выполнена с симметрично расположенными вертикальными ребрами, имеющими участки, прилегающие к наружной поверхности вставки, а днище корпуса снабжено радиальными ступенчатыми выступами, служащими опорой для вставки и размещенными в одной плоскости с вертикальными ребрами.

На чертеже показан описываемый ротор для разделения крови и промывки тяжелой фракции, разрез.

Ротор выполнен разборным и состоит из днища 1, корпуса 2 и конусообразной вставки 3, скрепленных вместе с помощью винтов 4 так, что между ними образована кольцевая рабочая полость. На внутренней поверхности днища 1 выполнены радиально ступенчатые выступы 5, служащие опорой для вставки 3. Вставка 3 состоит из колпака 6 и стойки 7, вставленных друг в друга, причем в нижней части стойки 7 вставлено уплотнительное резиновое кольцо 8, обеспечивающее герметизацию соединения колпака 6 со стойкой 7 по периметру вставки 3. Внутри нижней части корпуса 2 выполнены вертикальные ребра 9, расположенные симметрично и имеющие участки, прилегающие к наружной поверхности колпака 6 вставки 3 и предназначенные для прижима кромки вставки 3 через резиновое уплотнительное кольцо 8 к дну стойки 7, опирающемуся на ступенчатые выступы 5 днища 1.

Снаружи корпуса 2 размещена подвижная часть затвора - диск 10. Неподвижная часть затвора, выполненная в виде втулки 11 с патрубком 12, закреплена гайкой 13 на трубке 14 для подвода крови, промывной жидкости и отвода отмытой тяжелой фракции.

Снизу втулки 11 жестко закреплено кольцо 15 так, что между ним и втулкой 11 образована кольцевая полость для подвода охлаждающей жидкости через штуцер 16. В кольце 15 выполнены несколько капиллярных отверстий для прохода охлаждающей жидкости на трущиеся поверхности затвора.

Для отвода легкой фракции крови предусмотрены вставленные одна в другую втулки 17 и 18, смонтированные на трубке 14 над вставкой 3 таким образом, что между ними образовано узкое щелевидное пространство, начинающееся в рабочей полости ротора и заканчивающееся в верхней части втулки 11 патрубком 12.

Ротор работает следующим образом.

Собранный из чистых деталей ротор с неполностью затянутыми винтами 4 и гайкой 13 стерилизуется в специальном автоклаве, где перегретый пар поступает по штуцеру во внутреннюю полость ротора, стерилизуя все поверхности его, соприкасающиеся с кровью.

После охлаждения ротора винты 4 и гайка 13 затягиваются до упора, при этом обеспечивается герметичность соединения колпака 6 и стойки 7 по всему периметру вставки 3.

Ротор помещается на планшайбу приводного устройства (на чертеже не показано), а к штуцерам 16 подсоединяются трубки от насоса подачи физиологического раствора и емкости для сливной охлаждающей жидкости.

К трубке 14 ввода подсоединяются коммуникационная трубка от насоса подачи крови (на чертеже не показано), а к патрубку 12 - емкость для сбора плазмы. При небольшой скорости вращения ротора включается подача стерильного физиологического раствора, после чего скорость вращения ротора увеличивается до заданной, и насосом подается по трубке 14 кровь, которая, попадая на днище 1 ротора, центробежной силой откидывается к периферии его и разделяется на фракции: тяжелую (эритроцитную массу) и легкую (плазму) располагающуюся ближе к центру ротора. При достижении слоем плазмы наружных кромок втулок 17 и 18 плазма напором поступающих в ротор последующих порций крови вытесняется в вертикальную полость втулки 11 и отводится патрубком 12 в специальную емкость. После заполнения внутренней полости ротора эритроцитной массой, что соответствует объему эритроцитов в одной дозе крови, ротор останавливается, после чего насос подачи физиологического раствора отключается, эритроцитная масса стекает в нижнюю часть ротора, откуда обратным ходом насоса подачи крови по трубке 14 отбирается в специальную емкость.

