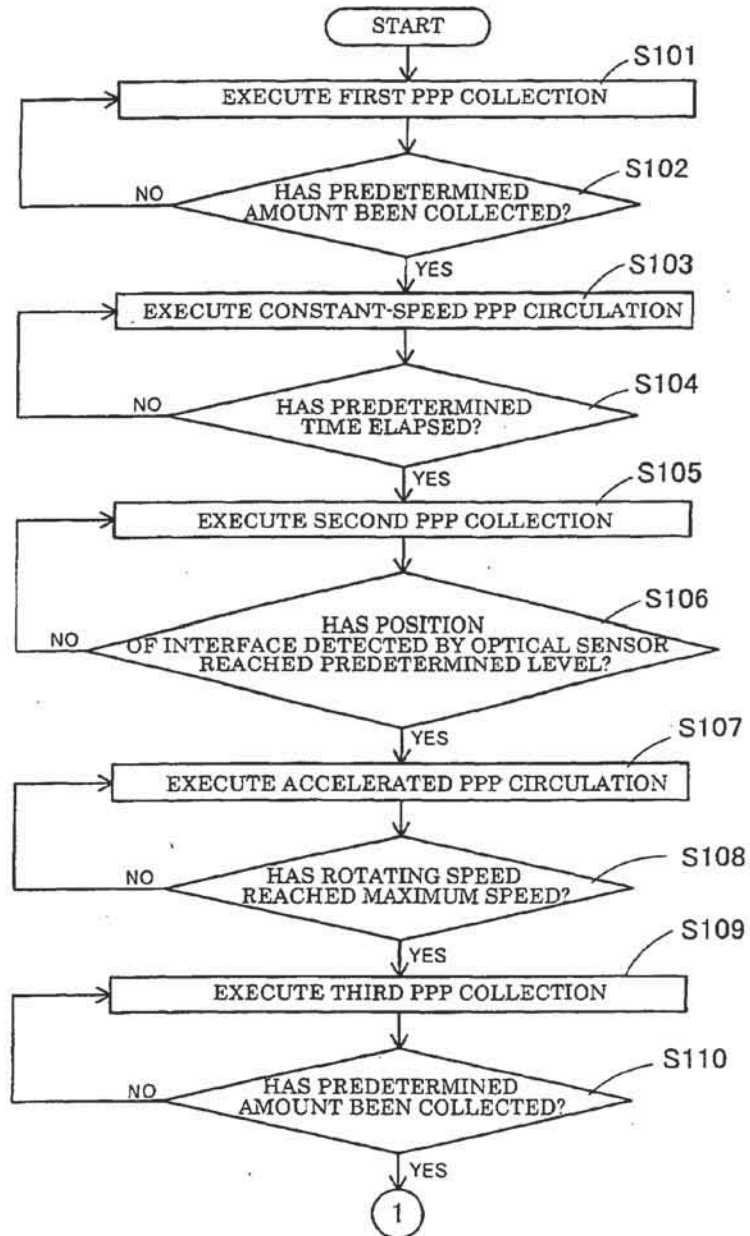


FIG.5

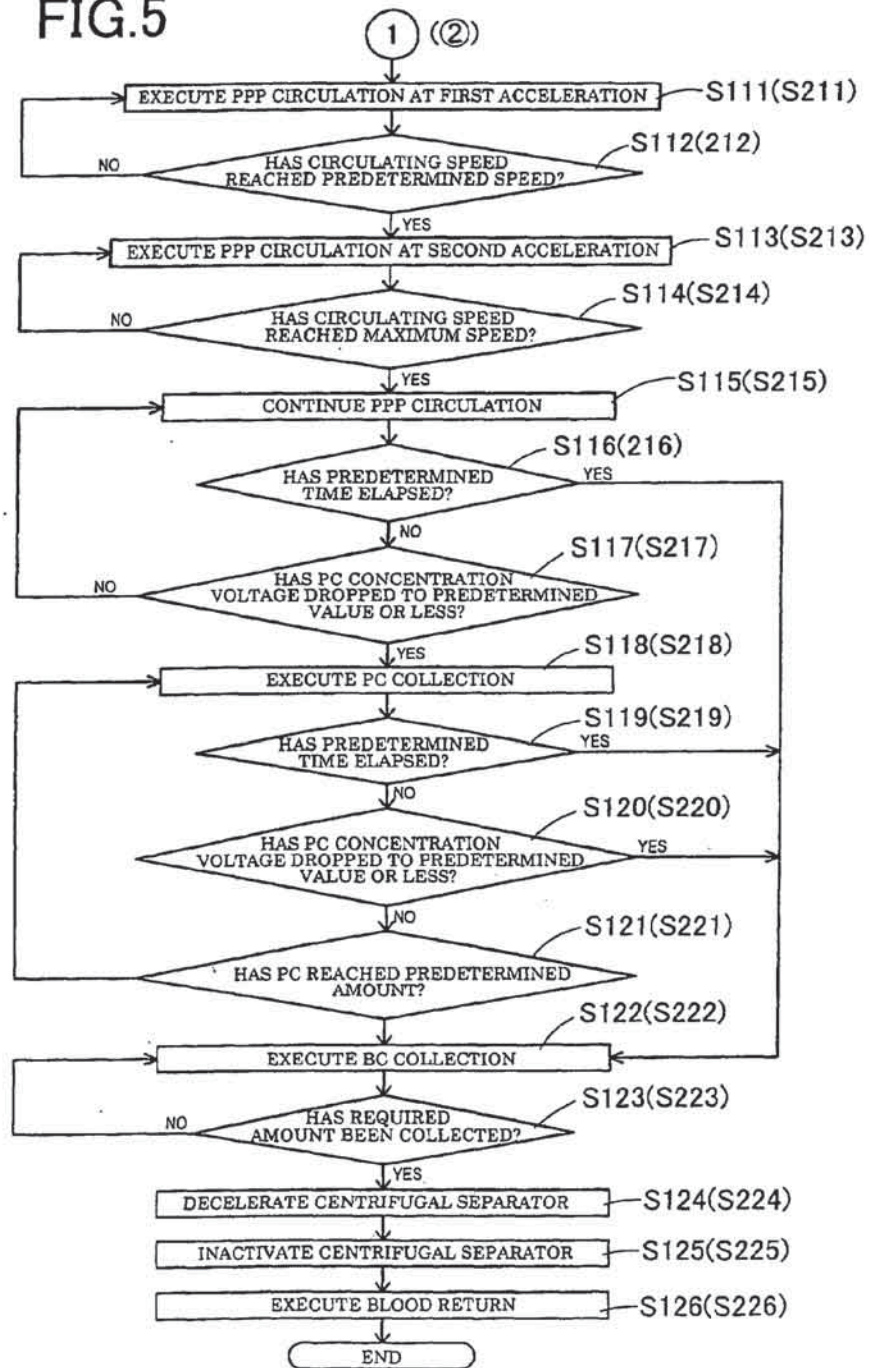


FIG.6

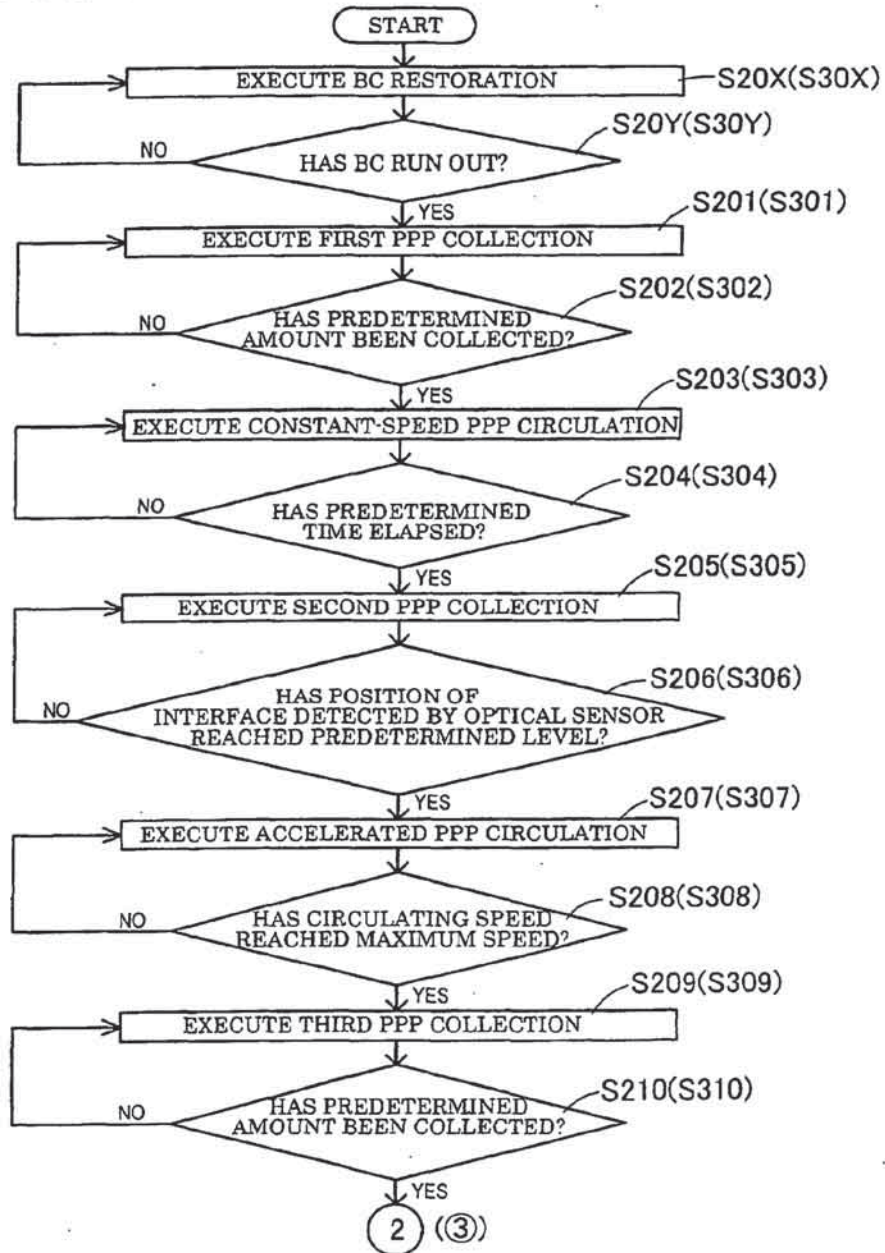


FIG. 7

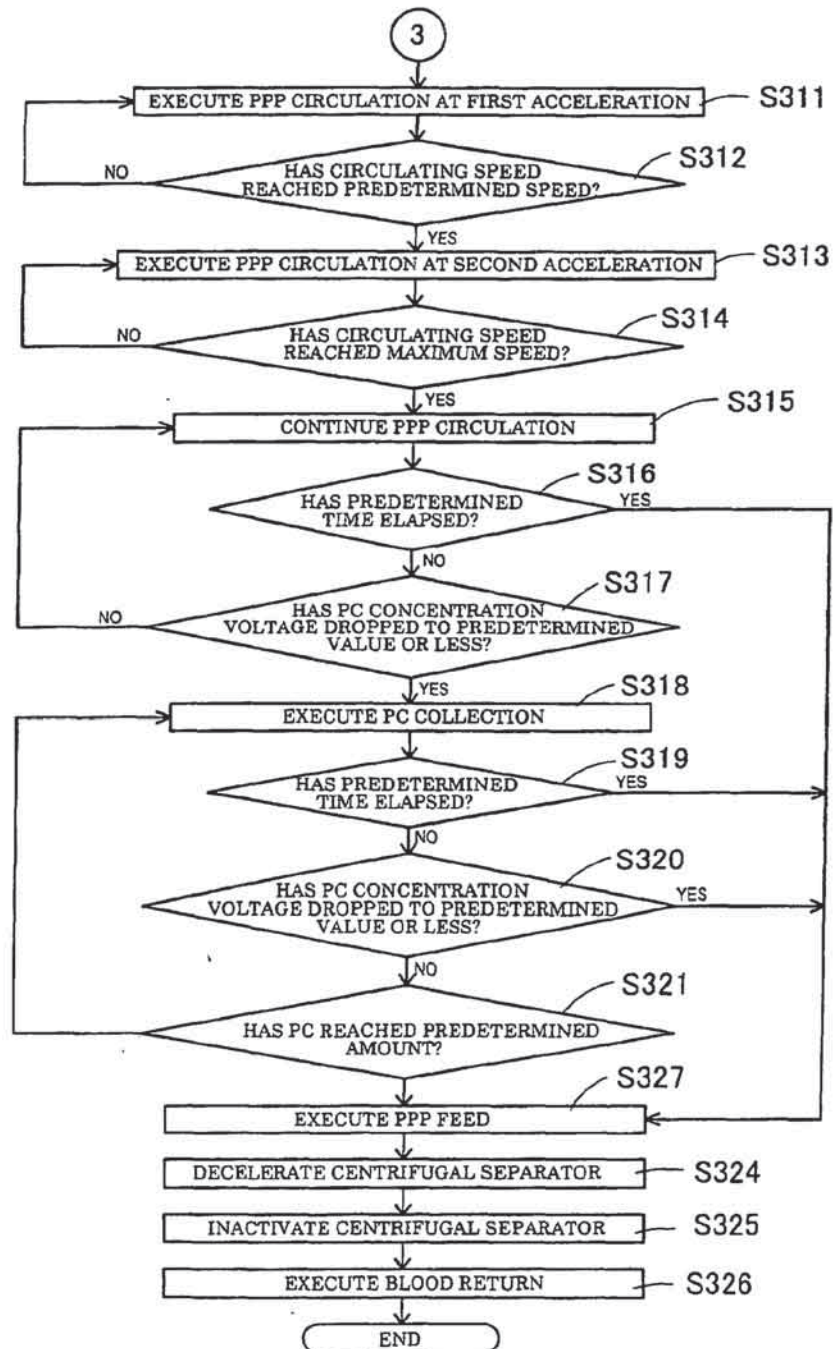
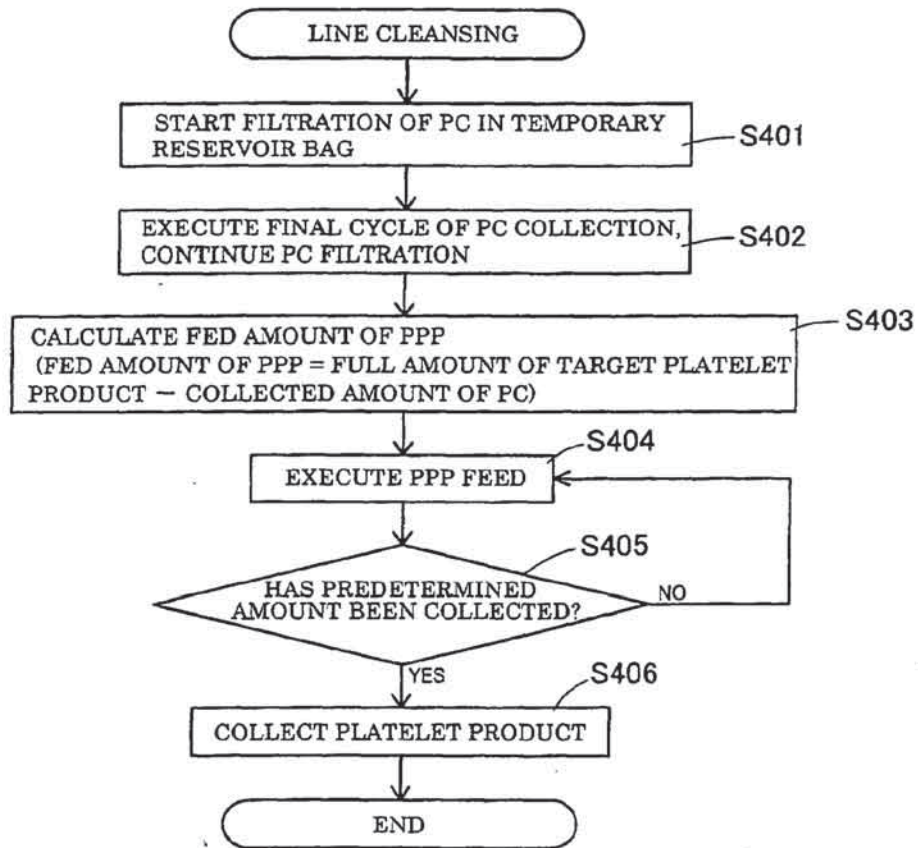


FIG. 8



INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP02/02625

A. CLASSIFICATION OF SUBJECT MATTER
Int. Cl.⁷ A61M1/02

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)

Int. Cl.⁷ A61M1/02

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho	1922-1996	Toroku Jitsuyo Shinan Koho	1994-2002
Kokai Jitsuyo Shinan Koho	1971-2002	Jitsuyo Shinan Toroku Koho	1996-2002

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.
A	JP 7-265407 A (Terumo Corp.), 17 October, 1995 (17.10.95), Full text; Figs. 1 to 5 (Family: none)	1-9

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:

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"&" document member of the same patent family

Date of the actual completion of the international search
06 June, 2002 (06.06.02)Date of mailing of the international search report
25 June, 2002 (25.06.02)Name and mailing address of the ISA/
Japanese Patent Office

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Form PCT/ISA/210 (second sheet) (July 1998)

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Confirmation Number:	7286
Title of Invention:	System and Method for Collecting Plasma
First Named Inventor/Applicant Name:	Michael Ragusa
Customer Number:	86738
Filer:	Jonathan Lovely
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Attorney Docket Number:	130670-08002
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Application Type:	Utility under 35 USC 111(a)

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Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	130670-08002_-_CN2735985Y.pdf	340053 363881fe4191b9e89c6f1da01d7a50d7d18e2943	no	8

Warnings:

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2	Foreign Reference	EP128683B1.PDF	1411250	no	20
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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: CN2735985 (Y) — 2005-10-26

Disposable blood cell separating device

Inventor(s): CHEN HUA [CN] ± (HUA CHEN)

Applicant(s): SHANGHAI DAHUA MEDICAL APPARAT [CN] ± (SHANGHAI DAHUA MEDICAL APPARATUS CO., LTD)

Classification: - **international:** **A61M1/38**; (IPC1-7): A61M1/38
- **cooperative:**

Application number: CN2004282755U 20040910

Priority number (s): CN2004282755U 20040910

Abstract of CN2735985 (Y)

The utility model relates to a blood cell separator with centrifugal separation principle, comprising a blood needle joint, a blood return needle joint, an anticoagulant bag and a salt water bag, which are connected to a centrifugation separator via a multi-cavity pipe; the centrifugation separator is composed of a centrifugation bin, a separation bag positioned in the centrifugation bin, and a collecting bag. A rich constituent blood plasma transporting pipe controlled and connected via a blood plasma pump is provided between the separation bag and the collecting bag. Adopting the structure chiefly solves the technical problem that the existing blood cell centrifugal separator adopts the single centrifugal separation structure to separate the blood cells, which leads to that the blood cells in the blood can not be fully utilized; disposable using and completing the complete-set the single blood sampling cell separation and recirculation processes of the blood sampling process, the centrifugation process, the separation process and the recirculation process can reduce the cross infections in high limit, protects the health of the blood donor and saves the blood resource.



[12] 实用新型专利说明书

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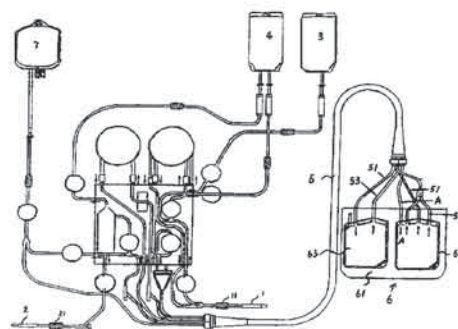
代理人 王敏杰

权利要求书 1 页 说明书 4 页 附图 1 页

[54] 实用新型名称 一次性使用血细胞分离器

[57] 摘要

一种离心分离原理的血细胞分离器，包括进血针接头、返血针接头、抗凝剂袋和盐水袋，它们通过多腔管路连接到一离心分离机构；该离心分离机构由一离心仓和位于离心仓内的分离袋、收集袋组成，分离袋和收集袋之间有一通过血浆泵控制连通的富成分血浆输送管。藉由上述结构主要解决现有的血细胞离心分离机采用单次离心分离结构分离血细胞，以致血液中的血细胞不能被充分利用的技术问题，一次性使用完成采血、离心、分离、回输全套单采血细胞分离、回输过程，能最大限度减少交叉传染，保护献血员健康，节约血资源。



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1、一种一次性使用血细胞分离器，包括进血针接头、返血针接头、抗凝剂袋和盐水袋，它们通过多腔管路连接到一离心分离机构，其特征在于：该离心分离机构由一离心仓和位于离心仓内的分离袋、收集袋组成，分离袋和收集袋之间有一通过血浆泵控制连通的富成分血浆输送管。

2、根据权利要求 1 所述的一次性使用血细胞分离器，其特征在于：连接进血针接头和返血针接头的管路上具有压力传感器。

3、根据权利要求 1 所述的一次性使用血细胞分离器，其特征在于：该离心仓内有温度探测器、湿度探测器及转子平衡探测器。

一次性使用血细胞分离器

技术领域：

本实用新型涉及一种一次性使用医用消耗器具，特别是一种离心分离原理的一次性使用血细胞分离器。

背景技术：

人体血液成分依其比重排列，分别是红细胞、粒细胞、淋巴细胞、血小板和血浆。医疗上根据需要只会给病人输入其所需要的成分，这样，对血液药源是一种节约。

目前，国内除了一些大城市的血液中心配备了血液分离机外，大部分地区血细胞分离均系手工采集。健康献血员的血液被采集后，经体外离心，再还输给献血员，这一过程不是密闭循环，极易出现还输失误和交叉传染。因此，中国实用新型专利说明书（授权公告号：CN2404534Y）公开了一种断续流动式血细胞分离机配套使用的一次性使用医用消耗器材，主要由抗凝剂袋、采样袋、血浆袋、产品收集袋、分离杯、采血针、药液过滤器、穿刺器及连接管、各种接头等构成，自成封闭式循环体系，能一次性使用完成采血、离心、分离、回输全套单采血细胞分离、回输过程，能最大限度减少交叉传染，保护献血员健康，节约血资源。

但是，这种血细胞分离机仍然存在一定缺陷，主要是分离杯采用单

次离心分离采集血细胞，使得血液中的血细胞不能被充分利用。

实用新型内容：

本实用新型的目的是提供一种一次性使用血细胞分离器，解决现有的血细胞离心分离机采用单次离心分离结构分离血细胞，以致血液中的血细胞不能被充分利用的技术问题。

为解决上述技术问题，本实用新型是这样实现的：

一种一次性使用血细胞分离器，包括进血针接头、返血针接头、抗凝剂袋和盐水袋，它们通过多腔管路连接到一离心分离机构，其特征在于：该离心分离机构由一离心仓和位于离心仓内的分离袋、收集袋组成，分离袋和收集袋之间有一通过血浆泵控制连通的富成分血浆输送管。

连接进血针接头和返血针接头的管路上具有压力传感器。

该离心仓内有温度探测器、湿度探测器及转子平衡探测器。

藉上述结构，本实用新型具有如下优点：

1、本实用新型的离心仓内具有分离袋和收集袋，当分离袋对血液进行第一次离心分离后，由血浆泵将富成分血浆输送到收集袋再进行二次离心分离，确保了对血液中的血细胞进行充分地利用。

2、本实用新型能一次性使用完成采血、离心、分离、回输全套单采血细胞分离、回输过程，能最大限度减少交叉传染，保护献血员健康，节约血资源。

附图说明：

图 1 是本实用新型的结构示意图。

具体实施方式：

请参阅图 1，它是本实用新型一次性使用血细胞分离器的结构示意图。如图所示：它包括进血针接头 1、返血针接头 2、抗凝剂袋 3 和盐水袋 4，它们通过多腔管路 5 连接到一离心分离机构 6。

该离心分离机构 6 由一离心仓 61 和位于离心仓 61 内的分离袋 62、收集袋 63 组成，分离袋 62 和收集袋 63 之间有一通过血浆泵控制连通的富成分血浆输送管 51。

连接进血针接头 1 和返血针接头 2 的管路上具有压力传感器 11、21。

该离心仓 61 内有温度探测器、湿度探测器及转子平衡探测器。

在运行过程中，抗凝的全血在全血泵的作用下，被泵入正在旋转的分离袋 62 中，血液成分分离的第一步发生在分离袋 62，可以看作是血液成分收集过程的第一次离心。当全血 A 进入分离袋后，较大密度的血液成分（主要是红细胞），在离心力的作用下，向分离袋 62 的外侧压积，然后通过 PRBC（压积红细胞）管路 52 退出分离袋；而那些密度较小的成分，如：血浆、血小板和/或白细胞可被血浆泵通过 CRP（富成分血浆）管路 51 运动到收集袋 63 内，血液成分分离的第二阶段在这里进行。可以看作是血液成分收集过程的第二次离心，当 CRP 进入收集袋 63 的底部，密度较大的成分入血小板和/或血细胞在离心力的作用下，向收集

袋 63 的外侧积压。所要收集的成分留在收集袋 63 内，而密度较小的 CPP（穷血浆）通过 CPP 管路 53 退出收集袋。CPP 和 PRBC 混合后返还给献血员/病人，（或收集 CPP 至转输袋 7 内）。

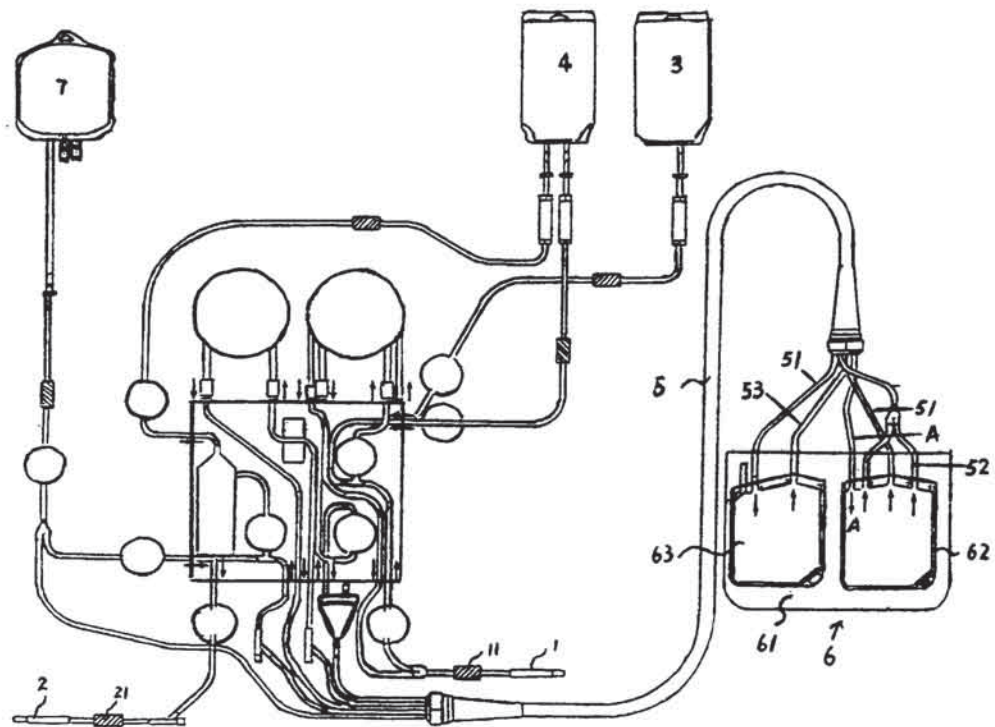


图 1

EUROPEAN PATENT SPECIFICATION

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(21) Application number: **84303509.8**
(22) Date of filing: **24.05.84**

(54) **Single needle blood fractionation system having adjustable recirculation through filter.**

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EP 0 128 683 B1

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Courier Press, Leamington Spa, England.

Description

Background of the invention

The present invention relates generally to systems and apparatus for processing whole blood, and more specifically to blood fractionation systems and apparatus having a filter component for separating and collecting a desired blood component, such as plasma, from whole blood through a single-lumen phlebotomy needle.

Various methods and apparatus have been developed for the in vivo processing of whole blood, wherein whole blood is taken from a donor, a desired blood component is separated and collected, and the processed blood is returned to the donor. Blood components typically collected using such processing include plasma (plasmapheresis), while blood cells (leukopheresis) and platelets (plateletpheresis).

In vivo blood processing apparatus may be of the centrifugal type, wherein the differing density of the collected blood component causes the component to congregate for collection at a particular radial distance in a centrifuge, or may be of the filter type, wherein the particle size of the collected component allows only that component to pass through a filter membrane into a collection chamber. Filter type apparatus is generally preferable for in vivo plasmapheresis applications, since such apparatus does not require complex rotating machinery and is more compact and less costly to manufacture.

One form of filter which is particularly attractive for use in plasmapheresis apparatus utilizes a plurality of parallel microporous hollow fibers arranged side-by-side in the form of a bundle within a hollow cylinder. As whole blood is caused to flow through the fibers the plasma component passes through the walls of the fibers to the surrounding container, which forms a collection chamber from which the component is transported to a collection container.

The efficiency of a flow-through filter in separating plasma from whole blood depends on the hematocrit of the donor, and the flow rate and pressure of the whole blood as it is pumped through the filter. Insufficient flow rates or whole blood pressures result in less than optimum yields. Excessive flow rates or whole blood pressures result in hemolysis, or damage to the red blood cells, within the filter, and possible failure of the filter to exclude red blood cells from the collected plasma. Thus, a practical limit exists for the percentage of plasma that can be recovered by a flow-through membrane filter in a single pass of whole blood.

To improve the efficiency of blood fractionation systems it has been proposed that once-filtered plasma-deficient whole blood be recirculated through the filter. This enables the filter to refilter the previously-filtered whole blood, recovering an additional percentage of the remaining plasma component.

However, in certain procedures, as where a high hematocrit is encountered in the whole blood drawn from a donor, the hematocrit of the once-filtered plasma-deficient whole blood may be so high as to require a reduction in the filter flow rate and pressure with an attendant reduction in filter efficiency, to avoid hemolysis in the second pass through the filter. This has the effect of increasing the time required to separate a given quantity of plasma, thereby increasing the inconvenience of the procedure to the donor. Accordingly, the need has developed for a blood fractionation system wherein recirculation through the filter is obtained while maintaining hematocrit, flow rate and pressure parameters which provide optimum system efficiency.

Furthermore, for user comfort it is desirable that in vivo blood fractionation systems withdraw and return whole blood to the donor through a single phlebotomy needle at a single injection site. This necessitates either the use of a single dual-lumen phlebotomy needle, in conjunction with a continuous flow non-batch system, or of a single-lumen phlebotomy needle in conjunction with a bidirectional batch system, whereby batches of whole blood are alternately drawn through the needle, passed through a plasma separation filter, and returned through the same needle. Such bidirectional single-lumen batch systems have the advantage of utilizing a smaller and potentially less traumatic single lumen needle. However, since such systems have heretofore not provided plasma separation from the batch in process during both the draw and return cycles, they have undesirably prolonged the time required to collect a desired volume of plasma.

The present invention is directed to a bidirectional single-needle batch type blood fractionation system which provides for user-controlled partial recirculation of plasma-deficient whole blood through the system filter during the blood return cycle, thereby enabling optimum plasma separation efficiency to be maintained in the system notwithstanding variations in whole blood hematocrit.

The present invention, by increasing the plasma separation efficiency of the system, makes a reduction in the volume of the system filter possible. This is advantageous in that it reduces the quantity of extracorporeal blood in process, and the cost of the system filter and the microporous filter material utilized therein.

DE—A—2745041 discloses a blood fractionation system for separating a blood fraction from whole blood comprising means including a donor interface conduit adapted for connection to a phlebotomy needle for alternately drawing whole blood from a donor and returning a component-deficient blood fraction to the donor. Whole blood is pumped through a main conduit to a separation means for separating the blood fraction and the blood fraction is stored in a reservoir. The pump is reversible, to return the component-deficient fraction through the main conduit back to the donor interface conduit and the donor,

in response to a predetermined quantity of the blood fraction having been collected. The pre-characterising clause of Claim 1 is based on this disclosure.

The present invention is characterised by second fluid conveyance means including a return pump responsive to the volume in said reservoir reaching a predetermined maximum level for conveying the component deficient blood fraction from said reservoir to said donor interface conduit to reduce the volume in said reservoir to a predetermined minimum level; and said second pump rate being set relative to said first pump rate whereby upon said operation of said second fluid conveyance means a selected portion of the flow from said reservoir is caused to recirculate through said separation means, while the remaining portion is caused to be returned through the phlebotomy needle to the donor.

The invention, together with the further objects and advantages thereof, may best be understood by reference to the following description taken in conjunction with the accompanying drawings, in the several figures of which like reference numerals identify like elements, and in which:

Figure 1 is a perspective view of a single-needle partial-recirculation plasmapheresis blood fractionation system constructed in accordance with the invention.

Figure 2 is a functional block diagram showing the principal components of the blood fractionation system of Figure 1.

Figure 3 is an enlarged front elevational view of the control panel of the blood fractionation apparatus of Figure 1.

Figure 4 is an enlarged front elevational view partially in section showing the electrical weight transducer of the system in conjunction with the in-process fluid reservoir of the system.

Figure 5 is a simplified schematic diagram of the mode control circuit of the blood fractionation system.

Figure 6a is a simplified schematic diagram of the inlet pump motor control circuit of the blood fractionation system.

Figure 6b is a simplified schematic diagram of a portion of the return pump motor control circuit of the blood fractionation system.

Figure 7 is a simplified schematic diagram of the ACD pump drive circuit of the blood fractionation system.

Figure 8a is a simplified flow diagram of the blood fractionation system showing the system in the draw portion of its operating cycle.

Figure 8b is a flow diagram similar to Figure 8a showing the blood fractionation system adapted for recirculation in the return portion of its operating cycle.

Figure 8c is a flow diagram similar to Figure 8a showing the blood fractionation system adapted for non-recirculation in the return portion of its operating cycle.

Figure 8d is a flow diagram similar to Figure 8a showing the plasmapheresis system in its prime mode.

Figure 9 is a simplified depiction of plasma collection versus time useful in comparing the operation of various types of blood fractionation systems.

Figure 10 is a simplified depiction of collected plasma volume versus time for various types of blood fractionation systems useful in comparing the systems.

Figure 11 is a top plan view of a disposable fluid circuit for use in conjunction with the blood fractionation system of the invention.

Description of the preferred embodiment

Referring to the Figures, and particularly to Figure 1, a blood fractionation apparatus 20 for use in conjunction with a single-needle filter-type blood fractionation system having filter recirculation in accordance with the invention is seen incorporated within a table-mounted housing 21. The housing preferably includes a pair of vertical support poles 22 and 23 from which a horizontal bar 24 is mounted to allow a plurality of collection and dispensing containers of conventional construction to be hung by means of appropriate hangers.

The fractionation apparatus 20 operates in conjunction with a disposable fluid circuit, generally identified by the reference numeral 25 in Figure 1 and shown schematically in Figure 2. The fluid circuit 25 includes a plurality of flexible plastic tubing segments which form fluid conduits between various components of the fluid circuit. As shown in Figure 2, whole blood derived from or returned to a donor is conveyed through the lumen of a single single-lumen phlebotomy needle 26 and a bidirectional donor interface conduit segment 27 to which the needle is connected. Conduit 27 communicates with a T-connector 28, which communicates with a tubing segment 30. Whole blood is conveyed through tubing segment 30 and an inline mixing chamber 31 by a peristaltic-type inlet pump 32 to a hollow fiber-type flow-through filter 33. The operation of the inlet pump is monitored by a positive pressure (+P) monitor circuit 34 connected to tubing segment 30 by a short tubing segment. Negative pressure, such as might occur upon the collapse of a vein, is monitored by means of a negative pressure (-P) monitor circuit 35 connected to tubing segment 30 upline of inlet pump 32 by another short tubing segment.

To prevent blood from clotting while in process anticoagulant (ACD) solution from a supply container 36 is introduced into conduit segment 30 through a tubing segment 37 and a T-connector 38. A drip chamber 39 may be provided inline in segment 37 to monitor ACD flow. A peristaltic-type pump 40 is

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provided along tubing segment 37 to provide a controlled rate of addition of the anticoagulant fluid to the whole blood.

Plasma separated from whole blood within filter 33 is conveyed by a tubing segment 41 to a plasma collection container 42. The pressure provided by inlet pump 32 provides flow through filter 33 to the collection container. A weight scale of conventional construction may be provided to provide an indication to the user of the volume of plasma collected.

Plasma-deficient blood from filter 33 is conveyed through a tubing segment 43 to an in-process fluid storage reservoir 44. In accordance with the invention, this plasma-deficient blood is periodically withdrawn from reservoir 44 through a tubing segment 45 by a peristaltic-type return pump 46 for return to conduit 27 at T-connector 28. The whole blood conveyed through tubing segment 45 passes through a combined bubble trap and fluid absence detector 47, which may be similar in structure and operation to that described in U.S. Patent No. 4,341,116 to Arnold C. Bilstad et al.

Reservoir 44 and plasma container 42 are preferably hung at the same height to avoid the need for an equalizer valve at the whole blood and collected plasma outlets of filter 33. However, under other circumstances an equalizer valve may be provided to restrict the plasma outlet port until the pressure of the plasma in the filter reaches that of plasma-deficient blood flowing from the filter, and thereafter to modulate plasma flow through line 41 to maintain the pressure equivalence. A transmembrane pressure (TMP) monitoring system 48 may be provided in apparatus 20 to assist the user in making adjustments for maximum operating efficiency of filter 33.

For system priming purposes, a saline fluid may be added to segment 30 through a tubing segment 51, which is connected at one end to a saline container 52 and at its other end to a T-connector in conduit segment 30. A second saline line 53 is provided between container 52 and bubble trap 47 for use in the purging procedure to enable trapped air to escape. Drip chambers and clamps of conventional construction may be provided in lines 51 and 53 to assist the procedure. A safety clamp 54 positioned along tubing segment 45 downline of bubble trap 47 actuates in the event of detection of a bubble or in the event of a malfunction in the apparatus to preclude uncontrolled infusion of fluid into the donor.

Referring to Figure 1, the blood fractionation apparatus 20 includes a sloped control panel 55 containing operator-actuated controls for operating the apparatus. As shown in Figure 3, control panel 55 includes a pair of selector switches 60a and 60b by which the draw and return mode operating speeds of anticoagulant pump 40 are set, a pair of potentiometer controls 61a and 61b and a digital readout 62 by which the draw and return mode operating speeds of the inlet pump 32 are controlled, and a pair of potentiometer controls 63a and 63b and a digital readout 64 by which the draw and return mode operating speeds of the return pump 46 are controlled. A plurality of push button switches 65 are provided to establish the operating mode of the apparatus. A plurality of status indicating lights 66a—66f provide status and alarm indications, and three pairs of indicator lights 66g and 66h associated with respective ones of the system pumps indicate the draw and return operating cycles of the pumps. An emergency stop switch 67 provides for an immediate operator-initiated shutdown in the event of a malfunction.

A display 68 displays the total volume of whole blood processed by the apparatus since the beginning of a particular procedure. A display 69 displays fluid pressure readings, as called for by a trio of pushbutton switches 69a—69c. Actuation of switch 69a causes the inlet pressure of filter 33 to be displayed. Actuation of switch 69b causes the collected plasma pressure of the filter to be displayed. Actuation of switch 69c causes the inlet transmembrane pressure (TMP) of the filter to be displayed as derived by TMP monitoring circuit 48.

Referring to Figure 2, the inlet pump 32 is driven by a motor 70. Power for operating motor 70 is provided by a motor control circuit 72 which responds to potentiometer controls 61a and 61b and a tachometer feedback signal from a tachometer (not shown in Figure 2) associated with the motor to maintain a desired motor operating speed. The inlet pump flow rate is displayed by readout 62 as part of a display circuit which responds to the tachometer output signal.

Similarly, the return pump 46 is driven by a motor 76. Power for motor 76 is provided by a motor control circuit 78 which responds to a tachometer feedback signal from a tachometer (not shown in Figure 2) associated with the motor and panel-mounted potentiometers 63a and 63b to maintain a desired constant motor speed. The return pump flow rate is displayed by readout 64 as part of the display circuit.

The anticoagulant pump 40 is driven by a stepper motor 79. Drive signals for motor 79 are developed by a motor control circuit 80 which responds to rate selection switches 60a and 60b to maintain a desired anticoagulant flow rate.

The operation of the various pump motors is controlled by a control circuit 81 which includes the mode select pushbutton switches 65 on control panel 55. Certain system conditions, such as negative pressure at pressure monitor 35, or excessive positive pressure at pressure monitor 34, or the occurrence of a bubble or other fluid absence as signalled at the output of the combined bubble trap and fluid absence detector 47, result in the application of an alarm signal to control circuit 81. This circuit in turn produces a control signal which is applied to motor control circuits 72, 78 and 80 by way of a motor control line 82 to interrupt operation of the motors. In addition, an alarm 83 associated with the control circuit may be sounded and an appropriate one of indicator lamps 66a—66f may be lit to alert the operator. Each of motor control circuits 72, 78 and 80 also includes internal stall protection whereby an alarm signal is developed and applied to

control circuit 81 by way of a control line 84 to terminate operation of blood fractionation apparatus 20 in the event of a pump malfunction.

Basically, the hollow fiber membrane-type filter device 33 employed in blood fractionation apparatus 20 includes a generally cylindrical housing within which a bundle of microporous hollow fibers are mounted. The housing includes end caps which close the ends of the housing to form a plasma collection chamber within the housing. A whole blood inlet port is formed on one end cap, and a whole blood outlet port is formed on the other end cap. Blood introduced through the inlet port enters the adjoining open ends of the hollow fiber membrane elements and proceeds to flow lengthwise through the fibers. Plasma in the whole blood flows through the micropores in the hollow fibers and out into the collection chamber formed within the housing circumferentially surrounding the bundle. The housing includes two side plasma outlet ports which communicate with the collection chamber. One outlet port communicates with the plasma collection container 42 to collect plasma separated by the filter. The other outlet port is used to sense plasma outlet pressure in conjunction with a tubing segment 85, a pressure transducer 86, and the transmembrane pressure (TMP) monitoring system 48. Plasma-deficient blood (containing red cells, leukocytes and platelets), having passed through the hollow fiber membrane elements, exists through the outlet port for temporary storage in the intermediate in-process fluid reservoir 44.

Plasma-deficient whole blood in reservoir 44 is periodically pumped by return pump 46 back to donor conduit segment 27. Inlet pump 32 continues to operate at this time at a rate set by the operator, so that a portion of the returned plasma-deficient blood dependent on the ratio of the return pump rate to the whole pump rate is recirculated through filter 33, thereby continuing plasma collection during the return cycle. For example, with inlet pump 32 continuously operating at 60 ml/min, and return pump 46 operating at 100 ml/min, 60 ml/min, or 60% of the processed plasma-deficient blood, is recirculated through the filter, and 40 ml/min, or 40%, is returned to the donor.

In performing a normal batch-mode procedure blood fractionation apparatus 20 operates in alternate draw and return cycles. During each draw cycle inlet pump 32 operates to draw whole blood through the phlebotomy needle into conduit 27 and to advance the whole blood through tubing 30 and mixing chamber 31 to filter 33. After a predetermined volume of plasma-deficient whole blood has been pumped through filter 33 into reservoir 44, the draw cycle is terminated and the return cycle is initiated. Return pump 46 then operates to pump plasma-deficient blood from reservoir 44 into conduit 30 at T-fitting 28. Depending on the relative operating speed of return pump 46 and inlet pump 32, a user-selectable portion of the plasma-deficient whole blood is pumped into mixing chamber 31 for subsequent recirculation through filter 33, and the remaining portion is returned to the donor through donor tubing segment 27 and needle 26. Upon the volume of the plasma-deficient blood in reservoir 44 reaching a predetermined minimum level, the return cycle is terminated and the draw cycle is again initiated. The cycles continue in alternation until a desired quantity of blood has been processed or a desired quantity of plasma has been collected.

The blood fractionation apparatus 20 is, in further accord with the invention, conditioned between the draw cycle and the return cycle by a circuit responsive to the weight of the intermediate in-process fluid reservoir 44. To this end, the blood fractionation apparatus 20 includes a weight transducer unit 100 from which the reservoir container 44 is suspended. As shown in Figure 4, the weight transducer unit 100 may include a housing 101 mounted by clamps 102 or other appropriate means to the horizontal support bar 24 of the apparatus. Within housing 101 reservoir 44 is suspended from the sense pin 103 of an electrical weight transducer 104, which may be conventional in construction and operation, provides an electrical output signal which is conveyed to the apparatus housing 21 through a connecting cable 106.

Within housing 21, blood fractionation apparatus 20 includes a mode control circuit 107 (Figure 2) which provides, in accordance with the magnitude of the signal from weight transducer 100, a pair of mode control signals for application to motor control circuits 72, 78 and 80 by way of a control line 108a and 108b. A mode select switch 109, located on control panel 55 (Figure 3), is provided to enable the user to selectively disable mode control circuit 107 when it is desired to operate the plasmapheresis apparatus as a continuously running system, as in conjunction with a continuous-flow two needle in vivo blood fractionation procedure.

Referring to Figure 5, within the weight transducer unit 100 the weight transducer 104 is seen to comprise a strain gauge bridge circuit 112. One input terminal of network 112 is connected to a source of positive current through a series-connected transistor 113, and the other input terminal is connected to ground. The conduction level of transistor 113, and hence the voltage applied to network 112, is controlled by a differential amplifier 115 having its non-inverting input connected to a source of regulated voltage, and its inverting input connected to a voltage divider comprising resistors 114a and 114b. The output of differential amplifier 115 is connected to the base of transistor 113 through a resistor 116, with the result that the voltage applied to network 112 is held constant at all times.

The output of bridge circuit 112, which depends on the force exerted on sense pin 103, is applied to a differential amplifier 120 included in mode control circuit 107. A necessary offset is introduced to this signal by an adjustable voltage divider network comprising resistors 121, 122, 123 and 124 connected between the regulated input terminal of network 112 and ground and the non-inverting input of differential amplifier 120.

To establish predetermined minimum and maximum volume thresholds for the plasma-deficient whole blood in reservoir 44 the output of differential amplifier 120 is applied to the non-inverting input of a

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comparator amplifier 125 and to the inverting input of a comparator 126. The inverting input of amplifier 125 is connected to a voltage divider comprising a resistor 127 and a potentiometer 128 connected between a source of regulated voltage and ground, and the inverting input. Depending on the setting of potentiometer 128, comparator amplifier 125 produces a logic high output signal as the volume of whole blood reaches a predetermined maximum level within reservoir 44. This output signal is applied to the set input of an RS-type flip-flop 130 which provides at its Q output the draw and return cycle mode control signal.

The non-inverting input of comparator amplifier 126 receives a reference voltage developed by a voltage divider comprising a resistor 131 and a potentiometer 132. Depending on the setting of potentiometer 132, the threshold of comparator amplifier 126 is varied to establish the minimum threshold level. Comparator 126 produces a logic low output which is applied to the reset input of flip-flop 130. Resistors 133 and 134 supply necessary operating current to the outputs of comparator amplifiers 125 and 126.

To enable blood fractionation apparatus 20 to be used for a continuous flow procedure wherein the ACD, inlet and return pumps are continuously controlled by controls 60a, 61a and 63a, respectively, an AND gate 136 is connected between the Q output of flip-flop 130 and control line 108a, and an OR gate 137 is connected between the Q output and control line 108b. One input of gate 136 is connected to a positive current source by a resistor 138, and to ground by mode switch 109. Gate 137 is similarly connected through an inverter 139. When switch 109 is open, corresponding to operator selection of a continuous-flow procedure, AND gate 136 is inhibited, rendering control line 108a logic low and control line 108b logic high, causing the pumps to operate continuously under the controls of 60a, 61a and 63b. However, when switch 109 is closed, AND gate 136 is enabled and the logic state of control line 108 is dependent on the operating state of RS flip-flop 130, and hence the volume of plasma-deficient blood accumulated in reservoir 44.

Referring to Figure 6a, the motor control circuit 72 provided for supplying operating power to the inlet pump motor 70 comprises a series-connected power transistor 140 and a reactance control network comprising an inductance 141 and a capacitor 142. These components supply power from a unidirectional motor current source (not shown) to the motor. The return line from the motor includes a series-connected current metering resistor 143.

Pump motor 70 is a direct current type motor and receives excitation over a variable duty cycle through power transistor 140. Conduction of this transistor is controlled by a pulse width modulator 144 which provides an apparatus control signal to the base electrode of the transistor. A tachometer formed by a light emitting diode 145 and a photodetector 146 operates in a conventional manner to provide output pulses indicative of incremental rotation of the pump motor. These pulses are applied to a tachometer output line through an amplifier 147 for use by other systems within the apparatus, and through an amplifier 148 to a frequency-to-voltage converter circuit 149. This circuit develops an analog output voltage in proportion to the frequency of the tachometer pulses. This signal is applied to the inverting input of a comparator amplifier 150, wherein it is compared with a speed control signal applied to the non-inverting input from potentiometer 61a or 61b through a trio of analog devices 151—153.

The control gate of switch device 151 is connected to the pump control line 82 so that in the absence of an appropriate motor enabling signal from the apparatus control circuit 81 no reference signal is applied to comparator 150. The control gate of switch device 152 is connected to mode control line 108a through an inverter 154 so that in the absence of a logic high signal on this control line an analog control signal may be applied to comparator 150 by the draw mode whole blood rate control potentiometer 61a. The control gate of switch device 153 is connected directly to mode control line 108a, so that in the presence of a logic high signal on this line the output of the return rate potentiometer 61b is applied to comparator 150.

Comparator amplifier 150 operates in a conventional manner to produce an output signal indicative of the difference between its inputs. This output signal is applied through an isolation circuit 155 to pulse width modulator 144, wherein it controls the duty cycle of power transistor 140, and hence the speed of pump motor 70.

Referring to Figure 6b, the return pump motor control circuit 78 may be identical to motor control circuit 72, except for the input circuit provided for potentiometer rate controls 63a and 63b and control line 108b.

To provide protection against overspeed operation, the excitation level applied to pump motor 70 is continuously monitored by an overspeed detection circuit 156. In the event of an overspeed condition, this circuit provides an output which is coupled through an OR gate 157 to the alarm output line 84, and to the inhibit input of pulse width modulator 144, wherein it prevents the application of current to the base of transistor 140, thereby stopping the motor. Additional protection against malfunction is provided by a stall detection circuit 158 which provides an input to OR gate 157 upon motor 70 becoming stalled, as detected by the voltage level across series-connected resistor 143.

Referring to Figure 7, a multi-phase drive signal is applied to the anticoagulant pump stepper motor 79 by a stepper motor drive circuit 160 of conventional design. Control pulses for initiating the multi-phase drive signal from drive circuit 160, and consequently each incremental rotation of the motor, are provided by a clock circuit 161. In the draw mode, output pulses from the clock are applied through a pair of analog switch devices 162 and 163 to a rate multiplier 164. Rate multiplier 164, which may be conventional in

construction and operation, responds to an operator-selected rate set by switch 60a to provide a preselected rate multiplication to the applied clock pulses. This results in stepper motor drive circuit 160 being impulsed at a user-selected rate, and consequently the stepper motor 79 being driven at the desired rate.

5 Alternatively, clock pulses from clock 161 are supplied to a second rate multiplier 165 through switch device 162 and a third analog switch device 166. When devices 162 and 166 are conductive, rate multiplier 165 is active to control motor speed according to the setting of return mode rate selector switch 60b.

Control over operation of stepper motor 79 is obtained by apparatus control circuit 81 by applying the pump enable control signal developed on control line 82 to analog switch device 162. During batch mode
10 operation of the blood fractionation apparatus, analog switch device 162 is enabled continuously. Switch device 163, which is connected to mode control line 108a through an inverter 167, is enabled during each draw cycle to render switch 60a operative. Switch device 166, which is connected directly to control line 108a, is conductive only during each return cycle. Consequently, switch 60b controls return rate. In a non-recirculation procedure, control line 108a provides a continuous logic low signal and only rate
15 multiplier 164 and switch 60a are utilized. The outputs of rate multipliers 164 and 165 are applied to stepper motor drive circuit 160 and a stall detection circuit 168 through an OR gate 169.

The anticoagulant pump drive circuit 80 also includes a tachometer comprising a light emitting diode 170, a slotted disk 171 and a photodetector 172. As disk 171 turns with motor 79, output pulses produced by photodetector 172 are supplied through a first inverter amplifier 173 to a tach output line. Pulses are also
20 supplied through a second inverter amplifier 174 to stall detector 168, which provides an output on alarm line 84 upon stepper motor 79 stalling.

The operation of blood fractionation system 20 is illustrated in Figures 8a—8d and 9. In the batch mode, the system operates as illustrated in Figures 8a and 8b. Where no recirculation through the filter is desired in the batch mode, the system operates as illustrated in Figures 8a and 8c. Where the system is to
25 be primed, the system operates as illustrated in Figure 8d.

During the draw cycle, as shown in Figure 8a, whole blood is drawn from a donor through a single-lumen phlebotomy needle 26 and the bidirectional donor interface conduit 27 by inlet pump 32, which pumps the whole blood along conduit segment 30 to mixing chamber 31. Within the mixing chamber, the freshly drawn whole blood is, in accordance with one aspect of the invention, mixed with
30 whole blood previously advanced along segment 30 by pump 32, and the resulting mixture is advanced through filter 33 to reservoir 44.

As the mixed whole blood from chamber 31 passes through filter 33, a portion of the plasma component contained therein is separated from the whole blood by the membrane element of the filter and is caused to flow through tubing segment 41 to plasma collection container 42. The volume of plasma thus
35 collected can be readily determined by reference to a conventional weight scale 180 from which the plasma collection container is suspended. Alternatively, a collected volume monitoring system such as that described in the copending application of Arnold C. Bilstad et al, entitled "Blood Fractionation Apparatus Having Collected Volume Monitoring System", Serial No. 330,899, filed December 15, 1981, may be utilized to provide a direct readout of collected plasma volume.

40 During the draw cycle the operating rate of the inlet pump 32 is set by potentiometer 61a. The operating rate of the return pump 46, which is normally not operative during the draw cycle, may be set to zero by setting potentiometer 63a to zero. As an alternative, to preclude operation of the return pump 46 during the draw cycle, potentiometer 63a may be eliminated in the replacement pump motor control circuit 78 and the input to analog switch device 152 in that circuit may be connected to ground, as shown in Figure
45 6b. The operating rate of ACD pump 40 is set by selector switch 60a to operate at a rate appropriate to the operating rate of inlet pump 32 to maintain a desired ratio of ACD to whole blood.

The plasma-deficient whole blood from the filter continues to collect in reservoir 44 during the draw cycle. As the weight of the whole blood in the reservoir increases, transducer 100 produces a progressively increasing output signal. When this signal reaches a level corresponding to fluid level l_r in reservoir 44, the
50 signal applied to comparator 125 (Figure 5) by differential amplifier 120 causes comparator 125 to produce an output signal which conditions RS flip-flop 130 to its set state. As a consequence, the Q output of flip-flop 130 becomes logic high, and, assuming AND gate 136 is enabled by mode switch 109 being open for batch operation, mode control line 108a conveys a logic high control signal. This causes termination of the draw cycle and initiation of the return cycle.

55 During the return cycle, as illustrated in Figure 8b, return pump 46 is operated to pump plasma-deficient whole blood from reservoir 44 back through conduit segment 45 to donor conduit 27 and conduit segment 30 at T-connector 28. The flow rate of the plasma-deficient whole blood, as established by return pump 46, under the control of potentiometer 63b, is set higher than the flow rate of the whole blood in conduit segment 30, as established by inlet pump 32 under the control of potentiometer 61b. As a result,
60 the plasma-deficient whole blood flowing from reservoir 44 is caused to divide between donor conduit 27, wherein it causes a flow reversal and flow into the donor through the lumen of the single-lumen phlebotomy needle, and conduit segment 30, wherein it is advanced toward mixing chamber 31 and filter 33.

Within mixing chamber 31 the recirculating portion of the plasma-deficient whole blood divided into
65 conduit segment 30 is caused to mix with whole blood previously pumped into the chamber, as during the

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previous draw cycle of the system. The resulting mixture, which has a hematocrit determined by the hematocrits of the recirculating plasma-deficient whole blood and the previously pumped resident whole blood, is advanced through filter 33 into reservoir 44 by inlet pump 32. This causes an additional quantity of plasma to be separated from the whole blood mixture by filter 33 and stored in plasma container 42.

5 The ratio of plasma-deficient whole blood returned to the donor to plasma-deficient whole blood recirculated through filter 33 is dependent on the relative operating rates of the inlet pump 32 and the return pump 46. For a relatively higher return pump rate, a higher percentage of plasma-deficient whole blood is returned to the donor. The actual operating rates of the inlet and return pumps during the return cycle are set by the operator by means of potentiometers 61b and 63b on panel 55. In practice, these rates
10 are limited by practical considerations, such as the flow rate and pressure requirements of filter 33, the maximum permissible draw and return rates of the donor, and the capacity of the conduit segments and associated system components. The ACD pump 40 may be operated during the return cycle at a rate selected by selector switch 60b to maintain a desired percentage of ACD solution in the in-process whole blood.

15 Operation in the return cycle continues until the volume of plasma-deficient whole blood in fluid reservoir 44 reaches a predetermined minimum level, corresponding to level I_2 in Figure 8b. At this time the output signal produced by weight transducer 100 causes comparator 126 (Figure 5) to toggle RS flip-flop 130 to its reset state, causing a logic low on mode control lines 108a and 108b. This causes analog switch devices 152 (Figures 6a and 6b) and 163 (Figure 7) to close and analog switch devices 153 and 166 to open,
20 thereby enabling the inlet pump draw cycle potentiometer 61a (and replacement pump draw cycle potentiometer 63a in a similar manner) and the ACD draw cycle rate selector switch 60a. Consequently, the return cycle is terminated and a new draw cycle is initiated.

Referring to Figure 9, during alternate draw and return cycles of blood fractionation system 20 the volume 181 of plasma-deficient blood in reservoir 44 is seen to vary between a predetermined maximum level, corresponding to level I_1 , and a predetermined minimum level, corresponding to level I_2 . At the same
25 time, the volume 183 of plasma collected in container 42 is seen to increase with each cycle, at a faster rate during draw cycles as freshly drawn blood is filtered, and at a slower rate during return cycles, as recirculated blood is filtered with previously drawn blood. Normally, the fractionation procedure is continued until a desired volume of plasma (or other-desired blood fraction) has been collected, as
30 determined by the weight of the collected plasma as read on scale 180.

As a result of the partial recirculation of plasma-deficient whole blood from reservoir 44 during each return cycle, the system filter operates during both draw and return cycles and the time required for separating a given volume of plasma is significantly reduced.

For example, the effect of recirculation through the filter for a system yield of 600 ml plasma, a donor of
35 5000 ml whole blood, a 200 ml/min return pump rate, a mixing chamber volume of 30 ml, and an in-process fluid reservoir having a predetermined maximum volume of 50 ml and a predetermined minimum volume of 30 ml, can be summarized for varying whole blood hematocrits and flow rates as follows:

Whole blood flow rate (ml/min)	Donor hemato- crit (%)	No recirculation			With recirculation		
		Procedure time (min)	Blood processed (ml)	Max filter hematocrit (%)	Procedure time (min)	Blood processed (ml)	Max filter hematocrit (%)
50	40	44.5	1690	41	39.7	1520	48
50	45	48.5	1831	46	42.9	1631	53
50	50	53.2	1990	51	46.7	1765	58
50	55	58.5	2178	56	51.3	1923	62
60	40	39.6	1667	41	34.0	1454	48
60	45	42.9	1802	46	36.6	1555	54
60	50	46.8	1958	51	39.9	1686	58
60	55	51.5	2138	56	43.6	1835	63
70	40	36.5	1694	41	30.5	1451	51
70	45	39.5	1826	46	33.1	1556	56
70	50	43.2	1985	51	35.9	1669	62
70	55	47.8	2183	56	39.3	1820	66

60 Thus, for hematocrits within the normally encountered range of 40—55% the single-lumen single needle partial-recirculation blood fractionation system of the present invention requires less processing time and less whole blood than a non-recirculation single-lumen single needle batch system wherein whole blood is drawn, filtered and returned in discrete batches and no recirculation through the filter takes place. Only the more complex and less convenient two needle continuous flow systems, which requires
65 two phlebotomy needles, has a greater system efficiency. This is illustrated in Figure 10, wherein collected

plasma volumes 183, 184 and 185 are depicted for two needle continuous, single needle recirculation and single needle batch systems, respectively.

Where it is desired to operate the blood fractionation system without recirculation, as where a donor is encountered having an unusually high hematocrit which raises the probability of hemolysis in a second pass through the filter, the operating speed of the inlet pump during the return cycle can be set to zero by means of potentiometer 61b. Then, as shown in Figure 8c, all of the plasma deficient whole blood pumped from reservoir 44 during the return cycle is caused to flow back to the donor through the donor interface conduit 27 and the single lumen phlebotomy needle 26. Inlet pump 32, being motionless, functions as a valve to prevent flow through tubing segment 30, thereby obviating the need for separate fluid flow control valves and their attendant control systems.

Where exceptionally low hematocrits are encountered, substantially all of the plasma deficient whole blood from reservoir 44 can be recirculated through filter 33 by setting the inlet pump 32 and the replacement pump 46 to operate at the same rate. It is contemplated that this procedure would be used only for short time periods, such as required to complete a second pass through the filter, to avoid subjecting the filter to excessively high hematocrits and attendant hemolysis.

During the draw and return cycles the ACD pump 40 introduces ACD solution into conduit segment 30 at respective rates selected by the operator. The operation of the ACD pump and the rate selected are options available to the physician and may vary according to the particulars of the procedure.

Prior to initial operation of the blood fractionation system a prime mode may be provided wherein air is removed from the conduit segments and fluid path elements of the system. As shown in Figure 8d, the saline lines 51 and 53, heretofore clamped closed during the drawn and return cycles, are opened. The donor conduit segment 27 is clamped shut and pumps 32, 40 and 46 are operated to pump saline solution from container 52 and ACD solution from container 36 throughout the system. Trapped air and bubbles are forced into the combined bubble trap and fluid absence detector 47, wherein they are collected and discharged through line 53 to saline container 52. Fluid absence detector 47 is disabled and the procedure continues until all trapped air has been exhausted. The procedure is then terminated by the operator, and after the system has been connected to the donor, an appropriate input is applied to control circuit 81 to initiate a draw cycle.

Thus, the blood fractionation system of the invention can be conveniently set up, and once in use can operate automatically without continuous operator intervention. By reason of its increased plasma separation efficiency, the system of the invention can utilize a smaller volume filter component and hence a smaller volume flow system, to accomplish a given blood fractionation procedure. Since the smaller filter requires a smaller microporous filter element, the cost of the filter component, and hence the cost of the system, is reduced.

The fluid flow system 25 utilized in conjunction with the system may be formed of vinyl and other plastic non-pyrogenic materials as a single use disposable flow set, as shown in Figure 11. The set is preferably individually packaged in a sterile condition for convenient long term storage prior to use.

The mixing chamber 31 is provided up-line of filter 33 to mix the plasma-deficient whole blood diverted for recirculation with previously drawn whole blood, thereby averaging the hematocrit of whole blood circulating through the filter over successive draw and return cycles and enabling the flow rate and pressure at the filter to be more nearly optimized. To this end, the mixing chamber preferably has a volume substantially equal to or greater than the volume of plasma-deficient whole blood pumped from reservoir 44 during the return cycle. This assures that the recirculated plasma-deficient blood will mix with at least an equal volume of previously pumped blood. In practice the mixing chamber may have a volume which is a multiple of the volume pumped from the in-process chamber. For example, in one successful application of the invention, which utilized an intermediate fluid reservoir having a volume of 100 ml, a high limit of 50 ml, and a low limit of 30 ml, a mixing chamber having a volume of 50 ml was provided in conjunction with a filter having a 5 ml volume. In this application, a return pump speed of 200 ml/min was utilized in conjunction with inlet pump speeds of 50—70 ml/min. This provided a ratio of 3:1 between the pump speeds, which has been found to provide good efficiency with the 40—55% hematocrit levels typically encountered, as shown in the previous tabulation.

While the use of a weight-responsive transducer has been shown for controlling the return cycle, it is possible to use other control means, such as electrical switches actuated by a mechanical weight scale linkage on which reservoir 44 is supported, or a pair of ultrasonic level detectors arranged to sense blood level in the reservoir. Also, the system may be used in conjunction with a pressure cuff.

The blood processing system of the invention has the further advantage of being dependent only on the volume of separated cellular component, or plasma-deficient whole blood, which is directly related to the volume of whole blood processed; and not on the volume of the collected non-cellular component, or plasma, which is dependent on the hematocrit of the whole blood and therefore not directly related to processed volume. This enables the system to draw and return without readjustment batches of uniform volume from different donors, notwithstanding differences in hematocrits between the donors.

While the invention has been shown in conjunction with a hollow fiber type filter, it will be appreciated that it can be utilized in conjunction with other types of filters, such as a flat membrane type filter, or a centrifugal separator. Also, in conjunction with the hollow fiber membrane filter shown, a pressure regulator valve and TMP monitoring system may be employed for more accurate TMP control.

Claims

1. A blood fractionation system for separating a blood fraction from whole blood, comprising means including a donor interface conduit (27) adapted for connection to a phlebotomy needle (26) for alternately
5 drawing whole blood from a donor and returning a component-deficient blood fraction to the donor; a fluid reservoir (44); separating means (33) for separating the blood fraction from whole blood; first fluid conveyance means (25) including an inlet pump (32) for conveying fluid from said donor conduit through said separation means to said reservoir (44); the system being adapted to return the component-deficient blood fraction to the donor interface conduit (27) from the reservoir (44), characterised by second fluid
10 conveyance means (45) including a return pump (46) responsive to the volume in said reservoir (44) reaching a predetermined maximum level for conveying the component deficient blood fraction from said reservoir to said donor interface conduit (27) to reduce the volume in said reservoir to a predetermined minimum level; and said second pump rate being set relative to said first pump rate whereby upon said operation of said second fluid conveyance means (45) a selected portion of the flow from said reservoir is
15 caused to recirculate through said separation means (33), while the remaining portion is caused to be returned through the phlebotomy needle to the donor.
2. A blood fractionation system according to Claim 1, wherein the second fluid conveyance means (45) is responsive to the weight of the contents of the reservoir (44).
3. A blood fractionation system according to Claim 1 or 2, wherein the rates of said inlet and return
20 pumps (32, 46) are operator-adjustable.
4. A blood fractionation system according to Claim 1, 2 or 3, wherein the volume of said first fluid conveyance means (32) is substantially equal to or greater than the volume of component-deficient blood fraction returned from said reservoir upon operation of said second fluid conveyance means (45).
5. A blood fractionation system according to Claim 4, wherein said first fluid conveyance means (32)
25 includes a fluid mixing chamber (31) upline of the separation means (33) having a volume substantially equal to or greater than the volume of component-deficient blood fraction returned from said reservoir (44) upon a single operation of said second fluid conveyance means (45).
6. A blood fractionation system according to any preceding claim, wherein said separation means (33) is a membrane type filter such as a hollow fiber type filter.
7. A blood fractionation system according to Claim 1 including means for monitoring the volume of the
30 component-deficient blood fraction, and control means for commencing return thereof to the donor when the volume of the collected component-deficient blood fraction reaches a predetermined maximum level, and for terminating the return of the cellular component when the volume thereof reaches a predetermined minimum level.
8. A blood fractionation system according to Claim 7, wherein said control means include an electrical
35 weight transducer providing an output signal indicative of the weight of the component-deficient blood fraction.
9. A blood fractionation system according to Claim 7 or 8, wherein the control means operates said inlet pump (32) at a preselected rate for continuously pumping blood through the first conveyance means
40 (25) and operates said return pump (46) intermittently at a preselected rate for intermittently pumping a predetermined aliquot of the component-deficient blood fraction through the second conveyance means (45).

Patentansprüche

1. Blut-Fraktionierungssystem zum Abtrennen eines Blutbestandteils vom Gesamtblut, umfassend
45 Mittel einschließlich einer Spender-Verbindungsleitung (27) zur Verbindung mit einer Phlebotomienadel (26) zum abwechselnden Abziehen von Gesamtblut von einem Spender und Zurückführen einer Blutfraktion, der eine Komponente fehlt, zum Spender; ein Flüssigkeitsreservoir (44); Abtrennungsmittel
50 (33) zum Abtrennen des Blutbestandteils vom Gesamtblut; erste Flüssigkeitsförderungsmittel (25), einschließlich einer Einlaßpumpe (32) zum Fördern von Flüssigkeit von der Spender-Leitung durch die Abtrennungsmittel zum Reservoir (44); wobei das System so ausgebildet ist, daß der Blutbestandteil mit fehlender Komponente zur Spender-Verbindungsleitung (27) vom Reservoir (44) zurückführbar ist,
55 gekennzeichnet durch zweite Flüssigkeitsförderungsmittel (45) einschließlich einer Rückförderpumpe (46), um in Antwort darauf, daß das Volumen im Reservoir (44) einen vorbestimmten Maximalpegel erreicht, den Blutbestandteil mit fehlender Blutkomponente vom Reservoir zur Spender-Verbindungsleitung (27) zur Verminderung des Volumens im Reservoir auf einen vorbestimmten Minimalpegel zu fördern; und wobei die zweite Pumprate in Relation zur ersten Pumprate eingestellt wird, wodurch bei Arbeiten der zweiten Flüssigkeitsförderungsmittel (45) ein ausgewählter Teil des Flusses vom Reservoir zur Rückströmung durch die
60 Abtrennungsmittel (33) veranlaßt wird, während der übrige Teil durch die Phlebotomienadel zum Spender zurückgeführt wird.
2. Blutfraktionierungssystem nach Anspruch 1, wobei die zweiten Flüssigkeitsförderungsmittel (45) auf das Gewicht des Inhaltes des Reservoirs (44) ansprechen.
3. Blutfraktionierungssystem nach Anspruch 1 oder 2, wobei die Raten der Einlaß- und
65 Rückförderpumpen (32, 46) von einer Bedienungsperson einstellbar sind.

4. Blutfraktionierungssystem nach den Ansprüchen 1, 2 oder 3, wobei das Volumen der ersten Flüssigkeitsförderungsmittel (32) im wesentlichen gleich oder größer als das Volumen des Blutbestandteils mit fehlender Komponente ist, welcher vom Reservoir beim Arbeiten der zweiten Flüssigkeitsförderungsmittel (45) zurückgeführt werden.

5 5. Blutfraktionierungssystem nach Anspruch 4, wobei die ersten Flüssigkeitsförderungsmittel (32) eine Flüssigkeitsmischkammer (31) umfassen, die stromauf der Abtrennungsmittel (33) liegen und ein Volumen aufweisen, das im wesentlichen gleich oder größer dem Volumen des Blutbestandteils mit fehlender Komponente ist, der vom Reservoir (44) auf eine einzige Inbetriebnahme der zweiten Flüssigkeitsförderungsmittel (45) zurückgeführt wird.

10 6. Blutfraktionierungssystem nach einem der vorhergehenden Ansprüche, wobei die Abtrennungsmittel (33) ein Membranfilter wie z.B. einen Hohlfasen-Filter umfassen.

7. Blutfraktionierungssystem nach Anspruch 1, umfassend Mittel zum Überwachen des Volumens des Blutbestandteils mit abgetrennter Komponente und Steuermittel zum Beginnen dessen Rückführung zum Spender, wenn das Volumen des Blutbestandteils mit fehlender Komponente einen vorbestimmten Maximalpegel erreicht und zum Beenden der Rückführung der zellulären Komponente, wenn deren Volumen einen vorbestimmten Minimalpegel erreicht.

8. Blutfraktionierungssystem nach Anspruch 7, wobei die Steuermittel einen elektrischen Gewichtswandler umfassen, der ein Ausgangssignal abgibt, welches des Gewicht des Blutbestandteils mit fehlender Komponente wiedergibt.

20 9. Blutfraktionierungssystem nach Anspruch 7 oder 8, wobei die Steuermittel die Einlaßpumpe (32) mit einer vorbestimmten Rate ansteuern, um kontinuierlich Blut durch die ersten Förderungsmittel (25) zu pumpen, und die Rückführungspumpe (46) intermittierend mit vorbestimmter Rate ansteuern, um einen vorbestimmten anderen Teil des Blutbestandteils mit fehlender Komponente durch die zweiten Förderungsmittel (45) zum pumpen.

Revendications

1. Système de fractionnement du sang pour séparer une fraction de sang du sang entier, comprenant des moyens comportant un conduit (27) d'interface de donneur prévu pour le raccordement à une aiguille de phlébotomie (26) pour alternativement extraire du sang entier d'un donneur et renvoyer une fraction de sang appauvrie en un composant au donneur; un réservoir de fluide (44); des moyens de séparation (33) pour séparer la fraction de sang du sang entier; des premiers moyens de transport de fluide (25) comportant une pompe d'entrée (32) pour faire circuler le fluide venant dudit conduit de donneur vers ledit réservoir (44), à travers lesdits moyens de séparation; le système étant prévu pour renvoyer la fraction de sang appauvrie en composant au conduit d'interface de donneur (27) à partir du réservoir (44), caractérisé en ce qu'il comprend des deuxièmes moyens de transport de fluide (45) comportant une pompe de retour (46) qui répond à l'arrivée du volume dans ledit réservoir (44) à un niveau maximal prédéterminé, pour faire circuler la fraction de sang appauvrie en composant dudit réservoir audit conduit d'interface de donneur (27) afin d'abaisser le volume dans ledit réservoir à un niveau minimal prédéterminé, le débit de ladite deuxième pompe étant fixé par rapport au débit de ladite première pompe de sorte que, lors dudit fonctionnement desdits deuxièmes moyens de transport de fluide (45), une partie déterminée du débit venant dudit réservoir est amenée à recirculer à travers lesdits moyens de séparation (33), tandis que la partie restante est renvoyée vers le donneur par l'intermédiaire de l'aiguille de phlébotomie.

2. Système de fractionnement du sang suivant la revendication 1, dans lequel les deuxièmes moyens de transport de fluide (45) sont sensibles au poids du contenu du réservoir (44).

3. Système de fractionnement du sang suivant la revendication 1 ou 2, dans lequel les débits desdites pompes d'entrée et de retour (32, 46) sont réglables par l'opérateur.

4. Système de fractionnement du sang suivant la revendication 1, 2 ou 3, dans lequel le volume desdits premiers moyens de transport (32) est sensiblement égal ou supérieur au volume de la fraction de sang appauvrie en composant renvoyée à partir dudit réservoir, lors du fonctionnement desdits deuxièmes moyens de transport de fluide (45).

5. Système de fractionnement du sang suivant la revendication 4, dans lequel lesdits premiers moyens de transport de fluide (32) comprennent une chambre de mélange de fluide (31) qui est située en amont des moyens de séparation (33) et qui a un volume sensiblement égal ou supérieur au volume de la fraction de sang appauvrie en composant renvoyée à partir dudit réservoir (44) lors d'un fonctionnement unique desdits deuxièmes moyens de transport de fluide.

6. Système de fractionnement du sang suivant l'une quelconque des revendications précédentes, dans lequel lesdits moyens de séparation (33) sont constitués par un filtre du type à membrane, tel qu'un filtre du type à fibres creuses.

7. Système de fractionnement du sang suivant la revendication 1, comprenant des moyens de contrôle du volume de la fraction de sang appauvrie en composant, et des moyens de commande pour commencer son renvoi au donneur lorsque le volume de la fraction de sang appauvrie en composant collectée atteint un niveau maximal prédéterminé, et pour terminer le renvoi du composant cellulaire lorsque son volume atteint un niveau minimal prédéterminé.

8. Système de fractionnement du sang suivant la revendication 7, dans lequel lesdits moyens de

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commande comprennent un transducteur de poids électrique fournissant un signal de sortie indicatif du poids de la fraction de sang appauvrie en composant.

9. Système de fractionnement du sang suivant la revendication 7 ou 8, dans lequel les moyens de commande actionnent ladite pompe d'entrée (32) à un débit prédéterminée, pour pomper continuellement le sang à travers les premiers moyens de transport (25), et actionnent ladite pompe de retour (46) de façon intermittente à un débit prédéterminé, pour pomper par intermittance une partie aliquote prédéterminée, de la fraction de sang appauvrie en composant à travers les deuxièmes moyens de transport (45).

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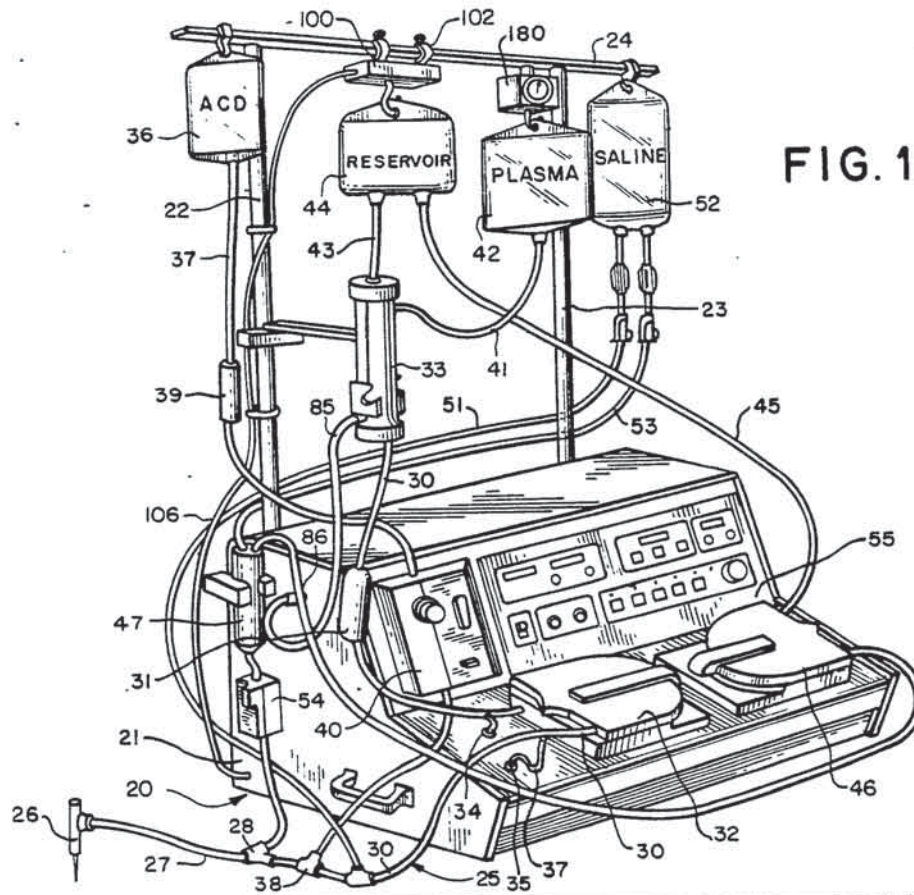


FIG. 1

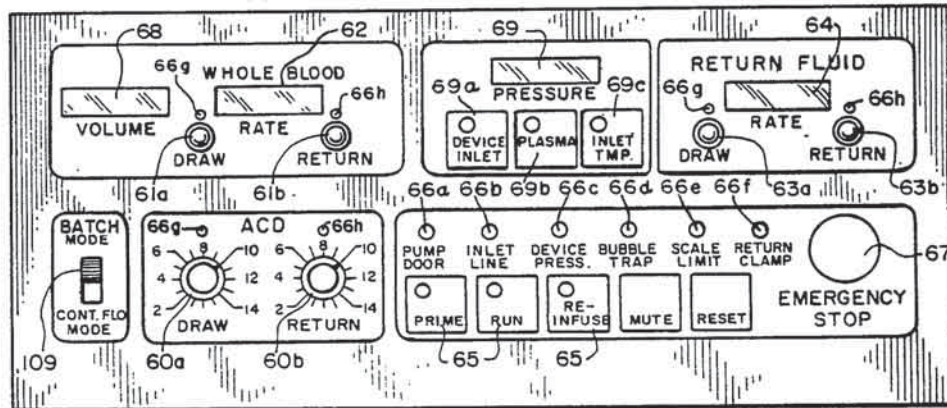
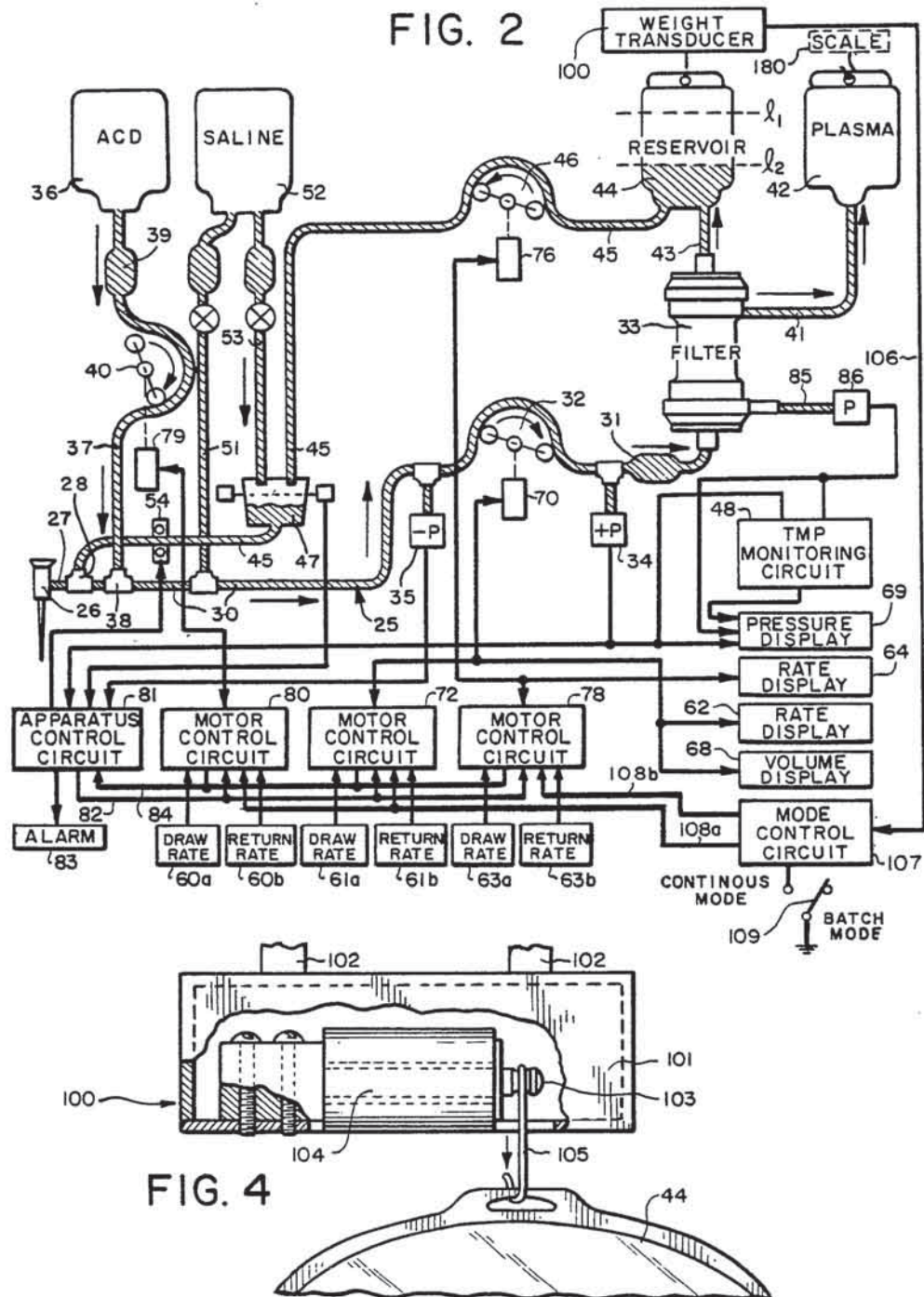


FIG. 3



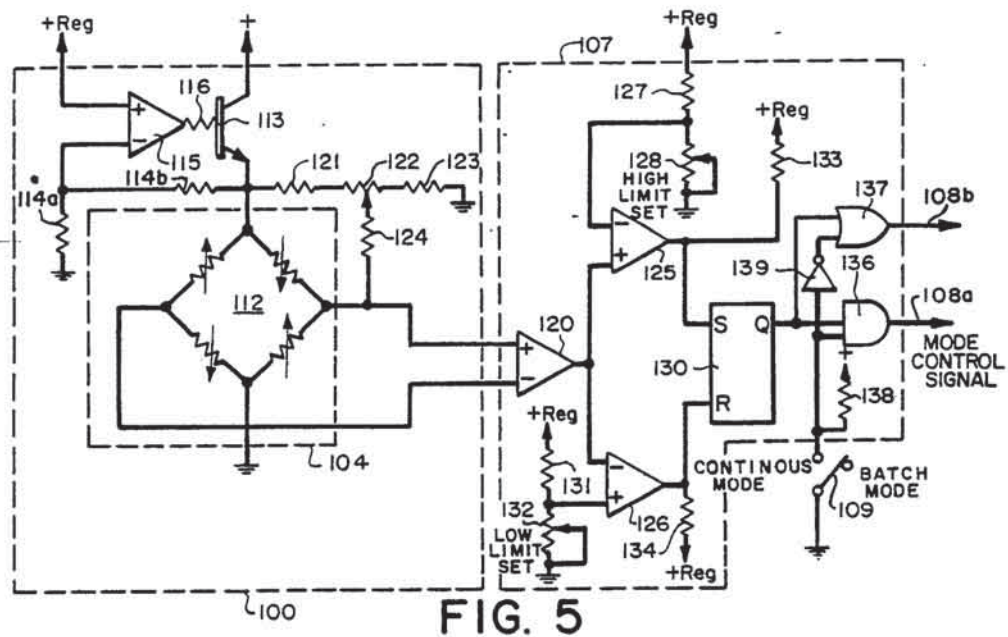
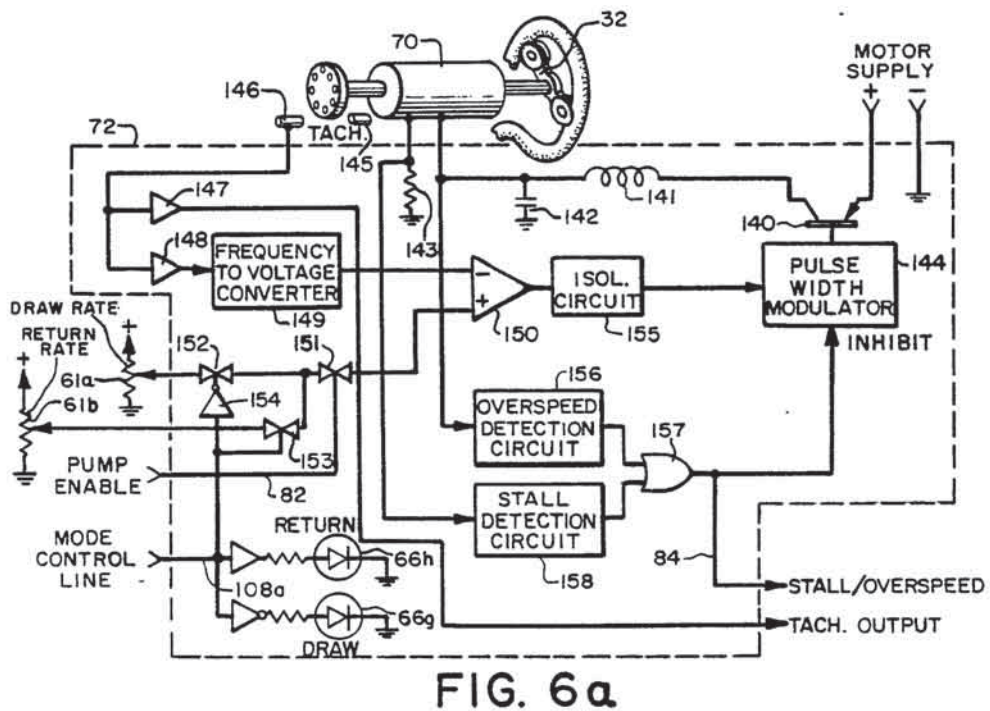


FIG. 7

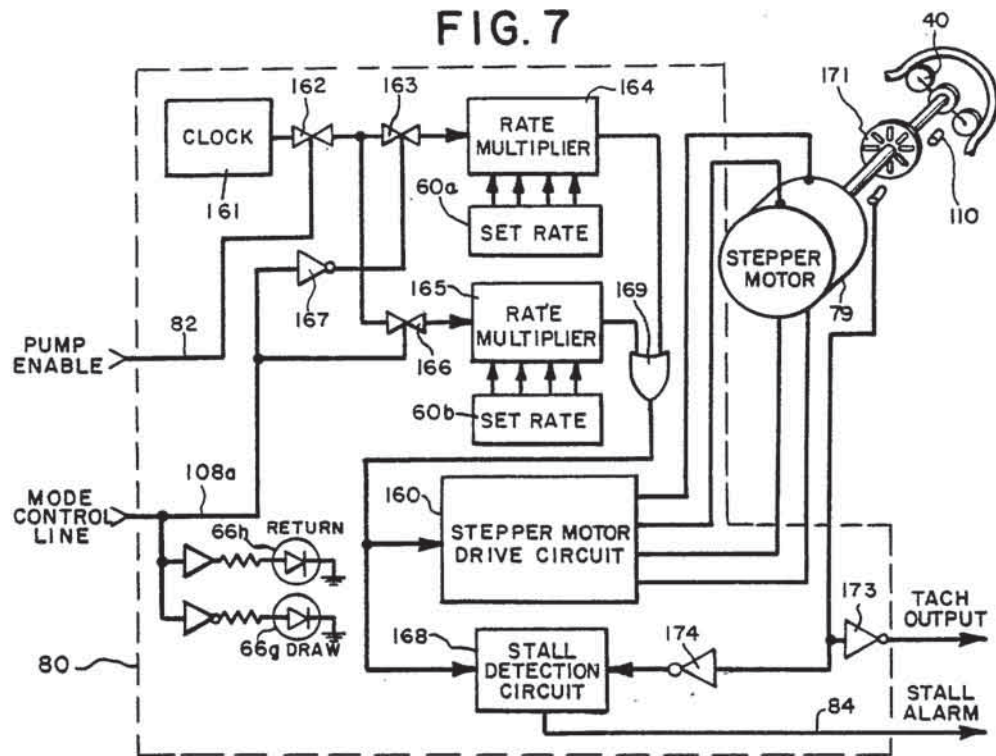


FIG. 6b

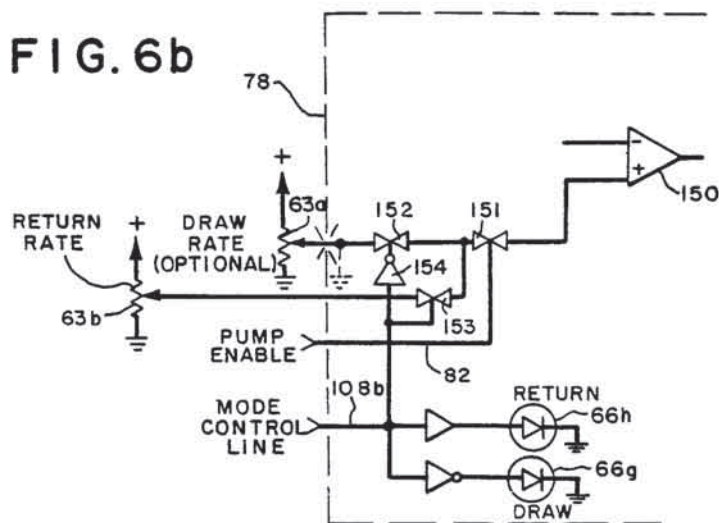


FIG. 8a
(DRAW)

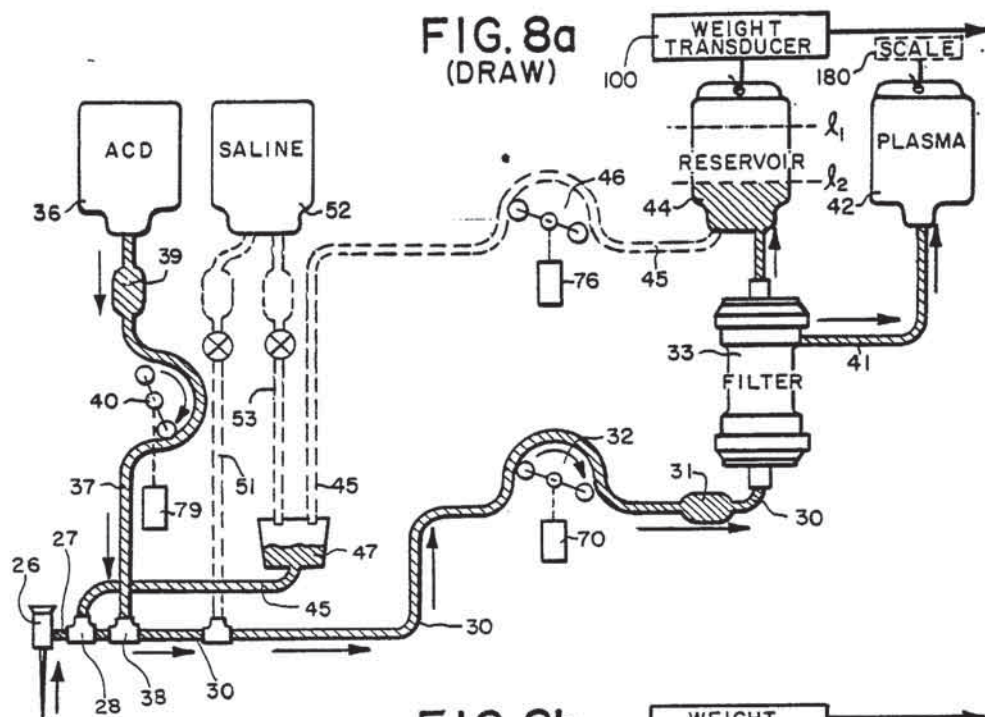
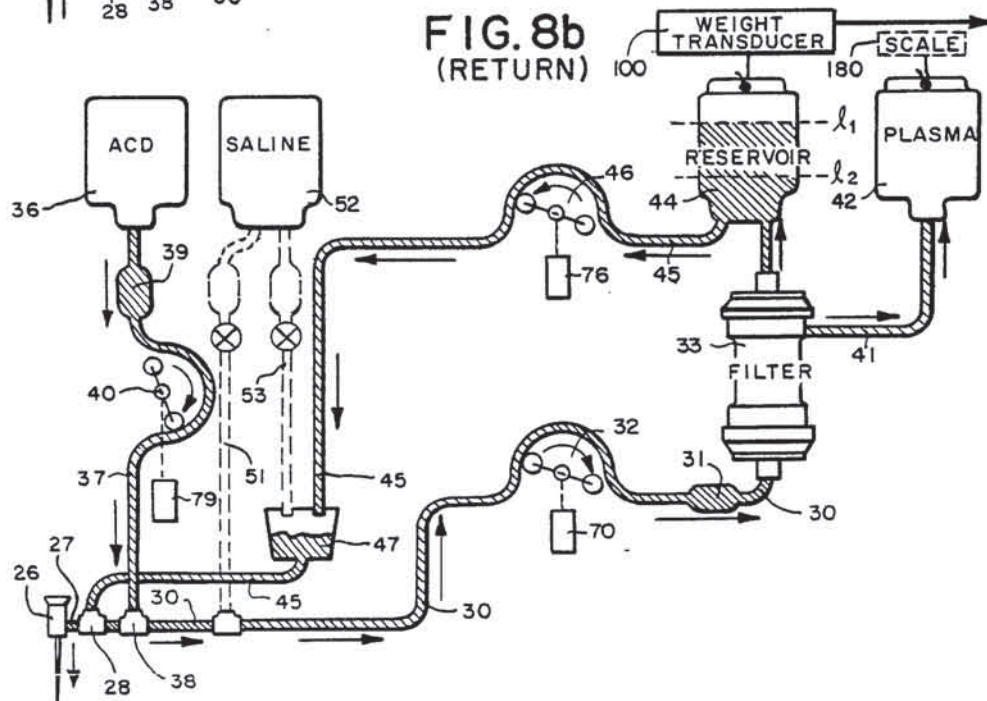
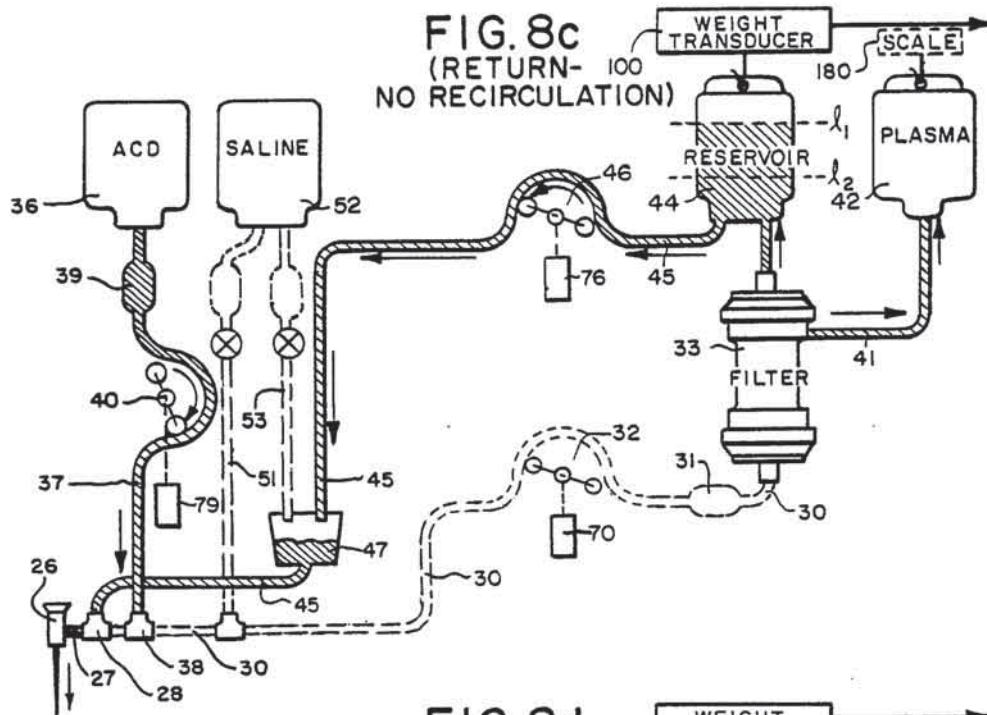
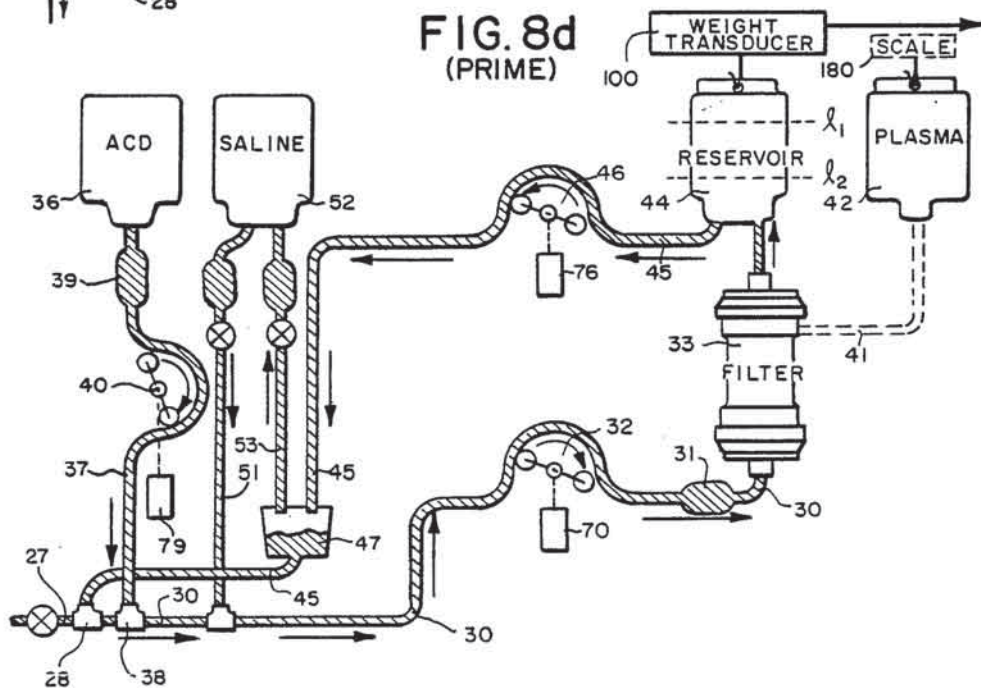


FIG. 8b
(RETURN)





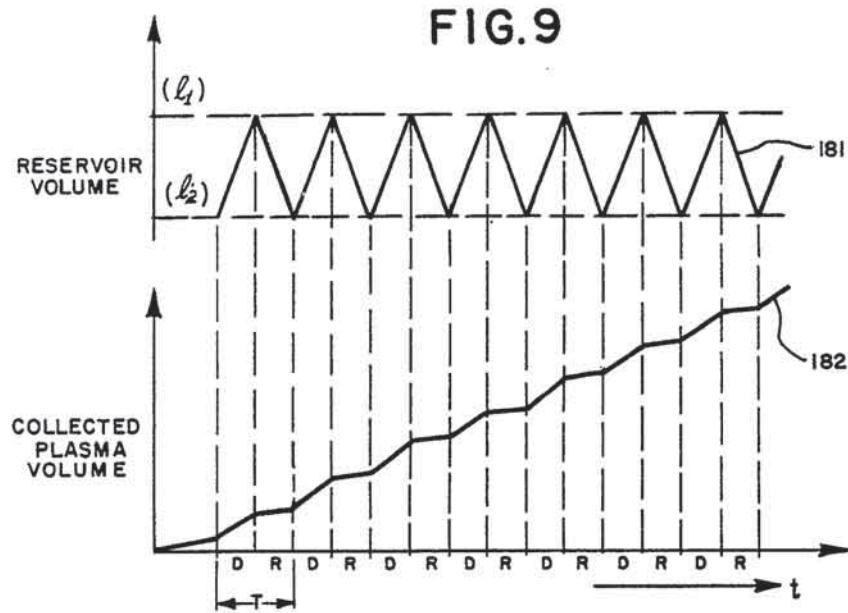
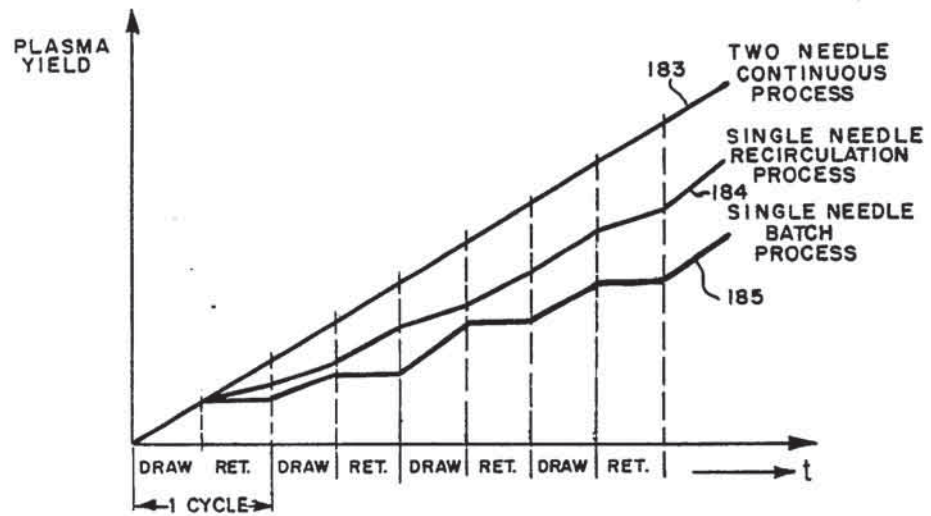


FIG.10

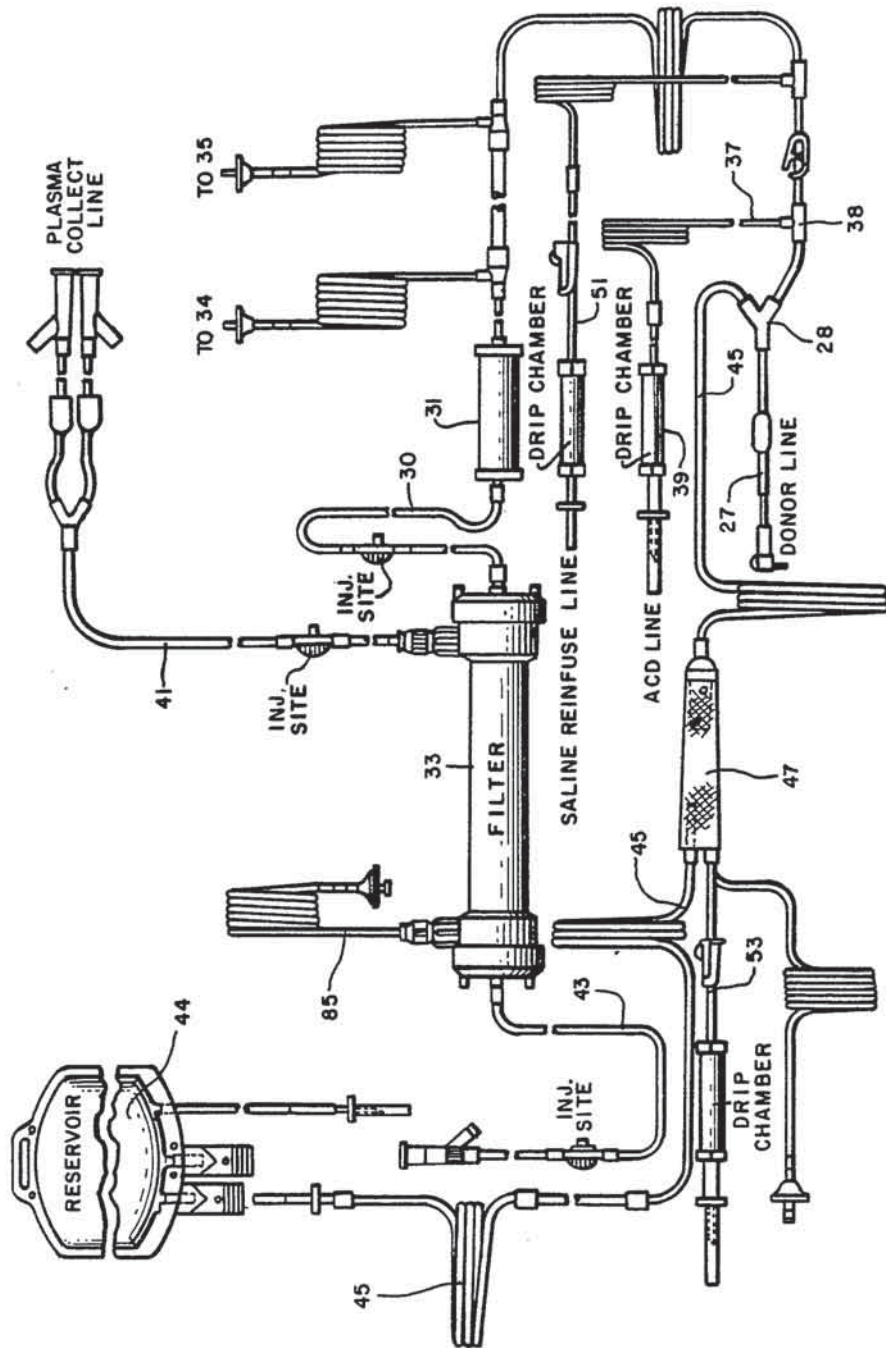


FIG.11

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22 Date of filing: **07.08.85**

54 **Apparatus for separating blood plasma, and apparatus therefor.**

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19.02.86 Bulletin 86/08

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WO-A-81/02979
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Courier Press, Leamington Spa, England.

Description

Background of the invention

1. Field of the invention:

5 This invention relates to an apparatus wherein a membrane-type blood plasma separator is used to separate blood plasma without continuously circulating blood externally of a donor, yet at an efficiency approximately equivalent to that of a continuous external circulation system by adopting a semicontinuous system in which blood is collected and returned in repeated fashion.

10

2. Description of the prior art

A well-known method of gathering blood plasma is to centrifugally separate whole blood taken from a healthy donor and collected in a blood bag. An apparatus has recently been developed for obtaining a large quantity of blood plasma from a single donor by means of semicontinuous or continuous centrifugation. 15 Membrane-type blood plasma separators have also appeared and make it possible to separate large quantities of blood plasma anywhere with facility, and much research has been done in the area of so-called plasma exchange therapy, in which a large amount of blood plasma is separated from a patient suffering from a serious immunological or metabolic illness and the patient is supplemented with blood plasma collected from a healthy donor. Blood plasma obtained from healthy donors is also used for such purposes as nutritional supply of gravity patients, supply of coagulation factor and invigoration of the immunity function, and demand for such plasma is ever increasing. For this reason, a variety of research is being conducted into methods of obtaining large quantities of blood plasma from healthy donors safely, inexpensively and with facility. The membrane-type plasma separator is particularly promising as it 20 features a higher separating speed than a continuous centrifuge and can be handled without costly specialized equipment.

However, with the conventional continuous separation of blood plasma using a membrane, it is necessary for a vein to be punctured at two locations, namely, on the side at which blood is collected from e.g., a donor, and on the side at which blood is returned to the donor, and it is also required that continuous extracorporeal circulation of blood be performed. Accordingly, the risk of injury to the donor is high. 30 Moreover, since a plasma pump is provided to prevent hemolysis due to a rise in TMP caused by resistance on the blood-return side, the separator operates at less than maximum performance. This results in a low separation efficiency.

With the conventional semicontinuous separation of blood plasma using a membrane, separator resistance at return of the blood from a blood reservoir rises owing to the concentrated blood obtained 35 from the separation process. The result is damage to the blood cells and an extended period of time for return of the blood. Though a bypass can be provided to alleviate the problem, this would result in loss time equivalent to the time needed for the bypass. Furthermore, since the TMP internally of the separator in a one-pump system becomes a negative pressure at return of the blood so that the collected plasma flows backward, it is necessary to interrupt the separation process at return of the blood or to provide a blood 40 return pump and a switching valve.

An apparatus according to the preamble part of Claims 1 and 6 is known from EP—A—0 085 016. This apparatus is adapted to sample blood from and to return blood to a donor via a single needle. Further, this apparatus includes a plasma separator for concentrating the blood and a reservoir for temporarily pooling concentrated blood. So, with the known apparatus the blood passes twice to separator, the first time when 45 blood is collected in the reservoir and a second time when the blood is returned to the donor via the plasma separator. However, in this known apparatus, all the blood concentrated by the plasma separator is collected in the reservoir, and it is only returned to the plasma separator when the blood from the reservoir is returned to the donor. So, the known apparatus cannot achieve a plasma separation with a good efficiency.

50 In EP—A—0 131 529, which is based on a prior application, but has not been published before the priority date of this application, a similar apparatus is described comprising additionally an internal circulating circuit. In this apparatus according to the prior art, the efficiency of the plasma separation is improved. However, there is another disadvantage. When the blood circulating in the plasma separator is concentrated, a rise in viscosity results whenever plasma is separated from the blood. As a result, it becomes progressively more difficult for the blood to flow internally of the separator, and so, there is an 55 increasing danger of hemolysis occurring.