Отмывка клеток крови от криоагентов производится аналогичным образом, только после подачи в ротор по трубке 14 размороженных эритроцитов насосом непрерывно подаются отмывные растворы определенного состава. Отмывные клетки крови отбираются после остановки ротора обратным ходом насоса подачи крови.

Благодаря выполнению в корпусе ротора симметрично расположенных вертикальных ребер, прилегающих к боковой поверхности колпака вставки, а на днище ротора - радиальных ступенчатых выступов, являющихся опорой для стойки, обеспечивается герметичность нижней части вставки в месте соединения колпачка и стойки за счет только внешних винтов, скрепляющих корпус и днище ротора.

При этом отпадает необходимость введения дополнительных крепежных деталей для вставки, что позволяет сократить металлоемкость и трудоемкость изготовления и полностью исключить деформацию вставки ротора при автоклавировании, являющуюся результатом различия коэффициентов термического расширения пластмассы и стали.

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Данная конструкция удобна в сборке, работе и стерильной обработке ротора после проведения экспериментов, так как все крепежные детали, сведенные до минимума, вынесены на наружную поверхность ротора. В то же время детали корпуса и днища, кроме основной функции изолирования разделяемого объема крови, выполняют функцию герметичного соединения деталей вставки в рабочем состоянии.

Выполнение на днище ротора ступенчатых выступов позволяет упростить конструкцию стойки днища, что улучшает технологию ее изготовления, а также исключает дополнительное сопротивление потоку крови, что может вызвать частичный гемолиз клеток, проталкиваемых во внутреннюю полость ротора через узкие отверстия.

В связи с тем, что во внутренней полости ротора исключены металлические крепежные детали, появилась возможность использования других способов стерилизации, например химическим дезоксоном, применяемым только для стерильной обработки изделий из пластмассы.

Таким образом, предлагаемая конструкция позволяет улучшить эксплуатационные характеристики ротора за счет легкости сборки и обработки деталей его, расширения видов стерилизации, исключения дополнительного сопротивления потоку крови, снижения гемолиза.

Упрощение конструкции за счет уменьшения количества деталей уменьшает трудоемкость изготовления, сокращает использование металла и снижает стоимость ротора.

Формула изобретения

Ротор для разделения крови и промывки тяжелой фракции, включающий корпус со съемным днищем, размещенную в нем с образованием кольцевой рабочей полости конусообразную вставку, состоящую из связанных между собой колпака, съемного днища и стойки, расположенной вертикально по оси ротора, укрепленную неподвижно концентрично стойке трубку для подвода крови, промывной жидкости и отвода отмытой тяжелой фракции, устройство для отвода легкой фракции, смонтированное над вставкой, и затвор ротора, *отличающийся* тем, что, с целью упрощения конструкции, повышения надежности работы и снижения стоимости, в рабочей полости нижняя часть корпуса выполнена с симметрично расположенными вертикальными ребрами, имеющими участки, прилегающие к наружной поверхности вставки, а днище корпуса снабжено радиальными ступенчатыми выступами, служащими опорой для вставки и размещенными в одной плоскости с вертикальными ребрами.