The present invention has been devised to solve the aforementioned problems of the prior art, and an object of the invention is to provide an apparatus for separating blood plasma, wherein the vein of a donor need be punctured at only one location, the risk of extracorporeal blood circulation can be avoided, and plasma can be separated continuously from blood collection to blood return, thereby enabling plasma to 60 be collected at an efficiency higher than that heretofore obtainable with a continuous system regardless of adoption of a semicontinuous plasma separation method in which blood collection and return are performed intermittently.

According to the present invention, the foregoing object is attained in a first embodiment with the 65 features of Claim 1 and in a second embodiment with the features of Claim 6.

According to the invention, the membrane-type blood plasma separating means is provided with means for varying the cross-sectional area of blood passages internally of the separating means.

Additionally, the blood reservoir means may comprise a sealed bag made of a flexible synthetic resin. Further, the blood feed means for introducing and discharging blood may comprise a roller pump capable of forward and reverse rotation. Preferably, the apparatus of the invention further includes at least two pumps, one for driving the blood feed means and the other for driving the circulating means.

Other features and advantages of the present invention will be apparent from the following description taken in conjunction with the accompanying drawings, in which like reference characters designate the same or similar parts throughout the figures thereof.

Brief description of the drawings

Figure 1(a) is a perspective view showing a blood plasma separating apparatus according to the present invention;

Figure 1(b) is a circuit diagram of a blood plasma separating apparatus according to the present invention;

Figure 1(C) is an enlarged sectional view showing an embodiment of a blood plasma separator;

Figure 1(d) is an enlarged sectional view showing a pressing device operatively associated with the separator of Figure 1(C);

Figures 2(A) and 2(B) are block diagrams illustrating the operating principle of the blood plasma separating apparatus at collection and return of blood.

Figure 3 is a graph illustrating the relation between the amount of blood plasma separated and the operating time of the apparatus;

Figure 4 is a circuit diagram of an experiment using the plasma separating apparatus for practicing the plasma separating method of the illustrated embodiment;

Figure 5 is a circuit diagram of an experiment indicative of the conventional continuous-type blood plasma separating method;

Figures 6(A) and 6(B) are block diagrams illustrating the operating principle of a modification of the blood plasma separating apparatus for practicing the blood plasma separating method of the illustrated embodiment;

Figure 7 is a circuit diagram of a second embodiment of a blood plasma separating apparatus according to the present invention;

Figures 8(A) and 8(B) are block diagrams illustrating the operating principle of the blood plasma separating apparatus at collection and return of blood;

Figure 9 is a circuit diagram of an experiment indicating the second embodiment of the plasma separating apparatus according to the present invention;

Figure 10 is a circuit diagram of an experiment indicating the conventional continuous-type separation method; and

Figures 11(A), 11(B), 12(A) and 12(B) are block diagrams illustrating modifications of the second embodiment of the blood plasma separating apparatus according to the present invention.

Description of the preferred embodiments

Figure 1(A) is a perspective view showing a blood plasma separating apparatus for practicing an embodiment of a blood plasma separating method, Figure 1(B) is a circuit diagram of the blood plasma separating apparatus shown in Figure 1(A), and Figures 2(A) and 2(B) are block diagrams illustrating the operating principle of the blood plasma separating apparatus at collection and return of blood.

With reference to Figure 1(A), the plasma separating apparatus of the present invention includes a membrane-type plasma separator 1, a recirculating pump 3 connected to the separator 1, a pressure monitoring air chamber 5 connected to the recirculating pump 3, a pressure gauge 6 connected to the air chamber 5, a blood feed pump 7 connected to the line between separator 1 and air chamber 5, a blood reservoir 8 connected to the line between the separator 1 and recirculating pump 3, a replacement liquid pump 9 connected to the blood feed pump 7, a vessel of anticoagulant 10 connected to the pump 9, a vessel of a replacement liquid 11 connected to the pump 9, and a plasma collecting vessel 12 connected to the separator 1. Also included are an air bubble detector 13, a negative pressure detector 14, a switching valve 15 for selecting either the anticoagulant 10 or the replacement liquid 11, a display and control section 17, a venipuncture needle 18, and a pressing device 19 serving as adjusting means for varying the cross-sectional area of blood flow passages in the separator 1.

As shown in the circuit diagram of Figure 1(B), the plasma separating apparatus separates plasma from blood by way of the membrane-type separator 1, includes a blood circulation circuit for recirculating the resulting concentrated blood from a blood outlet 2 of the plasma separator 1 to a blood inlet 4 thereof 1 by the recirculating pump 3, and causes blood collected from an individual, such as a donor or patient, to flow into the line of the circulation circuit between the recirculating pump 3 and the blood inlet 4 of plasma separator 1 by means of the blood feed pump 7, which is reversibly rotatable. Some of the concentrated blood from the blood outlet 2 of the plasma separator 1 branches from the circuit leading to the recirculating pump 3 and collects in the blood reservoir 8, with the amount of the blood fed to the plasma separator 1 being fixed. The arrangement is such that blood in the reservoir 8 and circulation circuit is

returned to the individual by reversing the rotation of the blood feed pump 7. The pressure of the blood flowing into the plasma separator 1 of the recirculating circuit is monitored by the pressure gauge 6 connected to the pressure monitoring air chamber 5.

Let us now describe the operation of the plasma separating apparatus of the illustrated embodiment.

5 The interior of the circuitry is primed with a physiologic saline solution or the like introduced from the terminus of the circuitry by driving the pump 7. Following priming, the recirculating pump 3 is set into operation to form the blood circulating circuit, after which blood is introduced from the needle 18 at the terminus of the circuitry by rotating the pump 7 in the forward direction. At this time the anticoagulant 10, such as heparin, ACD solution or sodium citrate solution, should be mixed with the blood by operating the
10 replacement liquid pump 9. The blood which has entered the recirculating circuit passes through the plasma separator 1, where plasma is separated from the blood and then collected in the plasma collecting vessel 12. Meanwhile, the concentrated blood resulting from the separation process in the plasma separator 1 is circulated through the circuit by the recirculating pump 3 to be diluted with blood obtained afresh from the donor and is reintroduced to the plasma separator 1 where further concentration is
15 performed. Some of the concentrated blood which flows out of the separator 1 is pooled in the blood reservoir 8. It is preferred that the blood reservoir 8 comprise a sealed bag made of a flexible synthetic resin, for a reservoir of such construction will automatically follow up changes in pressure.

As soon as a predetermined amount of blood has been collected from the donor, the blood feed pump 7 is rotated in the reverse direction to cause the concentrated blood in reservoir 8 to flow back into the
20 recirculating circuit. The concentrated blood thus enters the recirculating circuit, flows through the recirculating circuit and some of the concentrated blood is returned to the donor by the blood feed pump 7 while the remainder re-enters the plasma separator 1 from the blood inlet 4, whereby the blood is concentrated again. Some of this reconcentrated blood is returned to, e.g., the donor, by the blood feed pump 7. Plasma is continuously separated from the donor's blood by repeating this process. During this
25 process the amount of the blood in the recirculating circuit must be larger than that of the blood to be returned to the donor. In other words, the amount of blood which is recirculated is the amount of blood flow produced by pump 3 minus the amount of blood flow produced by pump 7. At this time the diluting liquid 11, such a physiologic saline or glucose solution, may be administered to the donor, rather than the anticoagulant 10, by the pump 9. Note that a prescribed amount of blood will circulate through the
30 membrane-type plasma separator 1 due to the inflow of blood to the reservoir 8 at blood collection and the outflow of blood from the reservoir 8 at blood return.

It is preferred that a separator of the kind shown in the enlarged sectional view of Figure 1(C) be used as the plasma separator 1. The structure of this separator will now be described.

The separator 1 comprises a case composed of a cylindrical case body 100 and a plunger 104, which
35 serves also as the separator cap. The case body 100 has a bottom centrally provided with a body fluid (blood) inflow port 101, and a side wall provided with a filtration residue (concentrated blood) outflow port 102. The plunger 104 has filtrate (blood plasma) outflow ports 103, 103, and has an O-ring 105 attached to its outer circumferential portion. Disposed within the case are a plurality of filtration membrane units 112. Each unit 112 includes two circularly shaped filtering membranas 107a, 107b which embrace, from above
40 and below, a filtrate flow passage forming plate 106 of circular shape comprising a screen mesh having a central opening 111 and filtrate passageways 108 located near the periphery of the plate. Each filtration membrane unit 112 has its outer circumferential portion as well as its inner circumferential portion about the central opening sealed as by thermal fusion or adhesive, and a sealing member 109 is bonded to the outer periphery of each filtrate passageway 108. It should be noted that the filtrate flow passage forming
45 plate 106 is not limited to the above mentioned mesh; what is essential is that flow passages for the filtrate be assured.

Arranged between neighboring ones of the filtration membrane units 112 is a body fluid flow passage regulating plate 110 of circular shape having a central opening 111' and filtrate passageways 108' corresponding to those in the units 112, as well as a multiplicity of projections on the upper and lower
50 surfaces thereof. Note that the outer peripheral portion of each filtrate passageway 108' has a flat configuration. Also provided in the case body 100 of the separator 1 are two body fluid flow passage regulating plates 113 each of circular shape having a multiplicity of projections on one side surface thereof. One of the plates 113 is arranged with its projections in abutting contact with the upper surface of the uppermost filtration membrane unit 112, and the other of the plates 113 is arranged with its projections in
55 abutting contact with the lower surface of the lowermost filtration membrane unit 112. Each of the body fluid flow passage regulating plates 113 is provided with a central opening 111'' and filtrate passageways 108'' corresponding to those in the units 112. Note that the outer peripheral portion of each filtrate passageway 108'' has a flat configuration. The filtration membrane units 112 and the body fluid flow passage regulating plates 110, 113 are stacked in the manner described and inserted in the case body 100, the entirety is capped under pressure by the plunger 104 to fit the assembly snugly into the case body 100,
60 and the O-ring 105 provides a liquid-tight seal between the plunger 104 and the case 100. The assembly that results is the plasma separator 1. Owing to the pressure applied by the plunger 104, the filtration membrane units 112 and the body fluid flow passage regulating plates 110, 113 are integrally joined at the outer peripheral portions of the filtrate passageways 108, 108', 108'' by means of the sealing members 109, so that these passageways are brought into communication with one another. It should be noted that
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Figure 1(C) depicts membrane thickness, the size of the projections and the spacing between the layers in exaggerated form.

Figure 1(D) is an enlarged sectional view showing the details of the pressing device 19 [Figure 1(A)]. A base 211 of suitable shape is provided with a pressing rod 212 capable of moving freely in the axial direction. The distal end of the pressing rod 212 is provided with a pressing plate 213 capable of being rotated freely about the axis of the pressing rod. Attached to the base 211 so as to rotate coaxially with respect to the pressing plate 213 is a frame-shaped holder 214 capable of accommodating the separator 1 in such a manner that the plunger 104 of the separator 1 may be abutted against the pressing plate 213. The holder 214 is provided with holder locking mechanisms 215 so that the holder can be fixed to the base 211 at a predetermined rotational position with respect thereto.

The arrangement for supporting the plasma separator 1 is thus characterized in that the pressing plate 213 is not only movable in unison with the pressing rod 212 in the axial direction thereof but is also freely rotatable about the axis of the pressing rod, the holder 214 is not only movable axially of the pressing rod 212 but is also rotatable coaxially with respect to the pressing plate 213, and the holder locking mechanisms 215 enable the holder 214 to be fixed to the base 211 at a predetermined rotational position.

The base 211 may consist of any suitable material and have any appropriate shape. As an example, the base 211 may have a columnar configuration and consist of cast iron. The pressing rod 212 is mounted on the base 211 so as to project therefrom and is freely movable axially of the plunger 104 held by the holder 214. In the illustrated embodiment, the pressing rod 212 is supported by the base 211 and by a bearing block 216 attached to the base 211 and, by turning a knob 217, may be moved freely in the axial direction so as to deliver a large axial thrust. A mechanism for rectilinear motion is interposed between the knob 217 and the pressing rod 212 and serves to convert horizontal motion of the knob 217 into axial motion of the rod 212. The mechanism may be of any suitable construction but in the illustrated embodiment includes a worm screw 218 coupled to the knob 217, and a worm 219 meshing with the worm screw 218. The pressing rod 212 is threadedly engaged with female screws provided on the worm 219 and is supported by the bearing block 216 (essentially the base 211) via a sliding key or spline 220, which prevents the pressing rod 212 from rotating. Turning the knob 217 rotates the worm 219 and the worm screw 218 meshing therewith, with the worm 219 rotating while in threaded engagement with the pressing rod 212. Since the pressing rod 212 is non-rotatable, it is free to move in the axial direction.

It should be noted that the bearing block 216 is essentially a part of the base 211. The amount by which the knob 217 is rotated is indicated by an indicator 221.

The pressing plate 213 is provided at the projecting end of the pressing rod 212 and is rotatable about the axis of the rod and movable axially in unison with the rod so as to apply pressure to the plunger 104 of the plasma separator 1.

In the illustrated embodiment, the pressing plate 213 comprises a disk portion 231 and a skirt portion 232 contiguous with the disk portion and covering the outer circumference of the flange portion 261 of the bearing block 216. The pressing plate 213 is fitted securely on the pressing rod 212 in such a manner that the skirt portion 232 covers a bearing flange 222 screwed securely onto the pressing rod 212.

The holder 214 surrounding the pressing plate 213 is mounted on the base 211 so as to be capable of rotating coaxially with respect to the pressing rod 212. The holder 214 has a frame-like construction and comprises a frame portion 241 having a cavity at a position facing the pressing plate 213 for receiving the plasma separator 1, and a hatch portion 242 for closing the cavity of the frame portion 241. The holder 214 is adapted to rigidly hold the case body 100 of the separator 1 in such a manner that the opening to the separator vessel confronts the pressing plate 213.

In the illustrated embodiment, the frame portion 241 of the holder 214 comprises a front part 241a and a pair of side parts 241b, 241b. The hatch portion 242 comprises a pressing part 242a and an arm part 242b. The hatch portion 242 may be swung open and closed relative to the frame portion 241 and, when closed, may be locked in place by fixing means 223. The front part 241a is fitted rotatably over the outer circumferential surface of the bearing block 216 and is embraced by the base 211 and the flange 261 of the bearing block 216. The two side parts 241b, 241b extend in parallel with the axis of the pressing rod 212 from respective ends of the front part 241a so as to surround the pressing plate 213, and each has a receiving projections 243, 243 on which the separator 1 is placed from below. The arm part 242b of the hatch portion 242 is formed integrally with the pressing part 242a and extends across the two side parts 241b, 241b of the frame portion 241. One end of the arm part 242b is pivotally connected by a pin shaft 244 to one end of one side part 241b, so that the other end of the arm part 242b may be swung about the pivot point. A slit (not shown) is provided in the arm part 242b so as to extend from said other end thereof to a point part of the way along the pressing part 242a and arm part 242b. Fitting the fixing means 223 into the slit locks the hatch portion 242 to the front part 241a in the closed condition.

The fixing means 223 has one end 331 thereof pivotally connected by a pin 224 to the side part 241b, and is formed to include a locking portion 332 at its other end. With the fixing means 223 fitted into the slit formed in the hatch portion 242, the locking portion 332 comes into abutting contact with the side face on the openable end of the arm part 242b from the outside thereof to lock the hatch portion 242 in place. Preferably, and by way of example, the fixing means 223 has a hatch locking mechanism for maintaining the locking engagement between the openable end of the arm part 242b and the corresponding side part 241b.

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The holder locking mechanism 215 has a locking recess 251, a locking projection 251a provided at one end of a pin body 252, a resilient member 253, and a locking release lever 254. The locking recess 251 is provided in the outer circumferential surface of the bearing block 216 (essentially in the base 211 at a position opposing the holder 214). The pin body 252 having the locking projection 251a, the resilient member 253 and the locking release lever 254 are provided in the holder 214. The pin body 252 is linked with the locking release lever 254, and the locking projection 251a at the one end of the pin body 252 is urged by the resilient means 253 into engagement with the locking recess 251 at a prescribed rotational position of the holder 214. The resilient member 253 may be any suitable resilient means, such as a spring.

The locking release lever 254 should be provided at a desired position and operable in the radial direction, namely in a direction perpendicular to the rotational axis of the holder 214. In the illustrated embodiment, the locking release lever 254 is provided on the outer surface of the side part 241b at a position in the proximity of the base 211 and is pivotally supported at an intermediate point by a pin shaft 255 in such a manner that both ends thereof are capable of being swung outwardly at right angles to the axis of the pressing rod.

The pin body 252, resilient member 253 and locking release lever 254 are provided at two diametrically opposed locations, namely at two locations 180° apart circumferentially of the holder 214. Accordingly, when the holder 214 is rotated through 180° to position the two side parts 241b thereof in a horizontal plane which contains the pressing rod 212, the holder 214 will be locked automatically to the base 211.

In order to assure rotation of the pressing plate 213 and holder 214, a thrust bearing 226 is provided between the bearing block 216 and the holder 214, and a thrust bearing 227 is mounted between the bearing flange 222 and the pressing plate 213.

In operation, either of the locking projections 251a of the holder locking mechanism 215 is mated with the locking recess 251 to lock the holder 214 to the base 211. Under these conditions, the hatch portion 242 of the holder 214 is swung open horizontally, the body fluid inlet port 101 of the separator 1 is pointed upward, and the separator 1 is placed in the holder 214 through the opening thereof with the plunger 104 being faced toward the pressing plate 213. This is followed by closing the hatch portion 242, fitting the fixing means 223 into the slit formed in the hatch portion 242, and locking the hatch portion 242 in the closed state by the hatch locking mechanism.

The plunger 104 is moved up and down by turning the knob 217 back and forth. Moving the plunger 104 up and down causes a change in the cross-sectional area of the blood flow passages in the plasma separator 1. The blood circulating in the plasma separator 1 is concentrated and, hence, experiences a rise in viscosity whenever plasma is separated from it. As a result, it becomes progressively more difficult for the blood to flow internally of the separator 1, the pressure loss rises and TMP increases. If unchecked, this can lead to hemolysis, namely damage to the red blood cells. Accordingly, if the plunger 104 is lowered by turning the knob 217, the cross-sectional area of the blood flow passages increases, thereby diminishing pressure loss internally of the separator 1 and regulating TMP to within a prescribed range, thus preventing hemolysis. The plasma separator 1 is thus capable of completely separating plasma from entrant blood.

With the plasma separating apparatus for practicing the plasma separating method of the illustrated embodiment, blood concentrated once and pooled in the blood reservoir 8 is recirculated through the recirculating circuit and concentrated again by the separator 1 at return of the blood to the individual, so that plasma is collected even when blood is returned. This enables separation to be performed continuously without interruption when blood is returned.

Let us describe this process in slightly more detail with reference to Figures 2(A) and 2(B). Figure 2(A) illustrates the blood collection cycle. Blood feed pump (P1) 7 is rotated in the forward direction to draw blood from the donor and feed the blood into the circulating circuit. Recirculating pump (P2) 3, which always rotates in the forward direction circulates the blood through the plasma separator (PS) 1, where plasma is separated and stored in the plasma collecting vessel, not shown in Figure 2(A). The concentrated blood resulting from this separation process exits from the plasma separator 1 and flows into the circulating circuit owing to the action of the pump 3. Some of the concentrated blood enters the blood reservoir (R) 8 and the remainder reenters the inlet side of the plasma separator 1 before mixing with fresh blood introduced from the donor by the feed pump 7 upstream of the separator. The mixture of concentrated blood and fresh blood is subjected to plasma separation by the plasma separator 1. The foregoing steps are then repeated.

Figure 2(b) shows the blood return cycle performed when a predetermined amount of blood has been introduced into the system. Here the blood feed pump 7 is operated in the reverse direction to return the blood cell fraction to the donor from the point between the recirculating pump 3 and the inlet side of the plasma separator 1. As mentioned above, however, the recirculating pump 3 continues rotating in the forward direction. Accordingly, the concentrated blood pooled in the blood reservoir 8 during the collection cycle is now withdrawn from the reservoir and introduced into the circulating circuit by the pump 3. Some of this concentrated blood is returned to the donor upstream of the plasma separator 1 by the action of the blood feed pump 7, as mentioned above, and the remainder enters the plasma separator 1 where it is again subjected to plasma separation and, hence, reconcentration. It will thus be understood that plasma separation takes place even while blood is being returned to the donor.

Figure 3 is a graph showing the relation between the amount of plasma separated and the operating time of the apparatus. Curve 510 represents the results achieved with a conventional semicontinuous

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membrane-type plasma separating apparatus, and curve 500 shows the results achieved with the apparatus of the illustrated embodiment. Curve 50 indicates that plasma separation takes place even during return of the blood and, hence, is carried out in a highly efficient manner. Curve 51 shows that since separation is suspended during return of the blood, a longer period of time is required to separate an equivalent amount of plasma with respect to curve 50.

Figure 4 illustrates an example of an experimental set-up indicative of an embodiment of the plasma separating apparatus of the present invention. In the experiment, use was made of a membrane-type plasma separator 1' in which were stacked eight porous membranes each consisting of cellulose acetate with a pore size of 0.45 μ m and having a donut-shaped configuration with an inner diameter of 3.6 cm and an outer diameter of 10 cm. The membranes presented an effective membrane surface area of 546.6 cm². The circuitry, inclusive of the separator 1', was arranged as shown. It should be noted that the membrane-type plasma separator is not limited to a flat membrane-type configuration, for a hollow fiber-type plasma separator can also be employed. Three liters of fresh bovine blood (hematocrit: 42%) with ACD serving as the anticoagulant was prepared in an Erlenmeyer flask 20 and the blood was stirred by a stirrer 22 in a water bath 21 at 37°C. The flask 20 containing the cow blood served as an imitation donor. After the interior of the circuitry was filled with a physiologic saline solution, the blood feed pump 7 was rotated to provide a blood flow rate (Q_B) of 60 ml/min. At the same time, the recirculating pump 3 was rotated to provide a blood flow rate (Q_R) of 110 ml/min. Plasma separation began immediately, with the separated plasma being received by a measuring cylinder 23 to measure the total amount (V) of plasma accumulated. Concurrently, blood inflow pressure (P) was measured for a requisite period of time by the pressure gauge 6 connected to the air chamber 5, with 0 min being taken as the start of blood extraction. When the total amount of blood extracted attained a value of 500 ml, the blood feed pump 7 was reversed to provide a return flow rate of 60 ml/min, and the recirculating pump 3 was rotated at a higher speed to increase the blood flow rate to 160 ml/min, thereby returning the blood to the flask 20. At the end of blood return, the Erlenmeyer flask 20 was replenished with an amount of physiologic saline 24 equivalent to the amount of plasma collected in the measuring cylinder 23. The foregoing process was repeated to provide the experimental results shown in the following Table 1:

TABLE 1

Time (min)	Pressure (mmHg) P	Collection/ return flow rate (ml/min) Q_B	Recirc. flow rate (ml/min) Q_R	Amt. of separated plasma (ml) V
0	75	+60	110	0
2	100	+60	110	60
4	135	+60	110	120
6	140	+60	110	175
8	145	-60	200	230
10	140	-60	200	250
12	145	+60	110	270
14	140	+60	110	325
16	145	+60	110	375
18	150	+60	110	425
20	135	-60	200	445
22	140	-60	200	460
24	120	+60	110	485
26	135	+60	110	515
28	140	-60	200	525
30	—	—	—	—

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In Table 1, the plus signs in the collection/return flow rate column indicate blood collection and the minus signs indicate blood return.

For the purpose of comparison, the inventor performed a plasma separation experiment using 3 l of fresh cow blood mixed with ACD, as in the experiment of Figure 4, employing a continuous separation method considered to be the most efficient at the present time. The experimental set-up, shown in Figure 5, utilizes the plasma separator 1', which has the same specifications as the separator 1' employed in the experiment of Figure 4. The results obtained are as shown in Table 2.

TABLE 2

	Time (min)	Pressure (mmHg)	Collection/ return flow rate (ml/min)	Amount of separated plasma (ml)
10	0	60	60	0
	2	135	60	40
15	4	140	60	75
	6	145	60	110
	8	145	60	145
20	10	145	60	180
	12	145	60	215
25	14	145	60	250
	16	145	60	280
30	18	145	60	310
	20	145	60	340
35	22	150	60	370
	24	145	60	405
40	26	145	60	435
	28	145	60	470
45	30	145	—	500

In the experiments of Figures 4 and 5, the cross-sectional area of blood flow passages in the separator 1 was so controlled by the pressing device as to keep the pressure from exceeding 150 mmHg.

A comparison of Tables 1 and 2 shows that 500 ml of plasma can be collected in less than 26 min with the separating method of the illustrated embodiment, while it takes 30 min to collect 500 ml of plasma with the continuous separation method of Figure 5. It will be appreciated that plasma can be separated from blood in a highly efficient manner according to the illustrated embodiment.

Figures 6(A) and 6(b) are block diagrams of a modification of the invention. In the illustrated arrangement, the reservoir 8 is incorporated into the recirculating circuit. Figure 6(A) illustrates operation at blood collection, and Figure 6(B) shows operation at blood return. The results obtained are the same as those with the arrangement of Figures 2(A) and 2(B). However, with the set-up shown in Figures 2(A), 2(B), the concentrated blood finds refuge in the blood reservoir 8 so that the concentration of the blood inside the reservoir 8 is substantially constant. With the set of shown in Figures 6(A), 6(B), on the other hand, blood in the reservoir 8 is being continuously circulated and concentrated at all times so that the blood concentration internally of the reservoir changes.

A second embodiment of the present invention will now be described. Figure 7 is a circuit diagram of a blood plasma separating apparatus of the second embodiment according to the present invention and Figures 8(A) and 8(B) are block diagrams illustrating the operating principle of the blood plasma separating apparatus at collection and return of blood for practicing the second embodiment of the plasma separation

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method. Portions similar to those shown in Figures 1(A) and 1(B) are designated by like reference characters. The second embodiment of the apparatus includes a three-way valve 31 in the line between the recirculating pump 3 and the blood reservoir 8, a vessel of physiologic saline solution 32, and a transfusion solution set 33 connected between the three-way valve 31 and the physiological saline solution vessel 32.

5 Numeral 34 denotes the forearm of a donor. Unlike the first embodiment, blood from the donor is introduced directly to the blood reservoir 8, rather than being fed directly into the blood circulating circuit.

In the operation of the second embodiment of the present invention, the three-way valve 31 is opened and the pump 3 is set into operation to fill the circuitry with the physiologic saline solution 32 introduced from the transfusion solution set 33. Next, the blood feed pump 7 is driven into rotation to collect blood 10 from the needle 18 inserted into a vein in the donor's forearm 34. The negative pressure monitor 14 for monitoring the state of blood collection from the donor and a brancher 35 can be provided in the tubing between the needle 18 and the blood feed pump 7, and the anticoagulant 10 or physiological saline 11 can be mixed with the blood by changing over the valve 15 and driving the pump 9 at a rate fixed in proportion to the operating rate of the blood feed pump 7. Whole blood collected by operation of the feed pump 7 15 begins to pool in the blood reservoir 8, which is made of a flexible synthetic resin. At the same time, the recirculating pump 3 is operated so that the blood pooled in the reservoir 8 flows into the plasma separator 1 from the blood inlet 4 thereof via the air chamber 5. Plasma separated inside the separator 1 flows from a filtrate outflow port 50 thereof into the tubing of the recirculating circuit for collection in the plasma collecting vessel (collecting bag) 12 by opening a valve 42.

20 The concentrated blood in the separator 1 resulting from separation of the plasma flows out from the blood outlet 2, returns to the reservoir 8 where mixing with newly collected blood takes place, and is then fed again, together with the fresh blood, from the reservoir 8 into the separator 1 by the pump 3. Repeating this process enables plasma to be separated from blood in continuous fashion. The concentration of the blood in the blood reservoir 8 is monitored by the pressure gauge 6.

25 When collection of a predetermined amount of blood from the donor by operation of the blood feed pump 7 ends, the valve 15 is switched so that the donor may be administered replacement physiological saline or glucose 11 in an amount equivalent to the amount of separated plasma by operation of the pump 9. At the same time, the blood feed pump 7 is reversed to return the blood in reservoir 8 to the donor. The recirculating pump 3 continues operating even during return of the blood, so that the plasma separator 1 30 goes on concentrating the blood up to the final target concentration. As soon as the concentrated blood have been returned to the donor, the blood feed pump 7 is again rotated in the forward direction to start collecting fresh blood from the donor so that the foregoing process may be repeated.

Thus, as in the first embodiment of the present invention, the above-described second embodiment also causes concentrated blood in the reservoir 8 to be subjected to concentration again by the separator 1 35 when blood is returned, so that plasma is separated from the concentrated blood even during the return stage of the process. Accordingly, the relation between the amount of plasma separation and the apparatus operating time is similar to that shown in the graph of Figure 3, so that approximately the same effect is obtained and a highly efficient blood collecting operation made possible.

Described next will be an experiment indicative of the plasma separating method of the second 40 embodiment. The set-up is as shown in Figure 9.

Three liters of fresh bovine blood (hematocrit: 42%) with ACD serving as the anticoagulant was prepared in an Erlenmeyer flask 20 and the blood was maintained at a temperature of 37°C by a constant temperature bath 21. At the same time, the blood in the flask 20 was stirred by a stirrer 22 so that the blood would separate by standing. Next, the pump 3 was set into operation to fill the circuitry with the minimum 45 amount of the necessary physiologic saline solution 51. The blood feed pump 7 was rotated to provide a blood flow rate of 60 ml/min and to introduce the blood into the blood reservoir 8.

At the same time, the recirculating pump 3 was rotated to provide a blood flow rate of 150 ml/min, introduce the blood through the air chamber 5 into the membrane-type separator 1', and then return the blood from the separator 1' to the reservoir 8, thereby setting up a circulating flow. At the same time that 50 this closed circuit became filled with blood, the filtrate outflow port 50 was opened to collect the separated plasma in the measuring cylinder 23. The pressure of the blood fed into the separator 1' by the pump 3 was monitored by the pressure gauge 6 connected to the air chamber 5. The membrane-type plasma separator 1' was composed of eight stacked flat-type porous membranes each consisting of cellulose acetate with a pore size of 0.45 μ m and having a donut-shaped configuration with an inner diameter of 3.6 cm and an outer diameter of 10 cm. The membranes presented an effective membrane surface area of 546.6 cm². The 55 plasma separator 1' was filled with 12 ml of blood. In order to hold the filtration pressure constant, the structure of the separator 1' was such that the cross-sectional area of the blood flow passages could be varied in accordance with the concentration of the blood in the reservoir 8 as monitored by the pressure gauge 6. Though not employed, a hollow fiber-type membrane configuration can be adapted to the separator 1'. The results of the experiment are as shown in Table 3.

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TABLE 3

	Operating time (min)	Flow rate		P (mmHg)	V (ml)
		QB1 (ml/min)	QB2 (ml/min)		
5	0	+60	0	0	0
	2	+60	150	78	—
10	3	+60	160	100	50
	6	+60	160	140	140
15	8	+60	160	150	200
	9	—60	160	150	230
	12	+60	160	165	255
20	14	+60	160	150	290
	18	+60	160	155	350
25	21	—60	160	157	400
	27	+60	160	160	440
	28	—60	160	160	475
30	30	+60	160	154	485
	31	—60	160	160	500
35	33	—60	160	0	—

The operating time column represents elapsed time immediately after start of blood collection. For example, the table shows that 500 ml of plasma were separated in 31 min. QB1 denotes the blood feed rate of the blood feed pump 7, where the plus sign indicates blood collection and the minus sign blood return. QB2 designates blood flow rate performed by the recirculating pump 3. P indicates that the blood flow passage pressure is controlled and held at a substantially constant value by monitoring the pressure at the inlet to the plasma separator 1' by the pressure gauge 6. V represents the total amount of plasma separated and shows that separation is carried out even when blood is returned to the donor. At return of the blood, physiologic saline 24 in an amount equivalent to the separated amount of plasma was returned to the flask 20. The maximum amount of blood collected in the reservoir 8 from the flask 20 was 500 ml.

For the purpose of comparison, the inventor performed a plasma separation experiment using 3 l of fresh bovine blood (hematocrit: 40%) mixed with ACD and employing the membrane-type plasma separator 1' of Figure 9. As shown in Figure 10, the plasma was separated by the conventional continuous process. The bovine blood, prepared in the flask 20, was held at 37°C in the constant temperature bath 21 and was stirred to uniformity in the flask 20 by the stirrer 22. At a collecting flow rate of 60 ml/min, blood was fed into the separator 1' through the air chamber 5 by the blood feed pump 7, and the separated plasma was collected in the measuring cylinder 23 from the filtrate outflow port 50 of the separator 1'. The physiologic saline 51 in an amount equivalent to that of the separated plasma was delivered by a pump 52 to a second air chamber 5', where the saline solution was mixed with the concentrated blood. The mixture of physiologic saline and concentrated blood was returned to the flask 20. The pressures on the inflow and outflow sides of the separator 1' were monitored by pressure gauges 6, 6' connected to the respective chambers 5, 5', and the flow passage pressure internally of the separator 1' was regulated to give a pressure loss similar to that obtained in the above experiment. The experimental results are shown in Table 4.

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TABLE 4

	Operating time (min)	Flow rate (ml/min)	Inflow pressure (mmHg)	Outflow pressure (mmHg)	Amount of separated plasma (ml)
5	0	60	145	0	—
	5	60	150	0	75
10	10	60	150	0	150
	15	60	150	0	230
15	20	60	150	0	295
	25	60	150	0	360
	30	60	150	0	420
20	35	60	154	2	480
	37	60	148	0	500
25	38	60	150	3	—

The operating time column represents elapsed time from the start of separation to the conclusion or blood return. Specifically, the table shows that 500 ml of plasma were obtained in 37 min and that 38 min was needed for the conclusion of the entire operation inclusive of blood return.

The blood flow rate is the flow rate established by the pump 7, the inflow and outflow pressures are those measured by the respective pressure gauges 6, 6', and the amount of separated blood plasma is the total accumulated amount measured by the measuring cylinder 23.

A comparison of Tables 3 and 4 clearly shows that the plasma separating apparatus for practicing the plasma separating method of the second embodiment separates plasma more efficiently than the conventional continuous separation method.

Figures 11(A) and 11(B) are block diagrams showing a modification of the second embodiment of Figures 7 and 8. Here the blood from the blood feed pump 7 does not flow directly into the blood reservoir 8. Figures 12(A) and 12(B) are block diagrams showing another modification of the second embodiment. Here the reservoir 8 is provided outside of the recirculating circuit, and the blood from the blood feed pump 7 does not flow directly into the blood reservoir 8. (A) in Figures 11 and 12 illustrates operation during blood collection, and (B) illustrates operation during blood return. The effects obtained with the arrangements of Figures 11 and 12 are similar to those obtained with the second embodiment shown in Figure 8. In the case of Figure 8, blood from the blood feed pump 7 and the concentrated blood from the plasma separator 1 mix in the blood reservoir 8, whereas in Figures 11 and 12 only the concentrated blood from the plasma separator 1 flows into the reservoir 8.

As many apparently widely different embodiments of the present invention can be made without departing from the spirit and scope thereof, it is to be understood that the invention is not limited to the specific embodiments thereof except as defined in the appended claims.

Concrete effects of the invention

According to the present invention as set forth above, plasma is separated from blood through a semicontinuous apparatus whereby a fixed amount of blood is repeatedly collected in and returned from a blood reservoir without requiring continuous circulation externally of a donor or patient. Therefore, unlike the conventional continuous arrangement that requires the donor or patient to be punctured at two locations, puncture at only one location is sufficient. Thus, a healthy donor is not subjected to the hazards of external circulation. Moreover, since plasma separation continues even during return of the blood and there is no need to operate the separator at less than peak performance as in the continuous system of the prior art, an equivalent or higher separation efficiency can be obtained, with one and the same plasma separator, as compared with the conventional external circulation-type continuous separation system heretofore considered to be the most outstanding in terms of effectiveness. The present invention therefore enables blood to be collected in a shorter period of time.

In the plasma separating apparatus of the present invention, the membrane-type plasma separating means is capable of having the cross-sectional area of its blood flow passages varied. This makes it possible to prevent hemolysis by suppressing a rise in pressure loss and stabilizing TMP even when blood viscosity changes. Since the blood reservoir means may comprise a sealed bag made of flexible synthetic

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resin, changes in pressure can be followed up automatically. Further, since the blood feed means for introducing and discharging blood may comprise a reversible roller pump, the cost of the apparatus can be lowered since only a single such roller pump need be used.

The plasma separating apparatus of the invention has at least two pumps, one for driving the blood feed means and the other for driving the circulating means. This enables a higher plasma separation efficiency to be achieved because the introduction, discharge and circulation of blood can be performed simultaneously.

10 Claims

1. An apparatus for separating plasma from blood comprising:
 - a single common needle (18) for introducing blood and returning blood, membrane-type plasma separating means (1) having an inlet port (4) for introducing blood therein and an outlet port (2) for
 - 15 discharging concentrated blood therefrom,
 - blood feed means which includes a reversibly rotatable blood feed pump (7) for introducing and discharging blood from said single common needle, and
 - blood reservoir means (8) connected to said plasma separating means for temporarily pooling or collecting concentrated blood, characterized in that
 - 20 a blood circulating circuit is provided having one end which is connected to said inlet port (4) of said plasma separating means (1) and another end connected to said outlet port (2) of said plasma separating means (1), the blood concentrated by said plasma separating means (1) flowing through said blood circulating circuit;
 - circulating means (3) is provided for circulating the blood internally of said blood circulating circuit
 - 25 from said outlet port (2) to said inlet port (4) of said plasma separating means (1);
 - said blood reservoir means (8) is coupled to said blood circulating circuit on an outlet side thereof for temporarily pooling or collecting an excess amount of concentrated blood which overflows in said blood circulating circuit;
 - said blood feed means is coupled between said single common needle (18) and said blood circulating
 - 30 circuit; and
 - said plasma separating means (1) further includes means (19) for varying the cross-sectional area of blood flow passages defined therein.
2. The apparatus according to Claim 7, wherein said blood reservoir means (8) comprises a sealed bag made of a flexible synthetic resin.
- 35 3. The apparatus according to Claim 7, further comprising at least two pumps (7, 3), one (7) for driving said blood feed means and the other (3) for driving said circulating means.
4. The apparatus according to Claim 7, further comprising at least two liquid-containing vessels (10, 11), and liquid feed means operatively associated with said blood feed means (7) for selectively delivering to said blood feed means a liquid from said liquid-containing vessels at a predetermined ratio.
- 40 5. The apparatus according to Claim 12, wherein the liquid contained in one (10) of said liquid-containing vessels is an anticoagulant, and the liquid contained in the other (11) of said liquid-containing vessels is a replacement liquid of an amount equivalent to an amount of separated plasma.
6. An apparatus for separating plasma from blood comprising:
 - a single common needle (18) for introducing blood and returning blood, membrane-type plasma
 - 45 separating means (1) having an inlet port (4) for introducing blood therein and an outlet port (2) for discharging concentrated blood therefrom,
 - blood feed means which includes a reversibly rotatable blood feed pump (7) for introducing and discharging blood from said single common needle, and
 - blood reservoir means (8) connected to said plasma separating means for temporarily pooling or
 - 50 collecting concentrated blood, characterized in that
 - a blood circulating circuit is provided having one end which is connected to said inlet port (4) of said plasma separating means (1) and another end which is connected to said outlet port (2) of said plasma separating means (1), the blood concentrated by said plasma separating means (1) flowing through said blood circulating circuit;
 - 55 circulating means (3) is provided for circulating the blood internally of said blood circulating circuit from said outlet port (2) to said inlet port (4) of said separating means (1);
 - said blood reservoir means (8) is provided in said blood circulating circuit, for temporarily pooling or collecting blood introduced through said single common needle (18) and concentrated by said plasma separating means;
 - 60 said blood feed means is coupled between said single common needle (18) and said blood reservoir means (8), and
 - said plasma separating means (1) further includes means for varying the cross-sectional area of blood flow passages defined therein.
7. The apparatus according to Claim 6, wherein said blood reservoir means (8) comprises a sealed bag
- 65 made of a flexible synthetic resin.

8. The apparatus according to Claim 6, further comprising at least two pumps (7, 3), one for driving said blood feed means and the other for driving said circulating means.

9. The apparatus according to Claim 6, further comprising at least two liquid-containing vessels (10, 11), and liquid feed means operatively associated with said blood feed means for selectively delivering to said blood feed means a liquid from said liquid-containing vessels at a predetermined ratio.

10. The apparatus according to Claim 9, wherein the liquid contained in one (10) of said liquid-containing vessel is an anticoagulant, and the liquid contained in the other (11) of said liquid containing vessels is a replacement liquid of an amount equivalent to an amount of separated plasma.

Patentansprüche

1. Vorrichtung zum Abtrennen von Blutplasma von Blut, welche aufweist:
eine einzelne gemeinsame Nadel (18) zum Zuführen und zum Rückführen von Blut,
eine membranartige Plasma-Trennvorrichtung (1) mit einer Einlaßöffnung (4) zum Einbringen von Blut
in diese und einer Auslaßöffnung (2) zum Austragen von konzentriertem Blut aus dieser,
eine Blutfördereinrichtung, welche eine reversibel drehbare Blutförderpumpe (7) zum Einführen und
Austragen von Blut von der einzelnen gemeinsamen Nadel enthält, und
einen Blutvorratsbehälter (8), welcher mit der Plasma-Trenneinrichtung verbunden ist, zum zeitweisen
Speichern oder Sammeln von konzentriertem Blut, dadurch gekennzeichnet,
daß ein Blutumwälzkreislauf vorgesehen ist, welcher mit einem Ende an die Einlaßöffnung (4) der
Plasmatrenneinrichtung (1) und mit einem anderen Ende an die Auslaßöffnung (2) der
Plasmatrenneinrichtung (1) angeschlossen ist, wobei das durch die Plasmatrenneinrichtung (1)
konzentrierte Blut durch den Blutumwälzkreislauf fließt,
daß eine Umwälzeinrichtung (3) vorgesehen ist, um das Blut innerhalb des Blutumwälzkreislaufes von
der Ausgangsöffnung (2) zu der Eingangsöffnung (4) der Plasmatrenneinrichtung (1) umzuwälzen,
daß der Blutvorratsbehälter (8) an den Blutumwälzkreislauf an dessen Auslaßseite angeschlossen ist,
um einen Überschußbetrag von konzentriertem Blut, welcher in dem Blutumwälzkreislauf in Übermenge
vorhanden ist, zeitweise zu speichern bzw. zu sammeln,
daß die Blutfördereinrichtung zwischen den einzelnen gemeinsame Nadel (18) und dem
Blutumwälzkreislauf eingeschaltet ist und
daß die Plasmatrenneinrichtung (1) außerdem eine Einrichtung (19) zur Veränderung der
Querschnittsfläche der in ihr definierten Blut-Strömungsdurchgänge aufweist.
2. Vorrichtung nach Anspruch 1, dadurch gekennzeichnet, daß der Blutvorratsbehälter (8) einen aus
flexiblem Kunstharzmaterial bestehenden abgedichteten Beutel umfaßt.
3. Vorrichtung nach Anspruch 1, dadurch gekennzeichnet, daß sie mindestens zwei Pumpen (7, 3), die
eine (7) zum Antrieb der Blutfördereinrichtung und die andere (3) zum Antrieb des Umwälzkreislaufes,
aufweist.
4. Vorrichtung nach Anspruch 1, dadurch gekennzeichnet, daß mindestens zwei Flüssigkeit
enthaltende Behälter (10, 11) und eine mit der Blutfördereinrichtung (7) wirkungsmäßig verbundene
Flüssigkeitsfördereinrichtung vorgesehen sind, um wahlweise eine Flüssigkeit von dem Flüssigkeit
enthaltenden Behälter in einem vorgegebenen Verhältnis zu der Blutfördereinrichtung zu liefern.
5. Vorrichtung nach Anspruch 12, dadurch gekennzeichnet, daß die in einem (10) der Flüssigkeit
enthaltenden Behälter enthaltene Flüssigkeit ein Antigeringungsmittel ist und daß die in dem anderen (11)
der Flüssigkeit enthaltenden Behälter enthaltende Flüssigkeit eine Ersatzflüssigkeit in einem dem Betrag
des abgetrennten Plasmas äquivalenten Betrag ist.
6. Vorrichtung zum Abtrennen von Blutplasma von Blut, welche aufweist:
eine einzelne gemeinsame Nadel (18) zum Zuführen und Rückführen von Blut,
eine membranartige Plasmatrenneinrichtung (1) mit einer Einlaßöffnung (4) zum Einführen von Blut in
diese und einer Auslaßöffnung (2) zum Austragen von konzentriertem Blut aus dieser,
eine Blutfördereinrichtung, welche eine reversibel drehbare Blutförderpumpe (7) zum Zuführen und
Austragen von Blut von der einzelnen gemeinsamen Nadel umfaßt, und
eine Blutbehältereinrichtung (8), welche mit der Plasmatrenneinrichtung verbunden ist, zum
zeitweiligen Speichern bzw. Sammeln von konzentriertem Blut, dadurch gekennzeichnet,
daß ein Blutumwälzkreislauf vorgesehen ist, welcher mit einem Ende an die Einlaßöffnung (4) der
Plasmatrenneinrichtung (1) und mit einem anderen Ende an die Auslaßöffnung (2) der
Plasmatrenneinrichtung (1) angeschlossen ist, wobei das durch die Plasmatrenneinrichtung (1) konzentrierte
Blut durch den Blutumwälzkreislauf fließt,
daß eine Umwälzeinrichtung (3) zum Umwälzen des Blutes innerhalb des Blutumwälzkreislaufes von
der Auslaßöffnung (2) zu der Einlaßöffnung (4) der Plasmatrenneinrichtung (1) vorgesehen ist,
daß die Blutvorratsbehältereinrichtung (8) in dem Blutumwälzkreislauf vorgesehen ist, um zeitweilig
durch die einzelne gemeinsame Nadel (18) eingeführtes und durch die Plasmatrenneinrichtung
konzentriertes Blut zu speichern bzw. zu sammeln,
daß die Blutfördereinrichtung zwischen die einzelne gemeinsame Nadel (18) und die
Blutvorratsbehältereinrichtung (8) eingeschaltet ist und
daß die Plasmatrenneinrichtung (1) außerdem eine Einrichtung zur Veränderung der
Querschnittsfläche der in ihr definieren Blutströmungsdurchgänge aufweist.

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7. Vorrichtung nach Anspruch 6, dadurch gekennzeichnet, daß die Blutvorratsbehältereinrichtung (8) einen aus flexiblem Kunstharz bestehenden, verseigelten Beutel aufweist.

8. Vorrichtung nach Anspruch 6, dadurch gekennzeichnet, daß mindestens zwei Pumpen (7, 3), die eine zum Antrieb der Blutfördereinrichtung und die andere zum Antrieb der Umwälzeinrichtung, vorgesehen sind.

9. Vorrichtung nach Anspruch 6, dadurch gekennzeichnet, daß sie mindestens zwei Flüssigkeit enthaltende Behälter (10, 11) sowie eine mit der Blutfördereinrichtung wirkungsmäßig verbundene Flüssigkeitsfördereinrichtung zur wahlweisen Lieferung einer Flüssigkeit von den Flüssigkeit enthaltenden Behältern in einem vorgegebenen Verhältnis an die Blutfördereinrichtung aufweist.

10. Vorrichtung nach Anspruch 9, dadurch gekennzeichnet, daß die in einem (10) der Flüssigkeit enthaltenden Behälter enthaltene Flüssigkeit ein Antigerinnungsmittel ist und daß die in dem anderen (11) der Flüssigkeit enthaltenden Behälter enthaltene Flüssigkeit eine Ersatzflüssigkeit in einem dem Betrag des abgetrennten Plasmas äquivalenten Betrag ist.

15 Revendications

1. Appareil pour séparer le plasma du sang comprenant:

une aiguille commune (18) unique destinée à l'introduction du sang et au retour du sang, un moyen de séparation de plasma (1) du type membrane comportant un orifice d'entrée (4) pour y introduire le sang et un orifice de sortie (2) pour en évacuer le sang concentré,

un moyen de transport de sang qui comporte une pompe de transport (7) pour le sang susceptible de tourner de façon réversible, destinée à l'introduction du sang et à l'évacuation du sang par ladite unique aiguille commune et un moyen (8) formant réservoir pour le sang, relié audit moyen de séparation de plasma pour accumuler ou recueillir temporairement le sang concentré, caractérise en ce que:

un circuit pour la circulation du sang est aménagé, dont l'une des extrémités est reliée audit orifice d'entrée (4) dudit moyen de séparation de plasma (1) et dont l'autre extrémité est reliée audit orifice de sortie (2) dudit moyen (1) de séparation de plasma, le sang concentré par ledit moyen (1) de séparation de plasma s'écoulant dans ledit circuit destiné à la circulation du sang;

un moyen de circulation (3) est installé en vue de faire circuler le sang à l'intérieur dudit circuit destiné à la circulation du sang, dudit orifice de sortie (2) audit orifice d'entrée (4) dudit moyen (1) de séparation de plasma;

ledit moyen (8) formant réservoir de sang est relié audit circuit pour la circulation du sang du côté de la sortie de celui-ci pour accumuler ou recueillir une quantité excédentaire de sang concentré, qui dépasse la capacité d'écoulement dudit circuit destiné à la circulation du sang;

ledit moyen de transport de sang est raccordé entre ladite aiguille commune (8) unique et ledit circuit destiné à la circulation du sang;

et le moyen (1) de séparation de plasma comporte en outre un moyen (19) destiné à faire varier la surface de la section transversale des passages pour le sang, définis à l'intérieur.

2. Appareil selon la revendication 7, dans lequel ledit moyen (8) formant réservoir le sang comporte une poche étanche fabriquée en résine de synthèse souple.

3. Appareil selon la revendication 7, comprenant en outre au moins deux pompes (7, 3), l'une (7) destinée à entraîner ledit moyen de transport de sang et l'autre (3) destinée à entraîner ledit moyen de circulation.

4. Appareil selon la revendication 7, comprenant en outre aux moins deux récipients (10, 11) contenant du liquide, et un moyen d'alimentation en liquide associé fonctionnellement audit moyen de transport de sang (7) pour fournir de façon sélective audit moyen de transport de sang un liquide provenant desdits récipients contenant du liquide selon un rapport prédéterminé.

5. Appareil selon la revendication 12, dans lequel le liquide contenu dans l'un (10) desdits récipients renfermant du liquide est un anticoagulant, et le liquide contenu dans l'autre (11) desdits récipients renfermant du liquide est un liquide de remplacement en quantité équivalente à la quantité de plasma qui a été séparé.

6. Appareil pour la séparation du plasma comprenant:

une aiguille commune (18) unique destinée à l'introduction du sang et au retour du sang, un moyen (1) de séparation de plasma, du type membrane, comportant un orifice d'entrée (4) pour y introduire le sang et un orifice de sortie (2) pour en évacuer le sang concentré,

un moyen de transport de sang qui comporte une pompe (7) de transport de sang, susceptible de tourner de façon réversible pour introduire et évacuer le sang par ladite unique aiguille commune, et un moyen formant réservoir (8) relié audit moyen de séparation de plasma pour accumuler ou recevoir temporairement le sang concentré, caractérise en ce que

un circuit pour la circulation du sang est aménagé, dont l'une des extrémités est reliée audit orifice d'entrée (4) dudit moyen (1) de séparation de plasma et dont l'autre extrémité est reliée audit orifice de sortie (2) dudit moyen (1) de séparation de plasma, le sang concentré par ledit moyen (1) de séparation de plasma s'écoulant dans ledit circuit destiné à la circulation du sang;

un moyen de circulation (3) est installé en vue de faire circuler le sang à l'intérieur dudit circuit destiné à la circulation du sang, dudit orifice de sortie (2) audit orifice d'entrée (4) dudit moyen de séparation (1);

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ledit moyen (8) formant réservoir de sang est installé dans ledit circuit destiné à la circulation du sang pour accumuler ou recueillir temporairement le sang prélevé par ladite unique aiguille commune (18) et concentré par ledit moyen de séparation de plasma;

et ledit moyen de transport de sang est raccordé entre ladite unique aiguille commune (18) et ledit
5 moyen (8) formant réservoir de sang
et ledit moyen (1) de séparation de plasma comporte en outre un moyen destiné à faire varier la surface de la section transversale des passages pour le sang, définis à l'intérieur.

7. Appareil selon la revendication 6, dans lequel ledit moyen (8) formant réservoir de sang comporte une poche étanche fabriquée en résine de synthèse souple.

10 8. Appareil selon la revendication 6, comprenant en outre au moins deux pompes (7, 3), l'une destinée à entraîner ledit moyen de transport de sang et l'autre destinée à entraîner ledit moyen de circulation.

9. Appareil selon la revendication 6, comprenant en outre au moins deux récipients (10, 11) contenant du liquide et un moyen d'alimentation en liquide fonctionnellement associé audit moyen de transport de sang pour fournir de façon sélective audit moyen de transport de sang un liquide provenant desdits
15 récipients contenant du liquide, selon un rapport prédéterminé.

10. Appareil selon la revendication 9, dans lequel le liquide contenu dans l'un (10) desdits récipients contenant du liquide est un anticoagulant, et le liquide contenu dans l'autre (11) desdits récipients contenant du liquide est un liquide de remplacement en quantité équivalente à la quantité de plasma qui a été
20 séparé.

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FIG. 1 (A)

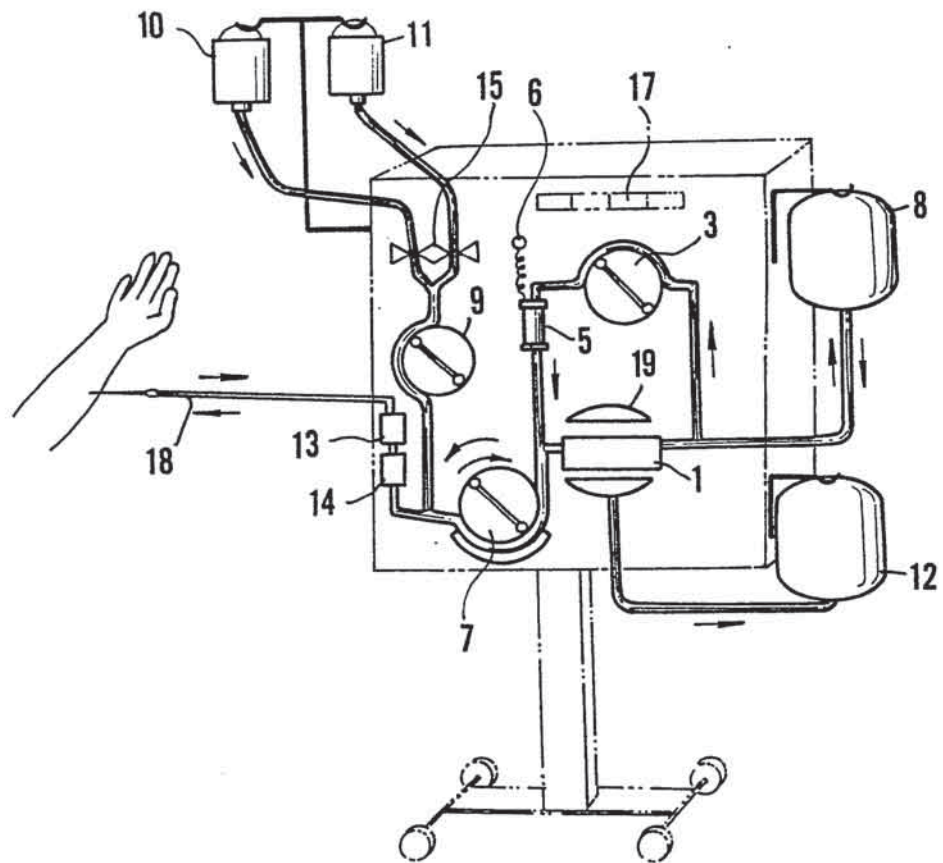


FIG. 1 (B)

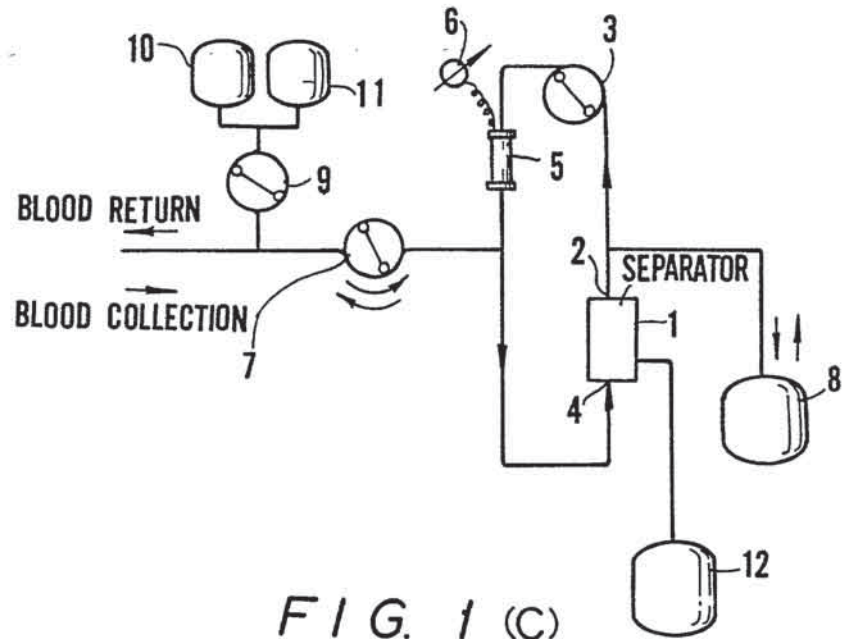


FIG. 1 (C)

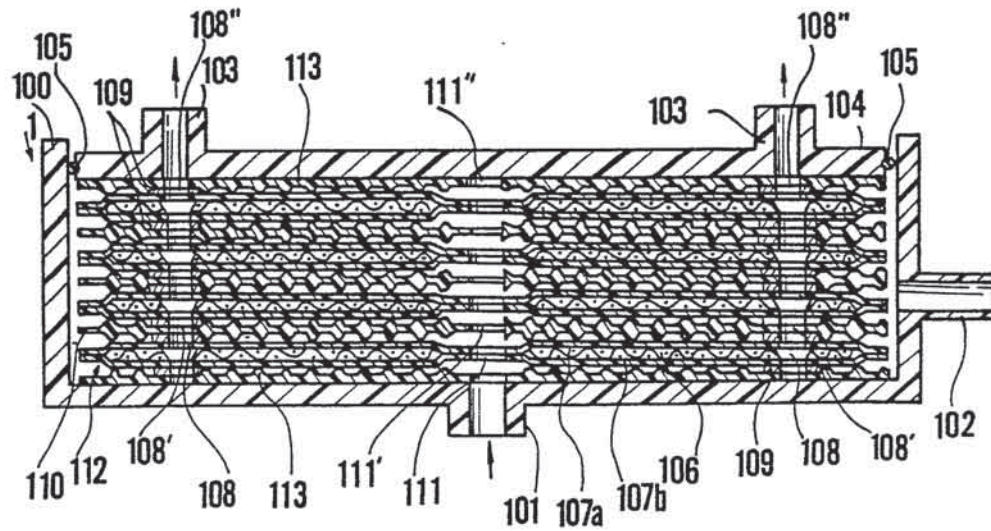


FIG. 1(D)

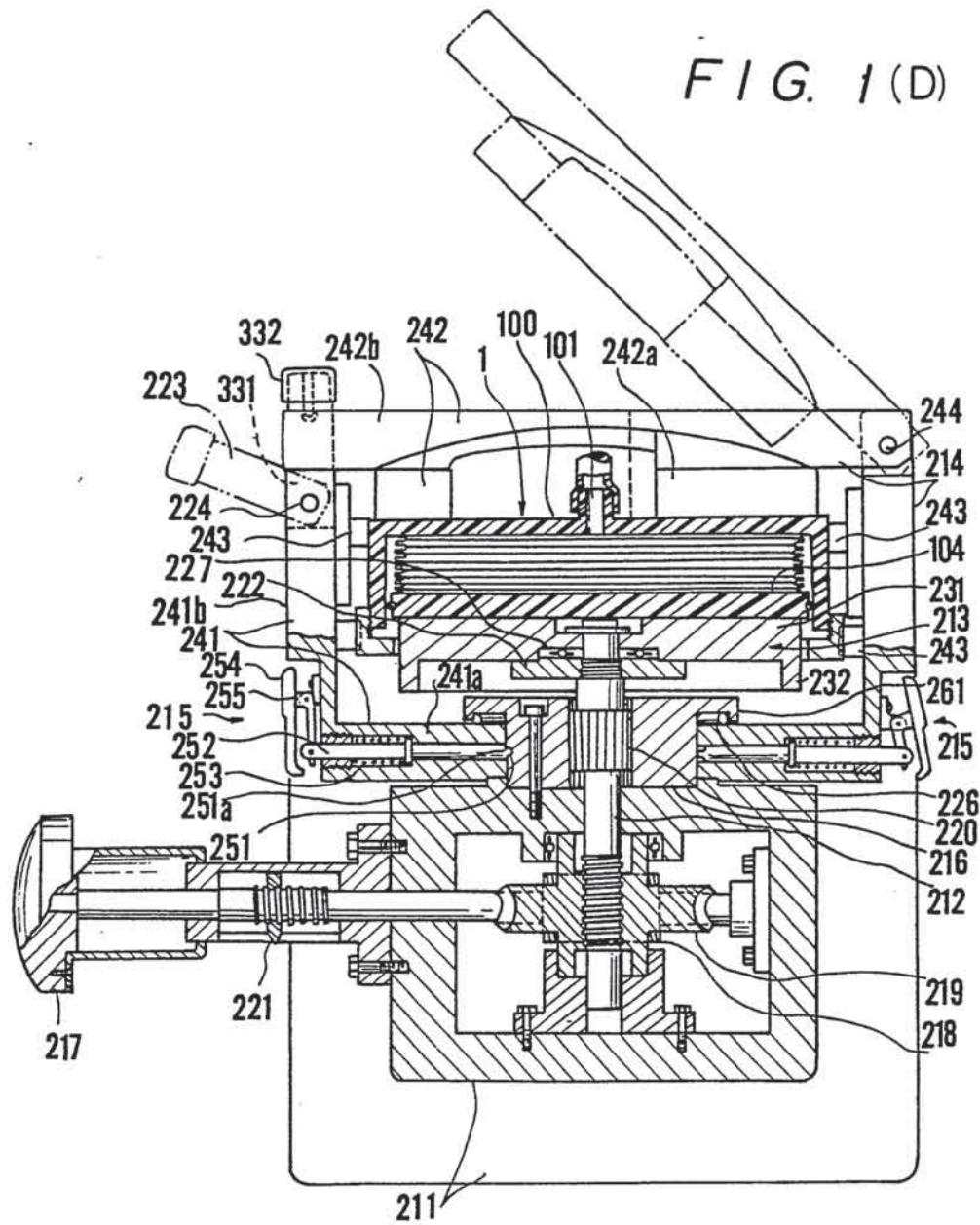


FIG. 2 (A)

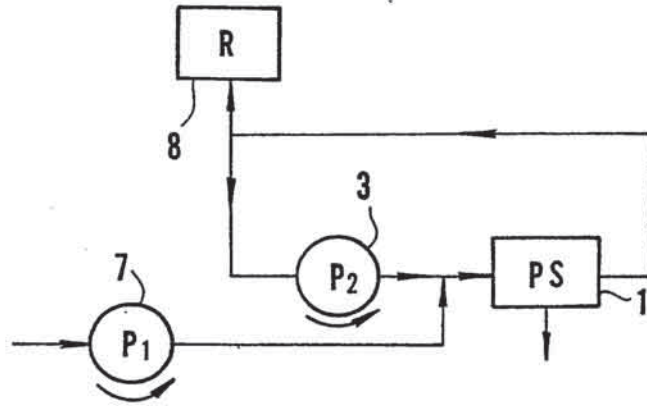
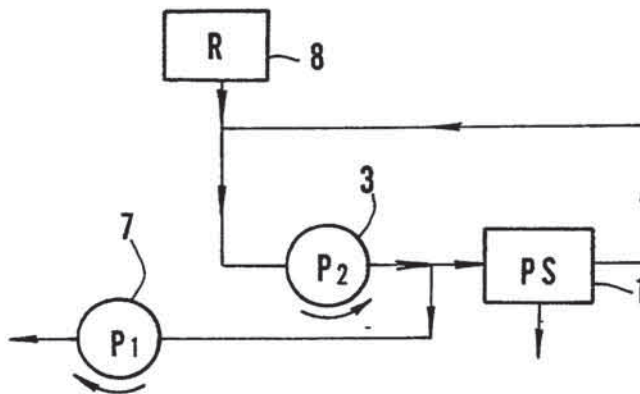


FIG. 2 (B)



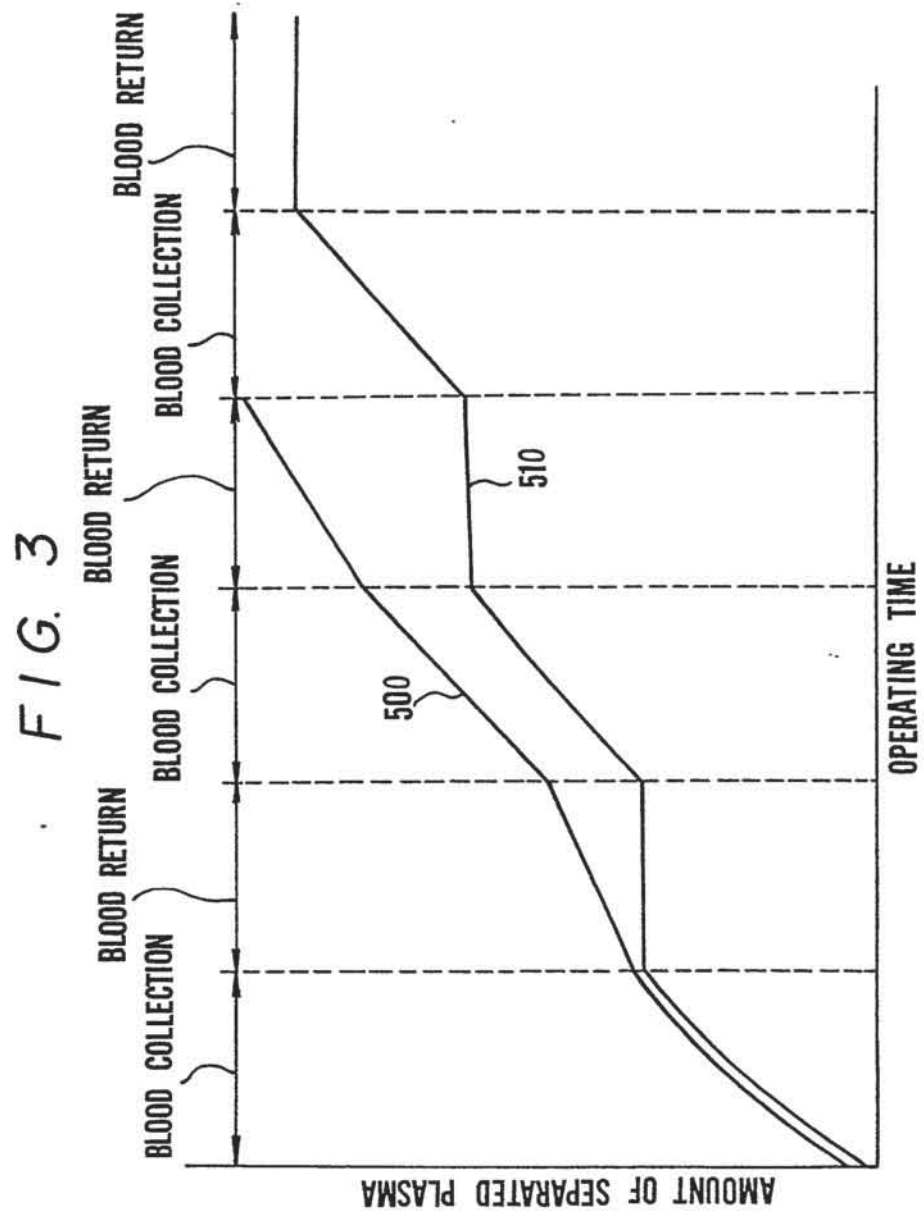


FIG. 4

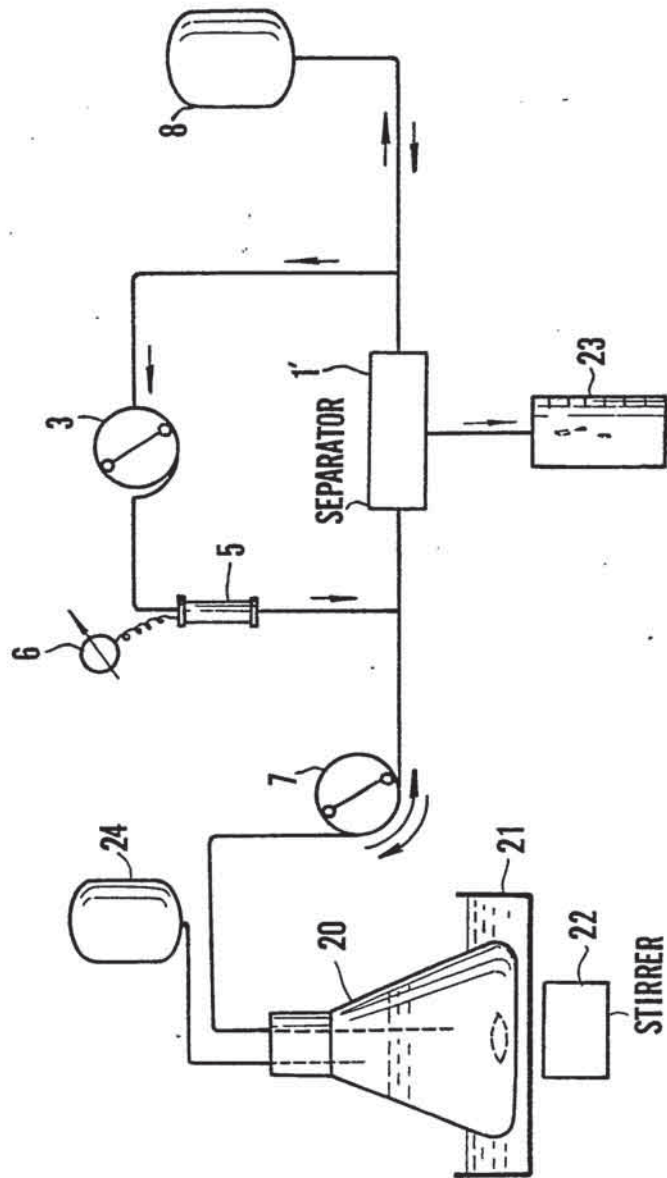


FIG. 5
PRIOR ART

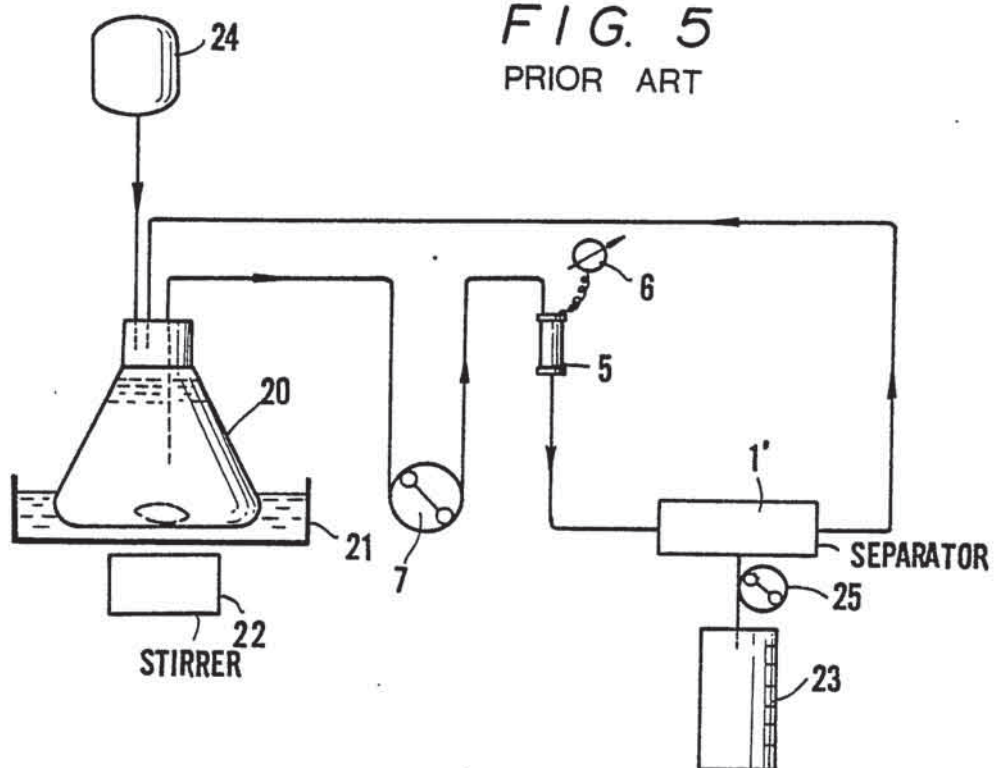


FIG. 8(A)

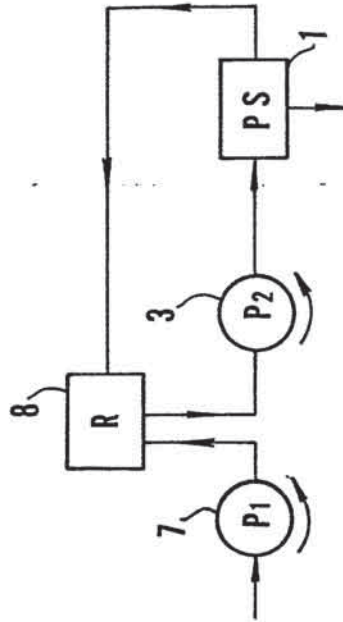


FIG. 8(B)

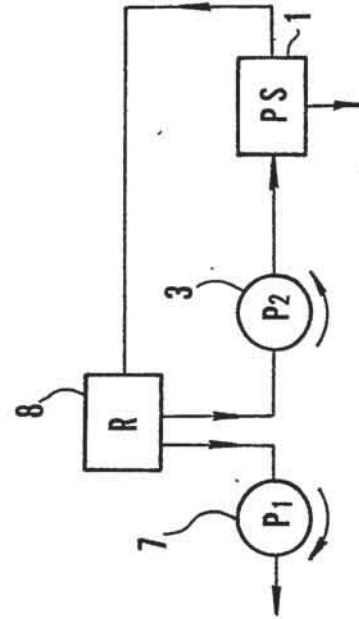


FIG. 6(A)

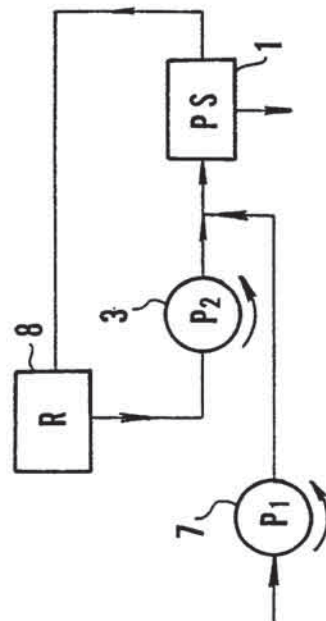


FIG. 6(B)

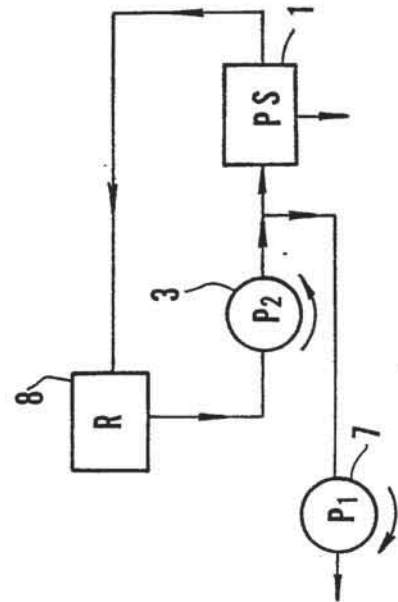
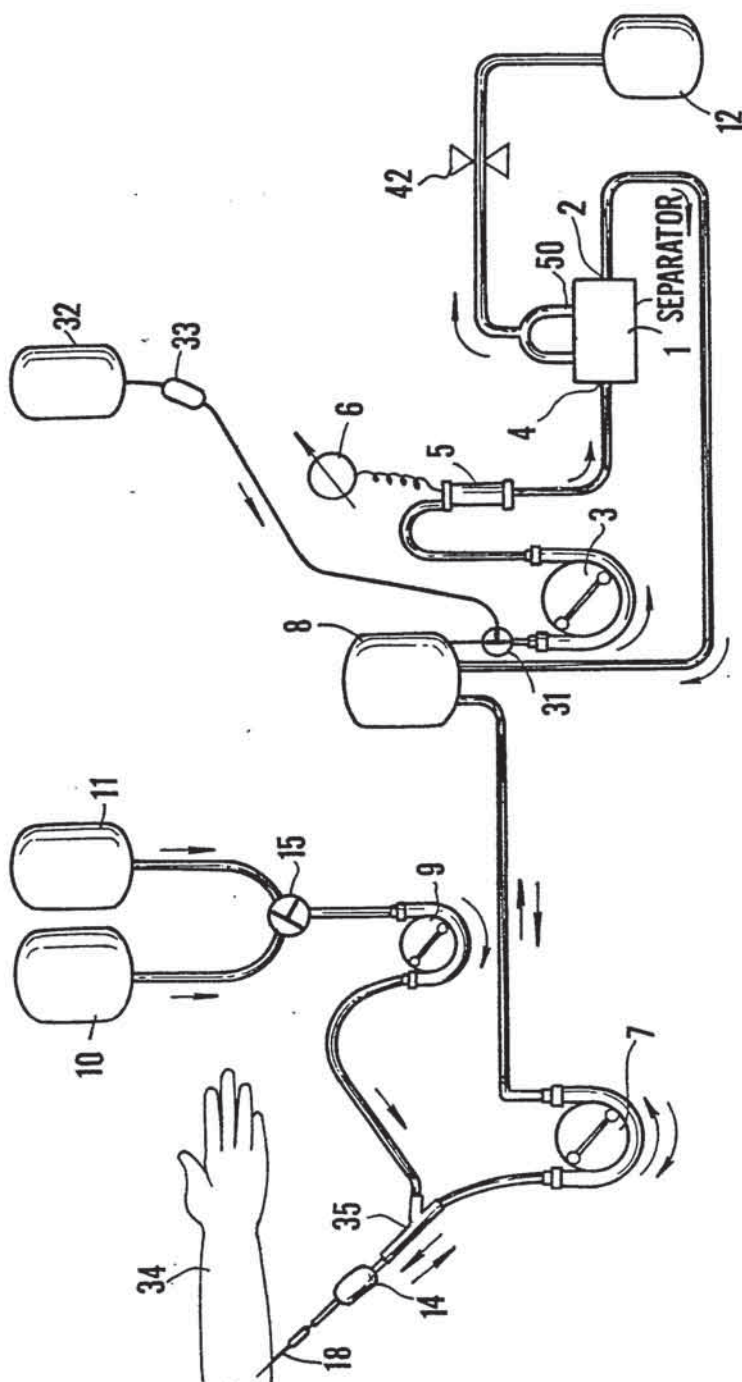


FIG. 7



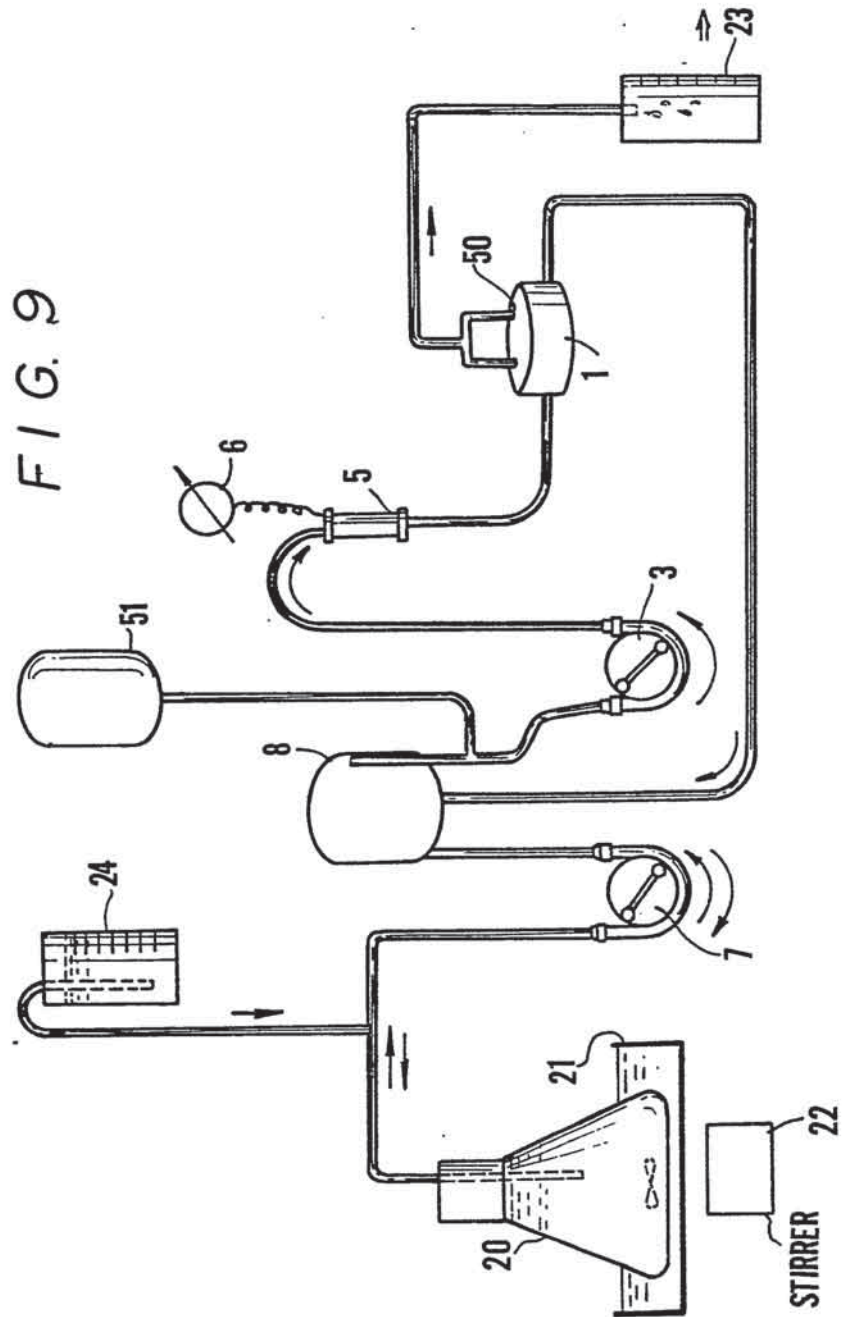


FIG. 10
PRIOR ART

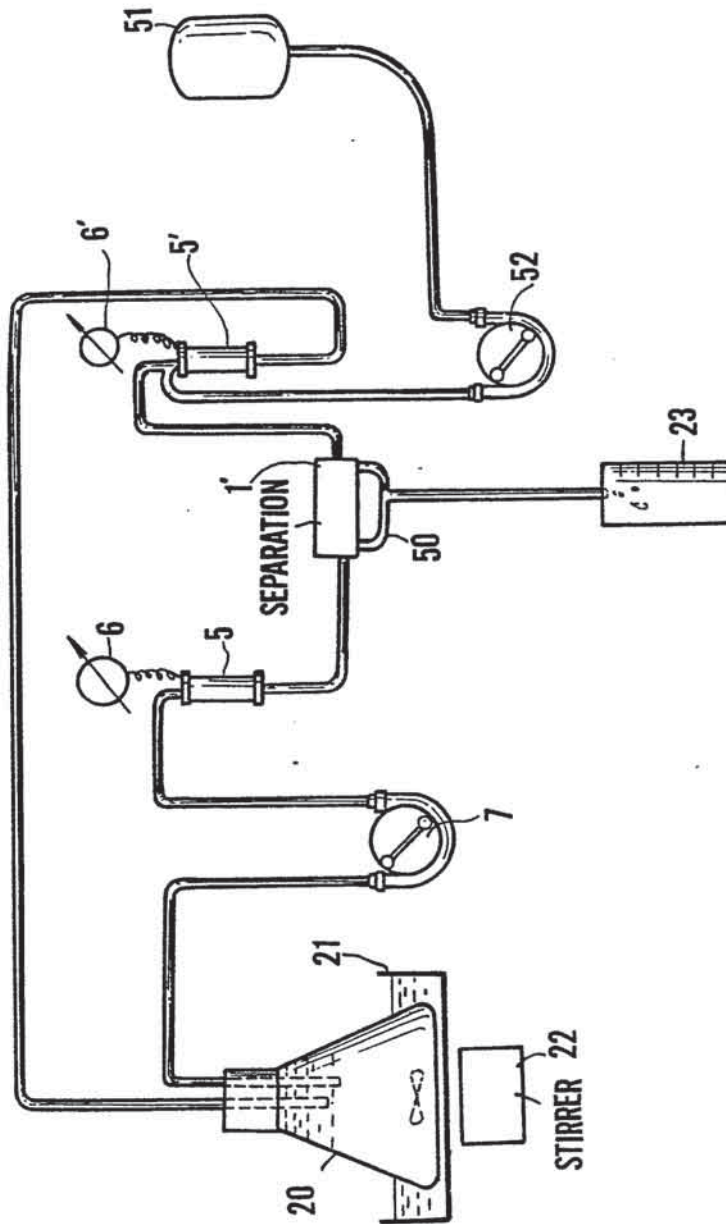


FIG. 12 (A)

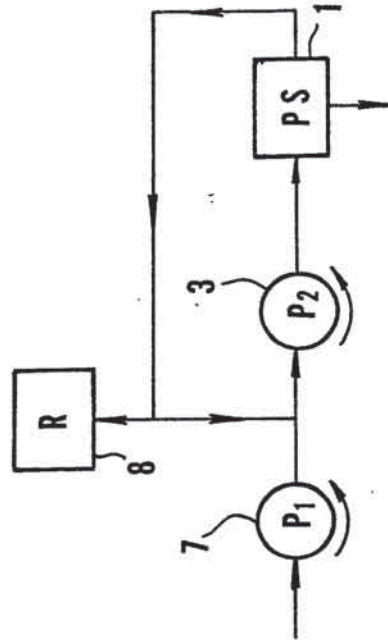


FIG. 12 (B)

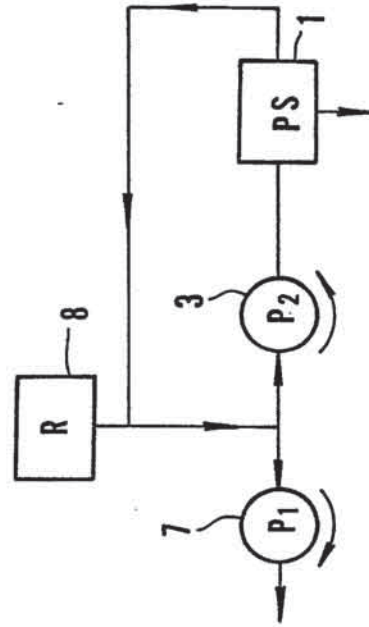


FIG. 11 (A)

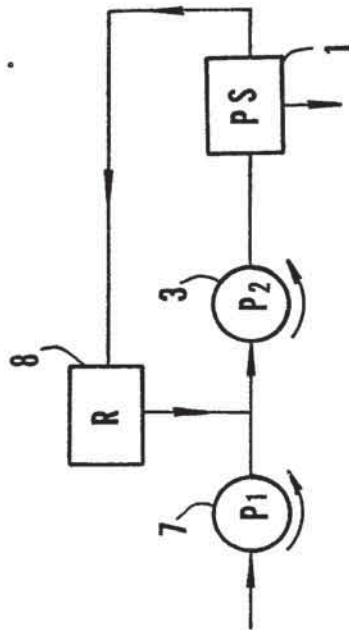
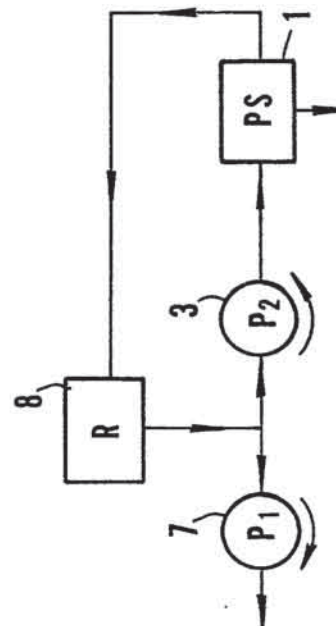


FIG. 11 (B)



(19)



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D-6230 Frankfurt am Main 80(DE)**(54) **Verfahren und Vorrichtung zur Gewinnung von Blutplasma.**

(57) Ein System zur Gewinnung von Blutplasma bei einer Blutentnahme vom lebenden Körper mit Blutentnahmekanüle (1) nach Stauung der entnahmefähigen Blutgefäße unter zusätzlicher Ausnutzung von äußerem Druck und Schwerkraft mit Hilfe einer Plasmafiltereinheit (4) als Trennvorrichtung bietet ein Optimum an Sicherheit für den Spender und an Funktionstüchtigkeit, wenn man Vorfüllungs-Lösung - (10) mit Hilfe eines separaten Anschlusses (2) zugebt, das gespendete Blutvolumen mißt, die Stabilisatorlösung (7) mit Hilfe einer Pumpe (8) entsprechend dem gemessenen gespendeten Blutvolumen zudosiert, das Blut durch eine zwischen Blutentnahmestelle (1) und Plasmafiltereinheit (4), jedoch nach dem Anschluß (11) für die Stabilisatorlösung (7) liegende Tropfkammer (6) mit eingebautem Transfusionsfilter führt und die Sammelstelle (5) für Plasma während des ganzen Verfahrens tiefer als Sammelstelle (3) für Blut anordnet, oder Blut in einen mit Stabilisatorlösung gefüllten Beutel (13) spendet, den vom Beutelsystem (12) abgetrennten Beutel (13) an oberes Ende eines Transfusionssystems (20) anschließt und Blut über Plasmafiltereinheit (4) und

Tropfkammer (6) mit Transfusionsfilter retransfundiert und während der Retransfusion Plasma sammelt.

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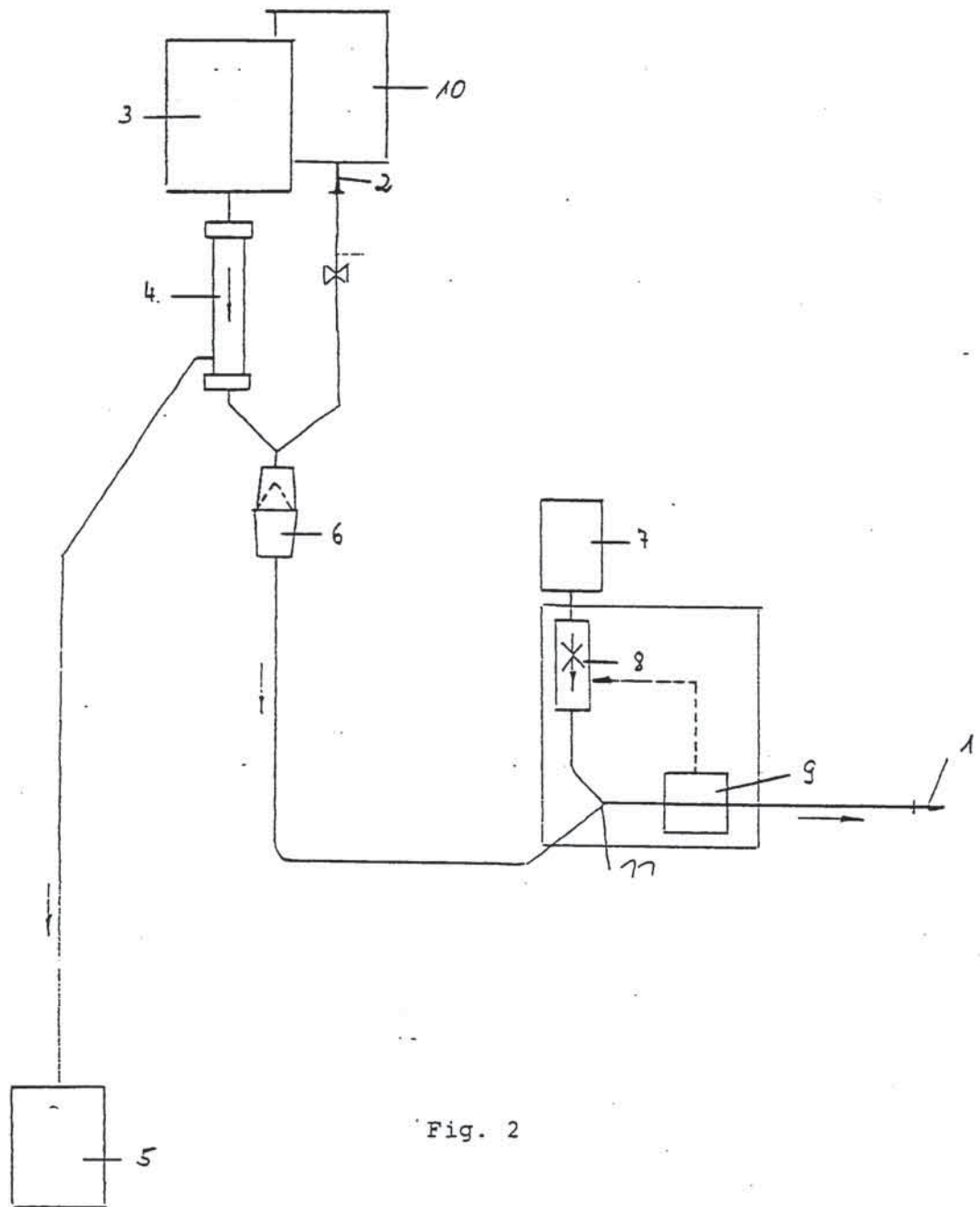


Fig. 2

Verfahren und Vorrichtung zur Gewinnung von Blutplasma

Die Erfindung betrifft ein Verfahren zur Gewinnung von Blutplasma nach dem Oberbegriff des Anspruchs 1 bzw. 4 sowie eine Vorrichtung zur Durchführung des Verfahrens.

Bei der routinemäßig mit Beutel durchgeführten Plasmaspende spendet der Spender eine bestimmte Menge Blut in einen Beutel, in dem eine auf die Blutmenge abgestimmte Menge Stabilisatorlösung bzw. Antikoagulanzlösung für Blut vorliegt. Nach der Spende wird der Beutel abgetrennt und die Bildung von Gerinnsel in der Venenkanüle im Arm des Spenders durch langsames Infundieren von isotoner NaCl-Lösung über ein Infusionsbesteck verhindert. Der Beutel wird dann zentrifugiert, um das Plasma von den Blutzellen abzutrennen, was meist in einem separaten Raum erfolgt. Anschließend werden die Blutzellen mit etwas isotoner NaCl-Lösung verdünnt und dem Spender über das Infusionsgerät retransfundiert. Dies wird in der Regel zweimal hintereinander durchgeführt, und man erhält so etwa 500 -600 ml Plasma. - ("Richtlinien für Plasmapheresen", Deutsches Ärzteblatt, Heft 5 (1977) 305-314; "Handbuch der Blutkomponenten-Therapie" American Association of Blood Banks (1969) 24-33)

Die Zentrifugen für das Zentrifugieren des Plasmas sind sehr groß und schwer und brauchen zur Energieversorgung einen Netzstromanschluß. Somit kann eine Plasmaspende nur in einem eingerichteten Spendezentrum durchgeführt werden.

Da zum Zwecke des Zentrifugierens das gespendete Blut vom Spender entfernt werden muß, kann es trotz aller Vorsichtsmaßnahmen zu Verwechslungen kommen, und dem Spender können falsche Blutzellen retransfundiert werden ("Manuel of Blood Component Preparation", American Association of Blood Banks (1969) 39-44).

Es war nun wünschenswert, auch bei Blutspendeterminen, die nicht in den Spendezentren stattfinden, Plasmaspenden durchführen zu können. Der Bedarf an Plasma ist größer als durch Blutspenden abgedeckt werden kann. Außerdem belastet eine Plasmaspende das blutbildende System weniger als eine Blutspende, so daß eine wöchentliche Spende von 500 ml Plasma möglich ist, während eine Blutspende von 500 ml Blut nur alle 12 Wochen erfolgen kann. Man versuchte ferner ein Verfahren zu finden, das das Wegtransportieren des Spenderblutes nicht mehr erforderlich macht.

Es wurden deshalb Verfahren und Vorrichtungen zur Gewinnung von Blutplasma bei einer Blutentnahme am lebenden Körper unter Verwendung einer Plasmafiltereinheit entwickelt, bei denen das Spenderblut mit Hilfe von Schlauchpumpen zur

Plasmafiltereinheit und durch diese hindurchgepumpt werden. Derartige Systeme sind jedoch sehr aufwendig und erfordern an mehreren Stellen Überwachungseinrichtungen für Drücke, Strömungen und Luftblasen.

Aus der DE-OS 33 02 383 bzw. Lysaght, M. et al.: "Plasmapheresis without pumps..."; Int. Workshop Plasma Separation and Plasma Fractionation 17.-19. März 1983, Rottach-Egern, Seiten 1-14, sind ein Verfahren zur Gewinnung von Blutplasma bei einer Blutentnahme nach dem Oberbegriff des Anspruchs 1 bzw. 4 und eine Vorrichtung nach dem Oberbegriff des Anspruchs 7 bzw. 8 bekannt.

Dieses Verfahren arbeitet ohne Blutpumpen, Tropfkammern oder andere Apparaturen, sondern unter Ausnutzung der Schwerkraft und ist somit wesentlich einfacher und weniger aufwendig als bisherige mit Pumpen und anderen Apparaturen arbeitende Verfahren. Es wird dort lediglich unter Verwendung einer Blutentnahmekanüle nach einer Stauung der entnahmefähigen Blutgefäße Spenderblut mittels eines Schlauches zu einer tiefer gelegenen Plasmafiltereinheit geleitet, worin Plasma und Blut getrennt und einer Sammelstelle für Plasma und einer davon getrennten Sammelstelle für Blut zugeleitet werden. Zwischen Blutentnahmestelle und Plasmafiltereinheit befindet sich ein Anschluß für eine Antikoagulanzlösung.

Bei diesem System braucht der Blutbeutel nicht zum Zwecke des Zentrifugierens wegtransportiert zu werden, sondern bleibt bei der Spende, wodurch eine geringere Verwechslungsgefahr besteht.

Neben dem Vorteil der einfachen Handhabung und der geringeren Verwechslungsgefahr weisen dieses Verfahren und die Vorrichtung jedoch einige Nachteile auf.

Das System sieht keine Messung des Spendevolumens vor, wobei die Gefahr besteht, daß ein zu großes Blutvolumen sich außerhalb des Körpers des Spenders befindet, wobei es zu einem Kreislaufkollaps kommen kann. Die Antikoagulanzlösung wird dem System in einer konstanten Menge zugeführt, jedoch unabhängig vom Blutfluß, nachdem dieser nicht gemessen wird. Der zu erwartende Blutfluß ist vor der Spende nicht bekannt und kann sich außerdem während der Spende ändern. Aus diesem Grunde kann Überdosierung oder Unterdosierung der Antikoagulanzlösung erfolgen. Überdosierung bedeutet bei der Retransfusion für den Spender eine zusätzliche, möglicherweise mit Komplikationen verbundene Belastung. Sehr unangenehm kann es für den Spender werden, wenn der Blutfluß stoppt wegen einer Verstopfung nach

der Antikoagulan-Zufuhrstelle. In diesem Falle läuft die Antikoagulan-Zufuhr weiter, und zwar in die Vene des Spenders. Es wird also reine Antikoagulanlösung infundiert, wovon auf dem Aufdruck von Behältern mit Antikoagulanlösung ausdrücklich gewarnt wird. Unterdosierung fördert die Bildung von Mikroaggregat und birgt die Gefahr der Gerinnungsaktivierung in sich, was bei Einsatz von Membranfiltern zur Plasmaabtrennung insofern besonders kritisch ist, als hier eine große Fremdoberfläche für das Blut vorliegt und die Gefahr einer Gerinnungsaktivierung besonders gegeben ist.

Vor Beginn der Spende muß das System mit isotoner Lösung vorgefüllt werden. Ist das System nicht von Anfang an vorgefüllt, so kann der Transmembrandruck (TMP) sogar negativ sein, wenn bei langsamem Blutfluß das für die Strömung notwendige Druckgefälle zwischen Plasmafiltereinheit und Blutsammelbeutel kleiner wird als die hydrostatische Druckdifferenz. Es findet dann keine Plasmafiltration statt. Es muß daher die Leitung zum Plasmabeutel mit Flüssigkeit gefüllt sein, um einen zusätzlichen Unterdruck aufgrund der Höhendifferenz zwischen Plasmafiltereinheit und Plasmabeutel sicherzustellen, so daß auf jeden Fall ein positiver TMP vorliegt, d.h. daß der Druck auf der Blutseite der Membran größer ist als auf der Plasmaseite.

Die Luft muß aus den Schlauchleitungen weitgehend entfernt werden, um bei der Retransfusion die Gefahr einer Luftembolie zu vermeiden. Beim bekannten System wird deshalb vor der Spende mit isotoner NaCl-Lösung über die Entnahmekanüle gespült. Beim Vorfüllen des Systems über die Blutentnahmekanüle kann letztere jedoch beim Einstechen in den Stopfen einer Flasche mit NaCl-Lösung verändert werden und eine Venenpunktion dann erschwert werden.

Wie bereits vorstehend ausgeführt, arbeitet das System ohne Tropfkammer und ohne Infusionsfilter, was, wie nachstehend genauer erläutert wird, sehr gefährlich sein kann.

Schließlich befinden sich die Sammelstelle für Plasma und die Sammelstelle für Blut bei der Blutspende praktisch auf einer Ebene. Mit einer solchen Anordnung kann über die kommunizierenden Schlauchleitungen bei Stillstand des Blutflusses das Plasma über die Plasmafiltereinheit in die Sammelstelle für Blut fließen, falls der Plasmabeutel geringfügig über dem Blutbeutel hängt, was sehr leicht auftreten kann.

Der Erfindung liegt die Aufgabe zugrunde, ein Verfahren und eine Vorrichtung zur Gewinnung von Blutplasma bei einer Entnahme vom lebenden Körper bereitzustellen, die leicht zu handhaben und einfach sind und sich keiner aufwendigen Blutpum-

pen und sonstiger Apparaturen bedienen, sondern unter Ausnutzung der Schwerkraft arbeiten, dabei jedoch ein Optimum an Sicherheit für den Spender bieten und keine Funktionsmängel aufweisen.

5 Diese Aufgabe wird bei einem gattungsgemäßen Verfahren durch die kennzeichnenden Merkmale des Anspruchs 1 bzw. 4 und bei einer gattungsgemäßen Vorrichtung durch die kennzeichnenden Merkmale des Anspruchs 7 bzw. 8 gelöst.

10 Nach einer Ausführungsform der Erfindung wird die Stabilisator-bzw. Antikoagulanlösung mit Hilfe einer Dosierpumpe entsprechend dem gemessenen Blutvolumen genau dosiert, wodurch ein optimales Stabilisator/Blut-Verhältnis eingehalten wird und weder durch Unterdosierung die Gerinnungsaktivierung begünstigt wird, noch durch Überdosierung der Spender bei der Spende gefährdet oder bei der Retransfusion zusätzlich belastet wird.

20 Um zu vermeiden, daß ein zu großes Volumen an Blut sich außerhalb des Körpers befindet und es somit zu einem Kreislaufkollaps kommen kann, wird erfindungsgemäß das gespendete Blutvolumen laufend gemessen. Die Messung erfolgt vorzugsweise mit einem Ultraschalldetektor an der Außenseite des blutführenden Schlauches. Eine geeignete Meßmethode wird in der EP-OS 83 100 079 beschrieben. Eine weitere, jedoch nicht so bevorzugte Meßmethode besteht in der Verwendung einer elektronischen Waage.

30 Als Dosierpumpe für Antikoagulanlösung läßt sich jede Art von auf dem Markt befindlichen Dosierpumpen verwenden. Besonders brauchbar sind Peristaltikpumpen, wie sie für diesen Zweck in der EP-OS 83 100 079 beschrieben werden.

35 Als ganz besonders brauchbar erwies sich ein Blutentnahmegesät (BEG 404) der Fa.Doltron AG. Bei diesem Gerät wird der Blutfluß mit einem Ultraschalldetektor gemessen und die Antikoagulanlösung über eine Peristaltikpumpe dem Blutfluß entsprechend zudosiert. Aus dem Blutfluß wird das Blutvolumen berechnet und angezeigt, wenn ein vorbestimmtes Volumen erreicht ist.

40 Es ist ferner nicht unbedingt erforderlich, die Vorfüllungs-Lösung am Anfang des Systems mit Hilfe der Blutentnahmekanüle einzufüllen, sondern dies ist auch mit Hilfe eines separaten Anschlusses an irgendeiner Stelle des Systems möglich. Erfindungsgemäß ist deshalb ein separater Anschluß für die Vorfüllungs-Lösung vorgesehen. Dadurch wird die Entnahmekanüle geschont, und die Venenpunktion wird nicht durch eine bereits vorher schon einmal eingestochene Kanüle erschwert.

45 50 55 Der Anschluß für die Vorfüllungs-Lösung kann mit einer Kanüle oder einem Dorn versehen sein zum Einstechen in eine mit Vorfüllungs-Lösung gefüllte Flasche oder einen Beutel.

Während der Retransfusion können sich aus dem System Luftblasen lösen, die beim Einfüllen mit isotoner Lösung und während der Blutspende nicht vollständig entfernt wurden (Gefahr der Luftembolie). Zum anderen besteht immer die Möglichkeit, daß im System trotz ausreichender Zugabe von Antikoagulanzlösung Gerinnungsvorgänge ablaufen, die zur Bildung von Mikroaggregaten führen können. Diese müssen bei der Retransfusion der Erythrozyten herausgefiltert werden (Gefahr der Thrombose). Aus Sicherheitsgründen, um diese Gefahren auszuschließen, ist erfindungsgemäß eine Luftblasenfalle mit eingebautem Transfusionsfilter vorgesehen. Diese Falle befindet sich hinter dem Anschluß für die Antikoagulanzlösung und vor der Plasmafiltereinheit, bezogen auf den Blutfluß während der Blutspende. Eine solche Luftblasenfalle mit Transfusionsfilter liegt in Form einer Tropfkammer mit Filter für Blut und Blutbestandteile vor, beispielsweise wie sie gemäß DIN 58 360 Teil 1 beschrieben wird.

Schließlich wurde gefunden, daß es zur Vermeidung eines Überfließens von Plasma aus der Sammelstelle für Plasma zur Sammelstelle für Blut, bei Stillstand des Blutflusses, der z.B. bei Verlegen der Venenkanüle durch die Venenwand eintritt, erforderlich ist, sowohl während der Blutspende als auch während der Retransfusion die Sammelstelle für Plasma tiefer als den Blutbeutel zu hängen.

Nach einer weiteren, bevorzugten Ausführungsform der Erfindung erfolgt die Abtrennung des Plasmas nicht mehr während der Blutspende, sondern nur noch während der Retransfusion.

Dabei erfolgt die Spende in einen Blutbeutel, dem eine bestimmte, auf die zu spendende Blutmenge abgestimmte Stabilisatorlösung vorliegt, auf ähnliche Weise, wie in der vorstehend genannten Literatur zur Plasmapherese beschrieben wird. Danach wird der Beutel vom Beutelsystem abgetrennt und an das obere Ende eines Transfusionsgerätes angeschlossen, das mehrere Einstichdorne am oberen Ende, eine Plasmafiltereinheit, eine Sammelstelle für Plasma und eine Tropfkammer mit eingebautem Transfusionsfilter enthält und mit dem unteren Ende mit dem Beutelsystem und somit der Spenderkanüle verbunden ist.

Das gespendete Blut kann nun über die Plasmafiltereinheit dem Spender retransfundiert werden. Während das Blut durch die Plasmafiltereinheit fließt, wird das Plasma abgetrennt und in einem Plasmasammelbeutel aufgefangen.

Diese bevorzugte Ausführungsform ist noch sicherer und noch einfacher als die vorstehend beschriebene Ausführungsform der Erfindung.

5 Sicherer deshalb, weil beim Durchströmen des Transfusionsfilters in beiden Richtungen Stoffe, z.B. Mikroaggregate, die bei der Blutentnahme im Filter zurückgehalten wurden, beim umgekehrten Durchströmen doch mal in den Spender retransfundiert werden können und weil diese Gefahr beim einfachen Durchströmen, d.h. nur beim Retransfundieren, ausgeschlossen ist.

10 Einfacher deshalb, weil kein Dosiersystem für die Stabilisatorlösung erforderlich ist und jeglicher apparativer Aufwand, wie die Dosierpumpe als solche und Leitungs-oder Batteriestrom, entfallen. Das Stabilisator-bzw. Antikoagulanzzproblem ist mit dieser Ausführungsform total gelöst.

15 Zur Gewinnung einer gewissen Plasmamenge sind zwar mehr Zyklen erforderlich als bei der ersten Ausführungsform, weil nur während der Retransfusion Plasma gewonnen wird, d.h. die Plasmaextraktion pro Volumeneinheit Blut ist etwas geringer, dafür ist aber die Zykluszeit kürzer, weil der Hämatokritwert niedriger ist.

20 Die Retransfusionszeit kann außerdem noch dadurch verkürzt werden, daß man um den gefüllten Beutel eine Druckmanschette legt, wie sie bei Drucktransfusion üblich ist.

25 Das Verfahren kann mehrere Male wiederholt werden, bis eine ausreichende Plasmamenge gespendet worden ist.

30 Am Beutelsystem befindet sich mindestens ein Blutbeutel, vorzugsweise drei, jedoch sind bis zu fünf Beutel möglich. Dementsprechend sollte auch die Anzahl der Einstichdorne am oberen Ende des Transfusionsgerätes sein. D.h. es sollten mindestens so viele Einstichdorne vorhanden sein, wie anzuschließende Blutbeutel vorgesehen sein können plus ein Einstichdorn für den Anschluß der Vorfüllungs-Lösung.

35 Als Vorfüllungs-Lösung wird vorzugsweise eine isotonische NaCl-Lösung verwendet.

40 Stabilisatorlösungen werden in der Literatur beschrieben. Zu den üblichen Lösungen gehören beispielsweise Na-Citrat- und CPD-(Citrat-Phosphat-Dextrose)Lösungen.

45 Als Plasmafiltereinheit lassen sich Module sowohl mit Flachmembranen als auch mit Hohlfasermembranen verwenden. Die Porengröße der Membranen sollte zweckmäßigerweise 0,2 bis 0,8 µm, vorzugsweise maximal 0,65 µm betragen. Bei einer zu kleinen Porengröße, z.B. unter 0,2 µm, könnten Proteine zurückgehalten werden. Der Innendurchmesser von Hohlfasermembranen kann

beliebig sein, jedoch werden durch das extrakorporale Blutvolumen Grenzen gesetzt. Deshalb sollte der Innendurchmesser nicht kleiner als 100 µm und nicht größer als 500 µm sein.