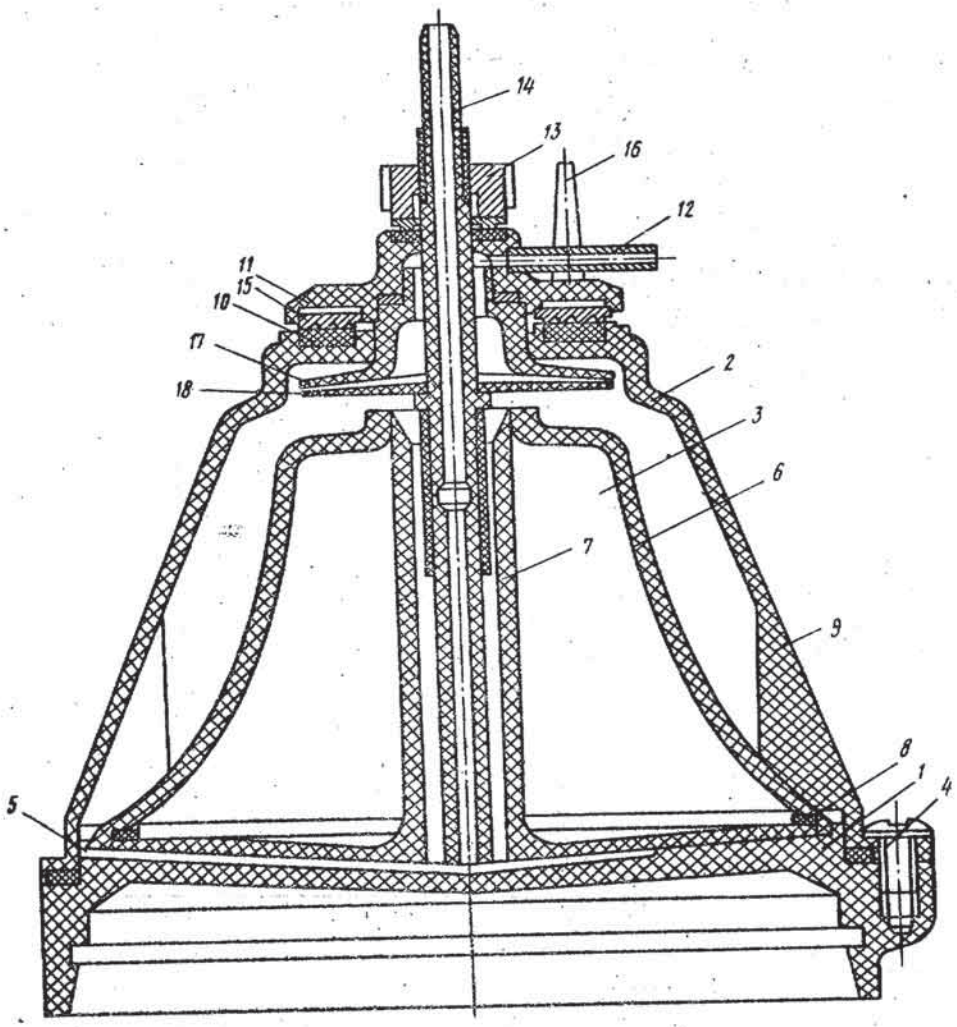
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FLEXIBLE DISPOSABLE CENTRIFUGE SYSTEM

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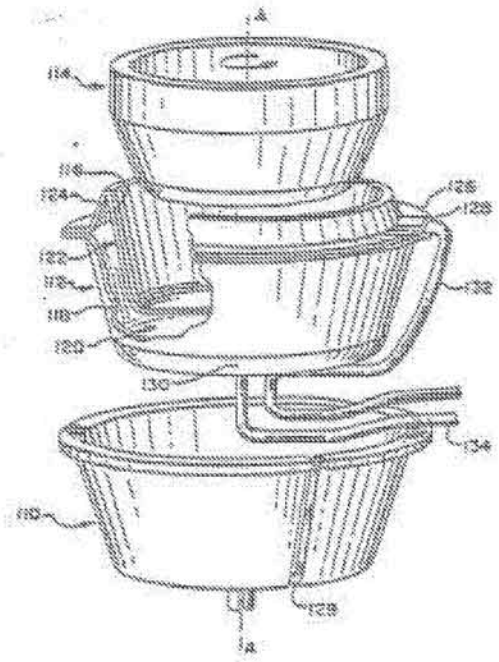
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A bowl-shaped chamber for use in centrifugal apheresis. The chamber is used for receiving whole blood, separating blood into therapeutic components and selectively collecting the therapeutic components. In one embodiment, the chamber (10) includes a bladder-like casing, which is formable into a bowl-like chamber having a bowl-shaped outer wall (32) and a bowl-shaped inner wall (34). The inner and outer walls (32, 34) define a blood processing cavity (37) therebetween and a flexible rim area (40) connects the inner and outer walls. The rim area (40) defines a rim edge (34c) and the bowl is substantially symmetric about a central spin axis. The rim area (40) is adapted to fold against itself so as to form the rim edge (34) which is adapted to advance and retract as the chamber volume changes. In another embodiment, the bowl (112) has inner and outer walls (116 and 118) which define bottom and side walls sections (120 and 122), a blood receiving cavity between said walls, and at least one port (128, 130) for fluid communication with said cavity. The bowl bottom section (120) defines a cylindrically-shaped plasma processing volume (136) and the side wall section defines an annularly-shaped red blood cell processing volume (140). The red blood cell processing volume (140) and the plasma processing volume (136) are approximately equal.