Eine brauchbare Plasmafiltereinheit mit Hohlfasermembran ist die Plasmapur®-Patrone, wie sie im Firmenprospekt "Pure plasma..... Plasmapur®" der Firma Organon Technika beschrieben wird. Ebenfalls brauchbar ist das Travenol CPS-10 Plasmafilter mit einer aktiven Hohlfaserlänge von 21 cm, wie es in der DE-OS 33 02 383 beschrieben wird.

Eine geeignete Plasmafiltereinheit mit Flachmembran wird beispielsweise in der DE-PS 29 25 143 beschrieben.

Als Sammelstelle für Blut und für Plasma lassen sich Blutflaschen oder Blutbeutel aus Kunststoff verwenden, wie sie allgemein zur Aufbewahrung von Blut üblich sind. Die Verbindungsschläuche zwischen den einzelnen Elementen der erfindungsgemäßen Vorrichtung können ebenfalls übliche Kunststoff- oder Gummischläuche sein, wie sie bei Transfusionsgeräten üblich sind und z.B. den Forderungen gemäß DIN 58 360 oder DIN 58 367 entsprechen. Derartige Schläuche haben einen Innendurchmesser von mindestens 3 mm.

Nachstehende Zeichnungen dienen der weiteren Erläuterung der Erfindung.

Es zeigen:

Fig. 1 eine erfindungsgemäße Vorrichtung in erfindungsgemäßer Anordnung zur Blutspende;

Fig. 2 eine erfindungsgemäße Vorrichtung in erfindungsgemäßer Anordnung zur Retransfusion;

Fig. 3 eine Vorrichtung ohne Anschluß an eine Vorfüllungs-Lösung in Anordnung zur Blutspende, wobei die Sammelstelle für Blut tiefer hängt als die Sammelstelle für Plasma;

Fig. 4 eine Vorrichtung ohne Anschluß an eine Vorfüllungs-Lösung in Anordnung zur Retransfusion, wobei die Sammelstelle für Blut höher hängt als die Sammelstelle für Plasma;

Fig. 5 eine bevorzugte Vorrichtung gemäß der Erfindung;

Fig. 6 eine stark vereinfachte Vorrichtung zur Effektivitätsmessung des bevorzugten Systems.

In Fig. 1 wird Blutentnahmekanüle (1) gezeigt, von der aus Blut durch ein Schlauchsystem, das mit einer Meßvorrichtung (9) für gespendetes Blutvolumen versehen ist, durch Tropfkammer mit eingebautem Transfusionsfilter (6) zur Plasmafiltereinheit (4) fließt. Zwischen Tropfkammer (6) und Blutentnahmekanüle (1) befindet sich der Anschluß (11) an Stabilisatorlösung (7), die mit Hilfe der Dosierpumpe (8) dem System in Abhängigkeit vom gespendeten Blutvolumen zudosiert wird. Beim Durchströmen durch die Plasmafiltereinheit (4) wird Plasma vom Blut getrennt und fließt zur Sammel-

stelle für Plasma (5), während Blut zur Sammelstelle für Blut (3) fließt. Der Anschluß (2) für die Vorfüllungs-Lösung (10) befindet sich bei dieser Ausführungsform zwischen Tropfkammer (6) und Plasmafiltereinheit (4), kann sich jedoch an jeder anderen beliebigen Stelle des Systems befinden, vorzugsweise zwischen Blutentnahmekanüle (1) und Plasmafiltereinheit (4). Ebenso kann sich die Meßvorrichtung (9) an irgendeiner beliebigen Stelle zwischen (1) und (4) befinden. Bei der Blutspende sind Blutentnahmekanüle (1) und Anschluß (11) mit Stabilisatorlösung (7) und Dosierpumpe (8) oberhalb der übrigen Elemente des Systems angeordnet, damit Blut mit Hilfe der Schwerkraft fließen kann. Die Sammelstelle für Plasma (5) befindet sich unterhalb der Sammelstelle für Blut (3).

In Fig. 2 haben alle Elemente die gleiche Bedeutung wie in Fig. 1. Die Fig. 2 unterscheidet sich von Fig. 1 lediglich dadurch, daß zum Zwecke der Retransfusion diesmal Sammelstelle für Blut (3), Plasmafiltereinheit (4) und Tropfkammer (6) höher als die Blutentnahmekanüle angeordnet sind, damit das nur zum Teil vom Plasma befreite Blut mit Hilfe der Schwerkraft zum Spender zurückfließen kann. Bei diesem Zurückfließen passiert das partiell deplasmatisierte Blut zum zweiten Mal die Plasmafiltereinheit (4) und eine weitere Plasmamenge wird vom Blut abgetrennt. Während der Retransfusion fördert die Dosierpumpe (8) keine Stabilisatorlösung (7).

In Fig. 3 haben ebenfalls alle Elemente die gleiche Bedeutung wie in Fig. 1. Fig. 3 unterscheidet sich von Fig. 1 dadurch, daß kein Anschluß (2) für Vorfüllungs-Lösung (10) vorgesehen ist und die Sammelstelle für Blut (3) tiefer angeordnet ist als die Sammelstelle für Plasma (5).

In Fig. 4 haben ebenfalls alle Elemente die gleiche Bedeutung wie in Fig. 1. Fig. 4 unterscheidet sich von Fig. 2 dadurch, daß kein Anschluß (2) für Vorfüllungs-Lösung (10) vorgesehen ist.

In Fig. 5 wird eine bevorzugte Vorrichtung gezeigt, bei der die Plasmagewinnung nur während der Retransfusion erfolgt.

Es wird dort Blutentnahmekanüle (1) gezeigt, von der das Spenderblut in das Beutelsystem (12) und in die Beutel (13, 13a, 13b) fließt. Es wird ferner das Transfusionsgerät (20) gezeigt, das die Plasmafiltereinheit (4), Sammelstelle für Plasma (5), Tropfkammer mit eingebautem Transfusionsfilter (6), Einstichdorne (14, 14a, 14b) zum Anschluß an die Blutbeutel (13, 13a, 13b), Einstichdorn (14c) zum Anschluß an die Vorfüllungs-Lösung (10) und Rollklemmen (15, 15a, 15b, 16, 17) enthält. Blutbeutelssystem (2) und Transfusionsgerät (20) weisen jeweils an einem Ende ein Verbindungssystem (18) auf, mit Hilfe dessen sie miteinander verbunden werden

können.

Nachdem diese Verbindung erfolgt ist, wird das gesamte System über Einstichdorn (14c) mit der Vorfüllungs-Lösung (10) vorgefüllt. Danach beginnt die Punktierung des Spenders mit Hilfe der Blutentnahmekanüle (1). Nachdem die mit Stabilisatorlösung vorgelegten Blutbeutel (13) mit Spenderblut gefüllt sind, werden sie vom Beutelsystem - (12) abgeklemmt und abgetrennt und mit Hilfe der Einstichdorne (14,14a,14b) an das höher liegende Transfusionssystem angeschlossen. Nun erfolgt die Retransfusion, bei der das Blut mit Hilfe von äußerem Druck und Schwerkraft durch Plasmafiltereinheit (4) fließt, wobei das Plasma abgetrennt und in der Sammelstelle für Blutplasma (5) gesammelt wird. Das deplasmatisierte Blut fließt dann weiter durch die Tropfkammer mit eingebautem Transfusionsfilter (6) zurück zum Spender.

In Fig. 6 wird eine stark vereinfachte Vorrichtung gezeigt, die dazu dienen soll, die Effektivität des bevorzugten Systems beim Durchströmen des stabilisierten Blutes durch eine Plasmafiltereinheit zu messen, ohne direkte Verbindung mit dem Spender.

Man sieht dort einen mit stabilisiertem Blut gefüllten Blutbeutel (13), Einstichdorn (14), Rollklemme (15), Plasmafiltereinheit (4), Sammelstelle für Plasma (5) und einen ca. 150 cm tiefer als der Blutbeutel (13) angeordneten Leerbeutel (21) zum Sammeln des durch die Plasmafiltereinheit (4) geflossenen Blutes.

Nachstende Beispiele dienen der weiteren Erläuterung der Erfindung.

Beispiel 1

Ein System bestehend aus:

Kanüle (Plasmapheresekanüle Fa. Biotest)

Tropfkammer mit Transfusionsfilter (TNSB-Gerät Fa. Biotest)

Hollow fiber Modul zur Plasmaabtrennung - (Plasmapur der Fa. Organon Technika)

Blutbeutel zum Sammeln des Blutes (Leerbeutel 500 ml Fa. Biotest)

Plasmabeutel zum Sammeln des Plasma - (Leerbeutel 500 ml Fa. Biotest)

Beutel mit Blutstabilisator (Na-Zitrat pH=7. Fa. Biotest) wurde gemäß Fig. 3 mit PVC-Schläuchen verbunden.

Die Dosierung der Stabilisatorlösung erfolgte mit einem Blutentnahmegesetz (BEG 404) der Fa. Doltron.

Der Blutbeutel hing tiefer als der Plasmabeutel. Ein Blutspender spendete 500 ml Blut direkt durch die Trenneinheit in den Blutsammelbeutel, ohne daß das System mit isotoner NaCl-Lösung vorgefüllt war. Das System füllte sich zu Beginn nur sehr langsam mit Blut, da die Schläuche nicht mit Flüssigkeit gefüllt waren, so daß das hydrostatische Druckgefälle noch nicht den Blutfluß unterstützen konnte.

Sobald das Blut die Trenneinheit gefüllt hatte, begann Plasma durch die Membrane zu treten und sammelte sich im Plasmabeutel. Der Blutfluß wurde zeitweilig durch Verlegen der Kanüle unterbrochen. Das Plasma strömte aus dem Plasmabeutel über die Trenneinheit in den Blutbeutel. Die Plasmaleitung war dann mit der Luft des Plasmabeutels gefüllt. Nach Korrektur der Lage der Kanüle in der Vene konnte der Blutfluß zwar wieder hergestellt werden, es trat jedoch keine Plasmafiltration mehr auf, da in der Plasmaleitung keine Flüssigkeitssäule mehr vorhanden war.

Beispiel 2

Es wurde das Beispiel 1 wiederholt, jedoch wurde das System mit isotoner NaCl-Lösung vorgefüllt und der Plasmasammelbeutel tiefer als der Blutsammelbeutel angebracht. Das Füllen des Systems mit isotoner NaCl-Lösung gestaltete sich - schwierig, da keine entsprechenden Anschlüsse hierfür vorgesehen waren. Es mußten Verbindungen geöffnet werden, um die Vorfüllungs-Lösung anschließen zu können und nach dem Füllen wieder umgesteckt werden.

In 8 Minuten wurden 500 ml Blut gespendet und dabei 160 ml Plasma gesammelt. Der Rückfluß des Blutes bei geänderter Schwerkraftlage (Fig. 4) in einen anstelle der Venenkanüle angeschlossenen Leerbeutel dauerte 7 Minuten, und es wurden weitere 80 ml Plasma gesammelt. In einem Zyklus konnten somit aus 500 ml Blut 240 ml Plasma gewonnen werden.

Beispiele 3 und 4

In das Schlauchsystem der Fig. 3 bzw. 4 wurde ein Anschluß für die Vorfüllungs-Lösung gemäß Fig. 1 bzw. 2 eingebaut. Die Komponenten entsprechen den Beispielen 1 bzw. 2.

Das System wurde mit isotoner NaCl gefüllt. Bei dieser Anordnung konnte durch Drücken auf die Tropfkammer die Tropfkammer selbst, die Plasmafiltereinheit und der Schlauch zwischen der Plasmafiltereinheit und dem Plasmasammelbeutel

gefüllt werden, ohne das System an einer Stelle öffnen zu müssen. Die restliche Luft, die sich im Schlauch zwischen der Blutentnahmekanüle und der Tropfkammer befand, sammelte sich bei der Blutspende in der Tropfkammer. Die Beispiele wurden analog des Beispiels 2 durchgeführt.

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	Beispiel <u>3</u>	Beispiel <u>4</u>
Spendezeit für 500 ml Blut	9 Min.	11 Min.
gesammeltes Plasma	140 ml	125 ml
Zeit für den Rückfluß des Blutes in einen Leerbeutel	8 Min.	8 Min.
zusätzlich gesammeltes Plasma	80 ml	75 ml
gesamte Plasmamenge	220 ml	200 ml

Aus den Beispielen 1 und 2 ist ersichtlich, daß es zwingend notwendig ist, das System mit einer Vorfüllungs-Lösung zu beschicken und daß auch bei der Blutspende der Plasmasammelbeutel tiefer angebracht sein muß als der Blutsammelbeutel.

Um eine einfachere Handhabung zu ermöglichen, wurde das Schlauchsystem für die Beispiele 3 und 4 modifiziert.

Diese Versuche dienen gleichzeitig der Feststellung, ob bei der Zugabe der Vorfüllungs-Lösung gemäß der Erfindung an einer separaten Anschlußstelle sich das System leichter handhaben läßt.

Wie aus diesen Beispielen ersichtlich ist, arbeitete unter Verwendung einer separat eingefüllten Vorfüllungs-Lösung und damit bei einfacherer Handhabung des Vorfüllvorganges sowie bei Anbringung des Plasmasammelbeutels tiefer als der Blutsammelbeutel dieses System einwandfrei.

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Beispiel 5

Ein System bestehend aus:

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Hollow fiber Modul zur Plasmatrennung (Plasmapur der Fa. Organon Technika)

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Plasmabeutel zum Sammeln des Plasma - (Leerbeutel 500 ml Fa. Biotest)

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wurde gemäß Fig. 6 installiert. Das System wurde mit isotoner NaCl-Lösung vorgefüllt. Ein mit stabilisiertem Blut gefüllter Beutel wurde über den Einstichdorn oberhalb der Plasmafiltereinheit angeschlossen und eine "Retransfusion" in einen Leerbeutel mit gleichzeitiger Plasmaabtrennung durchgeführt. Bei einem Höhenunterschied von 150 cm zwischen dem Blutbeutel und dem Leerbeutel wurden folgende Zeiten und Volumina gemessen:

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	Versuch	
	A	B
"Retransfusionszeit", Min.	12	10
Abgetrennte Plasmamenge, ml	145	132

Wird die Spendezeit für Blut berücksichtigt, so ergibt sich eine Effektivität wie folgt:

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Spendezeit für 500 ml Blut	5 Min.
Zeit für Retransfusion und Abtrennung des Plasmas	11 Min.
Handhabung des Gerätes	1 Min.
gesammeltes Plasma	140 ml

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Dieser Zyklus kann z.B. 3 * wiederholt werden, so daß man in ca. 50 Minuten einschließlich Retransfusion 420 ml Plasma erhält.

Ansprüche

1. Verfahren zur Gewinnung von Blutplasma bei einer Blutentnahme vom lebenden Körper, bei dem man nach einer Stauung der entnahmefähigen Blutgefäße mit Hilfe einer Blutentnahmekanüle Blut entnimmt und unter Ausnutzung von äußerem Druck und Schwerkraft und gegebenenfalls unter Verwendung einer Vorfüllungs-Lösung sowie nach Zusatz einer Stabilisatorlösung mit Hilfe eines Schlauches durch eine tiefer als die Blutquelle liegende Plasmafiltereinheit leitet, in der man Plasma vom Blut trennt, das abgetrennte Plasma einer Sammelstelle für Plasma und das partiell deplasmatisierte Blut einer davon getrennten Sammelstelle für Blut zuführt und gegebenenfalls das partiell deplasmatisierte Blut zum lebenden Körper in geänderter Schwerkraftlage durch dieselbe Plasmafiltereinheit retransfundiert, **dadurch gekennzeichnet**, daß man im Falle der Verwendung einer Vorfüllungs-Lösung diese mit Hilfe eines separaten Anschlusses zugeibt, das gespendete Blutvolumen mißt, die Stabilisatorlösung mit Hilfe einer Pumpe entsprechend dem gemessenen gespendeten Blutfluss bzw. Blutvolumen zudosiert, das Blut durch eine zwischen Blutentnahmestelle und Plasmafiltereinheit, jedoch nach dem Anschluß für die Stabilisatorlösung liegende Tropfkammer mit eingebautem Transfusionsfilter führt und die Sammelstelle für Plasma während des ganzen Verfahrens tiefer als die Sammelstelle für Blut anordnet.

2. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß die Messung des gespendeten Blutvolumens laufend erfolgt.

3. Verfahren nach einem der Ansprüche 1 oder 2, dadurch gekennzeichnet, daß die Messung des gespendeten Blutvolumens an der Schlauchaußenseite mit Hilfe eines Ultraschalldetektors erfolgt.

4. Verfahren zur Gewinnung von Blutplasma bei einer Blutentnahme vom lebenden Körper, bei dem man das System mit einer Vorfüllungs-Lösung

vorfüllt, nach einer Stauung der entnahmefähigen Blutgefäße mit Hilfe einer Blutentnahmekanüle Blut entnimmt, mit Stabilisatorlösung vermischt und unter Ausnutzung von äußerem Druck und Schwerkraft mit Hilfe mindestens eines Schlauches durch eine tiefer als die Blutquelle liegende Plasmafiltereinheit leitet, in der man Plasma vom Blut trennt, das abgetrennte Plasma einer Sammelstelle für Plasma zuführt und das partiell deplasmatisierte Blut zum lebenden Körper retransfundiert, **dadurch gekennzeichnet**, daß eine bestimmte Menge Blut in mindestens einen Beutel, der eine auf die Blutmenge abgestimmte Menge Stabilisatorlösung enthält, gespendet wird, der Beutel mit dem stabilisierten Blut vom Beutelsystem abgetrennt und an das obere Ende eines Transfusionsgerätes angeschlossen wird, das mit seinem unteren Ende mit dem Beutelsystem und der Spenderkanüle verbunden ist und das die Plasmafiltereinheit und die Sammelstelle für Plasma sowie eine Tropfkammer mit Transfusionsfilter enthält, das Blut über die Plasmafiltereinheit und die Tropfkammer dem Spender retransfundiert wird und während der Retransfusion das Plasma gesammelt wird.

5. Verfahren nach Anspruch 4, dadurch gekennzeichnet, daß die Vorfüllungs-Lösung mit Hilfe eines Einstichdorns am oberen Ende des Transfusionsgerätes dem System zugeführt wird.

6. Verfahren nach einem der vorstehenden Ansprüche, dadurch gekennzeichnet, daß man die Spende und die Retransfusion mehrere Male durchführt.

7. Vorrichtung zur Durchführung des Verfahrens nach einem der Ansprüche 1 bis 3, enthaltend eine Plasmafiltereinheit (4) zwischen einer Blutentnahmekanüle (1) und einer Sammelstelle für Blutplasma (5) sowie einer davon getrennten Sammelstelle für das partiell deplasmatisierte Blut (3) und einen Anschluß (11) für Stabilisatorlösung, **dadurch gekennzeichnet**, daß außerdem zwischen Injektionskanüle (1) und Plasmafiltereinheit (4) eine Tropfkammer mit eingebautem Transfusionsfilter - (6), eine Dosierpumpe (8) zur Dosierung von Stabilisatorlösung (7), die mit einer Meßvorrichtung (9) für das gespendete Blutvolumen gekoppelt ist, und ein Anschluß (2) an Vorfüllungs-Lösung (10) angeordnet sind, wobei Anschluß (11) mit Dosier-

pumpe (8) und Stabilisatorlösung (7) sich vor der Tropfkammer mit eingebautem Transfusionsfilter - (6), bezogen auf die Richtung des Blutflusses bei der Spende, befinden.

8. Vorrichtung zur Durchführung des Verfahrens nach einem der Ansprüche 4 bis 6, enthaltend eine Blutentnahmekanüle (1), eine Plasmafiltereinheit (4) und eine Sammelstelle für Plasma (5), dadurch gekennzeichnet, daß sich die Blutentnahmekanüle am Ende eines Beutelsystems (12) befindet, das mindestens einen mit Stabilisatorlösung zu

füllenden Blutbeutel (13) enthält, und die Plasmafiltereinheit (4) sowie die Sammelstelle für Plasma - (5) sich innerhalb eines Transfusionsgerätes (20) befinden, das am oberen Ende einen oder mehrere Einstichdorne (14), im Anschluß an die Plasmafiltereinheit (4) in Richtung des Retransfundierungsflusses eine Tropfkammer mit eingebautem Transfusionsfilter (6) und am unteren Ende ein Verbindungssystem (18) zum Anschluß an das Beutelsystem (12) aufweist.

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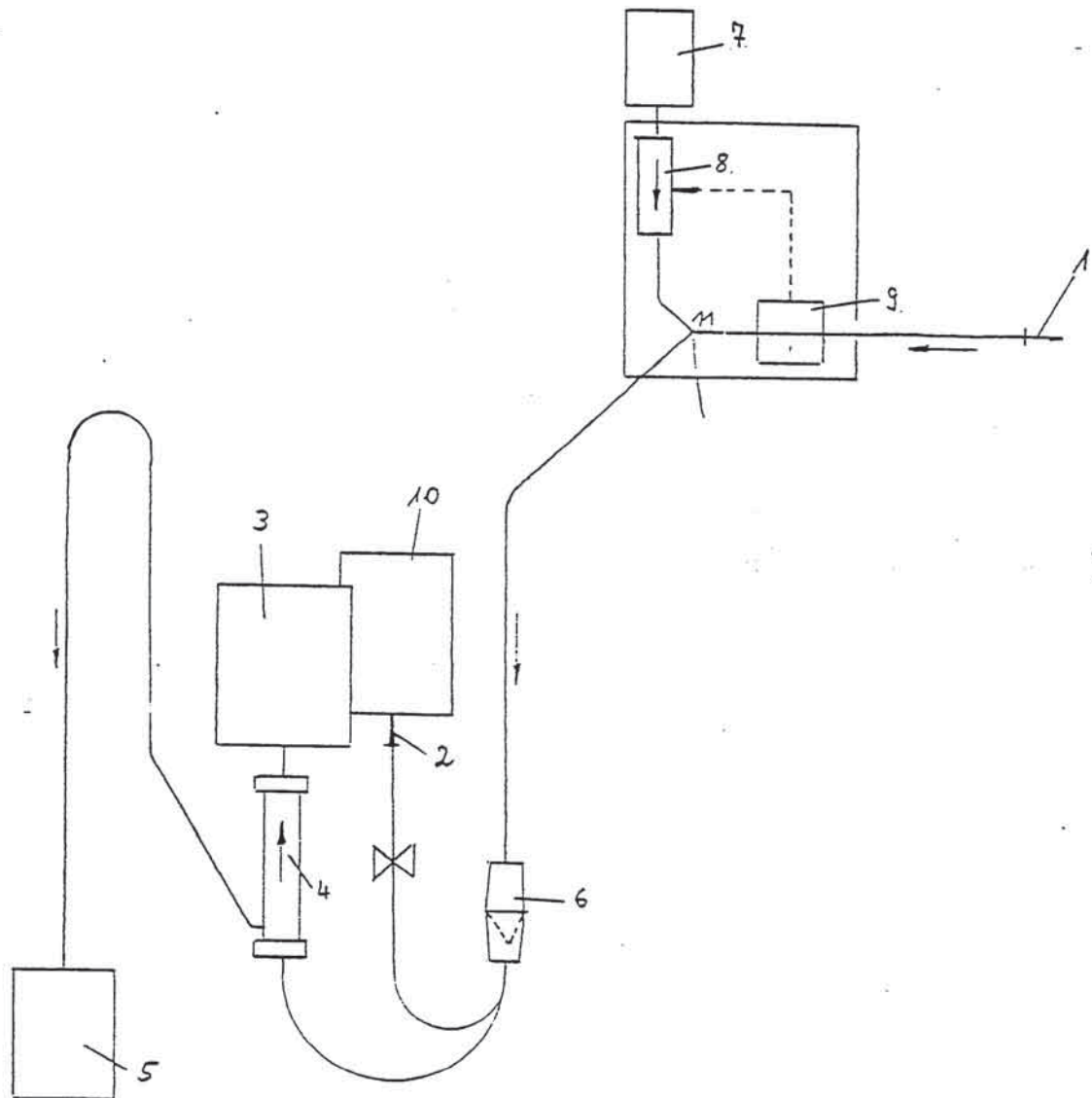
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Fig. 1



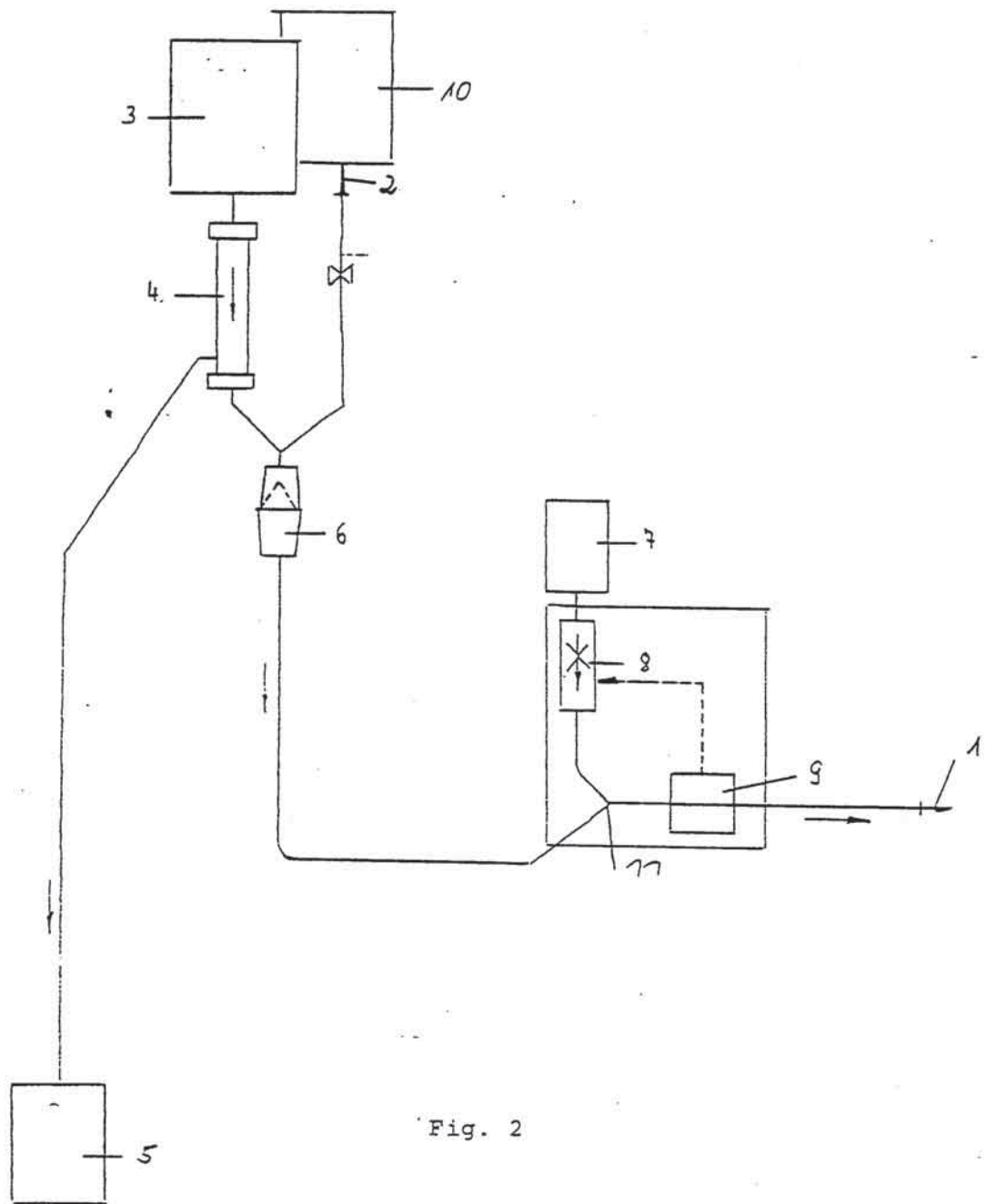


Fig. 2

Fig. 3

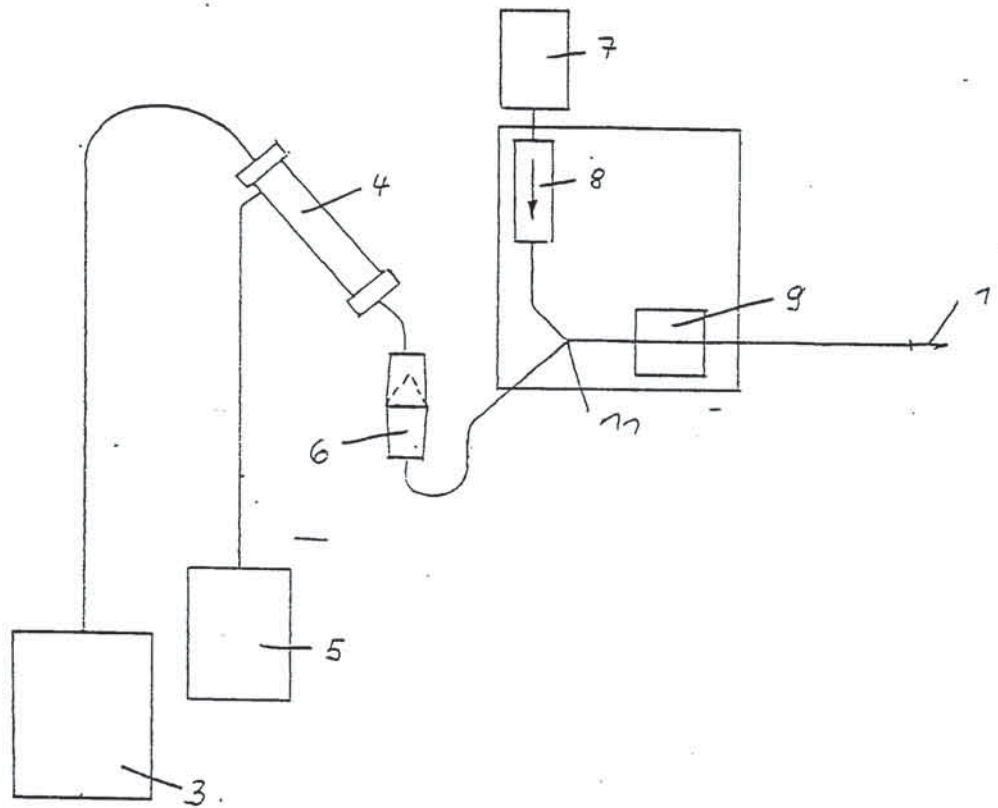
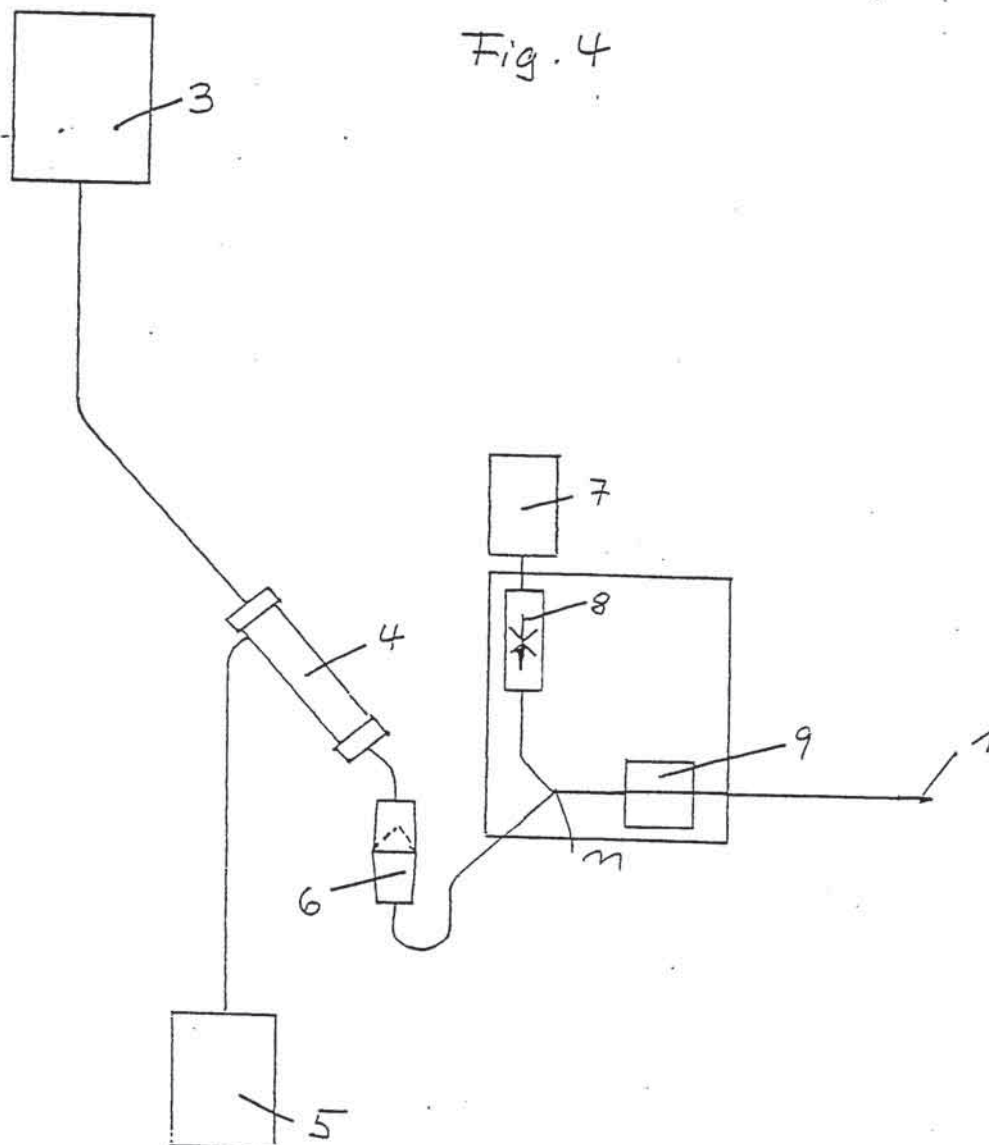


Fig. 4



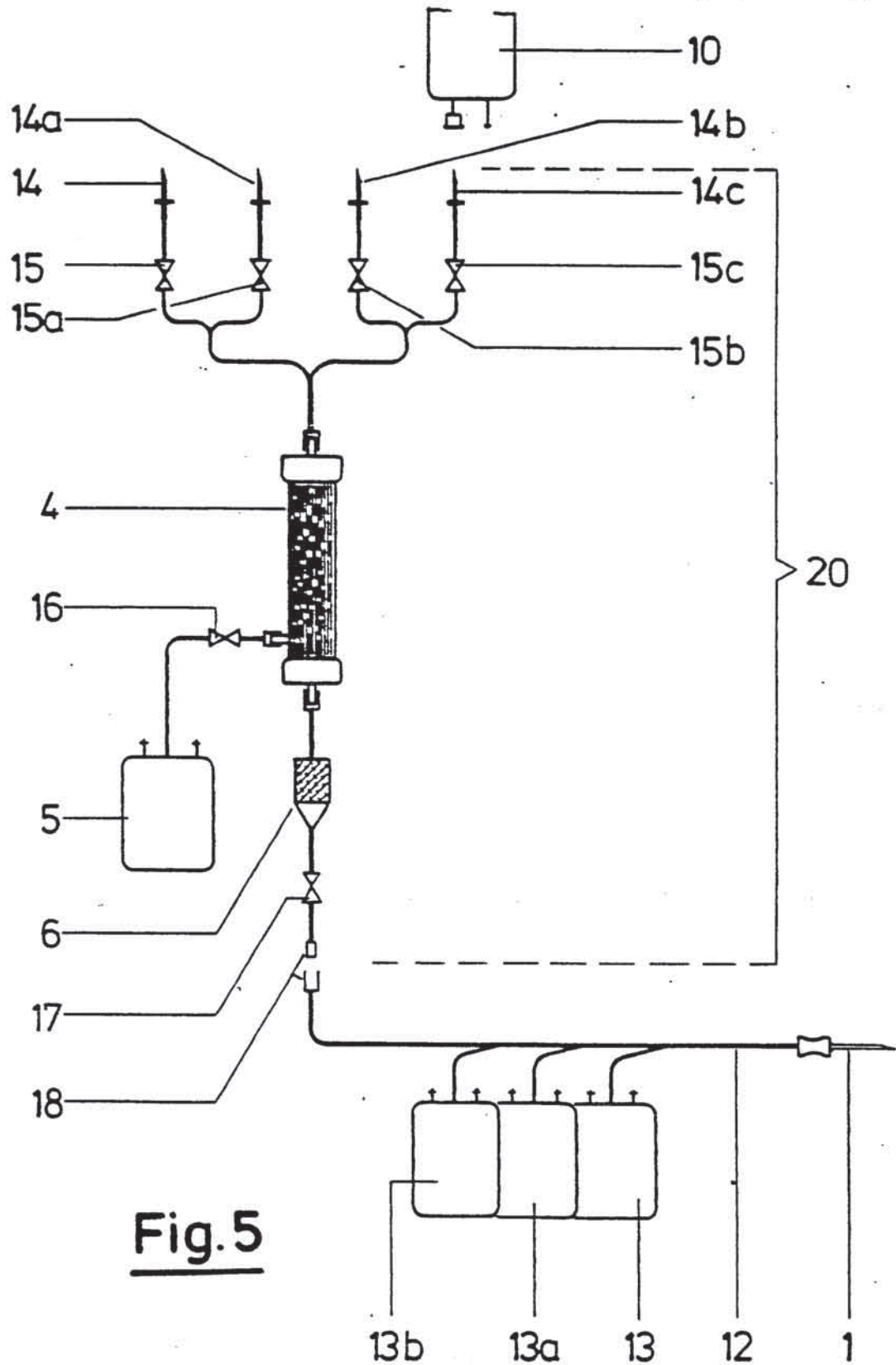
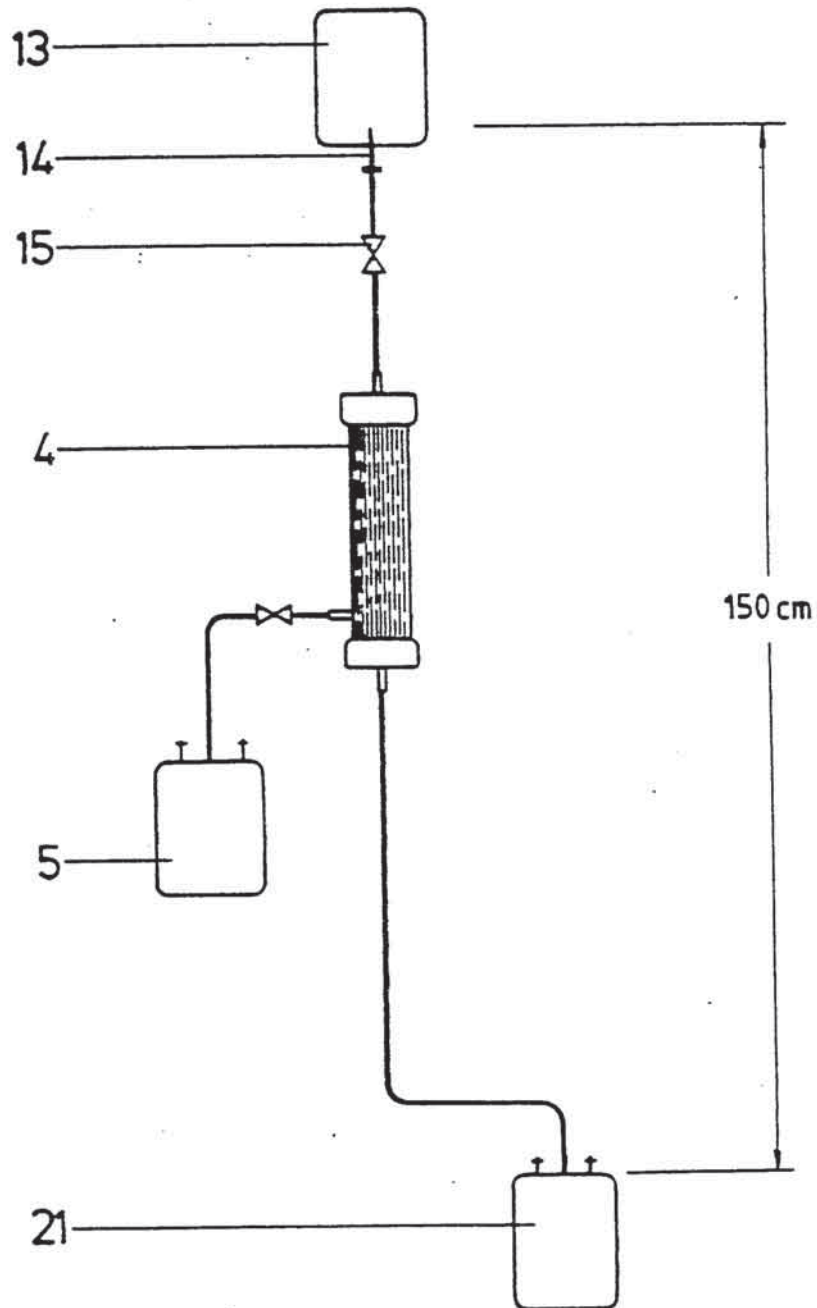
**Fig. 5**

Fig. 6



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EUROPÄISCHER TEILRECHERCHENBERICHT,
der nach Regel 45 des Europäischen Patent-
übereinkommens für das weitere Verfahren als
europäischer Recherchenbericht gilt

Nummer der Anmeldung

EINSCHLÄGIGE DOKUMENTE			EP 86104316.4
Kategorie	Kennzeichnung des Dokuments mit Angabe, soweit erforderlich, der maßgeblichen Teile	Betrifft Anspruch	KLASSIFIKATION DER ANMELDUNG (Int. Cl.4)
A	US - A - 4 498 983 (A.C.JILSTAD et al.) * Gesamt; insbesondere Fig. 1,2, 9a,b; Spalte 4, Zeile 54 - Spalte 5, Zeile 63; Spalte 6, Zeilen 18-49; Spalte 13, Zeile 21 - Spalte 14, Zeile 56 *	7,8	A 61 M 1/34 A 61 M 1/36
A	EP - A1 - 0 085 016 (RHONE POULENC S.A.) * Gesamt; insbesondere Fig. 2; Seite 7, Zeile 31 - Seite 12, Zeile 3 *	7,8	
D,A	DE - A1 - 3 302 383 (M. LYSAGHT et al.) * Gesamt *	7,8	
			RECHERCHIERTE SACHGEBIETE (Int. Cl.4)
			A 61 M 1/00 A 61 M 5/00
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<p>Nach Auffassung der Recherchenabteilung entspricht die vorliegende europäische Patentanmeldung den Vorschriften des Europäischen Patentübereinkommens so wenig, daß es nicht möglich ist, auf der Grundlage einiger Patentansprüche sinnvolle Ermittlungen über den Stand der Technik durchzuführen.</p> <p>Vollständig recherchierte Patentansprüche: 7,8 Unvollständig recherchierte Patentansprüche: 1-6 Nicht recherchierte Patentansprüche: 1-6 Grund für die Beschränkung der Recherche:</p> <p>(in Anwendung des Art. 52 (4))</p>			
Recherchenort WIEN		Abschlußdatum der Recherche 17-09-1986	Prüfer LUDWIG
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Kategorie	Kennzeichnung des Dokuments mit Angabe, soweit erforderlich, der maßgeblichen Teile	betrifft Anspruch	
A	GB - A - 2 112 293 (COBE LAB. INC.) * Gesamt; insbesondere Fig. 1; Seite 2, Zeile 94 - Seite 3, Zeile 8 *	7,8	
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A	US - A - 4 197 847 (I. DJERASSI) * Gesamt *		
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(54) **Apparatus and method for transferring separated components in liquid**

Gerät und Methode zur Transferierung einer in einer Flüssigkeit abgetrennten Komponente

Appareil et méthode pour transférer un composant séparé d'un liquide

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EP 0 578 086 B1

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Description

- [0001] This invention relates generally to apparatus and method for transferring a separated component in a liquid, and more particularly to apparatus and method for transferring or taking out a centrifugally separated component in a liquid such as blood contained in a blood bag.
- [0002] In carrying out blood transfusion, recently, blood collected from a donor is centrifuged with a centrifugal separator for separating the collected blood into blood components, and then only the component required for a patient is transfused, in order to utilize the blood effectively and to reduce a burden on the patient who receives a blood transfusion. Owing to this component transfusion, it has become possible to utilize blood more effectively, as compared with the whole blood transfusion so far adopted.
- [0003] In the above-mentioned component transfusion, connected bags (referred to as "multiple bag system") composed of a blood collecting bag and one or more bags are used.
- [0004] As one of the multiple bag systems, there is known a triple bag system, which comprises a blood collecting bag, a platelet concentrate preserving bag (hereinafter, referred to as "PC bag") and a plasma preserving bag (hereinafter, referred to as "plasma bag") which are connected to each other through tubes. The blood collected into the blood collecting bag is centrifuged at least once to separate the blood into three components of erythrocyte concentrate, platelet concentrate, and platelet-poor plasma (hereinafter, referred to as "PRP method"), and the separated components are preserved in the blood bag, the PC bag and the plasma bag, respectively.
- [0005] In the multiple blood bag system as described above, the respective bag is formed by laminating flexible polyvinyl chloride sheets and further fusing the periphery thereof. The reasons why the flexible polyvinyl chloride is used is that this material has an appropriate gas penetrability, and further that this material is excellent in preservation of cells such as erythrocyte, platelet, etc., in heat-resistance in autoclave sterilization, and in flexibility endurable to centrifugal separation and suitable for shake preservation. Further, the material is also low in manufacturing cost.
- [0006] The blood collected into a blood collecting bag is centrifuged by placing the blood collecting bag in a centrifugal cup formed of a hard material and formed into a cup-shaped container and mounting the centrifugal cup with the blood collecting bag to a centrifugal separator. Further, the separated components are collected in accordance with the following steps, that is, first the blood collecting bag is removed from the centrifugal cup; the blood collecting bag is then set to an automatic separating stand; and thereafter the blood collecting bag is pressed, so that the supernatant plasma layer is discharged. As the automatic separating stand, for example, one disclosed in U.S. Patent No. 4,976,851 can be used.
- [0007] In the method as described above, however, after the centrifugal separation, the following operations are required, that is, the blood collecting bag is removed from the centrifugal cup, the removed bag is then transferred to the separating stand, and thereafter the bag is set to the separating stand. Therefore, there are various problems in that the blood collecting bag is shaken or vibrated during the above-mentioned operations and further the bag is likely to be deformed because of its flexibility. With this result, the interfaces between the respective two layers of the three separated components are likely to be disturbed during the operations, thus leading to the problem that yield (quantity of collection or purity) of each of the separated components is deteriorated. When the yield of each of the separated components is lowered as described above, the quality of blood products is also degraded, and therefore there exists such a case that the blood collecting bag must be centrifuged again as occasion demands.
- [0008] In addition, since it takes a long time to take out the blood collecting bag from the centrifugal cup and further to set the bag to the separating stand. In particular, if these operations are carried out carefully so as not to disturb the interfaces between the respective separated components, a further long time is required.
- [0009] US-A-4,447,220 discloses an apparatus for separating blood components which comprises a centrifuge cup having two chambers. In a first chamber there is placed an elastically deformable inset cup tightly enclosing a blood bag filled with blood fluid. A deformable pressure pad is disposed in said first chamber between the inset cup and the inner surface of the first chamber.
- [0010] During centrifuging the pressure pad is inflated and the inset cup is thus compressed to transfer blood component into an empty bag disposed in the second chamber.
- [0011] The object of the present invention is to provide apparatus and method which can transfer a centrifugally separated component in a liquid contained in a flexible bag in which the number of the necessary components and steps are reduced and with improved yield for each separated component.
- [0012] A further object of the present invention is to provide apparatus and method which can collect the centrifugally separated component from the liquid with high yield, without removing out the flexible bag in which the liquid is contained from the centrifugal cup.
- [0013] As claimed the apparatus of the invention for transferring a separated component in a liquid contained in a flexible bag in airtight condition comprises a deformable centrifugal container for removably accommodating the flexible bag therein and pressing means provided outside said centrifugal container for pressing the flexible bag accommodated in said centrifugal container to increase the inner pressure of said flexible bag while the bag is released from the airtight

condition, so that a predetermined separated component can be discharged from the bag.

[0014] According to the invention, the centrifugal container includes a frame portion and a soft material part and the pressing means comprises a pair of opposing push members at least one of which is movable toward the other by a reciprocal motion driving mechanism. The push members are adapted for pressing the soft material part of said centrifugal container which is therefore deformed, so as to project in the inner direction of the centrifugal container, thus discharging the separated component of the liquid contained in the flexible bag.

[0015] Further, the present invention is also directed to a method of transferring a separated component in a liquid contained in a flexible bag under airtight condition; which comprises the steps of:

accommodating the flexible bag in which the liquid is contained under airtight condition into a centrifugal container which is removably attached to a centrifugal separator, said centrifugal container having a soft material part formed in at least one portion thereof;

centrifuging the flexible bag accommodated in the centrifugal container by the centrifugal separator to separate the liquid in the flexible bag into the components thereof;

removing said centrifugal container from the centrifugal separator together with the flexible bag contained therein and then fixing the centrifugal container to a fixing means, and

pressing the soft material part of the centrifugal container from the outside of said centrifugal container using a movable push member provided outside of the container for pushing said soft material part of said centrifugal container to increase inner pressure of the bag while releasing the airtight condition, thereby taking out a predetermined component in the liquid which has been separated by the centrifugation outside the flexible bag.

[0016] When the apparatus and method as described above are used to transfer separated blood components, the following steps are taken place.

[0017] A required amount of blood is collected into a flexible blood collecting bag. This bag is placed in the centrifugal container, and then the container in which the bag is accommodated is set to the centrifugal separator for centrifugal separation. The blood in the blood collecting bag is separated by the centrifugal separation into three layers, namely a plasma layer, a buffy coat layer, and an erythrocyte layer.

[0018] After completion of the centrifugal separation, the centrifugal container is removed from the centrifugal separator, and thereafter is fixed to a separating stand for instance. Then, the blood collecting bag accommodated in the centrifugal container is pressed by actuating at least one of the opposing push members. Since the inner pressure of the blood collecting bag increases, the upper plasma layer is discharged through a tube connected to the blood collecting bag, so that the plasma can be transferred to another bag or the like and collected therein.

[0019] In this case, since the plasma is transferred and collected, after centrifugal separation, without removing the blood collecting bag from the centrifugal container and further without setting the blood collecting bag to a separating stand, the time and labor required for the operation can be reduced. Further, the disturbance at the respective interfaces between two of the three separated component layers will not occur due to vibration or bag deformation which are likely to be caused when the blood collecting bag is removed, transferred or hanged. In addition, the yield of the collected plasma can be improved.

[0020] Further, in the present invention, since the upper plasma layer is raised and then discharged under the condition that the inner pressure of the blood collecting bag is kept increased and further the respective interfaces between the layers are kept stationary, it is possible to avoid that the other component in the lower layer below the plasma layer is mixed to the plasma, thereby enabling to increase the yield for the plasma. In addition, when the separated buffy coat layer is transferred and further collected, the yield therefore can be also improved in the same way as in the case of the plasma collection. In this regard, it should be noted that the liquid to be contained in the flexible bag is no limited to blood. Bone marrow fluid can be used instead of blood.

[0021] According to the invention, the push members are for pushing the soft material part of the centrifugal container in such a manner that the soft material part is deformed inwardly to project inside the container, and a reciprocal motion driving mechanism for driving the push member.

[0022] Further, in the apparatus and method according to the present invention, it is possible to use sucking means for sucking the separated component in the bag in addition to the pressing means. If the sucking means is provided in addition to the pressing means, it becomes possible to maintain high yield which is the same rate as that where the pressing means is used alone and shorten the time required for collecting the separated component.

[0023] Other objects, structures and advantages of the present invention will become apparent from the following descriptions of the preferred embodiments when taken in conjunction with the accompanying drawings.

Fig. 1 is a plan view showing an example of the connected bags to which the present invention is applied;

Fig. 2 is a side cross-sectional view showing an apparatus for transferring a centrifugally separated component in a liquid which is not according to the present invention but illustrating the general principles for such a transfer.

Fig. 3 is a perspective view showing a cuff as pressing means of the apparatus of figure 2;
 Fig. 4 is a perspective view showing an embodiment of the apparatus according to the present invention; and
 Fig. 5 is a side cross-sectional view showing the example in which a sucking means which can be used in the present invention is additionally provided to the apparatus of figure 2.

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[0024] An apparatus and a method for transferring a separated component in a liquid according to the present invention will be described in detail hereinbelow with reference to the attached drawings.

[0025] First, the typical multiple bag system used for the apparatus according to the present invention will be explained. Fig. 1 is a plan view showing an example of the multiple bag system. The multiple bag system shown in Fig. 1 is constituted as quadruple (four-connection) bags which are composed of a blood collecting bag, a PC bag, a plasma bag, and a sub-bag (buffy coat bag).

[0026] The blood collecting bag 1 shown on the right side in Fig. 1 is formed into a closed bag by laminating flexible sheets of a resin material such as soft polyvinyl chloride and further fusing a peripheral sealing portion 2 thereof in accordance with fusing method (e.g., thermal fusion, high frequency fusion, etc.) or bonding the portion 2. In the space defined by the two sheets and enclosed by the sealing portion 2, there is formed a blood component accommodating section 3 to which collected blood or erythrocyte concentrate obtained by centrifuging the blood is to be contained.

[0027] In the upper portion of the blood collecting bag 1, there is formed two opening portions 4 provided with a peeling tub, respectively. Further, a blood outlet 5 is formed between the two opening portions 4 so as to be connected to another bag. One end of a tube 14 is connected to this outlet 5 via a connecting member 15.

[0028] Further, a bifurcated connector 20 is connected to the other end of the tube 14. Another tube 21 is connected to this bifurcated connector 20. Further, another bifurcated connector 22 is connected to the other end of this tube 21.

[0029] Further, it is preferable to constitute the connecting member 15 so as to provide with a path closing member (not shown) inside thereof. The path closing member is adapted to be broken by bending the connecting member 15 to allow fluid communication in the connecting member 15. Accordingly, the closing member functions in such a way that fluid communication in the connecting member 15 is kept impossible before broken, but the fluid communication therein becomes allowed after breaking. As such a closing member, it is possible to use a Click Chip which is a product name of TERUMO Kabushiki Kaisha, for instance. In this invention, alternatively, it is possible not to provide the connecting member 15 as described above. In this case, it is preferable to close or open the tube 14 appropriately with the use of a clamp.

[0030] Further, one end of a flexible tube 6 communicating with the blood component accommodating section 3 is connected to the upper portion of the blood collecting bag 1. To the other end of this tube 6, a blood collecting needle 8 is attached via a hub 7. Further, there is provided a cap 9 which is attached to the hub 7 to cover the needle 8.

[0031] The plasma bag 10 shown at the second position from the left side in Fig. 1 is also formed into a closed bag by laminating flexible sheets of a resin material such as soft polyvinyl chloride and further bonding a peripheral sealing portion 11 thereof in accordance with fusing method (e.g., thermal fusion, high frequency fusion, etc.). In the space defined by the sheets and enclosed by the sealing portion 11, a plasma accommodating section 12 is formed to accommodate plasma (platelet-poor plasma, in particular) separated from the blood in the blood collecting bag 1.

[0032] In the upper portion of the plasma bag 10, there are formed two opening portions 13 provided with a peeling tub, respectively.

[0033] Further, one end of a flexible tube 23 communicating with the plasma accommodating section 12 is connected to the side of the opening portion 13 of the upper portion of the bag 10. The other end of this tube 23 is connected to the bifurcated end of the bifurcated connector 21. Therefore, the blood component accommodating portion 3 of the blood collecting bag 1 communicates with the plasma accommodating portion 12 of the plasma bag 10 through the tubes 14, 21 and 23 and the bifurcated connectors 20 and 22.