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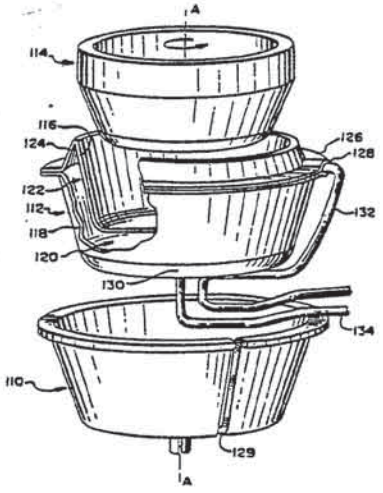
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(57) Abstract

A bowl-shaped chamber for use in centrifugal apheresis. The chamber is used for receiving whole blood, separating blood into therapeutic components and selectively collecting the therapeutic components. In one embodiment, the chamber (10) includes a bladder-like casing, which is formable into a bowl-like chamber having a bowl-shaped outer wall (32) and a bowl-shaped inner wall (34). The inner and outer walls (32, 34) define a blood processing cavity (37) therebetween and a flexible rim area (40) connects the inner and outer walls. The rim area (40) defines a rim edge (34c) and the bowl is substantially symmetric about a central spin axis. The rim area (40) is adapted to fold against itself so as to form the rim edge (34) which is adapted to advance and retract as the chamber volume changes. In another embodiment, the bowl (112) has inner and outer walls (116 and 118) which define bottom and side walls sections (120 and 122), a blood receiving cavity between said walls, and at least one port (128, 130) for fluid communication with said cavity. The bowl bottom section (120) defines a cylindrically-shaped plasma processing volume (136) and the side wall section defines an annularly-shaped red blood cell processing volume (140). The red blood cell processing volume (140) and the plasma processing volume (136) are approximately equal.



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FLEXIBLE DISPOSABLE CENTRIFUGE SYSTEM

BACKGROUND OF THE INVENTION:

This invention relates to a centrifugal liquid processing apparatus, and more particularly, to a novel processing or separation chamber and system for use in centrifugal apheresis (e.g., plasmapheresis or plateletapheresis).

In recent years long-term storage of human blood has been achieved by first obtaining whole blood from a donor at a collection center and, thereafter, separating the blood into therapeutic aomponents, such as plasma, platelets, and red cells at a central processing laboratory. The separated components are then collected and stored for future use.

The separation of the blood into constituent components is typically performed using a centrifuge or centrifugal liquid processing apparatus. Such systems are disclosed in U.S. Patents 3,987,961; 4,132,349; and 4,285,464. In such systems the processing chamber into which the whole blood is delivered for separation has in general been bowl-shaped, rigid and usually disposable. A number of different fluid connection systems are known for connecting the rotating processing chamber to external stationary blood sources or

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component collection containers. Some of these systems use stationary rather than rotating seals. See, for example, U.S. Patent 4,151,844; 4,285,464; and 4,389,207.

In addition to central processing laboratories, newer systems are being developed in which the centrifuge is located at the collection center and the donor is connected to the processing apparatus during the donation, separation and collection operations. A number of advantages are recognized from such systems, such as speed of collection, increased component yield, reduced cost, and the like.

It has been determined that in the newer systems it is particularly desirable that the volume of the separation chamber be variable so as to accommodate those volume changes occurring during the separation and collection procedures. Furthermore, the chamber should be one-piece and removable from the centrifugal processing apparatus for transporting of blood or components within the chamber.