[0034] The PC bag 16 shown on the left side in Fig. 1 is also formed into a closed bag by laminating flexible sheets of resins such as soft polyvinyl chloride and further bonding a peripheral sealing portion 17 thereof in accordance with fusing method (e.g., thermal fusion, high frequency fusion, etc.). In the space defined by the sheets and enclosed by the sealing portion 17, a platelet accommodating section 18 is formed to accommodate platelet (platelet concentrate plasma) obtained by centrifuging the blood.

[0035] In the upper portion of the blood PC bag 16, there are formed two opening portions 19 which are provided with a peeling tub, respectively. Further, an outlet 25 is formed on the side of the opening portion 19 of the upper portion of the bag 16. This outlet 25 is connected to one end of the flexible tube 24 through another connecting member 15 in the same way as the blood collecting bag described above. The other end of this tube 24 is connected to the bifurcated end of the bifurcated connector 22. Therefore, the platelet accommodating section 18 of the PC bag 16 communicates with the blood component accommodating section 3 of the blood collecting bag 1 and the plasma accommodating section 12 of the plasma bag 10, respectively, through the tubes 14, 21, 23 and 24 and the bifurcated connectors 20 and 22.

[0036] Between the blood collecting bag 1 and the plasma bag 10, there is provided a buffy coat bag 27 which is

used to accommodate buffy coat temporarily. The buffy coat bag 27 is also formed into a closed bag by laminating flexible sheets of a resin material such as soft polyvinyl chloride and further bonding a peripheral sealing portion 28 thereof in accordance with fusing method (e.g., thermal fusion, high frequency fusion, etc.). In the space defined by the sheets and enclosed by the sealing portion 28, a buffy coat accommodating section 29 is formed to accommodate buffy coat separated from the blood in the blood collecting bag 1.

[0037] On the upper portion of the buffy coat bag 27, one end of another flexible tube 26 is connected so as to communicate with the buffy coat accommodating section 29 of the buffy coat bag 27. The other end of this tube 26 is connected to the bifurcated end of the bifurcated connector 20. Therefore, the buffy coat accommodating section 29 of the buffy coat bag 27 communicates with the blood component accommodating section 3 of the blood collecting bag 1, the plasma accommodating section 12 of the plasma bag 10, and the platelet accommodating section 18 of the PC bag 16, respectively, through the tubes 14, 21, 23, 24 and 26 and the bifurcated connectors 20 and 22.

[0038] In use of the multiple bag system as described above, the blood collecting needle 8 is first inserted into a vein of a donor, and the blood is introduced into the blood component accommodating section 3 of the blood collecting bag 1 through the tube 6 and then stored therein. When the blood within the blood component accommodating section 3 reaches a predetermined quantity, the needle 8 is pulled out from the vein of the donor. Thereafter, the midway portion of the tube 6 is fused for instance to seal it, and the tube 6 on the side of the blood collecting needle 8 is cut off for removal. Under these conditions, the blood is accommodated within the blood collecting bag 1 in airtight condition.

[0039] In the above description, explanation is made with reference to the quadruple bag system. However, the multiple bag system to which the present invention is applied is not limited to only the quadruple bag system. That is, this invention can be applied to various bags, such as a single bag only having a blood collecting bag; a double bag system composed of a blood collecting bag and a plasma bag; a triple bag system composed of a blood collecting bag, a PC bag and a plasma bag; and a quadruple bag for use in the different purpose from that of the afore-mentioned quadruple bag. Further, this invention can also be applied to a double bag system, a triple bag system and a quadruple bag system connected to another bag for collecting cryo-precipitate (AHF), for instance.

[0040] Furthermore, this invention can also be applied to a multiple bag system having the blood collecting bag 1 in which a first discharge port and a second discharge port which are communicated with the upper portion and the bottom portion of the blood collecting bag, respectively, are formed in such a manner that the plasma in the upper layer is discharged from the first discharge port, the erythrocyte in the lower layer is discharged from the second port, and the buffy coat in the middle layer remains in the bag. As one of the examples of such a multiple bag system, one disclosed in US-A-5,102,407 can be used.

[0041] Moreover, a multiple bag system as disclosed in EP-A-484,751 or Japanese Laid-open Patent Publication No. 4-350556 can be used in particular with reference to the embodiment shown in Figs. 5 and 6 of this application which are described later.

[0042] Fig. 2 is a side cross-sectional view showing a separated component transferring apparatus which is not according to the present invention but useful for describing transfer of reparated component. As shown in the drawing, the apparatus 30 is provided with a centrifugal container (inner cup) 40 in which connected bags of the multiple bag system is to be placed. This centrifugal container 40 is formed into a cylindrical configuration having a bottom and adapted to be removably attached to a centrifugal separator. The bottom 41 of this cup 40 is formed into a semispherical shape.

[0043] The centrifugal container 40 is formed of a material having a rigidity of such an extent as not to be deformed easily even when it is centrifuged or even when the blood collecting bag 1 accommodated in the container 40 is pressed by the pushing means (described later). Preferably, the material is formed of an acrylic resin such as hard polyvinyl chloride, polyethylene, polypropylene, polycarbonate, polymethylmethacrylate (PMMA), or the like; a metal such as stainless steel or aluminum; various glasses or ceramics; or appropriate combinations of any of these materials.

[0044] In the centrifugal container 40 as described above, the connected bags having the blood collecting bag in which blood is stored are placed, and then centrifuged. The connected bags are put into the centrifugal container 40 by stacking the respective bags 1, 10, 16 and 27 and by directing the upper portion of the respective bag, that is the side on which the opening portion is formed toward the upper opening portion side of the centrifugal container 40.

[0045] When the connected bags are placed in the centrifugal container 40, it is not necessary to place all the bags in the centrifugal container 40. That is, it is possible to separate the blood collecting bag 1 from the remaining connected bags and then to place only the blood collecting bag 1 in the centrifugal container 40. For this reason, hereinafter, description is made based on a case where only the blood collecting bag 1 is placed in the centrifugal container 40.

[0046] Further, the method of removably setting the centrifugal container 40 to the centrifugal separator is not particularly limited. For example, the centrifugal container 40 may be constructed such that the container 40 is supported at opposite two portions of the upper annular edge thereof (not shown) so as to be rotatable with respect to the axis extending through the two supported portions.

[0047] The separated component transferring apparatus 30 is provided with a pressing means for pressing the blood collecting bag 1 in which blood is contained. In the apparatus shown in Fig. 2, the pressing means is composed of an

expandable and contractible cuff 50 to be interposed between the inner surface of the centrifugal container 40 and the outer surface of the blood collecting bag 1, and a fluid supplying means 51 for supplying a fluid such as air into the cuff 50 for expansion thereof.

[0048] The cuff 50 is formed into an annular tubular shape so as to be able to push or press the outer circumferential surface of the blood collecting bag 1 roughly uniformly. As shown in Fig. 3, the cuff 50 is constituted so as to provide a central space under the contracted condition thereof into which the blood collecting bag 1 containing the blood can be passed therethrough.

[0049] The cuff 50 is formed of a sheet material made of various rubbers (e.g., silicone rubber, etc.), various resins (e.g., soft polyvinyl chloride, polyethylene, polypropylene, etc.), cloth, and any appropriate combinations of these materials.

[0050] The dimensions of the cuff 50 are not limited to specific values. However, it is preferable to determine the width W of the cuff 50 within a range between 50 mm and 100 mm, in particular between 70 mm and 90 mm.

[0051] Further, the cuff 50 may be fixed to either the inner surface of the centrifugal container 40 or the outer surface of the blood collecting bag 1. Alternatively, the cuff 50 is simply interposed between the centrifugal container 40 and the blood collecting bag 1. Further, the shape of the cuff 50 is not limited only to the annular shape as shown. For instance, it is possible to arrange a pair of flat bags on the front and rear sides of the blood collecting bag 1, respectively.

[0052] The fluid supplying means 51 is composed of an air feeding tube 52 communicating with the inner side of the cuff 50; an air supply source 55 such as air cylinder, air compressor, compressed gas cylinder, etc.; another air feeding tube 53 connected to the air supply source 55; a pair of male and female connectors 54 connected between the two air feeding tubes 52 and 53; and open and close valve 56 disposed midway of the air feeding tube 53 to control the air supplied into the cuff 50. In this case, the open and close valve 56 may be constructed into the type in which the air pressure supplied to the cuff 50 can be adjusted by adjusting the opening rate thereof.

[0053] Further, the fluid for expanding the cuff 50 is not limited to only air, and other gas or water can be used.

[0054] The operation of the separated component transferring apparatus as described above will be described hereinafter.

[0055] In order to place the blood collecting bag 1 in the bag accommodating container 40 or centrifuge the blood collecting bag 1, first, the connector 54 is removed from the cuff 50 to contract the cuff 50.

[0056] Next, The blood collecting bag 1 in which blood is contained is placed in the centrifugal container 40, and the centrifugal container 40 accommodating the blood collecting bag 1 is then set to the centrifugal separator (not shown) for centrifugal separation. Therefore, the blood in the blood collecting bag 1 is separated into three layers i.e. a plasma layer, a buffy coat layer, and an erythrocyte layer in this order from the above.

[0057] After the centrifugal separation, under the condition that the blood collecting bag 1 is kept placed in the centrifugal container 40, the centrifugal container 40 is removed from the centrifugal separator, and further fixed to a fixing means (not shown) such as a stand or a mounting base. In this state, since the blood collecting bag 1 is not removed from the centrifugal container 40, the interfaces between two of the respective separated components are not disturbed. In this case, it should be noted that in the case where all the connected bags in the double, triple, or quadruple bag system are placed in the centrifugal container 40 for centrifugal separation, the bag or bags other than the blood collecting bag 1 are removed from the centrifugal container 40.

[0058] Successively, the plasma in the upper layer is collected from the separated components. In this case, the connecting member 15 of the upper portion of the blood collecting bag 1 is broken to allow the fluid communication and further the tube 26 is closed by a clamp or an electrically actuated solenoid pinch valve or the like. On the other hand, the connector 54 is connected. The air supply source 55 is actuated and the valve 56 is opened, to feed air into the cuff 50 through the air feeding tubes 52 and 53, so that the cuff 50 is expanded. In accordance with the expansion of the cuff 50, the blood collecting bag 1 is pressed and thereby the inner pressure thereof increases. With this result, the upper plasma layer is discharged through the outlet 5, and further fed into the plasma bag 10 through the tubes 14, 21 and 23, respectively. When the plasma is being discharged, the blood collection bag 1 is kept under the expanded condition, as already explained. Therefore, the lower components will not mixed with the plasma now being discharged and fed, thus improving the yield for the collection of the plasma.

[0059] In this case, the discharging speed of the plasma from the blood collecting bag 1 is preferably set in the rate under which no eddy that is likely to disturb the interface between the respective separated components is caused in the blood-collecting bag 1 and the time required for the collection of the plasma can be shortened as much as possible. The control of the discharging speed of the plasma can be conducted, for example, by controlling the pressure of the actuating fluid to be supplied to the cuff 50.

[0060] It is possible to use a sucking means (not shown) together with the pressing means for pressing the blood collecting bag 1. In this case, since the quantity of plasma discharged per unit time can be increased while keeping the high yield, it is possible to shorten the time required to collect the separated components.

[0061] Fig. 5 is a cross-sectional view showing one example of the sucking means. The sucking means 90 shown in the drawing comprises a vacuum chamber 91, a vacuum pump 92, a pipe 93 connected between the vacuum chamber

91 and the vacuum pump 92. On the middle portion of the pipe 93, there is formed a branch pipe 94, on which a valve 95 is provided.

[0062] The plasma bag 10 which is a container for collecting the separated plasma is adapted to be placed in the vacuum chamber 91. The tube 23 connected to the plasma bag 10 passes through a wall portion of the vacuum chamber 91 by means of a seal member. With this structure, the vacuum chamber 91 can be kept air-tight.

[0063] With valve 95 closed, when the vacuum pump 92 is actuated, the air in the vacuum chamber 91 is discharged through the pipe 93, and therefore the inner pressure of the vacuum chamber 91, that is, the atmosphere around the plasma bag 10 is reduced to be a negative pressure. Due to this reduced pressure, the plasma is sucked into the plasma bag 10. In this case, it is preferable to maintain the inner pressure of the vacuum chamber 91 to a constant value or within a predetermined value during the sucking operation. The adjustment of the inner pressure of the vacuum chamber 91 is made for example by on-off operation of the vacuum pump 92, open-close operation of the valve 95, or adjustment of the opening rate of the valve 95. The reduced inner pressure of the vacuum chamber 91 during the sucking operation is for example set to the rate between -0.133 bar (-100 mmHg) and -0.399 bar (-300 mmHg) (here, 0 mmHg is equal to the atmospheric pressure).

[0064] As an alternative for the sucking means, it is possible to provide a roller pump provided on the midway of the tube 14 connected to the blood collecting bag 1. The roller pump is adapted to squeeze the tube 14 so as to transfer the liquid within the tube to the side of the plasma bag 10.

[0065] In these cases, it is preferable that the quantity of air to be sucked is set to such an extent that a rising in the inner pressure of the blood collecting bag 1 by the pressing means is not reduced markedly.

[0066] Further, after almost all the quantity of the plasma is discharged from the blood collecting bag 1, the tube 21 is closed by a clamp or a solenoid pinch valve, while the tube 26 is opened. When the blood collecting bag 1 is further pressed under this condition in the same way as above, the intermediate buffy coat layer can be discharged. The buffy coat layer is fed into the buffy coat bag 27 through the tubes 14 and 26, respectively.

[0067] Upon discharging the buffy coat layer from the blood collecting bag 1, it is also possible to additionally provide such a sucking means as described above. In this case, the buffy coat bag 27 which is a container for collecting the buffy coat layer is placed inside the vacuum chamber 91 of the sucking means 90.

[0068] In this embodiment, it is possible to provide an optical sensor 80 at the midway of the tube 14 to detect the fact that almost all the quantity of the plasma in the blood collecting bag 1 has been discharged. This optical sensor 80 is constituted by light emitting element and light receiving element which are disposed on the opposite sides of the tube 14. When almost all the quantity of the plasma has been discharged from the blood collecting bag 1 and therefore the liquid flowing within the tube 14 is changed from the plasma to the buffy coat, the transmissibility of the light emitted from the light emitting element is reduced and therefore the amount of the light received by the light receiving element is also reduced. At this point of time, the fact that almost all the quantity of the plasma in the blood collecting bag 1 has been discharged is detected.

[0069] When the fact that almost all the quantity of the plasma is discharged from the blood collecting bag 1 is detected by the way described above, the transfer of the plasma to the plasma bag 10 is stopped by closing the tube 21 by clamping the midway of the tube 21 by a clamp or by actuating the solenoid pinch valve through the control performed by a micro computer (not shown). Thereafter, by opening the fluid path to the buffy coat bag 27, fluid communication is changed so as to allow the buffy coat is fed or transferred into the buffy coat bag 27. In this state, the actuating fluid from the fluid supply means 51 to the cuff 50 is supplied continuously, so that the buffy coat is being discharged from the blood collecting bag 1.

[0070] The weight of the buffy coat bag 27 is kept monitored by a weight sensor such as a load cell (not shown). When the weight sensor detects the fact that the weight of the buffy coat stored in the buffy coat bag 27 reaches a predetermined value, the transfer of the buffy coat from the blood collecting bag 1 to the buffy coat bag 27 is stopped.

[0071] The discharge of the buffy coat from the blood collecting bag 1 is stopped by stopping the supply of the actuating fluid from the fluid supply means 51 to the cuff 50 or closing the tube 14 or 26 with a clamp or the like. The supply of the actuating fluid is stopped by closing the valve 56 or stopping the operation of the air supply source 55.

[0072] As stated in the foregoing, if the apparatus is constituted such that the discharge of the blood component from the blood collecting bag 1 can be stopped or changed so as to direct toward a different bag in good timing based on the detected information by the optical sensor 80 or the weight sensor, the yield for the component is further improved.

[0073] Fig. 4 is a perspective view showing a separated component transferring apparatus according to the present invention. In the apparatus 32 shown in Fig. 4, at least one part of the centrifugal container 40, that is, the side portion 42 thereof is formed of a soft material to provide a soft material part 48. When this soft material part 48 is pressed by a movable push member 57, the soft material part 48 is deformed so as to project in the inner direction of the centrifugal container 40.

[0074] The movable push member 57 is composed of a movable piston 58 and a head 59 fixed to an end of the piston 58, and driving means (not shown) are provided for driving the movable push member 57.

- [0075] The pressing means of this embodiment is composed of a pair of opposing push members 57 and the driving means (not shown) for driving the push members 57 both roughly in the horizontal direction. When two opposing pistons 58 are moved in the direction that both the heads 59 approach each other, the soft material part 48 of the centrifugal container 40 is pressed by the two heads 59 and then deformed in the inner direction of the centrifugal container 40.
- 5 As a result, the blood collecting bag 1 placed in the centrifugal container 40 is also compressed, so that the plasma in the upper layer is discharged from the blood collecting bag 1.
- [0076] In this embodiment, it should be noted that the pressing means is constructed such that one of the push members 57 is not movable and only the other push member 57 is movable so as to press the soft material part 48 of the centrifugal container 40.
- 10 [0077] The soft material part 48 of the centrifugal container 40 is formed of a soft synthetic resin like a polyester such as soft polyvinyl chloride, polyethylene, polypropylene, polyethyleneterephthalate, or a combination of these materials. Further, the soft material part 48 can be formed at a bottom portion 41 of the centrifugal container 40, without being limited to only the side portion 42 thereof as described in the drawing.
- [0078] As one of the example of the centrifugal container 40 used in the apparatus 32 of this embodiment, a portion
- 15 excepting a frame portion 401, that is, a cylindrical portion thereof can be formed of the soft material as described above.
- [0079] Further, any types of the pressing means such as rollers, fastening members, etc. can be used instead of the pair of the heads 59 as described above, as far as the soft material part 48 of the centrifugal container 40 can be deformed inwardly.
- [0080] In accordance with the separated component transferring apparatus 32 as shown in Fig. 4, there are advantages such as follows. Namely, the blood collecting bag 1 can be pressed from the front and rear side thereof, the interfaces between the respective component layers are kept more stationary when the separated component is being discharged, thus leading to improvement of the yield for the blood component. Further, since the driving means of this embodiment is formed from the mechanism which merely perform reciprocal motion, the mechanism can be constructed with simple structure.
- 20 [0081] Further, it should be noted that the sucking means described with reference to Fig. 5 can also be applied to the apparatus according to the present invention.
- [0082] Furthermore, it should be also noted that this invention can be applied to the case other than the transfer of the centrifugally separated blood component. For example, this invention can be used for collecting or taking out a layer including the effective component of eupyrene cells from a bone marrow fluid, for instance.
- 25 [0083] Hereinafter, practical experiments will be described hereinbelow.

[Experiment 1]

- [0084] A quadruple bag system (four-connected bags) as shown in Fig. 1 was manufactured as follows: a blood
- 35 collecting bag (400 ml in volume), a PC bag (60 ml in volume), a plasma bag (300 ml in volume) and a buffy coat bag (60 ml in volume) are all manufactured by use of a soft polyvinyl chloride sheet with a thickness of 0.39 mm. Further, these bags are connected through soft polyvinyl chloride tubes as shown in Fig. 1.
- [0085] On the other hand, a centrifugal container 40 as shown in Fig. 2 was manufactured by use of polypropylene. The wall thickness of the container 40 was 2.5 mm, the inner diameter thereof was 95 mm, and the maximum depth
- 40 thereof was 130 mm.
- [0086] As the pressing means for pressing the blood collecting bag, an annular cuff (width (W) = 80 mm) was formed of soft polyvinyl chloride so as to be expandable and contractible. The annular cuff was placed on an inner surface of the centrifugal container 40 at a position 30 mm away from the bottom of the container 40, and further connected to an air supplying source (i.e. air compressor) through an air feeding tube.
- 45 [0087] A whole blood was collected in the blood collecting bag of the above-mentioned connected bags, and the blood collecting bag was placed in the centrifugal container under the condition that the annular cuff was contracted together with other bags. Then, the centrifugal container was set to a centrifugal separator (MODEL: DPR-6000 MODEL made by IEC Corp.), and centrifuged under 420rpm for 5 minutes.
- [0088] Thereafter, the centrifugal container 40 was removed from the centrifugal separator, and further the bags
- 50 other than the blood collecting bag were also removed from the centrifugal container 40. The connecting member 15 was then broken to effect the fluid communication therethrough, and further the tube 26 is closed by a clamp. Successively, the compressor was actuated, and compressed air of 0.6 Kg/cm² is fed into the annular cuff to expand the annular cuff gradually, so that the blood collecting bag in the centrifugal container was pressed to discharge the plasma in the upper layer through the tube 14. The discharged plasma was then transferred and collected into the plasma bag
- 55 10.

[Experiment 2]

[0089] In this experiment, the connected bags, the centrifugal container and the pressing means which are all the same as with those of the Experiment 1 were used, by which the whole blood was centrifuged under the same conditions as those in Experiment 1.

[0090] After the centrifugal separation, the blood collecting bag accommodated in the centrifugal container was pressed in the same way as in Experiment 1, while the plasma bag 10 was placed in a pressure reducing chamber kept at a vacuum of - 0.239 bar (- 180 mmHg), to suck the plasma in the upper layer in the blood collecting bag in order to transfer and collect it into the plasma bag 10 through the tube 14.

[Comparative Experiment]

[0091] The connected bags and the centrifugal container which are the same as those used in the Experiment 1 were used, but no pushing means was used. Further, the whole blood was centrifuged under the same conditions as those in Experiment 1.

[0092] Thereafter, the connected bags were removed from the centrifugal container 40, and only the blood collecting bag was set between a pair of plates of a separator stand by hanging a small hole formed in the blood collecting bag on a hook of the separator stand. Then, the blood collecting bag was sandwiched between the two plates of the separator stand for pressurization, to discharge the plasma in the upper layer and transfer and collect it to the plasma bag 10.

[0093] The quantities of the blood and the collected plasma, and the time-required to collect the plasma were measured. Table 1 below lists these measured results.

TABLE 1

	QUANTITY OF BLOOD [g]	QUANTITY OF PLASMA [g]	TIME REQUIRED TO COLLECT PLASMA [sec]
EXPRMT 1	426. 2	318. 4	36. 0
EXPRMT 2	428. 3	320. 2	27. 5
COMPAR	424. 2	314. 0	97. 4

[0094] As indicated in Table 1, the yield for plasma collection (purity) is high in Experiments 1 and 2, as compared with Comparative Experiment. In particular, in the case of Experiment 2 in which the plasma is collected under the condition that the suction is performed in addition to the pressing motion, the time required to collect plasma can be shortened.

[0095] In addition, in the case of Experiment 1 or 2, even when the pressing means for pressing the blood collecting bag was replaced with another means as shown in Fig. 4 similar results were obtained.

[0096] In this connection, as the method of discharging each of the separated components without removing the blood collecting bag from the centrifugal container, it may be possible to use only the sucking method as described above which sucks the supernatant plasma layer through a tube connected to the upper end portion of the blood collecting bag and discharge it, without using the pressing means.

[0097] However, it has been found that the above-mentioned method is not appropriate due to the following reasons. That is to say, where the above-mentioned method is adopted alone, the inner pressure of the blood collecting bag is reduced into a vacuum pressure. For this reason, when the plasma layer is being discharged with the advance of pump suction, the two opposing inner surfaces of the bag are brought into contact with each other in particular at the upper portion of the bag. In addition, since gaps (channels) are produced between the inner surfaces of the bag so as to extend from the upper end discharge port 5 (outlet) of the bag to the vicinity of the fused edge portions of the bag, the separated component lower than the plasma layer, in particular the lowermost erythrocyte layer is sucked upwardly along the produced gaps. As a result, the erythrocyte is likely to be mixed with the plasma, thus causing another problem in that the yield for plasma collection is lowered.

[0098] Further, when the lower buffy coat layer is required to be collected after the plasma layer has been collected, the quantity of liquid within the blood collecting bag is further reduced, so that the two opposing inner surfaces of the bag are brought into further tight contact with each other. Therefore, a great quantity of erythrocyte is likely to be discharged through the gaps formed between the inner surfaces of the bag. In other words, the collection of the buffy coat layer must be stopped before the erythrocyte is mixed. This means that a quantity of the buffy coat layer remains within the blood collecting bag. As a result, it is difficult to separate the buffy coat layer from the erythrocyte layer effectively.

[0099] In contrast with this, if the suction motion for the separated component by the sucking means is taken place in addition to the pressing motion for the blood collecting bag 1, the two opposing inner surfaces of the bag are not brought into contact with each other at the upper portion of the bag and further any channel is not be produced between the opposite two sheets, so that it becomes possible to transfer and collect the separated component with high yield.

5 [0100] As described above, in the separated component transferring apparatus and method according to the present invention, it is possible to improve the yield for the blood component obtained by the centrifugal separation, and further to reduce the time and labor required for separation.

10 Claims

1. An apparatus (32) for transferring a separated component in a liquid contained in a flexible bag (1) in airtight condition comprising :

15 a deformable centrifugal container (40) for removably accommodating the flexible bag (1) therein; pressing means provided outside said centrifugal container (40) for pressing the flexible bag (1) accommodated in said centrifugal container (40) to increase the inner pressure of said flexible bag (1) while the bag (1) is released from the airtight condition, so that a predetermined separated component can be discharged from the bag (1),

20 characterized in that said centrifugal container (40) includes a frame portion (401) and a soft material part (48); said pressing means comprises a pair of opposing push members (57), at least one of which is movable toward the other by a reciprocal motion driving mechanism, said push members (57) being adapted for pressing the soft material part of said centrifugal container (40) which is therefore deformed, so as to project in the inner direction of the centrifugal container, thus discharging the separated component of the liquid contained in the flexible bag.

2. The apparatus of claim 1, wherein each of said pushing members includes a roller for pushing the soft material part.

30 3. The apparatus as claimed in anyone of claims 1 to 2, wherein the apparatus further comprises sucking means (90) for sucking the separated component in the bag (1).

4. The apparatus of claim 3 which further comprises a container (10) for receiving the separated component, wherein said sucking means (90) includes means for reducing the pressure of an atmosphere in which said separated component receiving container (10) is placed.

35 5. A method of transferring a separated component in a liquid contained in a flexible bag (1) under airtight condition, which comprises the steps of:

40 accommodating the flexible bag in which the liquid is contained under airtight condition into a centrifugal container (40) which is removably attached to a centrifugal separator, said centrifugal container having a soft material part formed in at least one portion thereof; centrifuging the flexible bag (1) accommodated in the centrifugal container (40) by the centrifugal separator to separate the liquid in the flexible bag (1) into the components thereof; removing said centrifugal container (40) from the centrifugal separator together with the flexible bag contained therein and then fixing the centrifugal container to a fixing means; and pressing the soft material part of the centrifugal container (40) from the outside of said centrifugal container (40) using a movable push member (57) provided outside of the container (40) for pushing said soft material part of said centrifugal container (40) to increase inner pressure of the bag (1) while releasing the airtight condition, thereby taking out a predetermined component in the liquid which has been separated by the centrifugation outside the flexible bag (1).

6. The method as claimed in claim 5, further comprising the step of sucking the separated component in the flexible bag (1) while pressing the flexible bag (1).

55 7. The method as claimed in claim 5, further comprising the step of sucking the separated component in the flexible bag (1) by reducing the pressure of an atmosphere in which a separated component receiving container (10) is put, while pressing the flexible bag (1).

Patentansprüche

1. Vorrichtung (32) zum Übertragen eines getrennten Bestandteils in einer Flüssigkeit, welche in einem flexiblen Beutel (1) in luftdichtem Zustand enthalten ist, umfassend:
5 einen verformbaren Zentrifugalbehälter (40) zum lösbaren Aufnehmen des flexiblen Beutels (1) darin;

 eine außen an dem Zentrifugalbehälter (40) vorgesehene Drückeinrichtung zum Drücken des in dem Zentrifugalbehälter (40) aufgenommenen flexiblen Beutels (1), so daß der Innendruck des flexiblen Beutels (1) erhöht wird, während der Beutel (1) aus dem luftdichten Zustand freigegeben wird, so daß ein vorbestimmter getrennter Bestandteil aus dem Beutel (1) abgegeben werden kann,
10 dadurch gekennzeichnet, daß der Zentrifugalbehälter (40) einen Rahmenabschnitt (401) und einen Abschnitt (48) aus weichem Material umfaßt;
15 wobei die Drückeinrichtung ein Paar gegenüberliegender Druckelemente (57) umfaßt, wobei mindestens eines davon hin zu dem anderen durch eine Reziprokbewegungs-Antriebsvorrichtung bewegbar ist, wobei die Druckelemente (57) angepaßt sind, den Abschnitt aus weichem Material des Zentrifugalbehälters (40) zu drücken, welcher dadurch verformt wird, so daß dieser in die Innenrichtung bezüglich des Zentrifugalbehälters vorsteht, wodurch der getrennte Bestandteil der in dem flexiblen Beutel enthaltenen Flüssigkeit abgegeben wird.
20 2. Vorrichtung nach Anspruch 1, wobei jedes der Druckelemente eine Rolle zum Drücken des Abschnitts aus weichem Material umfaßt.

 3. Vorrichtung nach einem der Ansprüche 1 bis 2, wobei die Vorrichtung ferner eine Saugeinrichtung (90) zum Saugen des getrennten Bestandteils in dem Beutel (1) umfaßt.
25 4. Vorrichtung nach Anspruch 3, welche ferner einen Behälter (10) zum Aufnehmen des getrennten Bestandteils umfaßt, wobei die Saugeinrichtung (90) eine Einrichtung zum Verringern des Drucks einer Atmosphäre umfaßt, in welcher der Behälter (10) zum Aufnehmen des getrennten Bestandteils angeordnet ist.
30 5. Verfahren zum Übertragen eines getrennten Bestandteils in einer in einem flexiblen Beutel (1) in luftdichtem Zustand enthaltenen Flüssigkeit, folgende Schritte umfassend:

 Aufnehmen des flexiblen Beutels, in welchem die Flüssigkeit in luftdichtem Zustand enthalten ist, in einem Zentrifugalbehälter (40), welcher abnehmbar an einer Trennzentrifuge angebracht ist, wobei der Zentrifugalbehälter einen Abschnitt aus weichem Material umfaßt, welcher in mindestens einem Abschnitt davon ausgebildet ist;
35 Zentrifugieren des in dem Zentrifugalbehälter (40) aufgenommenen flexiblen Beutels (1) durch die Trennzentrifuge, so daß die Flüssigkeit in dem flexiblen Beutel (1) in die Bestandteile davon getrennt wird;
40 Entfernen des Zentrifugalbehälters (40) von der Trennzentrifuge zusammen mit dem darin enthaltenen flexiblen Beutel und anschließendes Befestigen des Zentrifugalbehälters an einer Befestigungseinrichtung; und

45 Drücken des Abschnitts aus weichem Material des Zentrifugalbehälters (40) ausgehend von dem Äußeren des Zentrifugalbehälters (40) unter Verwendung eines beweglichen Druckelements (57), welches außen an dem Behälter (40) vorgesehen ist, zum Drücken des Abschnitts aus weichem Material des Zentrifugalbehälters (40), so daß der Innendruck des Beutels (1) erhöht wird, während der luftdichte Zustand freigegeben wird, wodurch ein vorbestimmter Bestandteil in der Flüssigkeit entnommen wird, welcher durch die Zentrifugierung außerhalb des flexiblen Beutels (1) getrennt wurde.
50 6. Verfahren nach Anspruch 5, ferner umfassend den Schritt des Saugens des getrennten Bestandteils in dem flexiblen Beutel (1), während der flexible Beutel (1) gedrückt wird.

55 7. Verfahren nach Anspruch 5, ferner umfassend den Schritt des Saugens des getrennten Bestandteils in dem flexiblen Beutel (1) durch Verringern des Drucks einer Atmosphäre, in welcher ein Behälter (10) zum Aufnehmen eines getrennten Bestandteils angeordnet wird, während der flexible Beutel (1) gedrückt wird.

Revendications

1. Appareil (32) servant à transférer un composant séparé dans un liquide contenu dans une poche souple (1) sous condition étanche à l'air comprenant :
 - un récipient centrifuge déformable (40) destiné à recevoir, de manière amovible, la poche souple (1);
 - un moyen de pressage prévu à l'extérieur dudit récipient centrifuge (40) pour presser la poche souple (1) logée dans ledit récipient centrifuge (40) pour accroître la pression interne de ladite poche souple (1) tandis que la poche (1) est libérée de la condition étanche à l'air, de sorte qu'un composant séparé prédéterminé peut être déchargé de la poche (1),
 - caractérisé en ce que ledit récipient centrifuge (40) comprend une partie cadre (401) et une partie en matériau mou (48);
 - ledit moyen de pressage comprend une paire de poussoirs opposés (57), au moins l'un d'entre eux pouvant être déplacé vers l'autre par un mécanisme d'entraînement à mouvement de va-et-vient, lesdits poussoirs (57) étant adaptés pour presser la partie en matériau mou dudit récipient centrifuge (40) qui est par conséquent déformée, afin de faire saillie vers l'intérieur du récipient centrifuge, en déchargeant de ce fait le composant séparé du liquide contenu dans la poche souple.
2. Appareil selon la revendication 1, dans lequel chacun desdits poussoirs comprend un rouleau servant à pousser la partie en matériau mou.
3. Appareil selon la revendication 1 ou 2, l'appareil comprenant en outre un moyen d'aspiration (90) servant à aspirer le composant séparé dans la poche (1).
4. Appareil selon la revendication 3 qui comprend en outre un récipient (10) destiné à recevoir le composant séparé, ledit moyen d'aspiration (90) comportant un moyen servant à réduire la pression de l'atmosphère dans laquelle est placé ledit récipient (10) de réception du composant séparé.
5. Procédé de transfert d'un composant séparé dans un liquide contenu dans une poche souple (1) sous condition étanche à l'air, qui comprend les étapes consistant à :
 - placer la poche souple contenant le liquide sous condition étanche à l'air dans un récipient centrifuge (40) qui est attaché de manière amovible à un séparateur centrifuge, ledit récipient centrifuge comportant une partie en matériau mou formée dans au moins une portion de celui-ci;
 - centrifuger la poche souple (1) logée dans le récipient centrifuge (40) au moyen du séparateur centrifuge pour séparer le liquide contenu dans la poche souple (1) en ses composants;
 - retirer ledit récipient centrifuge (40) du séparateur centrifuge en même temps que la poche souple contenue dedans puis fixer le récipient centrifuge à un moyen de fixation; et
 - presser la partie en matériau mou du récipient centrifuge (40) depuis l'extérieur dudit récipient centrifuge (40) en utilisant un poussoir mobile (57) prévu à l'extérieur du récipient (40) pour pousser ladite partie en matériau mou dudit récipient centrifuge (40) pour accroître la pression interne de la poche (1) tout en libérant la condition étanche à l'air, pour extraire de ce fait un composant prédéterminé du liquide qui a été séparé par la centrifugation hors de la poche souple (1).
6. Procédé selon la revendication 5, comprenant en outre l'étape consistant à aspirer le composant séparé dans la poche souple (1) tout en pressant la poche souple (1).
7. Procédé selon la revendication 5, comprenant en outre l'étape consistant à aspirer le composant séparé dans la poche souple (1) en réduisant la pression de l'atmosphère dans laquelle est placé un récipient (10) de réception de composant séparé, tout en pressant la poche souple (1).

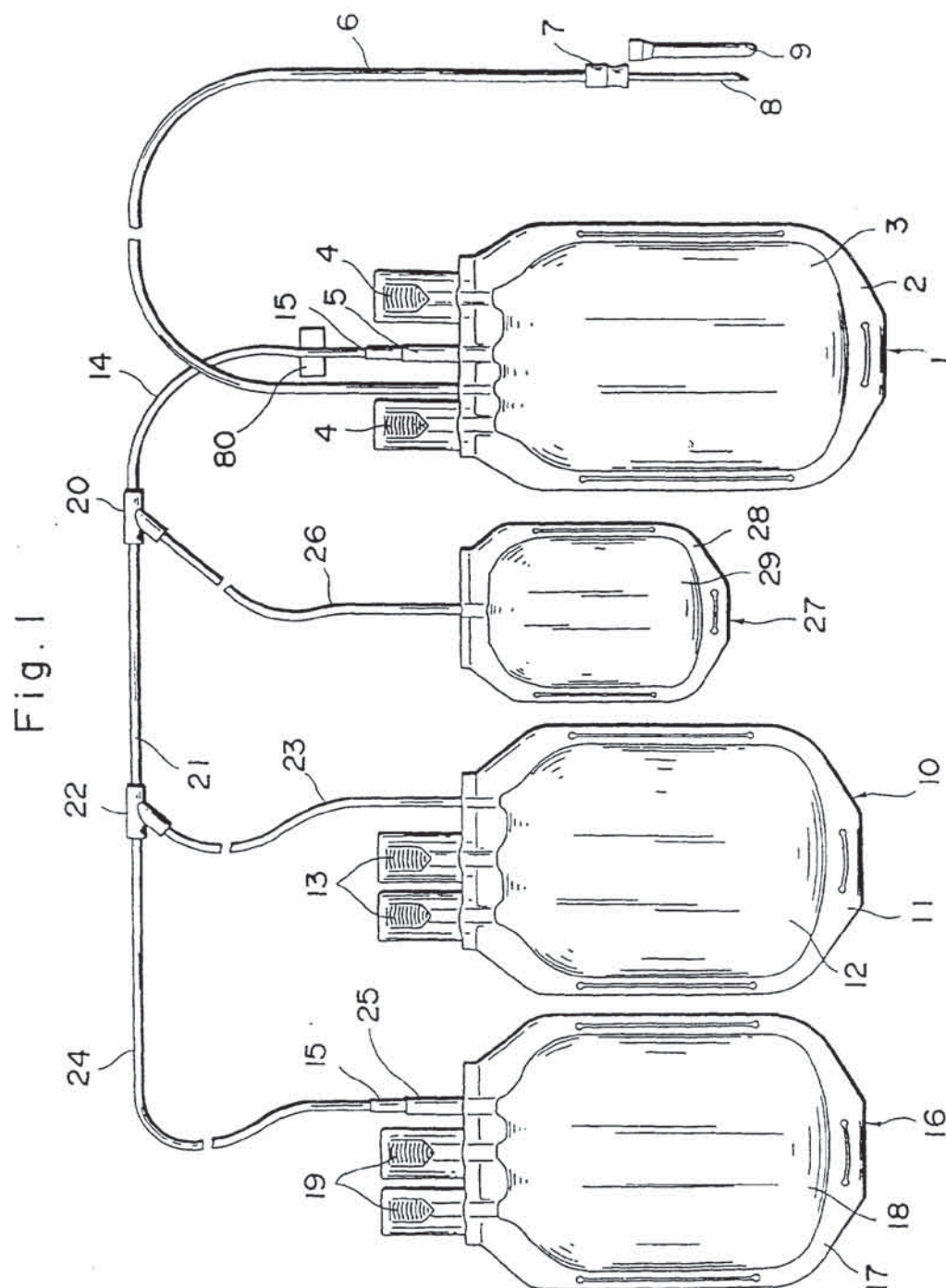


Fig. 2

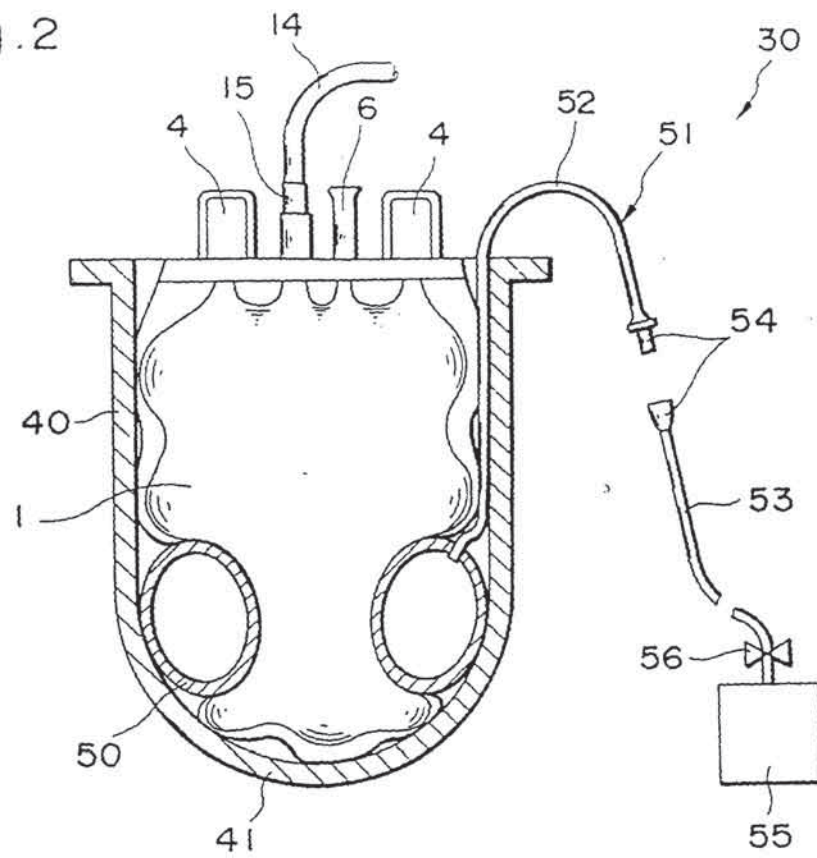


Fig. 3

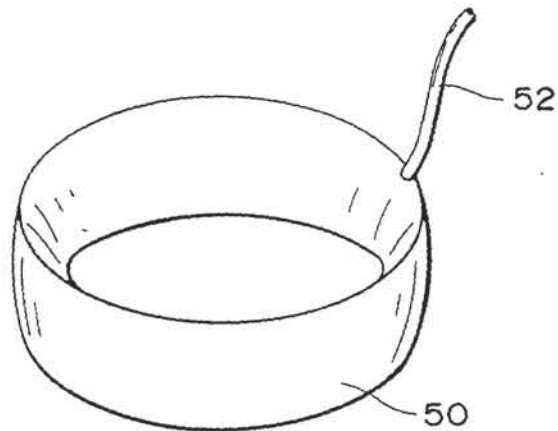


Fig. 4

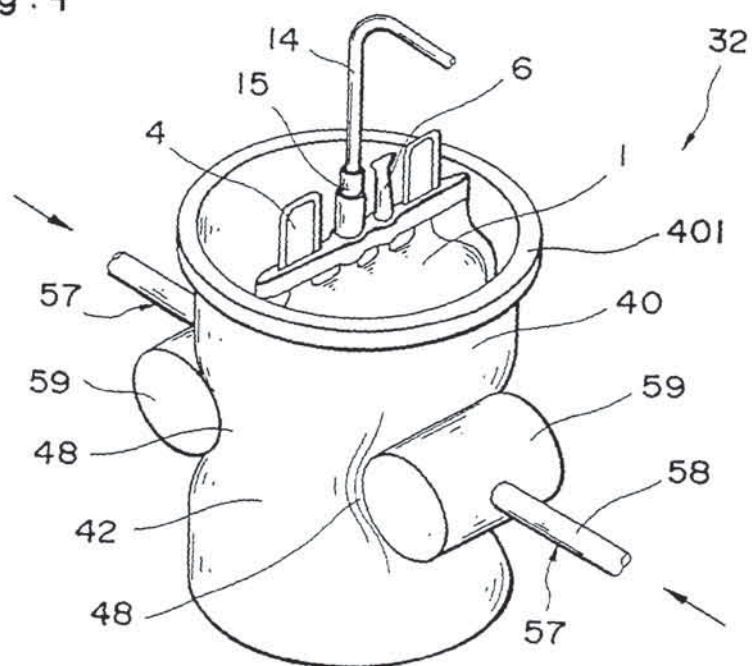
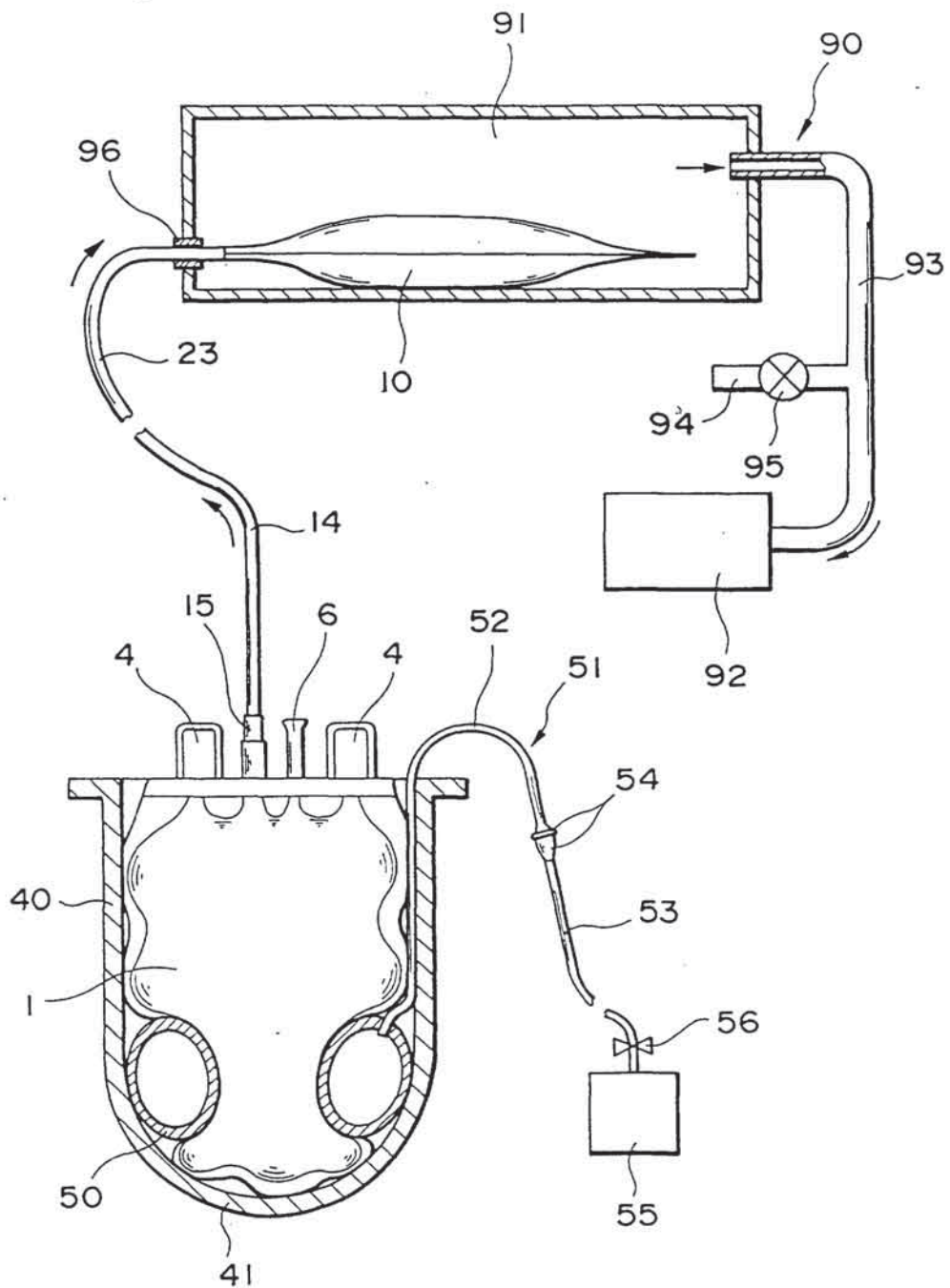


Fig. 5





Espacenet

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Optimized blood component collection system

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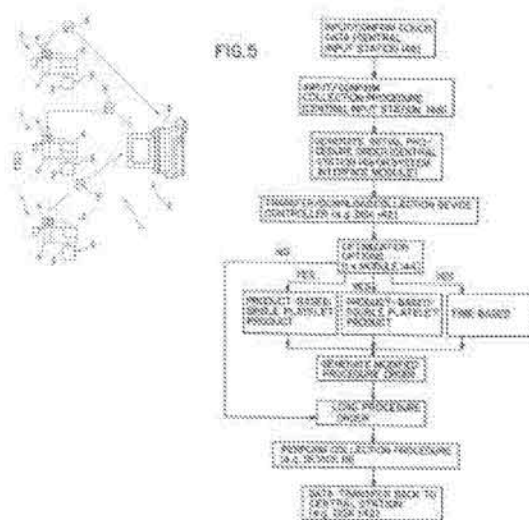
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Abstract of EP0654277 (A1)

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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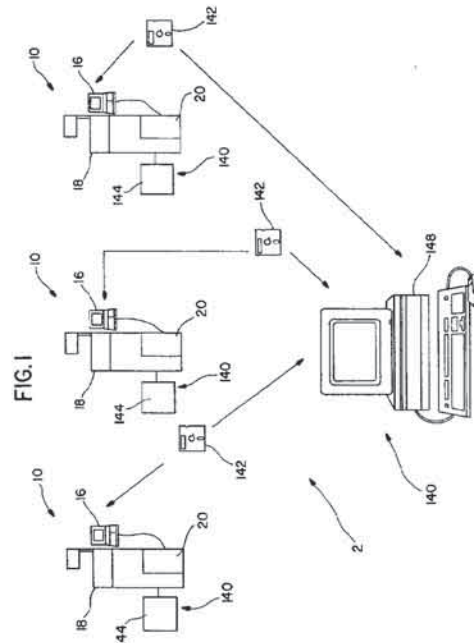
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(54) **Blood component collection system with optimizer.**

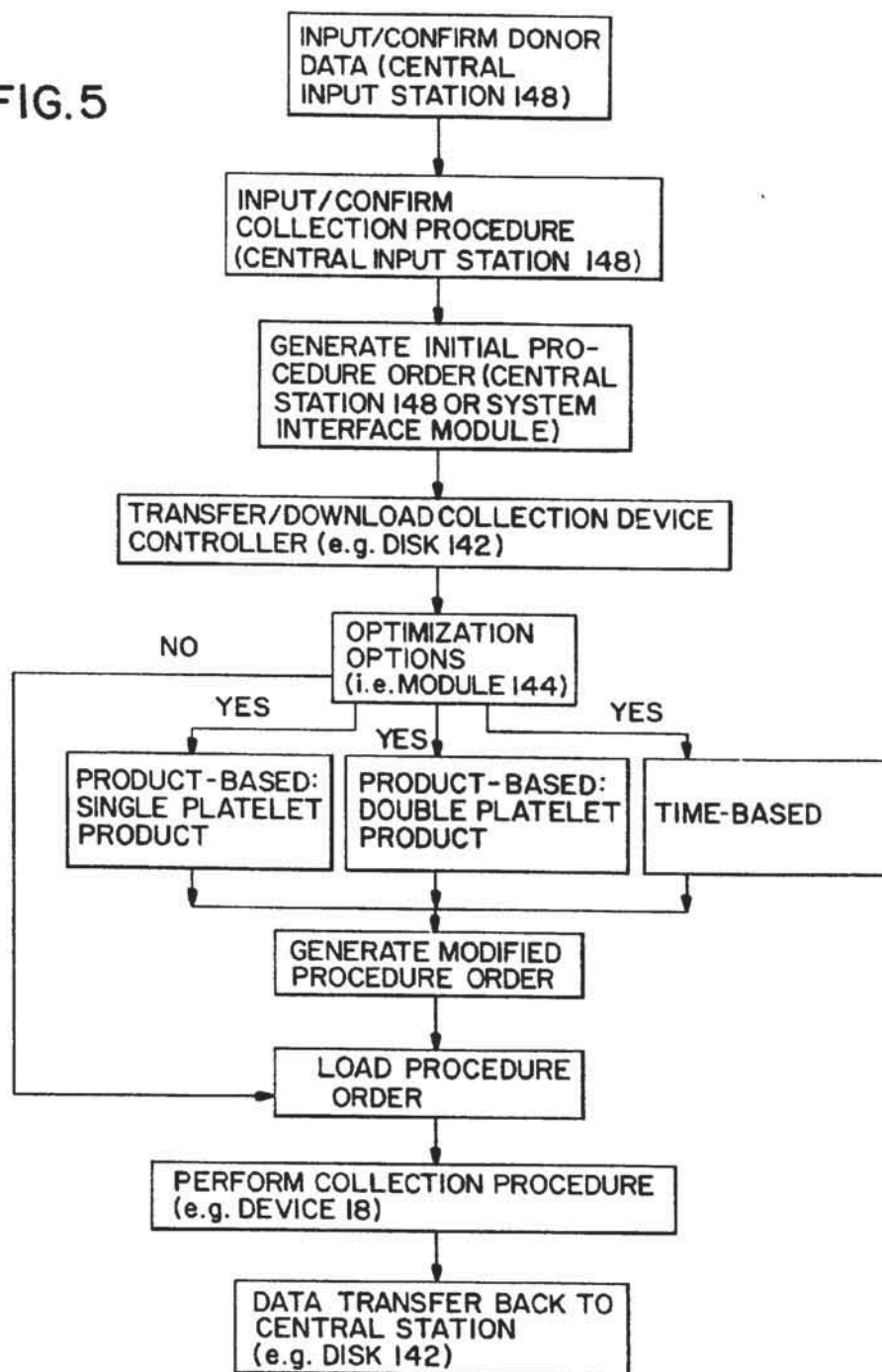
(57) A blood component collection system with optimization capabilities. In one embodiment, process parameters are derived from an input/configured predetermined blood component yield and which is based upon the maximization of at least one process parameter. Thereafter, the blood component collection 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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FIG.5



Field of the Invention

The present invention generally relates to the field of blood component collection systems and, more particularly, to providing management capabilities by incorporating optimization principles into such systems.

Background of the Invention

The utilization of blood taken from donors and infused into recipients is well known for purposes of treating medical emergencies and other conditions. More recently, selected blood components have been separated and collected from blood for subsequent infusion into recipients requiring blood component therapy. The primary blood components include platelets, red blood cells, white blood cells, and plasma.

In order to collect blood components, blood is removed from a donor by a needle assembly or other blood access device and is thereafter processed utilizing centrifugation or other appropriate separation techniques to isolate and collect the desired components. This procedure is carried out most effectively in an on-line process wherein blood is removed from a donor, processed through a disposable extracorporeal circuit to obtain the desired components, and thereafter returned to the donor. One blood component collection system which provides for this type of blood component collection procedure is the COBE Spectra™ which is commercially available from the assignee of the present application.

The yield of a particular collection of blood components is an important factor. For instance, presently in the United States a yield must be associated with a collection of blood components in order to be a useful blood component product. COBE Spectra™ presently accommodates for this requirement by processing certain donor biological data such as height, weight, sex, and hematocrit, preconfigured/operator-input data such as the total procedure time, and system-related data such as the type of collection procedure (e.g., single or double needle) and collection efficiency to generate certain process parameters such as the inlet flow to COBE Spectra™ (a combined flow of whole blood from the donor plus typically a flow of anticoagulant) and a predicted blood component yield as well.

An additional consideration presently in the United States relating to blood component yield is that it is determinative of the product classification. With regard to platelets, presently a single platelet product is considered to be a collection of 3×10^{11} platelets and a double platelet product is considered to be a collection of 6×10^{11} platelets. If the collection is between 3×10^{11} and 6×10^{11} platelets it is still considered to be a single platelet product. This classification as a single or double platelet product is relevant to blood component collection facilities (e.g., blood banks/centers) since a double platelet product has a higher selling price associated therewith than a single platelet product and also typically benefits more patients. The yield of a particular collection of blood components may also be a relevant consideration for certain therapeutic treatments.