In addition, the chamber should be sterilely sealed to external sites such as component collection bags and catheters. Desirably, the entire system should be integral and disposable.

It is also desirable to provide a processing chamber which is less expensive to manufacture than the existing bowl systems.

It is therefore an object of this invention to provide a one-piece, variable-volume processing chamber which can be economically manufactured and which may be part of a complete collection and separation system.

In the processing of blood, it is generally desirable to first separate red blood cells from the whole blood and thereafter separate and collect platelets from the remaining plasma. It is also desirable to maximize platelet collection in general and, more specifically, to maximize collection of platelets which may be associated with the red blood cells.

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During centrifugal processing the red blood cells separate or sediment against the bowl wall. In existing bowls the plasma forms a layer inwardly of and adjacent the red blood cell layer with an interface of "buffy layer" of platelets forming therebetween. In such a situation three adjacent layers are formed: the red blood cell layer, the platelet or buffy layer, and the plasma layer. However the discreteness of the layers may not be as precise as desired.

Thus when collecting the components, it may be difficult to precisely separate each component without including another component. For example, some platelets may be collected during collection of the red blood cells. Thus separation and collection of the components will not have been maximized.

It is particularly important in collecting platelets to maximize the collection of platelets from whatever quantity of blood is taken from the donor. To this end it is believed to be desirable to minimize the separation of platelets from plasma during the separation of red blood cells.

It is therefore an object of this invention to provide a processing chamber which is shaped to assure maximum separation of red blood cells while also minimizing platelet separation.

These and other objects of this invention will become apparent from the following description and appended claims.

SUMMARY OF THE INVENTION

There is provided herein a flexible, one-piece, variable-volume processing chamber for use in centrifugal apheresis (e.g., plasmapheresis or plateletapheresis) which can be easily and economically manufactured. The chamber is useful in receiving whole blood, separating the blood into therapeutic components, and the selective collection of such components.

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The chamber includes a flexible, bladder-like casing which is formable to a bowl-like shape having an outer wall and an inner wall which when spaced from each other define the blood-receiving and processing cavity. A flexible rim area connects the inner and outer walls and defines a flexible rim edge. The resulting bowl is substantially symmetric about a central spin axis, is flexible, and the rim area is constructed to fold or lay against itself and to roll in an axial direction or advance and retract as the chamber is filled and emptied. At least one port provides fluid communication between the flood-receiving cavity and external sites.

The chamber may be one component of an integral sterile and disposable separation and collection system which also includes fluid-carrying tubing, collection bags, and a catheter.

There is also disclosed herein an enclosed processing bowl for use in centrifugal apheresis which minimizes platelet separation during red blood cell separation and collection and which maximizes platelet collection by maximizing the blood sedimentation surface area and minimizing the buffy layer interface area.

The bowl has inner and outer walls which define bottom and side wall sections, a blood receiving cavity between said walls, and at least one port for fluid communication with said cavity. The bowl bottom section defines a cylindrically-shaped plasma processing volume, and the side wall section defines an annularly-shaped red blood cell processing volume. The red blood cell processing volume and the plasma processing volume are approximately equal.

The plasma processing volume and red blood cell processing volume form a generally cylindrical interface at the transition from the bottom section to the side wall section. The buffy layer forms at this interface.

The outer wall of the side wall section forms a red blood sedimentation surface and the area of the sedimentation surface is greater than the surface area of the blood cell/plasma interface.

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BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is a perspective view showing the flexible, variable-volume, bowl-shaped chamber with mating parts of a centrifugal processing apparatus;

FIGURE 2 shows the bowl-shaped chamber distended to show the bladder-like casing shape and show how the bowl-shaped chamber is formed;

FIGURE 3 shows a rim edge and a portion of the rim area rolled back upon itself in advanced and retracted positions;

FIGURE 4 shows another version of the chamber with the rim edge;

FIGURE 5 through FIGURE 12 show the operation of a centrifuge system using the bowl-shaped chamber;

FIGURE 13 shows a integral sterile and disposable separation and collection system.