Other important considerations relating to blood component collection systems relate to the donor. For instance, blood component collection facilities are not only experiencing an increase in the overall demand for blood components, but the demand now typically varies between the blood component types as well. Moreover, not only is the supply of donors unfortunately in many cases inadequate, but donor time constraints are becoming more prevalent. Furthermore, obtainable yields from a given donor may vary from one blood component to another (i.e., one donor may be a better platelet source than a red blood cell source).

Based upon the foregoing, the management of the various aspects of blood component collection systems is becoming increasingly important.

Summary of the Invention

The present invention relates in one application to a blood component collection system which provides management capabilities by incorporating optimization principles. Generally and in this case, the present invention utilizes principles of optimization in terms of the donor, blood component collection system, and/or desired blood component product. For instance, the present invention may be adapted to provide for the collection of a predetermined quantity of at least one predetermined blood component (or more typically the collection of such blood components within a particular range) in a "minimum" amount of time and/or for the collection of a "maximum" quantity of at least one predetermined blood component in a fixed amount of time, all based upon certain process conditions. Moreover, the present invention may be adapted to provide for blood component inventory control by basing donor selection and/or collection procedure selection in terms of the type of blood component to be collected on blood component demand and/or existing inventory. In addition, the present invention may be adapted to provide for further donor management by collecting that blood component type(s) from the donor which provides a maximum yield.

In one aspect, the present invention may be characterized as a blood component collection system having

blood component product-based optimization-like capabilities. One embodiment comprises a method for collecting at least one predetermined blood component (e.g., a collection of platelets, red blood cells) from a source of whole blood using a blood component collection system which includes a blood component collection device and which utilizes a collection procedure. More particularly, a desired yield of the predetermined blood component(s) is identified (such yield including a single yield or range of yields) and biological data relating to the source is provided to the blood component collection system. Moreover, a value or magnitude is associated with each of the various process parameters used in the collection procedure. A magnitude of at least one of these process parameters is derived from the biological data and the desired yield. These magnitudes, including all magnitudes of process parameters derived from the desired yield, are input to the blood component collection system. Thereafter, the collection procedure is performed with the blood component collection device and with the input process parameters to collect the desired yield of at least one predetermined blood component(s) from the whole blood source.

In another aspect, the present invention may be characterized as a blood component collection system having time-based optimization-like capabilities. One embodiment of such is a method for collecting at least one predetermined blood component from a source of whole blood using a blood component collection system which includes a blood component collection device and which utilizes a collection procedure. A flow of the whole blood from the source, as well as a flow of anticoagulant, is provided to the blood component collection system and collectively constitutes an inlet flow. In the method, a total procedure time for the collection procedure is identified (e.g., based upon donor time availability). One potential inlet flow to the system is derived from at least this identified total procedure time. Another potential inlet flow to the system is derived which provides an "optimum" collection efficiency and is effectively the apex of a bell-shaped yield/inlet flow curve (i.e., the inlet flow which provides the maximum blood component yield). Consequently, if the total procedure time-based inlet flow is greater than the maximum yield-based inlet flow, and thus is an inlet flow on the decreasing slope portion of the yield/inlet flow curve, the maximum yield-based inlet flow magnitude is used in the performance of the collection procedure. However, if the total procedure time-based inlet flow is less than the maximum yield-based inlet flow, and thus is an inlet flow on the increasing slope portion of the yield/inlet flow curve, the total procedure time-based inlet flow magnitude is used in the performance of the collection procedure.

The subject invention provides greater efficiency in blood component collection and management. For example, the present invention can be used to compare blood bank/center component inventories with projected needs, and adjust collection procedures to meet these needs. Further, the present invention provides benefits to donors. In particular, certain information relating to the donor's physical and medical characteristics may be stored in the system and utilized during subsequent visits by the donor to derive magnitudes for the various process control parameters. For example, for a donor with an anticoagulant intolerance, the magnitude of the anticoagulant infusion rate may be set so as to not exceed the donor's tolerance.

Brief Description of the Drawings

Fig. 1 is a schematic representation of a blood component collection system in accordance with principles of the present invention;
 Fig. 2 is a schematic representation of one embodiment of a blood component separation assembly which utilizes a dual needle configuration and which may be incorporated into the blood component collection system of Fig. 1;
 Fig. 3 is a schematic representation of one embodiment of a blood component separation assembly which utilizes a single needle configuration and which may be incorporated into the blood component collection system of Fig. 1;
 Figs. 4a and 4b are perspective and top views, respectively, of one type of a disposable processing channel used in the blood component collection device of Figs. 2 and 3;
 Fig. 5 is a flow chart of a blood component collection procedure utilizing principles of the present invention;
 Fig. 6 is a flow chart of one optimization model for deriving at least one optimal process parameter from a desired blood component yield or from a total procedure time in accordance with principles of the present invention;
 Fig. 7 is a flow chart of one optimization model for deriving at least one optimal process parameter from a desired blood component yield or from a total procedure time in accordance with principles of the present invention; and
 Fig. 8 is a yield/inlet flow curve.

Detailed Description

The present invention will be described with reference to the accompanying drawings which assist in illustrating the pertinent features thereof. One application of the present invention is embodied within a blood component collection system which separates, removes, and collects at least one type of blood component (e.g., platelets, red blood cells, white blood cells, plasma) from a source of whole blood (e.g., a donor) through utilization of a collection procedure derived from a typically site-configured/operator-input goal(s) and the "maximization" of at least one process control parameter. This type of derivation is referred to herein as an "optimization process" and the derived process control parameters are referred to herein as "optimal values."

Referring to Fig. 1, the present invention is embodied within the blood component collection system 2 which would typically be implemented at a blood bank/center (not shown). The system 2 includes an optimization assembly 140 (e.g., appropriate microprocessor(s) such as an IBM compatible PC and software) and at least one blood component collection assembly 10 (three shown) which each includes a blood component collection device 18 as an integral part thereof. As will be discussed below, the optimization assembly 140 (or at least a portion thereof) and associated blood component collection assemblies 10 are preferably appropriately interfaced but may be completely separate as well. That is, optimization procedures in accordance with principles of the present invention are not limited to being performed at any particular location.

Generally, the optimization assembly 140 includes a central input station 148 (e.g., an appropriate microprocessor such as an IBM compatible PC and attendant software) for inputting and maintaining donor-related data, and also typically for preparing an initial procedure order (the process control parameters derived from the donor-related data and other considerations) for a given donor. These procedures may also be performed at the appropriate operator interface module 16 as well such that a central input station 148 is not required. However, where a central input station 148 is used, this donor-related data and/or initial procedure order is transferred to one of the operator interface modules 16 (e.g., an appropriate microprocessor such as an IBM compatible microprocessor and interfaced with the device 18 via an RS232 or other lab specific interface, including the Digital Equipment Corp. PCP 30, which is also known as the DEC pc 325SL and which utilizes a 386 processor) which are located at each blood component collection device 18 and which as noted preferably interfaces with an optimizer module 144 (part of the optimizing assembly 140) for providing the operator with one or more optimization options. These optimization options provide a different set of process control parameters than the initial procedure order based upon one or more specified conditions/goals (e.g., input blood component yield, input procedure time) and a particular derivation for the process control parameters. If an optimization option is selected the procedure order is modified to reflect the results of the optimization, the collection procedure is initialized/reinitialized (i.e., the collection procedure would be reinitialized in the case of an optimization which is performed after the collection procedure has been initiated and such is referenced to as a downstream optimization) with the results of the optimization, and the collection procedure is thereafter performed with the blood component collection device 18.

Various embodiments of blood component collection assemblies may incorporate principles of the present invention. However, as noted above on-line techniques have been determined to be quite effective and thus the present invention is being described with reference to such techniques. One embodiment of an on-line technique and attendant apparatus which may be incorporated into the blood component collection system 2 of Fig. 1 is illustrated in Fig. 2. The blood component collection assembly 10' utilizes an on-line technique in that a donor 14 (e.g., the whole blood source) is directly integrated with the system 10' by fluid interconnection with the blood component collection device 18. This particular on-line technique is more particularly referred to as a dual needle configuration since there are two fluid interconnections between the donor 14 and the blood component collection device 18.

The donor 14 is fluidly connected to the blood component collection device 18 by an inlet line 22 and appropriate needle assembly (not shown). Whole blood from the donor 14 is thus continuously provided to the blood component collection device 18 through the inlet line 22 for separation of the desired blood component(s) therefrom, utilizing an inlet pump 26 (e.g., a peristaltic pump) to maintain this flow if desired/required. Prior to the blood of the donor 14 entering the blood component collection device 18, anticoagulant from an anticoagulant ("AC") container 30 may be provided to the whole blood, utilizing an AC pump 32 (e.g., a peristaltic pump) to maintain this particular flow if desired/required. Consequently, the inlet flow to the blood component collection device 18 typically includes both a flow of whole blood from the donor 14 and a flow of anticoagulant from the AC container 30.

The blood component collection device 18 separates the whole blood provided on line by the donor 14 into three primary constituents, namely platelets, a combination of red and white blood cells ("RBC/WBC"), and plasma. The platelets collected from the blood component device 18 are directed through a platelet collect line(s) 34 to one or more platelet collect bags 38 via a collect pump 36. The plasma and RBC/WBC are provided

back to the donor 14 through a plasma line 42 and RBC/WBC line 46, respectively, both of which are interconnected with a second needle assembly (not shown) on the donor 14 via a donor return line 50. The plasma line 42 includes a plasma pump 40 (e.g., a peristaltic pump) to maintain the flow of plasma if desired/required. Although plasma may be provided back to the donor 14 in the above manner, it may be desirable to collect the separated plasma in some cases. In this regard, a plasma collect bag 54 may be provided and interconnected with the plasma line 42 (interconnection shown in phantom). In this case, appropriate valving 56 may be incorporated in the plasma line 42.

The blood component separation assembly 10" of Fig. 3 is similar to that of the dual needle configuration of Fig. 2 except that a single needle assembly (not shown) integrates the donor 14 within the blood component collection assembly 10". Consequently, similar components are similarly identified where appropriate. With regard to the single needle configuration of Fig. 3, whole blood of the donor 14 initially flows through a donor access line 62 and into an inlet line 66 which is fluidly connected with the blood component collection device 18 such that the platelets are separated and collected in the above-described manner. The plasma and RBC from the blood component collection device 18 flow through the plasma and RBC/WBC lines 42, 46, respectively, both of which are fluidly interconnected with a return flow controller 74. As above, however, the plasma may alternatively be directed to a plasma collect bag 54. In the event that plasma is not collected, the RBC/WBC and plasma are provided back to the donor 14 through the return flow controller 74 via a donor return line 70 which is interconnected with the donor access line 62. As can be appreciated, since only a single line is directly connected to the donor 14, namely the donor access line 62, blood is either being removed from or provided back to the donor 14 such that the procedure is effectively two-step versus continuous in relation to the donor 14.

The blood component collection device 18 used in the blood component collection assembly 10 is more particularly illustrated in Figs. 4A-B. This device 18 is the subject of U.S. Patent No. 4,387,848 to Kellog et al., entitled "CENTRIFUGE ASSEMBLY", issued June 14, 1983, and the disclosure of which is incorporated by reference in its entirety herein. This device 18 is also commercially available from the assignee of the present application as such is incorporated in COBE Spectra™.

Referring to Figs. 4A-B, the blood component collection device 18 utilizes a processing channel 80 to provide the desired disposable extracorporeal circuit. The channel 80 is positioned within a groove formed directly or indirectly in a centrifuge rotor (not shown) (e.g., a separate filler may receive the channel 80 and be attached to the centrifuge rotor), and is illustrated in the shape which it assumes during processing (i.e., during flow of blood therethrough). All subsequent references herein to the structural and operational characteristics of the blood component collection device 18 will be to the processing channel 80 in the illustrated condition.

The processing channel 80 generally includes a first stage 84 for collectively separating red blood cells ("RBC") and white blood cells ("WBC") from platelet-rich plasma, a second stage 92 for thereafter separating platelets from the platelet-rich plasma, a transition portion 88 defining a separation between the first stage 84 and second stage 92, and a control chamber 124 for maintaining a proper interface between the first stage 84 and second stage 92, namely the position of the interface between the RBC/WBC and platelet-rich plasma within the transition portion 88.

The first stage 84 extends from one end of the control chamber 124 along an arcuate path generally inwardly, toward the axis 132 about which the processing channel 80 rotates via the centrifuge rotor, until terminating at the transition portion 88. Specifically, the end of the first stage 84 adjacent the control chamber 124 is positioned at a greater radial distance from the axis 132 than the end of the first stage 84 adjacent the transition portion 88. An inlet tube 96 is fluidly connected with the first stage 84 between its two ends to introduce whole blood into the processing channel 80 and a RBC/WBC tube 100 is provided in the control chamber 124 for removing the separated RBC/WBC from the channel 80. Both the inlet tube 96 and RBC/WBC tube 100 extend externally of the rotatable device 18 for interconnection with the donor 14 and/or collection bags 38, 54.

As RBC/WBC sediment against the outer wall in the first stage 84 during rotation of the centrifuge rotor they are directed and counterflow toward the RBC/WBC tube 100 for removal from the channel 80 due to the increased centrifugal forces at the RBC/WBC tube 100 in comparison with the transition portion 88. That is, since the first stage 84 extends along an arcuate path generally outwardly away from the axis 132 proceeding from the transition portion 88 to the control chamber 124, the centrifugal force differential along the first stage 84 establishes the described counterflow of the separated RBC/WBC. Moreover, the transition portion 88 also assists in providing for this counterflow since it extends along an arcuate path generally inwardly toward the axis 132 proceeding from the first stage 84 to the second stage 92.

The platelet-rich plasma, which has a lower density than the RBC and WBC, flows beyond the transition portion 88 from the first stage 84 into the second stage 92 for further processing, while the RBC/WBC are directed back toward the RBC/WBC tube 100 in the above-described manner. The second stage 92 initiates

at the radially inwardmost part of the transition portion 88 and extends along an arcuate path generally outwardly away from the axis 132 to a platelet collection chamber 104. Platelets are removed from the processing channel 80 at the platelet collection chamber 104 by a platelet tube 108 which interfaces with the outer wall of the processing channel 80 at the platelet collection chamber 104. Thereafter, the second stage 92 extends
 5 along an arcuate path generally inwardly toward the axis 132 until terminating at the plasma tube 112. Both the platelet tube 108 and plasma tube 112 extend externally of the rotatable device 18 for interconnection with the platelet collect bag(s) 38 and donor 14/plasma collect bag(s) 54, respectively.

Platelets which do not separate from the plasma in the initial portion of the second stage 92 between the transition portion 88 and platelet collection chamber 104 are separated in the portion of the second stage 92
 10 between the platelet collection chamber 104 and the plasma tube 112. These platelets will flow back towards the platelet collection chamber 104 in the opposite direction of the flow of platelet-rich plasma/platelet-poor plasma through the second stage 92 due to the configuration of this portion of the second stage 92. That is, the platelet collection chamber 104 assumes the radially outwardmost position in the second stage 92 such that all platelets, regardless of where separation occurs in the second stage 92, flow towards the platelet collection chamber 104 for removal from the channel 80.

Platelet-poor plasma exits the second stage 92 and flows out through the plasma tube 112 which interfaces with the inner wall of the processing channel 80 and/or continues to flow through the remaining portion of the processing channel 80 to the control chamber 124. Plasma which flows to the control chamber 124 exits the channel through the control tube 114 which joins with the RBC/WBC tube 100 into a single outlet tube 120.
 20 The positionings and diameters of the RBC/WBC tube 100 and control tube 114 and the joinder of such into the common outlet tube 120 regulate the position of the RBC/WBC-platelet-rich plasma interface within the transition portion 88 using conservation of mass principles.

The blood component collection device 18 includes a prediction model 20 (appropriately interfaced with the operator input module 16 as shown in Fig. 1 as noted above and which may be used to configure the prediction model 20 and/or to allow operator input of various parameters to be used by the prediction model 20)
 25 for predicting a platelet yield before a collection procedure is initiated using a compilation of algorithms. The prediction model 20 may be used by the optimizer assembly 140 which is associated with principles of the present invention and thus will be briefly described herein. Notwithstanding the following discussion of the specifics of the prediction model 20, those skilled in the art will appreciate that the prediction model 20 is associated with the functional and operational characteristics of the blood component device 18 described herein. Therefore, the algorithms used in the prediction model 20 could and likely would vary in the case of other blood component collection devices which may be used by the present invention. Moreover, different algorithms could of course be used even for the prediction model 20. Furthermore, the algorithms are specific to platelet collection and therefore may and likely would change if used in relation to other blood component types such as
 35 red blood cells.

The prediction model 20 is typically configured by the site (e.g., the blood bank/center) for a particular blood component collection procedure (e.g., single or dual needle) used by the site and will be presented with regard to the dual needle procedure of Fig. 2 and in relation to a platelet-collecting procedure. In this regard, an AC infusion rate (i.e., the rate at which anticoagulant is provided to the donor 14 per the blood volume of the donor 14) and the AC ratio (i.e., the collective flow of AC and blood through the inlet line 22 in relation to the flow of AC through the line 22) must be specified (through configuration or modified input as will be discussed below). Moreover, in the event that plasma is to be collected into the plasma collect bag 54 in the collection procedure, the maximum amount of plasma which should be collected considering the medical and physical characteristics of the donor 14 must also be provided.

There are two alternatives for establishing the plasma volume limit. The first alternative relating to the plasma volume limit is to provide a weight cutoff (e.g., 0-500 pounds), associated with the weight of the donor 14 which is input as will be discussed below. In this regard, a plasma volume upper limit (e.g., 10-1500 ml.) may be established for a weight of a donor 14 in excess of this cutoff, and a plasma volume lower limit (e.g., 10-1500 ml.) may be established for a weight of such donor 14 which is less than this cutoff. For instance, if the weight cutoff is 175 pounds, the plasma volume upper limit can be 600 ml. for a donor 14 weight greater than or equal to 175 pounds, and the plasma volume lower limit can be 500 ml. for a donor 14 weight less than 175 pounds.
 50

The second alternative for a plasma volume limit is to configure the prediction model 20 such that the plasma volume limit is expressed as a percentage of the total blood volume of the donor 14 which is calculated pursuant to Eq. 10 below. For instance, the plasma volume limit may be established as 1-15% of the total blood volume of the donor 14, and is preferably established as about 12% of such volume.

Further information is required by the prediction model 20 prior to performing its yield prediction function. For instance, the total procedure time is typically input by the operator or preconfigured by the user (e.g., the

blood bank/center). When configured the procedure time is typically 100 minutes. Moreover, the total procedure time is affected by whether a stepdown option is utilized for the blood component collection device 18 so as to enhance separation of the various blood components. When this stepdown option is selected, the angular velocity of the blood component collection device 18 is incrementally reduced during the platelet-collection procedure. For instance, the stepdown option could provide for angular velocities for the device 18 of 2400, 2200, and 2000 RPM, each of which would be for a specified duration.

Based upon the foregoing, the configuration of the prediction model 20 in relation to the blood component separation assembly 10' and associated protocol in effect standardizes site protocol for purposes of "normal" operations. However, for a particular donor 14 it may be desirable to alter the "configuration" for one processing run. Consequently, the prediction model 20 utilizes a procedure in which certain parameters utilized in the following equations may be adjusted on a one-at-a-time basis. Such is referred to as modified input data and the associated parameters are procedure time (e.g., 10-999 minutes), inlet flow rate to the device 18 (e.g., 0-150 ml/min. for the Fig. 2 assembly and 0-50 ml/min. for the Fig. 2 assembly), AC ratio option as discussed above (3-50), the desired platelet collect volume (e.g., 10-9999 ml.), the desired platelet collect concentration (e.g., 100-8000 x 10⁶/ml.), and the desired source plasma volume to be collected (e.g., 0-9999 ml.). Moreover, other parameters such as AC infusion rate (0.8-1.1), stepdown option (yes or no), needle option (single or double), and high flow option (yes or no) may also be entered as modified input data by an operator.

Having configured the prediction model 20 in the above-described manner, the following additional information is provided and is utilized in the various calculations of Equations 1-22 presented below: (1) needle option, namely whether the procedure is dual needle (Fig. 2) or single needle (Fig. 3); (2) run identification number for purposes of associating the data/output generated by the various equations with a particular donor 14 and processing run; (3) the sex of the donor 14; (4) the height of the donor 14; (5) the weight of the donor 14; (6) the total blood volume as calculated in Eq. 10 below; (7) the hematocrit of the donor 14, either based upon an initial estimation and thereafter updated based upon analysis of the donor's 14 blood sample (e.g., by a cell counter) or input directly from such an analysis; (8) the platelet precount, either based upon an initial estimation and thereafter updated based upon analysis of the donor's 14 blood sample (e.g., cell counter) or input directly from such an analysis; and (9) whether plasma collection is desired in conjunction with the platelet collection.

Based upon the above initial configuration and subsequent data input (except when entered as modified input data), the following output is generated by the prediction model 20: (1) platelet yield; (2) inlet flow rate; (3) AC ratio; (4) procedure time; (5) platelet collect volume; (6) platelet collect concentration; (7) source plasma volume; (8) AC in the platelet and plasma collect bags 38, 54; (9) platelet postcount; (10) AC infusion rate; and (11) output approval. This information is utilized at least in part in the following equations to generate, *inter alia*, the predicted platelet yield value of the collected platelets for the case of the dual needle procedure of Fig. 2 and also for the case of the single needle procedure of Fig. 3. The differences between those procedures with regard to the prediction model 20 are identified herein. As will be appreciated, some of the equations are utilized in the calculation of the predicted platelet yield, whereas other equations are used to generate additional information for output and informational purposes. The variables or parameters and the units associated therewith of the equations are presented after the equations in the Variables Index.

Platelet Yield:

$$Y = 1 \times 10^6 C_{PR} V_B F_Y [1 - \exp[-E_C (f_{BP} - 0.12)]] \quad (\text{Eq. 1})$$

where:

$$f_{BP} = (Q_{IN} t_E + 50) (1 - 1/R) / V_B \quad (\text{Eq. 2})$$

and where:

$$Q_{IN} = R Q_{AC} = 0.001 / V_B PR \leq 150 \quad (\text{Eq. 3})$$

Alternatively, the platelet yield may be expressed as:

$$Y = 1 \times 10^6 C_{PR} V_B F_Y [1 - \exp[-E_C (0.001 I(R-1) P t_E + 50 (1 - 1/R) / V_B - 0.12)]] \geq 0 \quad (\text{Eq. 4})$$

Platelet Collection Efficiency:

$$E_C = C_1 - C_2 \exp[9.91 (1 - 1/R) H] Q_{INA} \geq 0 \quad (\text{Eq. 5})$$

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where the constant C_1 is defined as follows:

$C_1 = 0.803$ - dual needle, without stepdown

$C_1 = 0.840$ - dual needle, with stepdown

where the constant C_2 is defined as follows:

5 $C_2 = 4.08 \times 10^{-5}$ - dual needle, without stepdown

- dual needle, with stepdown

and where:

$$Q_{INA} = Q_{IN} (t_E/t_P) \quad (\text{Eq. 6})$$

10 In Eq. 6, t_P may be provided as configuration data or modified data as provided above, or alternatively may be derived from the solution of Eq. 4 for t_E .

Effective Procedure Time:

$$15 \quad t_E = t_P, Q_{IN} \leq 45$$

$$= t_P - 500 (1/45 - 1/Q_{IN}), Q_{IN} > 45 \quad (\text{Eq. 7})$$

Only high-flow protocol is used for $Q_{IN} > 45$.

20 AC Infusion Rate Constant:

$$I = 1000 Q_{IN}/(PRV_B) \quad (\text{Eq. 8})$$

Alternatively to the use of Eq. 8 for the derivation of the AC infusion rate constant I, such may be provided as configuration or modified input data pursuant to the above.

25 AC Ratio:

Initially, the AC ratio may be provided as configuration or modified input data pursuant to the above. In configuration, it is defined as follows:

30

$$R = 1 + 2.51/H \quad \text{low}$$

$$= 1.33(1 + 2.51/H) \quad \text{medium} \quad (\text{Eq. 9})$$

$$= 1.67(1 + 2.51/H) \quad \text{high}$$

35

Total Blood Volume:

$$40 \quad V_B = 604 + 0.006012 L^3 + 14.6 W \text{ ml (male)} \quad (\text{Eq. 10})$$

$$= 183 + 0.005835 L^3 + 15.0 W \text{ ml (female)}$$

Plasma Collect Factor:

45 AC infusion rate control maintains the AC flow to the donor as:

$$Q_{ACD} = 0.001 / V_B \quad (\text{Eq. 11})$$

where the inlet flow associated with this is:

$$Q_{INO} = R Q_{ACD} = 0.001 I R V_B \quad (\text{Eq. 12})$$

50 Q_{IN} is proportional to the total AC flow, as given by Eq. 3, which includes the AC that flows to the platelet collect bag 38 and the plasma collect bag 54. P (Eq. 13) is the factor by which Q_{IN} is increased by collecting AC, relative to not collecting AC. That is,

$$P = Q_{IN}/Q_{INO} = (\text{average } Q_{AC})/Q_{ACD} \quad (\text{Eq. 13})$$

where:

$$P = 1 + (f_{ACP}/Q_{ACD}) [V_C (t_P - 150/Q_{IN}) + V_{SP} (t_P - 500/Q_{IN})] \quad (\text{Eq. 14})$$

55 and where:

$$f_{ACP} = [(R - 1) (1 - H)]^{-1} \quad (\text{Eq. 15})$$

Platelet Collect Volume:

$$V_C = 1 \times 10^{-6} Y / [C_B (1 + f_{ACP})] \quad (\text{Eq. 16})$$

5 Source Plasma Volume:

The four choices provided are as follows:

$$\left. \begin{aligned} V_{SP} &= 0 \\ &= V_{CON} - V_C \\ &= f_{SP} V_B - V_C \\ &= \text{specified as modified input} \end{aligned} \right\} \geq 0 \quad (\text{Eq. 17})$$

15 where:

$$\begin{aligned} V_{CON} &= V_{CONL}, W < W_C \\ &= V_{CONH}, W \geq W_C \end{aligned} \quad (\text{Eq. 18})$$

20

and where:

$$0.01 \leq f_{SP} \leq 0.15 \quad (\text{Eq. 19})$$

Donor Postcount:

25

$$C_{PO} = C_{PR} \exp[-E_C(0.001 / (R - 1)Pt_E + 50(1 - 1/R)/V_B - 0.12)] \leq C_{PR} \quad (\text{Eq. 20})$$

A warning is given if $C_{PO} < 100$.

Collect Volumes:

30

$$V_{CB} = V_C (1 + f_{ACP}) \quad (\text{Eq. 21})$$

$$V_{SPB} = V_{SP} (1 + f_{ACP}) \quad (\text{Eq. 22})$$

The primary equation to be solved for purposes of the yield prediction by the prediction model 20 is Eq. 4. Consequently, Eqs. 1-3 and 5-22 are ancillary to Eq. 4 although they may be used to calculate other output data and/or information required by Eq. 4. With regard to the manner in which Eqs. 1-22 are solved, all the iteration loops are based on the technique of successive approximation, in which each iteration is a repeat of the previous one, but using updated parameter values calculated in the previous iteration. This process continues until all the convergence criteria are met. The convergence criteria are that, on successive iterations, the variable difference is ≤ 1 for V_C , ≤ 0.2 for t_E , and ≤ 10 for C_B .

40 As noted above, the foregoing was based upon a dual needle configuration as illustrated in Fig. 2. In the event that a single needle configuration such as that illustrated in Fig. 3 is utilized, the following Eq. 7' is used in place of Eq. 7 and the constants C_1 and C_2 for Eq. 5 are as follows:

$$C_1 = 0.803$$

$$C_2 = 8.54 \times 10^{-5}$$

45

$$\begin{aligned} t_E &= t_P, Q_{IN} \leq 20 \\ &= t_P - 215 (1/20 - 1/Q_{IN}), Q_{IN} > 20 \end{aligned} \quad (\text{Eq. 7'})$$

50

Variables Index

Symbols for Equations:

- 55 C_1, C_2 = constants in platelet collection efficiency equations
 C_B = platelet concentration in collect bag, expressed as 10^3 platelets/microliter
 C_{PO} = donor postcount, expressed as 10^3 platelets/microliter
 C_{PR} = donor precount, expressed as 10^3 platelets/microliter

	E_C	= platelet collection efficiency
	f_{ACP}	= AC expressed as a fraction of pure plasma volume
	f_{BP}	= fraction of V_B processed in platelet collection procedure
	f_{SP}	= V_{CON} expressed as a fraction of V_B
5	F_Y	= user-specific (e.g., blood bank/center) yield calibration factor
	H	= hematocrit of donor or patient
	I	= AC infusion rate constant
	L	= donor or patient height, inches
	P	= plasma collect factor
10	Q_{AC}	= AC flow, ml/min
	Q_{ACD}	= AC flow infused into donor for platelet collection procedures, ml/min
	Q_{IN}	= inlet flow, ml/min
	Q_{INA}	= average inlet flow for platelet procedures, ml/min
	Q_{INO}	= RQ_{ACD} = inlet flow associated with Q_{ACD} , ml/min
15	R	= AC ratio
	t_E	= equivalent procedure time, min
	t_P	= procedure time, min
	V_B	= total blood volume of donor or patient, ml
	V_C	= volume of pure plasma in platelet collect bag, ml
20	V_{CB}	= total volume in platelet collect bag, ml
	V_{CON}	= volume constraint for total pure plasma collected, ml
	V_{CONH}	= higher value of V_{CON} , ml
	V_{CONL}	= lower value of V_{CON} , ml
	V_{SP}	= volume of pure plasma in source plasma bag, ml
25	V_{SPB}	= total volume in source plasma bag, ml
	W	= donor or patient weight, lbs
	W_C	= weight constraint associated with V_{CON} , lb
	Y	= platelet yield, number of platelets.

As noted above, the optimizer assembly 140 associated with principles of the present invention interfaces with or at least provides information to one or more blood component collection assemblies 10 to provide a blood component collection system 2. That is, although there are definite advantages to having an interface between the optimizer assembly 140, particularly the optimizer module 144, and the blood component collection device 18, the optimization procedure may be performed at any location and input into the blood component collection device 18 in any manner. Since the general principles of the blood component collection assembly 10 were described with relation to the collection assemblies 10, 10" which included the blood component collection device 18 and its various features, the optimizer assembly 140 will be described in relation to such assemblies 10', 10". However, it will be appreciated that the fundamental optimization principles of the present invention are not limited to these collection procedures and/or apparatus.

As noted (Fig. 1), the optimization assembly 140 generally includes a central input station 148, as well as an optimizer module 144 for each blood component collection device 18. Initially, it should be noted that the optimizer module 144 may be separate from the internal control of the blood component collection device 18 which is accessible by the operator interface module 16. However, typically the optimizer module 144 will be integrated with this internal control along with the above-described prediction model 20.

Referring to Fig. 5, the optimizer assembly 140 will be described with regard to a standard procedure. The central input station 148 will typically be used by blood banks/centers as the primary means for donor data input and donor data management. Information relating to a donor such as sex, height, weight, and demographics will be input at the central input station 148. Moreover, information relating to the donor's hematocrit and a blood component precount, both of which may be obtained from a donor blood sample and determined by known techniques such as cell counters, may also be entered at the central station 148. In addition to donor-related data, the particular type of collection procedure to be used for the donor (e.g., single needle or double needle) may be input/confirmed at the central input station 148. Based upon this information and certain site-standardized conditions (e.g., total procedure time, collection efficiency, AC infusion rate), an initial procedure order is thereafter generated which specifies the various process control parameters associated with the selected collection procedure.

The initial procedure order may be transferred/downloaded onto the internal control of a blood component collection device 18 by a computer disk 142 (Fig. 1) or electronically if a network system is implemented (not shown), through use of the operator interface module 16 if required/desired. When this operator interface module 16 exists, it may of course be used for the initial donor data input and/or to generate the initial procedure

order and thereby alleviate the need for a central input station 148. However, it may be more efficient to use the central input station. Although this initial procedure order may be used in the collection process, the initial procedure order may be optimized in accordance with principles of the present invention to obtain one or more optimal values for the process control parameters. As noted, this optimization process may be utilized before the collection procedure is actually initiated, but may also be initiated during a given collection procedure and such is referred to as downstream optimization.

With regard to the various optimization options, process control parameters may be derived for a product-based optimization. More particularly, the optimizer assembly 140 and specifically the optimizer module 144 derives process control parameters for achieving a predetermined yield of blood components through a maximization of at least one process parameter as will be discussed below in relation to the optimization models 152 (Fig. 6), 172 (Fig. 7). As noted above, in the United States a single platelet product (SPP) is 3×10^{11} platelets and a double platelet product (DPP) is 6×10^{11} platelets. Consequently, the optimizer module 144 may be configured to provide a number of product-based optimizations such as SPP and DPP. Although the exact values for a current U.S. SPP and DPP could be configured into the optimizer module 144, in order to increase the probability that the actual yield will equal or exceed the yield requirements for a current U.S. SPP or a DPP, the site may configure a SPP to be 3.5×10^{11} platelets and a DPP to be 7.0×10^{11} platelets (e.g., to effectively provide a given confidence level that the specified yield will actually be met).

The optimizer module 144 may also be configured to provide a time-based optimization. That is, for a given amount of time which a donor is available, the optimizer module 144 will derive those process parameters which allow for the collection of a "maximum" amount of platelets in this time period in relation to a maximization of at least one of the process control parameters.

Once the optimization is complete, the values for the various process control parameters generated thereby, as well as any ancillary/previously specified values, are downloaded to the internal control of the blood collection device 18 such that the collection procedure may be initiated or reinitiated (downstream optimization) as the case may be in accordance with these values. Once the procedure is completed, certain data is transferable (via the disk 142 or electronically as noted) back to the central input station 148 for further use with regard to the particular donor. In addition, this information as well as the initial input may be used to generate various types of reports which may further assist in the management of the blood bank/center (e.g., individual run, donor/patient, summary reports). That is, this information may be used in the derivation of subsequent procedure orders for the particular donor. For instance, in the event that a certain AC infusion rate was used in the collection procedure which had certain effects on the donor, this may be recorded in the central input station 148 such that a lower AC infusion rate would be suggested/required for subsequent donations by the donor.

One model which may be incorporated into the optimization module 144 is illustrated in Fig. 6 and will be described with regard to platelet collections in accordance with the dual needle configuration of Fig. 2, although the module 144 may be used with a variety of other collection procedures and including the single needle configuration of Fig. 3, as well as with various other blood components. Initially, it should be noted that all references in Fig. 6 to "derivations" are actually provided by the prediction model 20 discussed above such that there is either an appropriate interface between the prediction model 20 and optimizer module 144 or the optimization module 144 actually includes the prediction model 20. Moreover, as noted the prediction model 20 is specific to the blood component collection device 18 and to platelet collections. Therefore, if other devices are used the associated prediction model would also likely change as noted. Moreover, the associated prediction model may also vary in the case where different blood components such as red blood cells are to be collected.

The optimizer model 152 of Fig. 6 may be used for both product-based and time-based optimizations. Initially, the optimizer model 152 will be described with regard to a product-based optimization. That is, the fundamental premise of the optimization is to achieve a predetermined platelet (or other blood component type) yield (or within a yield range), preferably in the minimum amount of time.

The optimizer model 152 of Fig. 6 is comprised of four iterative loops. Generally, the first loop 156 is a derivation of an inlet flow (Q_{IN}) associated with a specified AC infusion rate (I_{SPEC}) which is typically set at a maximum value for purposes of the present invention and which is entered at the input station 154. This derivation is thereafter performed by the processing station 158 and includes the solution of Eqs. 4, 8, 14, and 16 and/or equations ancillary thereto by the prediction model 20 as discussed above.

There are of course various convergence criterion/criteria which may be incorporated into the first loop 156. For instance, convergence may be based upon the current inlet flow (Q_{IN-C}) in the first loop 156 through use of a binary search technique. In this case, in solving the noted equations at the processing station 158 certain parameters remain fixed in the iterative derivation of the inlet flow (Q_{IN}) which achieves the 'specified AC infusion rate (I_{SPEC}) and these parameters are also specified at input station 154. These include the total blood

volume (V_B) which can be calculated using Eq. 10 since the donor's height, weight, and sex are entered at the central input station 148, and the AC ratio (R), which can be calculated using Eq. 9 since the donor's hematocrit (H) has been determined, or may be specified at some value. Moreover, the total procedure time (t_p) remains fixed in each iterative derivation of the inlet flow (Q_{IN}) associated with the specified AC infusion rate (I_{SPEC}) in the first loop 156. However, since the total procedure time (t_p) is not known in the case of a product-based optimization and thus cannot be specified at the input station 154, a current total procedure time (t_{p_c}) initially will be assumed (e.g., this assumption is configured in the optimizer model 152 and since a range of total procedure times is provided in the prediction model 20 as noted above, the mean total procedure time (t_p) is typically configured into this portion of the optimizer model 152 as the initial current total procedure time (t_{p_c})). The "current" designation is used for the total procedure time in this case since the optimizer model 152 provides for an adjustment of the total procedure time after each iterative determination of the inlet flow (Q_{IN}) which provides the specified AC infusion rate (I_{SPEC}) in the second loop 160 in order to achieve the desired yield (Y) if required in the case of a product-based optimization as will be discussed in more detail below.

Generally, the inlet flow-based binary search technique convergence may be provided by assuming a current value for the inlet flow (Q_{IN_c}), calculating a current plasma collect factor (P_c) using the current total procedure time (t_{p_c}), calculating a current AC infusion rate (I_c) using the current inlet flow (Q_{IN_c}) and current plasma collect factor (P_c), and adjusting the current inlet flow (Q_{IN_c}) (at the parameter update in the first loop 156) in accordance with the selected binary search technique until there is a predetermined convergence between the two most recent values for the current inlet flow (Q_{IN_c}) (i.e., wherein the difference between the two most recent values of Q_{IN_c} is less than some predetermined amount which means that the convergence criterion is met). In the case of a binary search technique, there will always be convergence (i.e., the convergence criterion will always be met) such that the optimizer model 152 will always exit the first loop 156 and enter the second loop 160.

As an alternative to the noted inlet flow-based convergence criterion/criteria and the noted binary search technique, another possibility is to base convergence on the specified AC infusion rate (I_{SPEC}) and use an iterative derivation to determine the desired inlet flow (Q_{IN}). In this case, the first loop 156 is used to once again iteratively derive the inlet flow (Q_{IN}) which provides the specified AC infusion rate (I_{SPEC}) at the processing station 158 from certain specified parameters. That is, the first loop 156 is still a maximization of the inlet flow (Q_{IN}) based upon the specified AC infusion rate (I_{SPEC}) which should be associated with the donor 14. This is again primarily through the solution of Eqs. 4, 8, 14, and 16 and/or equations ancillary thereto by the prediction model 20 discussed above.

For purposes of solving the above-identified equations in relation to the infusion rate-based convergence criterion, certain parameters remain fixed in the iterative derivation of the inlet flow (Q_{IN}) which achieves the specified AC infusion rate (I_{SPEC}) in the first loop 156 and these parameters are also specified at the input station 154. These include the specified AC infusion rate (I_{SPEC}) which is known and which is typically a maximum value for the donor 14, the total blood volume (V_B) which can be calculated using Eq. 10 since the donor's 14 height, weight, and sex are entered in the central input station 148, and the AC ratio (R) which can be calculated using Eq. 9 since the donor's 14 hematocrit (H) has been determined and input in the central input station 148, or may be entered as modified input data. Moreover, the total procedure time (t_p) remains fixed in each iterative derivation of the inlet flow (Q_{IN}) associated with the specified AC infusion rate (I_{SPEC}). However, once again the total procedure time (t_p) is not known in the case of a product-based optimization and thus cannot be specified at the input station 154. Therefore, a current total procedure time (t_{p_c}) initially will be assumed (e.g., this assumption is configured in the optimizer model 152, and since a range of total procedure times is provided in the prediction model 20 as noted above, the mean total procedure time (t_p) is typically configured into the first loop 156 of the optimizer model 152). The "current" designation for the total procedure time is used for the above-identified reasons relating to the adjustment of the total procedure time in the second loop 160 if required to attain the desired yield (Y).

The solution of Eqs. 4, 8, 14, and 16 also requires that certain values be assumed for certain of the remaining parameters with still other parameters being derived from this assumption. In this case, an iterative procedure is used and updated/current values are used in the next iterative calculation(s). All parameters which change on each iteration of the first loop 156 are identified herein with a "c" subscript to designate that the most current value is to be used. Although the derivation of that inlet flow (Q_{IN}) which provides the specified AC infusion rate (I_{SPEC}) may be accomplished in a variety of manners via Eqs. 4, 8, 14, and 16, one way is to assume a current value for the plasma collect factor (P_c), then calculate the current inlet flow (Q_{IN_c}) using the specified AC infusion rate (I_{SPEC}), then calculate the current yield (Y_c), then calculate the current plasma collection factor (P_c) using the current yield (Y_c), and repeat this procedure with the current values until there has been acceptable convergence on the current inlet flow (Q_{IN_c}) in relation to the specified AC infusion rate (I_{SPEC}) (e.g., when the particular convergence criterion/criteria is met/established). When there is acceptable

infusion rate-based convergence, the optimizer model 152 exits the first loop 156 and enters the second loop 160. In order to offer protection for cases when there is no such convergence, a maximum number of iterations for the first loop 156 may be specified (not shown).

The second loop 160 of the optimizer model 152 is a total procedure time (t_p) iteration. That is, the second loop 160 is an iterative adjustment of the current total procedure time ($t_{p,c}$). Initially, in the second loop 160 and in the case of a product-based optimization the model 152 will never exit at the first comparator 162 since a total procedure time (t_p) is not specified at the input station 154. Consequently, the optimizer model 152 proceeds to the second comparator 166 where convergence criteria (i.e., more than one check) is made. One convergence criterion which is checked at the second comparator 166 is whether the current yield (Y_c) is greater than or equal to the desired and specified yield (Y). In this case, the current yield (Y_c) may be calculated based upon the values specified at the input station 158, values derived at the processing station 158, and the current total procedure time ($t_{p,c}$) for comparison with the desired and specified yield (Y) (in some cases, this current yield calculation (Y_c) may have been performed in the first loop 156 and need not be repeated in the second loop 160). If the yield convergence criterion is met, the model 152 exits the second loop 160 and actually exits all the way through to the exit 151, as will be discussed below. In this case, the specified/derived values are "optimal" and the collection procedure could be performed on the device 18 using the noted values for the various control parameters.

In the event that the yield-based criterion is not met at second comparator 166, the second comparator 166 looks to a total procedure time-based convergence criterion which may be similar to that discussed above with regard to the inlet flow-based criterion (e.g., using a binary search technique with the convergence criterion then being a predetermined difference between the two most current values of the total procedure time ($t_{p,c}$)). On the first time through the second loop 160 after the noted yield-based convergence criterion has failed and the total procedure time convergence criterion has failed, the current total procedure time ($t_{p,c}$) is adjusted and the model 152 returns to the first loop 156. That is, each time that the current total procedure time ($t_{p,c}$) is adjusted in the second loop 160, the entirety of the first loop 152 is repeated (i.e., a new inlet flow (Q_{IN}) associated with the specified AC infusion rate (I_{SPEC}) is derived using the current total procedure time ($t_{p,c}$) provided by the adjustment in the second loop 160). Other convergence criterion/criteria could be used in the second loop 160, such as specifying a maximum number of iterations to be performed by the second loop 160.

In the event that the yield-based convergence criterion is not met on the second loop 160 and the total procedure time-based convergence criterion is met at the second comparator 166 in the second loop 160, the optimizer model 152 exits the second loop 160 and enters the third loop 164. The third loop 164 is an iterative adjustment of the AC ratio (R). However, the model 152 initially enters the third comparator 169 where convergence criteria (i.e., more than one) are checked. One convergence criterion is again the above-noted yield-based convergence criterion. If this yield-based convergence criterion is again not met, an AC ratio-based convergence criterion is checked at the third comparator 169. This may be similar to the inlet flow-based criterion discussed above (e.g., using a binary search technique with the convergence criterion being the two most current values of the AC ratio). On the first time through the third loop 164 after the yield-based criterion has failed and the AC ratio-based convergence criterion has failed, the AC ratio is adjusted and the optimizer model 152 returns to the first loop 152. That is, each time that the AC ratio (R) is adjusted in the third loop 164, the entirety of the first and second loops 156, 160, respectively, is repeated. Other convergence criterion/criteria could be used in the third loop 164, such as specifying a maximum number of iterations of the third loop 164.

In the event that the yield-based convergence criterion is not met in the second or third loops 160, 164, respectively, and the second and third comparator 166, 169, respectively, and the AC ratio-based convergence criterion is met at the third comparator 169 in the third loop 164, the optimizer model 152 exits the third loop 164 and enters the fourth loop 168. The fourth loop 168 is an iterative adjustment of the specified AC infusion rate (I_{SPEC}). However, the optimizer model 152 initially enters the fourth comparator 170 where convergence criteria (i.e., more than one) are checked. One convergence criterion is the noted yield-based convergence criterion. If the noted yield-based convergence criterion is not met at the fourth comparator 170, an AC infusion rate-based criterion is checked at the fourth comparator 170. This may be similar to the inlet-flow based criterion discussed above (e.g., using a binary search technique with the convergence criterion being the two most current values of the AC infusion rate). On the first time through the fourth loop 168 after the yield-based criterion has failed and the AC infusion rate-based convergence criterion has failed, the AC infusion rate is adjusted and the model 152 returns to the first loop 152. That is, each time that the specified AC infusion rate (I_{SPEC}) is adjusted, the entirety of the first, second and third loops 156, 160, 164, respectively, is repeated (with the AC ratio set back to its initial value as entered at the input station 154 on each iteration of the fourth loop 168). Other convergence criterion/criteria could be used in the fourth loop 168, such as specifying a maximum number of iterations of the fourth loop 168. In cases where the specified AC infusion rate (I_{SPEC}) is actually the maximum AC infusion rate, typically the fourth loop 168 will execute only a single time with a one-time

increase in the AC infusion rate of, for instance, 20% (e.g., may be site-configured).

In the foregoing loops where a yield-based convergence criteria are identified, when the criteria are met the optimizer model 152 exits to exit 151 and the specified/derived (i.e., current) values for the various process control parameters may be provided to the device 18 for performing the collection procedure. However, there may be cases where no optimization occurs, such as when the optimizer model 152 exits to the exit 151 based upon the AC infusion rate based convergence criterion being met.

The optimizer model 152 may also be used for a time optimization. That is, the optimizer model will derive optimal process parameters for a predetermined total procedure time (t_p) through maximization of at least one of the process parameters in order to maximize the platelet collection (or for other blood component types). In this case, the optimizer model 152 only executes the first loop 156 to derive the inlet flow (Q_{IN}) associated with a specified AC infusion rate (I_{SPEC}) (typically a maximum value) using the input total procedure time (t_p) in this iterative derivation instead of the assumed total procedure time (t_p) referenced above. Once there is acceptable convergence as defined above in the product-based optimization such that model 152 exits the first loop 156, the current yield (Y_C) may be calculated in the first loop 156 (but again may already have been calculated in the first loop 156 at the processing station 158 such that no further calculation is required) and the convergence criterion will be met at the first comparator 162 when entering the second loop 160 (i.e., in a time-based optimization when a total procedure time is specified at the input station 154, the model 152 will exit when entering the second loop 158). As a result, the inlet flow (Q_{IN}) and AC infusion rate (I) will be optimal and the collection procedure may be performed with such values.

Another optimization model is presented in Fig. 7 and may be used for both product-based and time-based optimizations. As in the case of the optimizer model 152, the optimizer model 172 may interface with the prediction model 20 or actually integrally incorporate the prediction model 20, and thus reference to Eqs. 1-22 will be further made herein. Generally, the optimizer model 172 is based upon the principle that optimization occurs when an optimal inlet flow (Q_L) associated with an optimum system collection efficiency is used in the derivation of various process control parameters. Referring to Fig. 8, a representative inlet flow (Q_{IN})/yield (Y) curve is presented to show the optimal inlet flow (Q_L) associated with the maximum yield (Y_{MAX}). This optimal inlet flow (Q_L) is mathematically expressed by Eq. 23 presented below which results from differentiating Eq. 4 of the prediction model 20 with regard to the inlet flow (Q_{IN}). As can be appreciated, where different algorithms are used in the associated prediction model (whether based upon collection of blood components other than platelets, different collection apparatus, or alternative derivations of the various parameters with the same collection procedure and apparatus), the optimal inlet flow may be mathematically expressed in a different manner.

$$Q_L = \left(\frac{C_1}{2C_2} \right) e^{-9.91(1-1/R)H} - C_3 \quad (\text{Eq. 23})$$

$$C_3 = \frac{1}{2(t_p/K_7 - 1/K_9)}, \quad \begin{matrix} Q_0 \geq 45 \text{ for Dual Needle ("DN")} \\ \geq 20 \text{ for Single Needle ("SN")} \end{matrix}$$

(Eq. 24)

$$= 0, \quad \begin{matrix} Q_0 < 45 \text{ for DN} \\ < 20 \text{ for SN} \end{matrix} \quad (\text{Eq. 25})$$

$$\begin{matrix} K_7 = 500 \text{ (DN)} \\ = 215 \text{ (SN)} \end{matrix} \quad \begin{matrix} K_9 = 45 \text{ (DN)} \\ = 20 \text{ (SN)} \end{matrix} \quad (\text{Eq. 26})$$

$$\begin{aligned} C_1 &= 0.803 \text{ (SN, DN without stepdown)} \\ &= 0.840 \text{ (DN with stepdown)} \end{aligned} \quad (\text{Eq. 27})$$

$$\begin{aligned} C_2 &= 4.08 \times 10^{-5} \text{ (DN)} \\ &= 8.54 \times 10^{-5} \text{ (SN)} \end{aligned} \quad (\text{Eq. 28})$$

Based upon the foregoing, the optimal inlet flow (Q_L) is really "optimal" in terms of the collection apparatus. Referring again to Fig. 7, the optimizer model 172 will initially be described with regard to a product-based optimization wherein the desired yield (Y) is specified at input station 184. Generally, the inlet flow (Q_{IN}) associated with a specified AC infusion rate (I_{SPEC}) (typically the maximum AC infusion rate and also specified at input station 184) is iteratively derived from certain other specified parameters. This inlet flow calculation, particularly when the maximum AC infusion rate (I_{MAX}) and maximum AC ratio (R_{MAX}) are specified, the inlet flow (Q_{IN}) is optimal based on the physiological considerations of the donor 14. This is primarily through the solution of Eqs. 4, 8, 14, and 16 and/or equations ancillary thereto by the prediction model 20 discussed above. For purposes of solving these equations certain parameters remain fixed in the iterative derivation of the inlet flow (Q_{IN}) which achieves the specified AC infusion rate (I_{SPEC}) and these parameters are also specified at input station 184. These include the total blood volume (V_B) which can be calculated using Eq. 10 since the donor's height, weight, and sex are entered in the central input station 148, and the AC ratio (R), which can be calculated using Eq. 9 since the donor's hematocrit (H) has been determined, or may be specified at some maximum value. Moreover, the total procedure time (t_P) remains fixed in each iterative derivation of the inlet flow (Q_{IN}) associated with the specified AC infusion rate (I_{SPEC}). However, since the total procedure time (t_P) is not known in the case of a product-based optimization and thus cannot be specified at the input station 184, a current total procedure time (t_{P-C}) initially will be assumed (e.g., this assumption is configured in the optimizer model 172 and since a range of total procedure times is provided in the prediction model 20 as noted above, the mean total procedure time (t_P) is typically configured into this portion of the optimizer model 172 as the initial current total procedure time (t_{P-C})). The "current" designation is used for the total procedure time in this case since the optimizer model 172 provides for an adjustment of the total procedure time after each iterative determination of the inlet flow (Q_{IN}) which provides the specified AC infusion rate (I_{SPEC}) in order to achieve the desired yield (Y) if required in the case of a product-based optimization as will be discussed in more detail below.

The solution of Eqs. 4, 8, 14, and 16 also requires that certain values initially be assumed for certain of the remaining parameters. In this case, an iterative procedure is used in the solution of the yield equation (Eq. 4) (and including equations ancillary thereto as noted above) and updated values are used in the next iterative calculation(s) at the processing station 188. Although the derivation of that inlet flow (Q_{IN}) which provides the specified (typically maximum) AC infusion rate (I_{SPEC}) may be accomplished in a variety of manners via Eqs. 4, 8, 14, and 16, one way is to assume a current value for the plasma collect factor (P), then calculate the current inlet flow (Q_{IN-C}) using the specified AC infusion rate (I_{SPEC}), then calculate the current yield (Y_C), then calculate the current plasma collection factor (P_C) using the current yield (Y_C), and repeat the foregoing with the updated parameters, all within the processing station 188, until there has been acceptable convergence on the current inlet flow (Q_{IN-C}) in relation to the specified AC infusion rate (I_{SPEC}).

In addition to the calculation of the current inlet flow (Q_{IN-C}) associated with the specified AC infusion rate (I_{SPEC}), the above-discussed optimal inlet flow (Q_L) is calculated at processing station 192. Consequently, a comparison can be made between the current inlet flow (Q_{IN-C}) which was derived in the above-described manner and the optimal inlet flow (Q_L) at the first comparator 176. If the current inlet flow (Q_{IN-C}) is less than the optimal inlet flow (Q_L) at the first comparator 176, the specified values for the various parameters associated with the inlet flow Q_{IN} are "optimum", namely the AC ratio (R) and the AC infusion rate (I) specified at the input station 184. Thereafter, the current yield (Y_C) (which was calculated in the derivation of the current inlet flow (Q_{IN-C}) associated with the specified AC infusion rate (I_{SPEC}) at the processing station 188) is compared with the input yield (Y) at second comparator 180. In the event that there has been acceptable convergence between these yield values, the current total procedure time (t_{P-C}) is also "optimal". However, in the event that there has not been acceptable convergence between these yield values, the current total procedure time (t_{P-C}) is adjusted at adjusting station 196 and the foregoing iterative derivation of the current inlet flow (Q_{IN-C}) associated with the specified AC infusion rate (I_{SPEC}) is repeated until such convergence is achieved (i.e., using the initially specified AC infusion rate (I_{SPEC}) and the now adjusted current total procedure time (t_{P-C}), a new current inlet flow (Q_{IN-C}) is iteratively derived in the above-described manner).

Referring back to the first comparator 176, if the current inlet flow (Q_{IN-C}) associated with the specified AC infusion rate (I_{SPEC}) derived at processing station 188 is greater than the optimal inlet flow (Q_L), a current AC infusion rate (I_C) associated with this particular inlet flow (Q_L) is iteratively derived at the processing station 188 generally in the above-described manner (i.e., the initially specified AC infusion rate (I_{SPEC}) is disregarded in this derivation and a current AC infusion rate (I_C) is iteratively derived to coincide with the inlet flow (Q_L)). In this case, the current inlet flow (Q_{IN-C}) will always be equal to the optimal inlet flow (Q_L) at the first comparator 176 and the optimizer model 172 thereafter proceeds to the second comparator 180 for the yield comparison in accordance with the above-described procedure.

The optimizer model 176 may also be used for a time-based optimization. In this case, the total procedure time (t_p) is specified at the input station 184 as a specified total procedure time (t_{p-SPEC}) and thus is not assumed as in the product-based optimization. The optimizer model 172 thereafter proceeds in the same manner discussed above with regard to the product-based optimization except at the second comparator 180. Since no yield was input there is no yield comparison made at the second comparator 180. Instead a total procedure time comparison is made at the second comparator 180. Since the current total procedure time (t_{p-C}) was set equal to the specified total procedure time (t_{p-SPEC}) prior to the model 172 proceeding to the processing station 188 in this time-based optimization, the model 172 will exit each time at the second comparator for a time-based optimization.

In addition to the above-described product-based and time-based optimizations, the principles of the present invention may be extended to other applications relating to enhancing blood component system management. For instance, an optimization in accordance with principles of the present invention may be extended to encompass donor management issues. In one such case, another "optimization" associated with the blood component collection process would be to collect blood components as dictated by existing inventory (i.e., use optimization as dictated by existing inventory (i.e., use optimization as an inventory control). That is, information relating to the inventory of the various types of blood components in the blood bank/center and/or the demand for one or more blood component types could be maintained such that specific collection procedures could be selected to accommodate for a low supply of a given blood component type and/or a high demand for such blood component type. More specifically, in the event that the supply of red blood cells was low and/or the demand for red blood cells was high, or anticipated to be so in the near future, prompts could be provided to operators that red blood cells should be selected for collection if possible from donors during a given time period. Relatedly, the optimization principles of the present invention would be applicable to maintaining data on blood component collections from a given donor such that a determination could be made as to what type or types of blood components from the particular donor provided the maximum yield in the collection procedure. That is, information could be collected and maintained from prior blood component donations such that a determination could be made for a specific donor as to which type or types of blood components the donor has had a propensity to produce maximum yields therefor.

Notwithstanding the foregoing description of the present invention in relation to an on-line blood component collection process, those skilled in the art will appreciate that the source of blood may be provided to the blood component collection device from an appropriate blood container (not shown) interconnected with the blood component collection device 18 versus receiving such directly from the donor. Moreover, the blood of course may be provided from alternative sources such as animals. Furthermore, as illustrated in Fig. 3 the described platelet harvesting procedure may be performed utilizing a single needle configuration. In addition, the present invention is applicable to the collection of other types of blood components such as red blood cells, white blood cells, and/or plasma, and is further applicable to the simultaneous collection of more than one blood component type. In the case of red blood cell collection and optimization in accordance with principles of the present invention, the donor's blood type should be known and used in various algorithms. Moreover, the present invention is not limited to the source being whole blood. That is, the principles of the present invention may be applicable to removal of a component from any liquid.

The foregoing description of the present invention has been presented for purposes of illustration and description. Furthermore, the description is not intended to limit the invention to the form disclosed herein. Consequently, variations and modifications commensurate with the above teachings, and skill and knowledge of the relevant art, are within the scope of the present invention. The embodiments described hereinabove are further intended to explain best modes known of practicing the invention and to enable others skilled in the art to utilize the invention, and such other embodiments, and with various modifications required by the particular applications or uses of the present invention. It is intended that the appended claims be construed to include alternative embodiments to the extent permitted by the prior art.

Claims

1. A method for collecting at least one predetermined type of blood component from a source of whole blood using a blood component collection system comprising a blood component collection device and collection procedure, said collection procedure having a plurality of parameters associated therewith, **characterized in that** said method comprises the steps of:
 - providing biological data relating to said source;
 - identifying a desired yield of said at least one predetermined blood component;
 - associating a magnitude with each of said parameters, said associating step comprising performing a first deriving step comprising deriving a magnitude for at least one of said parameters from said providing and identifying steps;
 - inputting said magnitude of each said parameter into said blood component collection system after said associating step; and
 - performing said collection procedure on said blood component collection device using said inputting step to collect said desired yield of said at least one predetermined blood component from said source of whole blood.
2. A method as claimed in Claim 1, **characterized in that:**
 - said source is a human donor and said biological data comprises said donor's hematocrit, height, weight, and sex.
3. A method as claimed in Claim 1 or 2 **characterized in that:**
 - one of said parameters is an inlet flow to said blood collection device and another of said parameters is a flow of anticoagulant into said blood component collection system, wherein said inlet flow comprises a flow of whole blood from said source and said flow of anticoagulant, wherein said source of said blood has a volume, wherein at least part of said flow of anticoagulant is provided to said source, wherein an AC ratio is a ratio of said inlet flow to said flow of anticoagulant, and wherein an AC infusion rate is said at least part of said flow of anticoagulant per said volume.
4. A method as claimed in any one of Claims 1-3 **characterized in that** said performing a first deriving step further comprises:
 - deriving said magnitude of said inlet flow associated with a predetermined magnitude of said AC infusion rate.
5. A method as claimed in Claim 4, **characterized in that** said deriving said magnitude of said inlet flow step comprises:
 - using said predetermined magnitude of said AC infusion rate and a current magnitude for a total procedure time, said total procedure time being another of said parameters.
6. A method as claimed in Claim 5, **characterized in that** said deriving said magnitude of said inlet flow step further comprises:
 - assuming a current magnitude for said inlet flow and performing a first iteration procedure comprising calculating a current magnitude for said AC infusion rate from at least said current magnitude of said inlet flow, evaluating convergence criteria relating to said current magnitude of said inlet flow, and adjusting said current magnitude of said inlet flow and repeating said first iteration procedure until said convergence criteria is established.
7. A method as claimed in Claim 5 or 6 **characterized in that:**
 - said deriving said magnitude of said inlet flow step comprises:
 - deriving a current magnitude for said AC infusion rate, said performing a first deriving step further comprising iteratively calculating a current blood component yield using at least said current magnitude of said inlet flow and said current magnitude of said AC infusion rate and by using said providing step and by iteratively adjusting said magnitude of said current total procedure time until achieving said desired yield of blood components.
8. A method as claimed in any one of Claims 5-7 **characterized in that:**
 - said deriving said magnitude of said inlet flow step comprises:
 - deriving a current magnitude for said AC infusion rate, said performing a first deriving step further comprising performing a second iteration procedure after said deriving said magnitude of said inlet flow

step, said second iteration procedure step comprising calculating a current yield from said current magnitude of said inlet flow, said current magnitude of said AC infusion rate, and said current magnitude of said procedure time, comparing said current yield with said desired yield, performing said inputting step after said comparing step when said current yield is within a predetermined amount of said desired yield, adjusting said current magnitude of said total procedure time when said current yield differs from desired yield by more than said predetermined amount, repeating said deriving a magnitude of said inlet flow step after said adjusting said current magnitude of said total procedure time step, and repeating said second iteration procedure step after said repeating said second iteration procedure step until predetermined convergence criteria relating to said current total procedure time is established.

9. A method as claimed in any one of Claims 5-9, **characterized in that:**

said performing a first deriving step further comprises deriving a total procedure time after said deriving said magnitude of said inlet flow step which provides a current yield within a predetermined amount of said desired yield, said total procedure time being another of said parameters.

10. A method as claimed in Claim 8 or 9 **characterized in that:**

said performing a first deriving step further comprises:

performing a third iteration procedure after said second iteration procedure step and when said convergence criteria associated with said second iteration procedure is established, said third iteration procedure step comprising adjusting said magnitude of said AC ratio, repeating said first and second iteration procedure steps, and repeating said third iteration procedure step until predetermined convergence criteria relating to said magnitude of said AC ratio is established.

11. A method as claimed in Claim 10, **characterized in that:**

said maximum AC infusion rate is increased by a predetermined amount when said convergence criteria associated with said third iteration procedure step is established, wherein said performing a first deriving step further comprises repeating said first, second, and third iteration procedure steps using said increased AC infusion rate.

12. A method as claimed in any one of Claims 3-11 **characterized in that:**

said associating step comprises selecting a maximum magnitude for said AC infusion rate, and wherein said associating step further comprises generating a calculated magnitude of said inlet flow using at least said maximum magnitude of said AC infusion rate.

13. A method as claimed in Claim 12, **characterized in that:**

said performing a first deriving step further comprises:

calculating a theoretical magnitude of said inlet flow which provides a maximum yield of said at least one predetermined blood component and comparing said theoretical and calculated magnitudes of said inlet flow, and wherein said inputting step comprises inputting the lesser of said theoretical magnitude and said calculated magnitude of said inlet flow.

14. A method as claimed in Claim 13, **characterized in that:**

another of said parameters is a total procedure time, wherein a current magnitude for said total procedure time is assumed, and wherein said performing a first deriving step further comprises performing a first iteration procedure, said performing a first iteration procedure step comprising calculating a current blood component yield using the lesser of said calculated and theoretical magnitudes of said inlet flow of whole blood, said current magnitude of said total procedure time, and said maximum AC infusion rate, comparing said current blood component yield with said desired blood component yield, and repeating said first iteration procedure using an adjusting current total procedure times until said current magnitude of said blood component yield is within a predetermined amount of said desired blood component yield.

15. A method as claimed in Claim 13, **characterized in that:**

another of said parameters is a total procedure time and said performing a first deriving step further comprises assuming a current magnitude for said total procedure time and performing a first iteration procedure, said performing a first iteration procedure step comprising calculating a current yield from the lesser of said actual and theoretical magnitudes of said inlet flows, said maximum AC ratio, and said maximum AC infusion rate, and said current magnitude of said procedure time, comparing said current yield with said desired yield, incrementally adjusting said current magnitude of said total procedure time when

said current yield differs from desired yield by more than a predetermined amount, and repeating said first iteration procedure step until at least one of a first and second condition is satisfied, said first condition being that said current yield is within said first predetermined amount of said desired yield and said second condition being that said second iteration procedure step has been performed a predetermined number of times.

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16. A method, as claimed in any one of Claims 3-15 **characterized in that:**

said at least one of said parameters is a total procedure time, said performing a first deriving step comprising maximizing said inlet flow and minimizing said total procedure time.

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17. A method, as claimed in any one of Claims 1-16, **characterized in that:**

providing a magnitude for each of said parameters before said identifying step;

performing said collection procedure on said blood component collection device before said identifying step, using said providing a magnitude step, and for a first time period, wherein said associating step is performed after expiration of said first time period.

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18. A method, as claimed in any one of Claims 1-17 **characterized in that:**

one of said parameters is a total procedure time, and wherein said performing a first deriving step comprises minimizing said magnitude of said total procedure time based upon said magnitude of at least one of said parameters other than said total procedure time.

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19. A method, as claimed in Claim 18, **characterized in that:**

one of said parameters is an inlet flow to said blood collection device and another of said parameters is a flow of anticoagulant into said blood component collection system, wherein said inlet flow comprises a flow of whole blood from said source and said flow of anticoagulant, wherein said blood within from said source has a volume, wherein at least part of said flow of anticoagulant is provided to said source, wherein an AC ratio is a ratio of said inlet flow to said flow of anticoagulant, wherein an AC infusion rate is said at least part of said flow of anticoagulant per said volume, and wherein said at least one of said parameters associated with said minimizing step comprises said magnitude of said AC infusion rate and said magnitude of said inlet flow.

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20. A method, as claimed in any one of Claims 1-19, **characterized in that:**

said associating step comprises optimizing said magnitude of at least one of said parameters.

21. A method for collecting a blood component from a source of whole blood using a blood component collection system comprising a blood component collection device and collection procedure, wherein an inlet flow to said blood component collection system comprises a flow of whole blood from said source and a flow of anticoagulant, said method **characterized in that** it comprises the steps of:

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identifying a total procedure time for said collection procedure;

deriving a first inlet flow to said collection system which provides a maximum yield of said blood components;

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deriving a second inlet flow to said collection system using at least said identifying a total procedure time step;

identifying a smallest magnitude of said first and second inlet flows as an actual inlet flow to said blood component collection system; and

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performing said collection procedure with said blood component collection device, using said actual inlet flow, and for said total procedure time to collect said blood components from said source of whole blood.

22. A method, as claimed in Claim 21, **characterized in that:**

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said blood within said source has a volume, wherein at least part of said flow of anticoagulant is provided to said volume, wherein an AC ratio is a ratio of said inlet flow to said flow of anticoagulant, wherein an AC infusion rate is said at least part of said flow of anticoagulant per said volume, and wherein said deriving a second inlet flow step further uses a maximum AC ratio and a maximum AC infusion rate.

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23. A method for collecting a blood component from a donor using a blood component collection system comprising a blood component collection device and a collection procedure, said collection procedure comprising a plurality of parameters, **characterized in that** said method comprises the steps of:

providing biological data relating to said donor;

associating a magnitude with each said control parameter based upon at least said providing step;
 optimizing said magnitude of at least one of said control parameters in relation to both donor constraints and system constraints, said optimizing step allowing for achieving at least one of first and second conditions, said first condition being collecting a predetermined quantity of said blood components in a minimum amount of time and said second condition being collecting a maximum quantity of said blood components in a predetermined amount of time;
 inputting said magnitudes of said parameters into said blood component collection device after said optimizing step; and
 performing said collection procedure on said blood component collection device using said parameters to collect said blood components from said donor to achieve at least one of said first and second conditions.

24. A blood component collection control and information communication system used in conjunction with a blood component collection device in a procedure performed on a donor to separate, remove and collect components from blood received from the donor, comprising:

an information communication medium;

a first station interactive with the communication medium to transmit and receive information on the medium describing biological data of the donor, describing process parameters for controlling the collection device during the procedure performed on the donor, describing physical and medical characteristics of the donor observed during performance of a prior procedure on the donor, and describing the yield of at least one component obtained from the donor during performance of the procedure; the first station including an information input device by which to supply donor data, process parameters, prior procedure characteristics and component yield information to communication medium; the first station further including a computer responsive to the donor data, prior procedure characteristics and component yield information received from the communication medium to determine at least one process parameter to be used for controlling the blood component collection device during performance of a subsequent procedure on the donor; and the first station also including a display by which to display the donor data, process parameters, prior procedure characteristics and component yield information;

a second station interactive with the communication medium to transmit and receive information on the medium describing biological data of the donor, describing process parameters for controlling the collection device during the procedure performed on the donor, describing physical and medical characteristics of the donor observed during performance of a prior procedure on the donor, and describing the yield of at least one component obtained from the donor during performance of a procedure; the second station including an information input device by which to supply donor data, process parameters, prior procedure characteristics and component yield information to communication medium; the second station further including a computer responsive to the donor data, prior procedure characteristics and component yield information received from the communication medium to determine at least one process parameter to be used for controlling the blood component collection device during performance of a subsequent procedure on the donor; and the second station also including a display by which to display the donor data, process parameters, prior procedure characteristics and component yield information; and

an interface of at least one of the first or second stations which connects to the blood component collection device to the one station, the interface adaptable for controlling the blood collection device to perform the procedure in response to the process parameter information transmitted to the one station by the communication medium; the interface further supplying information to the medium at the one station describing the yield of at least one component obtained from the donor during performance of the procedure performed.

25. A method of controlling a blood component collection device in a procedure performed on a donor to separate, remove and collect components from blood received from the donor and for communicating information describing the procedure, comprising the steps of:

establishing first and second stations, each of which includes a computer, an information input device and a display;

connecting one of the first and second stations to the blood component collection device;

communicating information between the first and second stations which describes biological data of the donor, process parameters for controlling the collection device during the procedure performed on the donor, physical and medical characteristics of the donor observed during performance of a prior procedure on the donor, and the yield of at least one component obtained from the donor during performance of the procedure;

using the information input device at either the first or the second station to create at least some of one of the donor data information, the process parameter information, the prior procedure characteristics information and the component yield information;

5 deriving at least some of the process parameter information by processing the donor data, prior procedure characteristics and component yield information with the computer at one of the first or second stations; and

controlling the operation of the blood component collection device in response to the process parameter information which was communicated, created by using the information input device and derived from the computer.

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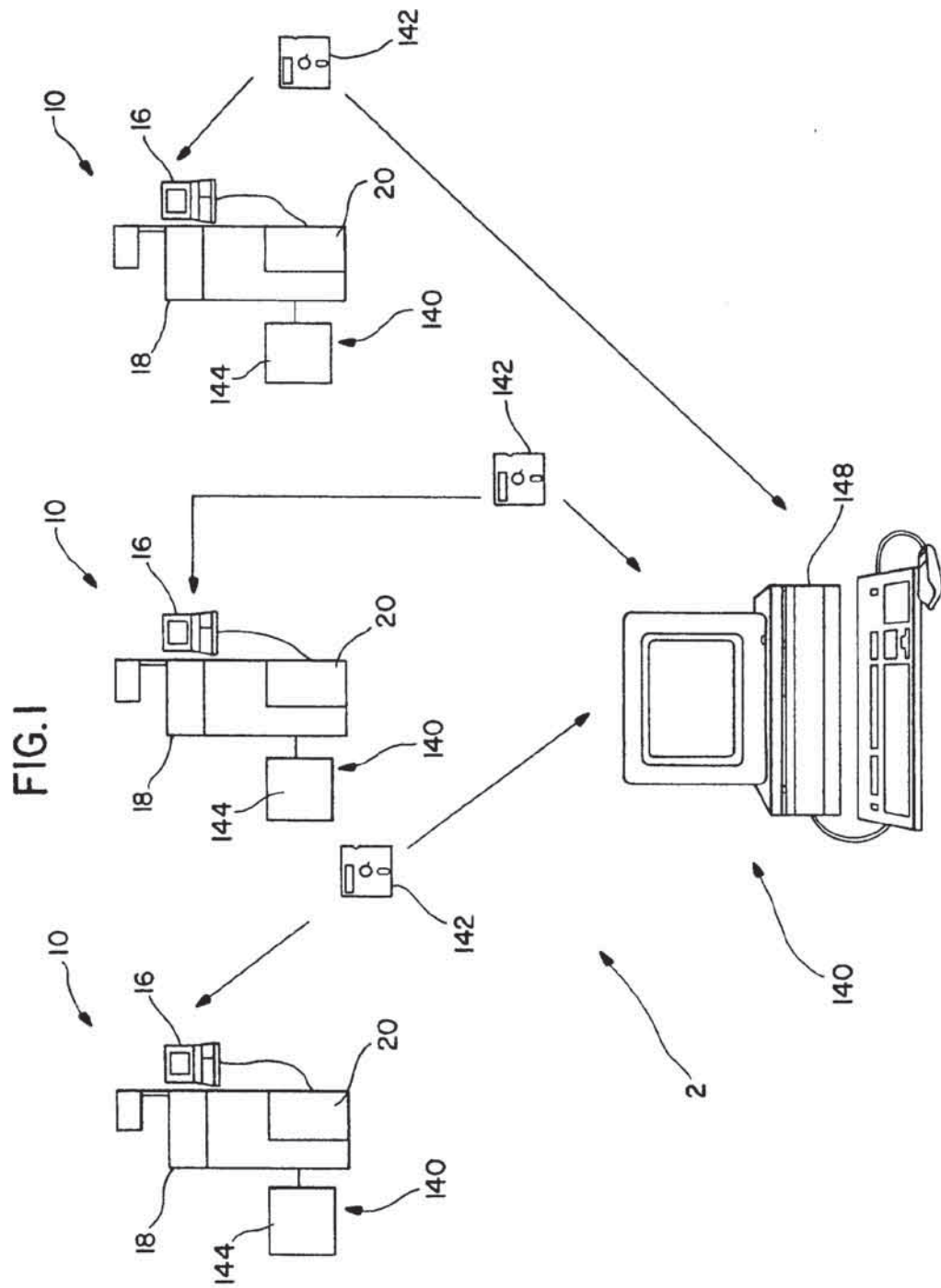
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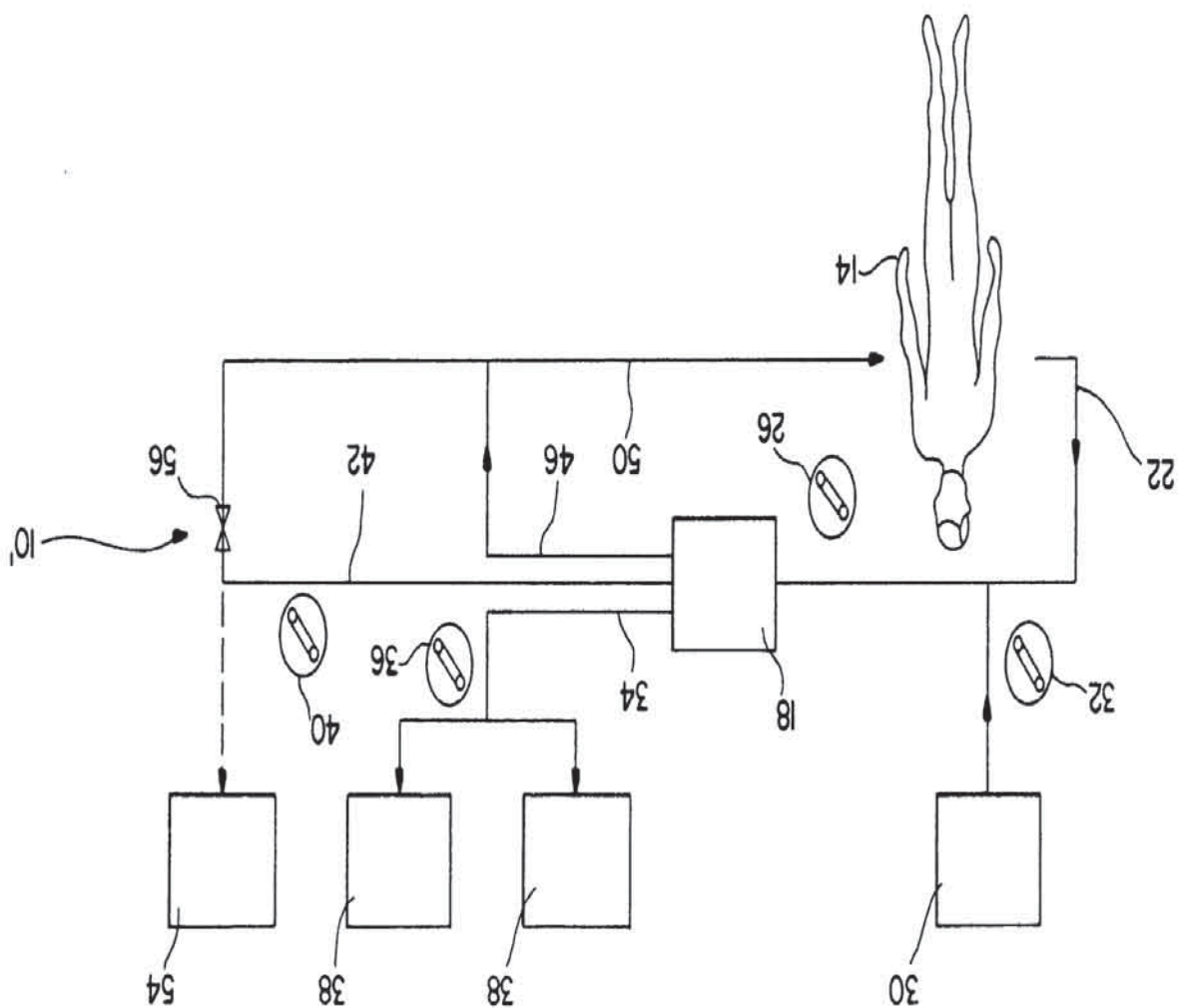
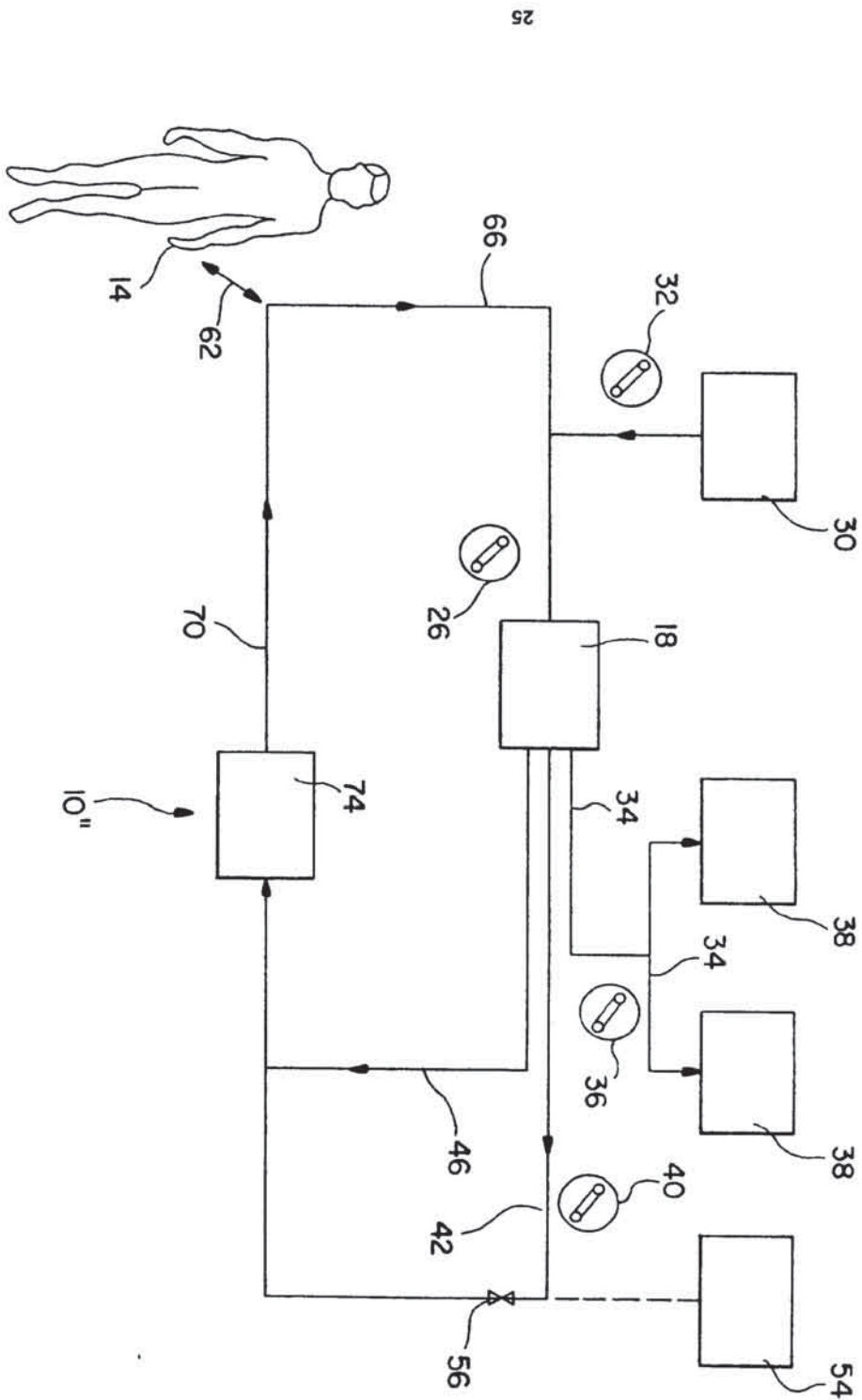


FIG. 3



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FIG. 4A

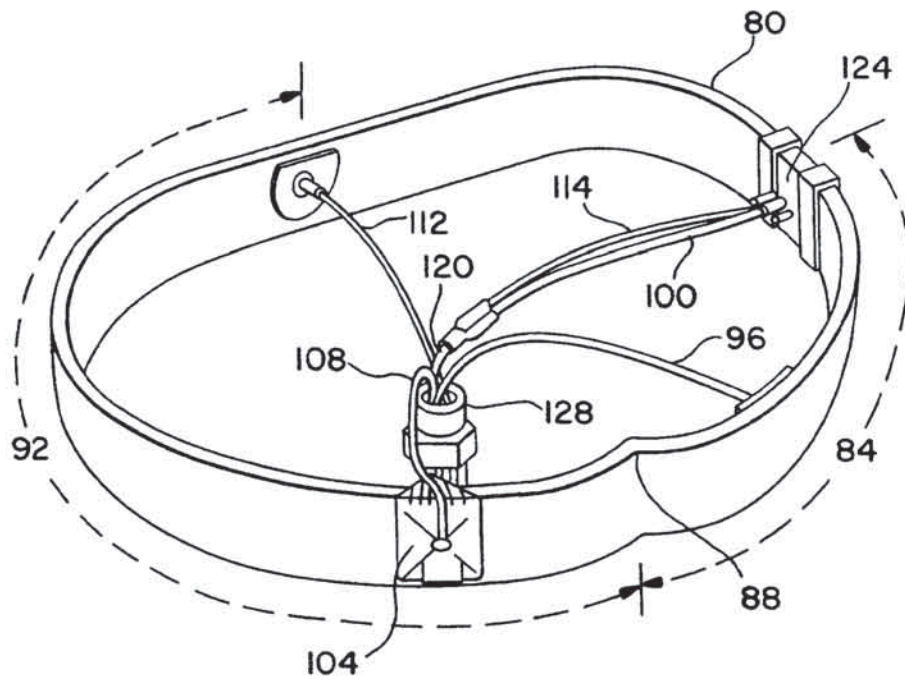


FIG. 4B

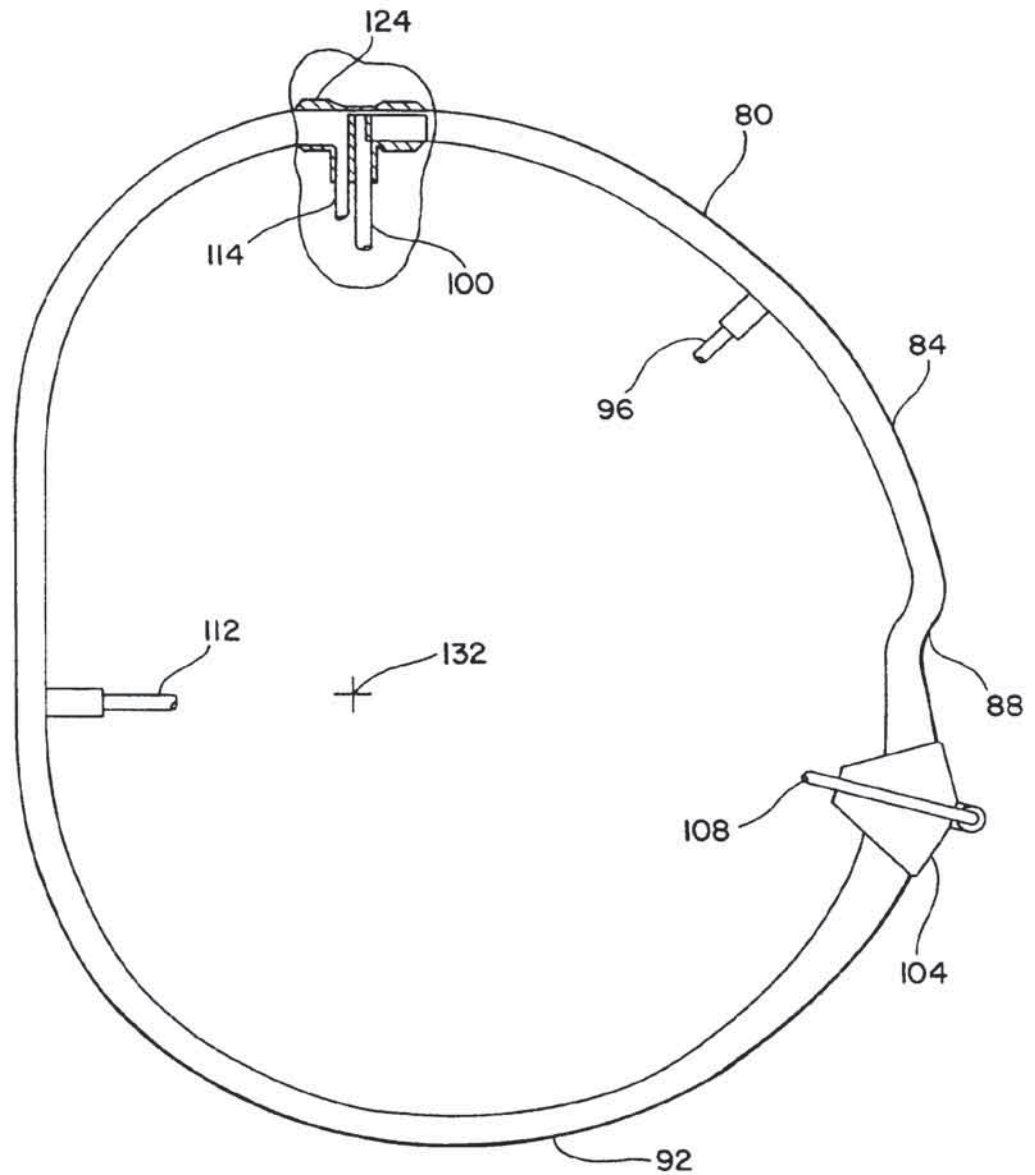
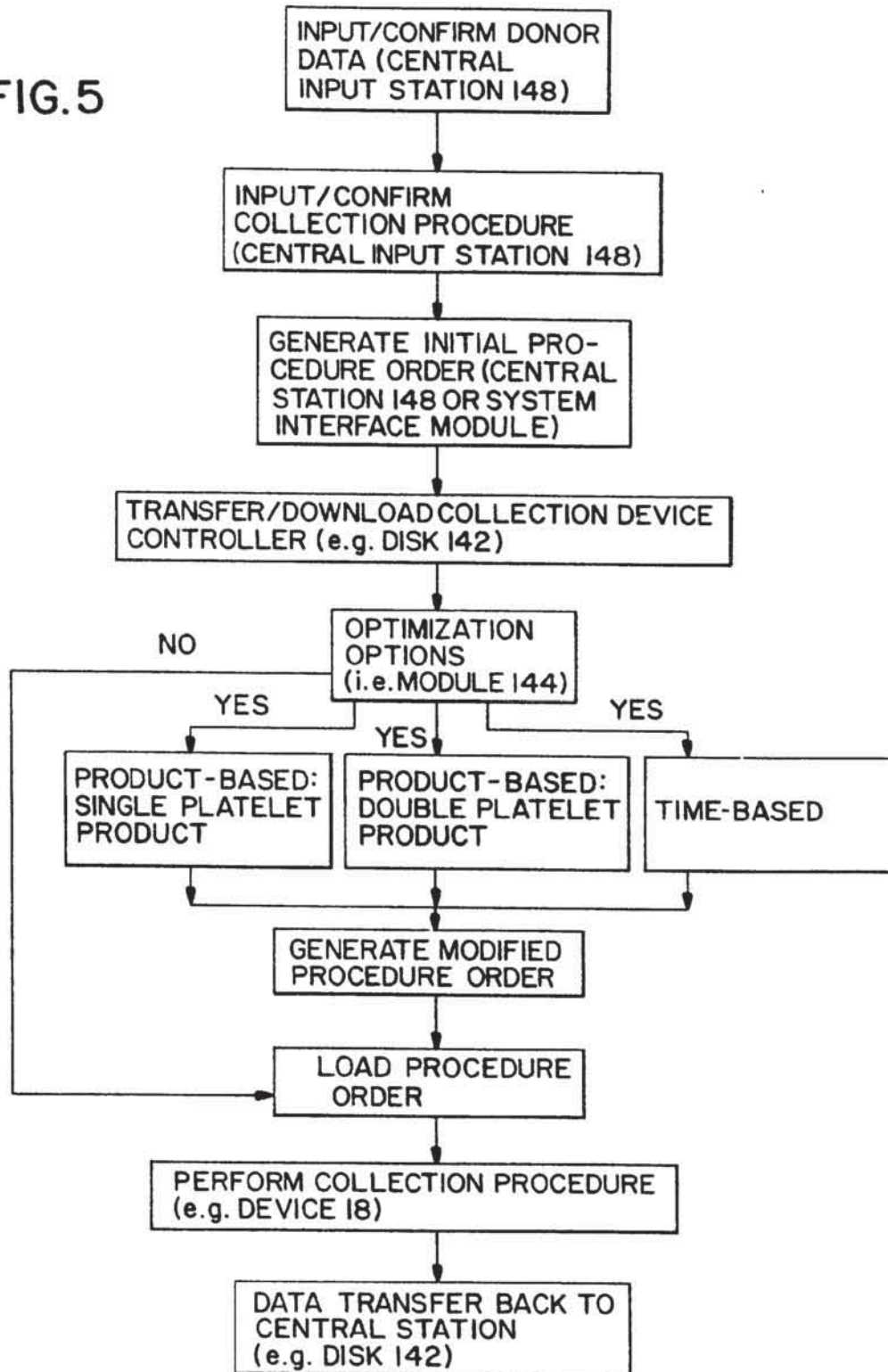


FIG. 5



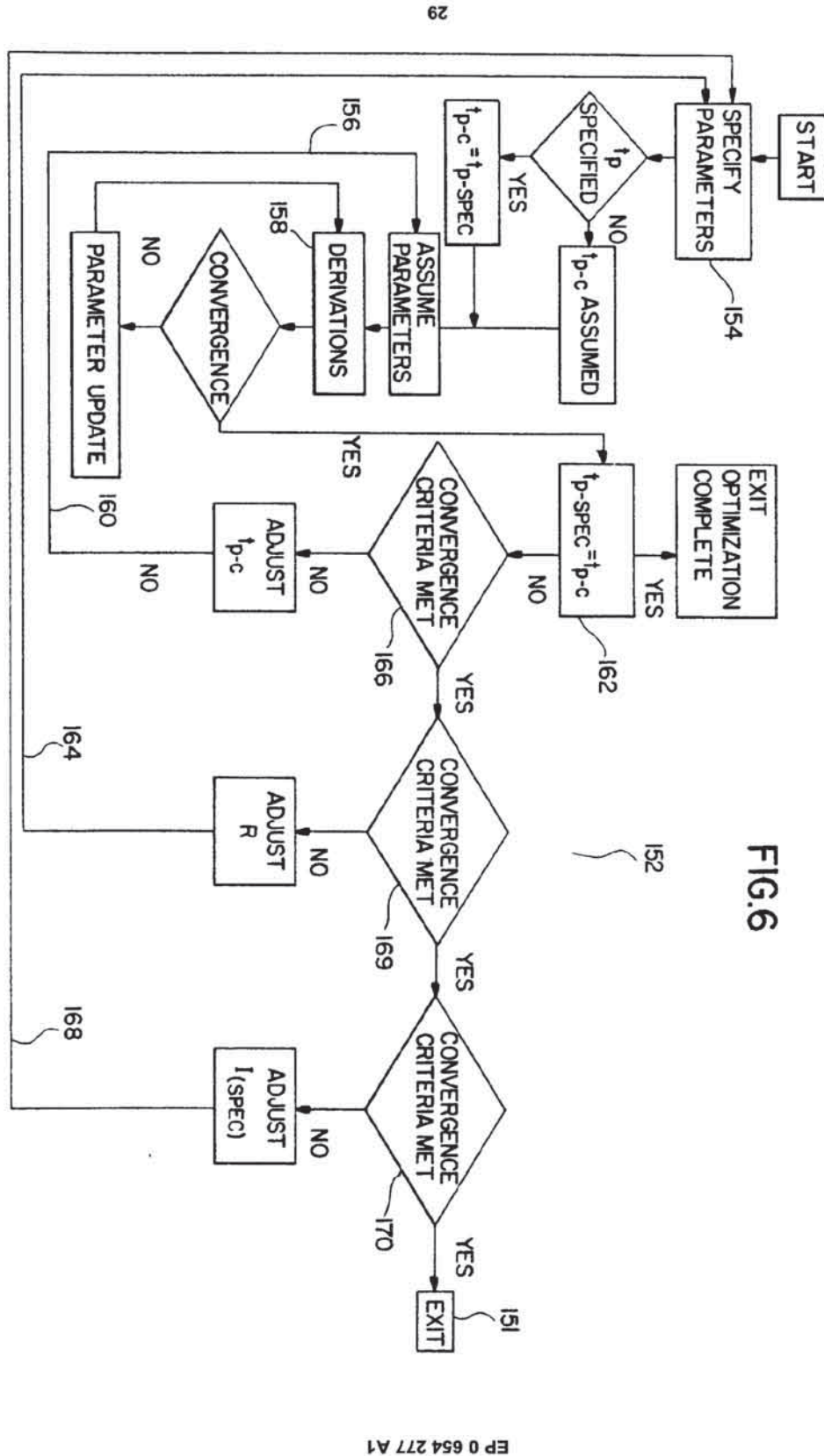


FIG. 7

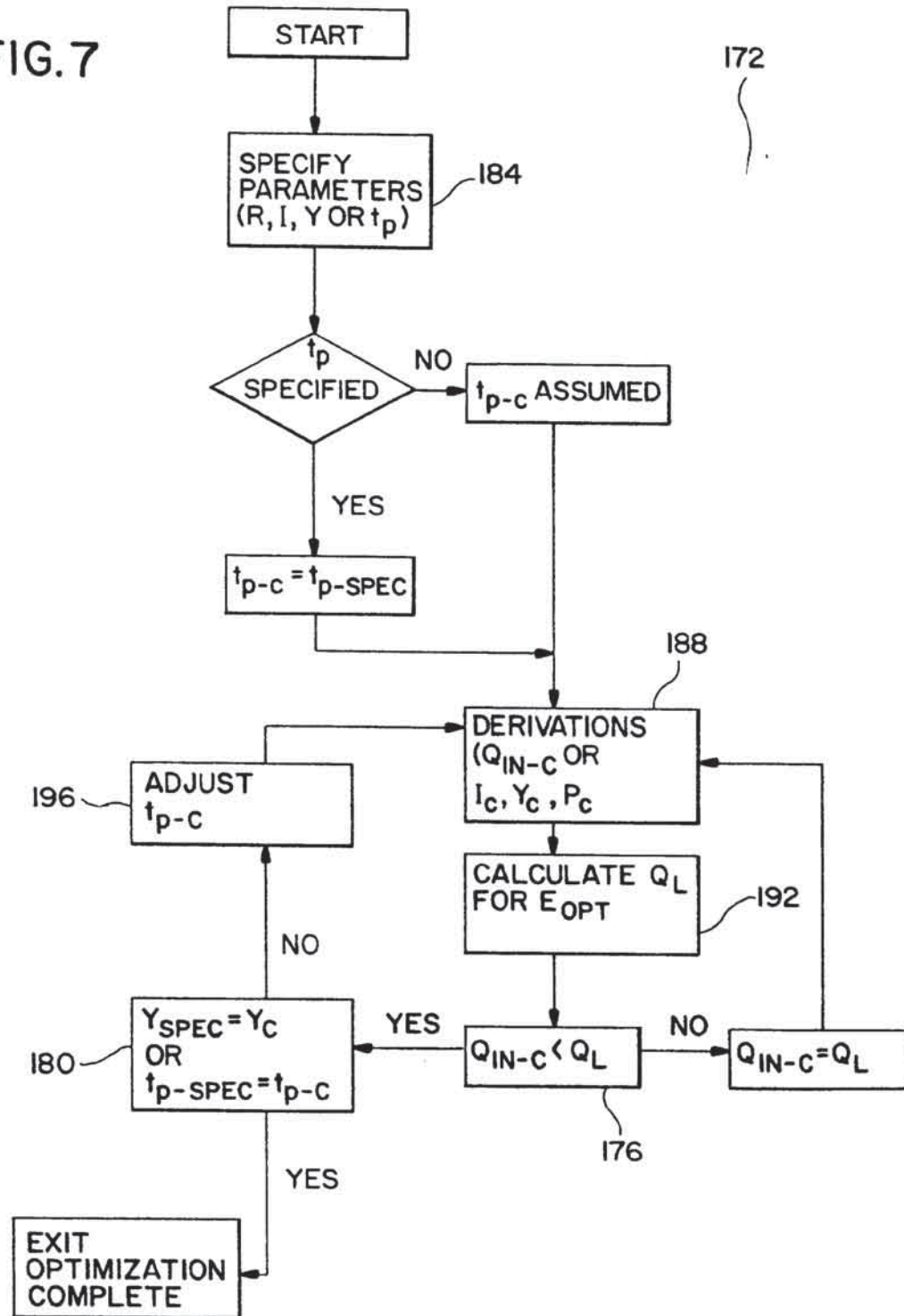
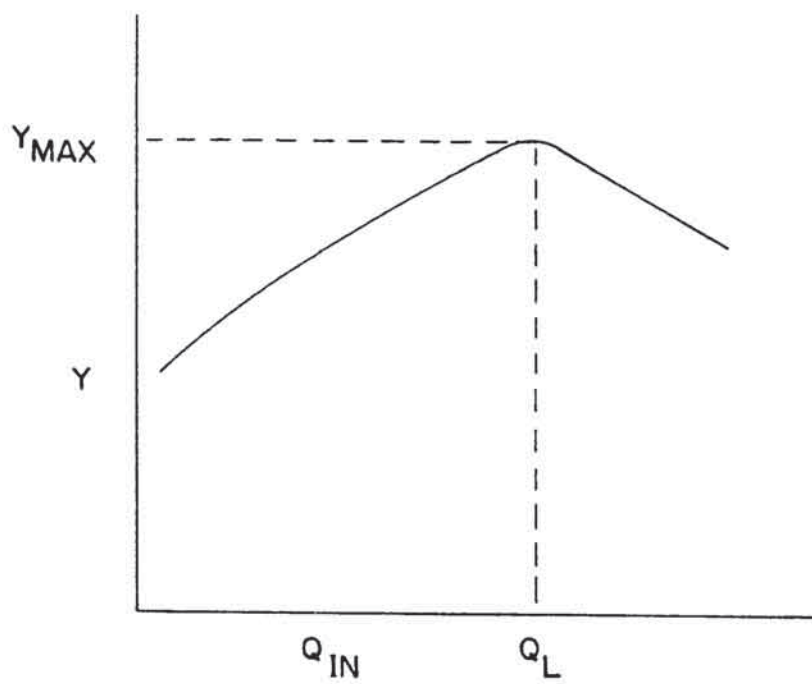


FIG. 8





European Patent
Office

EUROPEAN SEARCH REPORT

Application Number

DOCUMENTS CONSIDERED TO BE RELEVANT			EP 94307735.4
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. 6)
X, P, A	<u>EP - A - 0 580 299</u> (COBE LAB.) * Totality, especially page 2, lines 34-50; page 4, lines 18-26; page 5, line 47 - page 6, line 27; page 7, lines 7-20; page 10, lines 22-37 *	1-4, 12, 16, 18, 21, 23-25	A 61 M 1/36
A	<u>US - A - 4 968 295</u> (H.J. NEUMANN) * Totality *	1-4	
			TECHNICAL FIELDS SEARCHED (Int. Cl. 6)
			A 61 M
The present search report has been drawn up for all claims			
Place of search VIENNA		Date of completion of the search 10-02-1995	Examiner LUDWIG
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

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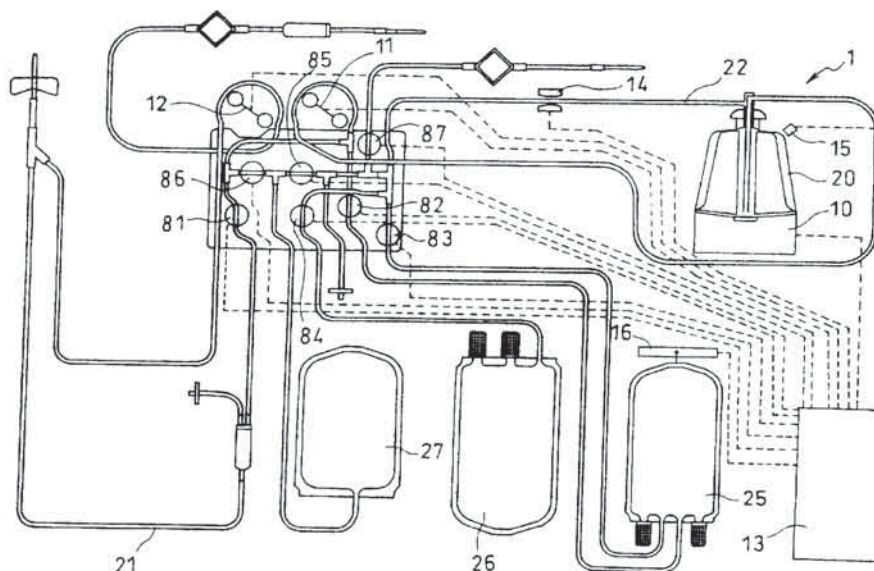
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(54) Blood component collecting apparatus

(57) A blood component collecting apparatus 1 is provided with a controller 13 for controlling a centrifugal separator drive unit 10, a pump 11, a pump 12 and a plurality of flow path shutters so as to execute plasma collecting-circulation steps including a plasma collecting step for collecting the blood containing added anticoagulant by starting the first and the second pumps 11, 12 and collecting a predetermined amount of plasma ob-

tained from the blood in a plasma collecting bag 25 by activating the centrifugal separator drive unit 10; and a plasma circulation step for temporarily suspending blood collection subsequent to the plasma collecting step and circulating the plasma contained in the plasma collecting bag 25 to the centrifugal separator 20, which is followed by a platelet collecting step and a blood returning step.

Fig. 4



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Description**BACKGROUND OF THE INVENTION**

5 The present invention relates to a blood component collecting apparatus and a blood component collecting circuit for separating predetermined blood components from the blood.

For effectively utilizing the blood and reducing the burden on the blood donor in the blood-collection, the collected blood is separated into various blood components centrifugally to extract only the components required for the donee, and the remaining components are returned to the donor.

10 In the case where a platelet product is produced from this blood component collection process, the blood donated from the donor is introduced to a blood component collecting circuit, separated into four components of plasma, white cells, platelets and red cells by a centrifugal separator called the centrifugal bowl installed in the blood component collecting circuit. Among these blood components, the platelets are recovered in a container to produce a platelet product. Meanwhile the remaining components including the plasma, white cells and red cells are returned to the donor.

15 Methods of collecting the platelets, first and second methods, are disclosed in WO 94/25086. In the first method, a liquid is sent to the centrifugal bowl and added to the whole blood while being diluted at a predetermined flow rate. According to the second method, the whole blood is sent to the centrifugal bowl and centrifugally separated into a low-density component, a middle-density component and a high-density component. The low-density component is retrieved in a first container, and the circuit is switched to circulate the low-density component at a first flow rate (fixed rate) to expand the middle-density component area in the centrifugal bowl, and the middle-density component, while being recirculated at a second flow rate (acceleration), is retrieved.

20 The first method, however, requires three pumps including an ACD pump, a blood collecting-returning pump and a circulation pump, and thus enlarges the apparatus size. In the second method, on the other hand, the platelets can be collected by two pumps, thus reducing the apparatus size. Nevertheless, the collected platelets are likely to be mixed with white cells, which fails to meet the requirement of the liquid containing platelets for a platelet product demanded to contain as few white cells as possible.

25 Accordingly, the object of the present invention is to provide a compact blood component collecting apparatus and a blood component collecting circuit used therein which is capable of producing a high-concentration platelets-contained liquid with low content of white cells at a high platelet collecting efficiency.

30 **SUMMARY OF THE INVENTION**

The aforementioned object of the invention can be achieved by a blood component collecting apparatus which comprises a blood component collecting circuit including: a centrifugal separator having a rotor having an internal blood storage space, an inlet and an outlet communicating with said blood storage space for centrifugally separating the blood introduced therein through said inlet by rotation of said rotor; a first line for connection between a blood-collection needle or a blood-collection unit connector and said inlet of said centrifugal separator; a second line connected to said outlet of said centrifugal separator; a third line connected to said first line for injecting an anticoagulant; a plasma collecting bag having a first tube connected to a middle point of said first line and a second tube connected to said second line; and a platelet collecting bag connected to said second line; said blood component collecting apparatus further comprising a centrifugal separator drive unit for rotating said rotor of said centrifugal separator, a first liquid supply pump for said first line arranged at a position of said first line between said centrifugal separator and a connecting portion for connecting said first tube to said first line, a second liquid supply pump for said third line, a plurality of flow path shutter means for opening/ closing the flow paths of said blood component collecting circuit; and a controller for controlling said centrifugal separator drive unit, said first liquid supply pump, said second liquid supply pump and said plurality of flow path shutter means; wherein said controller controls said centrifugal separator drive unit, said first liquid supply pump, said second liquid supply pump and said plurality of flow path shutter means so as to execute a platelet collecting operation which includes at least twice of plasma collecting-circulation steps including a plasma collecting step for collecting blood added anticoagulant by starting said first and second liquid supply pumps and collecting said plasma obtained from said blood in said plasma collecting bag by activating said centrifugal separator drive unit and a plasma circulation step for temporarily suspending blood-collection subsequent to said plasma collecting step and circulating said plasma contained in said plasma collecting bag to said centrifugal separator by activating said centrifugal separator drive unit, subsequent to said plasma collecting-circulation steps, a platelet collecting step for collecting platelet released from said centrifugal separator into said platelet collecting bag by accelerating a plasma circulation rate by said first liquid supply pump; and to execute a blood returning step, subsequent to said platelet collecting step, for returning said blood contained in said centrifugal separator.

Further, the aforementioned object of the invention can be achieved by a blood component collecting circuit which comprises a centrifugal separator having an inlet and an outlet; a blood-collection needle or a blood-collection unit

connector; a first line having a first pump tube for connection between said blood-collection needle or said blood-collection unit connector and the inlet of said centrifugal separator; a second line connected to the outlet of said centrifugal separator; a third line having a second pump tube connected to a portion near said blood-collection needle or said blood-collection unit connector of said first line; a plasma collecting bag having a first tube connected to a portion of said first line between said blood-collection needle or said blood-collection unit connector and said first pump tube and a second tube connected to said second line; a platelet collecting bag having a third tube connected to said second line; and a cassette housing for partially containing and partially holding said first line, said second line, said third line, said first tube, said second tube and said third tube; wherein said first pump tube and said second pump tube are fixed on said cassette housing so as to extend therefrom; wherein said cassette housing includes a first opening for exposing the portion of said, first line between said blood-collection needle or said blood-collection unit connector and said first pump tube and capable of being intruded by a flow path shutter means, a second opening for exposing said first pump tube and capable of being intruded by a flow path shutter means, a third opening for exposing said second tube and capable of being intruded by a flow path shutter means, a fourth opening for exposing said third tube and capable of being intruded by a flow path shutter means, a fifth opening for exposing the portion of said second line between said centrifugal separator and a connecting portion for connecting said fourth tube to said second line and capable of being intruded by a flow path shutter means.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic drawing of an example configuration of a blood component collecting circuit used in a blood component collecting apparatus according to the present invention.

Fig. 2 is a plan view showing a cassette housing portion of the blood component collecting circuit shown in Fig. 1.

Fig. 3 is a partially cutaway sectional view showing the state in which a drive unit is mounted on a centrifugal separator used in a blood component collecting circuit.

Fig. 4 is a schematic drawing of a blood component collecting apparatus according to an embodiment of the invention having a blood component collecting circuit mounted thereon.

Fig. 5 is a flowchart representing the operation of a blood component collecting apparatus according to the invention.

Fig. 6 is a flowchart for explaining the operation of a blood component collecting apparatus according to the invention.

Fig. 7 is a flowchart representing the operation of a blood component collecting apparatus according to the invention.

Fig. 8 is a flowchart representing the operation of a blood component collecting apparatus according to the invention.

Fig. 9 is a flowchart representing the operation of a blood component collecting apparatus according to the invention.

Fig. 10 is a flowchart representing the operation of a blood component collecting apparatus according to the invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

A blood component collecting apparatus according to the present invention will be described with reference to an embodiment shown in the accompanying drawings.

A blood component collecting apparatus 1 according to the invention is provided with a blood component collecting circuit 2 including a centrifugal separator 20 having a rotor 142 having an internal blood storage space, an inlet and an outlet communicating with the blood storage space for centrifugally separating, in the blood storage space, the blood introduced therein through the inlet by the rotation of the rotor 142, a first line 21 for connection between a connector of a blood-collection needle 29 or a blood pool and the inlet of the centrifugal separator 20, a second line 22 connected to the outlet of the centrifugal separator 20, a third line 23 connected to the first line 21 for injecting an anticoagulant, a plasma collecting bag 25 having a first tube 25a connected to the first line 21 and a second tube 25b connected to the second line 22, and a platelet collecting bag 26 connected to the second line 22.

The blood component collecting apparatus 1 has a centrifugal separator drive unit 10 for rotating the rotor 142 of the centrifugal separator 20, a first liquid supply pump 11 for the first line 21, a second liquid supply pump 12 for the third line 23, a plurality of flow path shutter means 81, 82, 83, 84, 85, 86, 87 for opening/closing the flow paths of the blood component collecting circuit 2, and a controller 13 for controlling the centrifugal separator drive unit 10, the first liquid supply pump 11, the second liquid supply pump 12 and a plurality of the flow path shutter means 81, 82, 83, 84, 85, 86, 87.

First, the blood component collecting circuit 2 will be explained.