FIGURE 14 is a perspective view showing a processing apparatus and variable volume bowl;

FIGURE 15 is a sectional and perspective view showing a fully filled bowl and the red blood cell and the plasma volumes;

FIGURE 16 is a sectional and perspective view showing a partially filled bowl and the red blood cell and the plasma volumes;

FIGURE 17 is a perspective view, partially in section, showing a fixed volume and the red blood cell and the plasma volumes.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to Figure 1, a flexible, variable-volume, bowl-shaped processing chamber 10 generally is shown positioned between a bowl-shaped rotor 12 and a conformingly-shaped and movable mandrel 14.

As previously indicated, centrifugal liquid processing apparatus of the type used in centrifugal apheresis are known in the art. Drive systems for spinning the separation chambers, speed

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control systems, and the like, are also known in the art. Those systems are not shown herein as they are known in the art, and as this invention is directed to the flexible, variable-volume chamber and the system of which it may be a part.

The rotor bowl 12 includes a bottom wall portion 16, upwardly-extending side wall 18, an upper lip or edge 20, a tube-receiving slot 21, and is generally symmetric about a vertical spin axis 22-22. The rotor bowl also includes at least one port or passageway 24, which is located in the bottom wall 16 at the spin axis 22-22.

The flexible chamber 10 is constructed to fit within the rotor bowl 12 for rotation therewith, and the chamber may have a shape which is generally complementary to that of the rotor bowl.

The mandrel 14 is a cup-shaped member, similar in shape to the rotor bowl 12, and is adapted to nest therein. The mandrel 14 includes a bottom wall 26, an upwardly-extending side wall 28, and skirt 30. The mandrel is axially movable toward and away from the chamber 10 so that the chamber's volume may be controlled by the cooperation of the mandrel 14 and rotor bowl 12. The mandrel is mounted to the processing apparatus so as to spin with the rotor bowl 12 and the chamber 10 about axis 22-22.

The flexible chamber 10, as shown herein, includes an outer wall 32 and an inner wall 34 which are joined along a flange or shoulder-like seal 36 to form an enclosed casing. The space between the walls defines a blood-receiving cavity 37.

The inner and outer walls, as shown here, are formed of a flexible, medical-grade, polymeric material, such as polyvinylchloride. In the preferred embodiment, the walls are sealed, flexible and pliable. The outerwall 32 includes a fluid port 38 and integral conduit 39, which provides fluid communication between the cavity 37 and external blood sources or therapeutic component collection sites. The port 38 is shown as aligned with

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the spin axis and forms what is known as the low-gravity or low-G port. The inner wall 34 is shown as depressed inwardly toward the outer wall 32 and forming a rim area 40 generally adjacent the flange 36.

As can be seen in Figure 1, the flexible processing chamber 10 fits within the rotor bowl 12, and since it is flexible, the outerwall 32 will conform to the shape of the rotor wall when the chamber is filled and spinning. The conduit 39 and port 38 are positioned in the cover 12 through the slot 21. The mandrel 14 fits within the depression or space formed in the inner wall 34, and the inner wall 34 will conform to the mandrel. Axial movement of the mandrel 14 cooperates in controlling the volume of the cavity 37 as well as the pressure within the chamber.

The chamber 10 is vacuum formed by separately vacuum forming each of two polyvinyl sheets over a male die, and thereafter, nesting the formed sheets and RF (radio frequency) sealing the sheets along the peripheral edge or flange line. When a high-G port is desired, tubing is sealed in place between the sheets at the flange area and provides fluid communication with the cavity 37 via a high-G port.

When the chamber is distended, as suggested in Figure 2, the casing assumes a bladder-like configuration which may be referred to as a prolate ellipsoid. From the distended position, the top end of the inner wall 34 is depressed inwardly so as to form the depression which receives the mandrel 14.

In some situations, it is important at the end of the separation procedures to fully express all liquid from the processing chamber. This requires that the chamber walls be capable of being flattened against themselves and that the only space provided between the rotor bowl 12 and mandrel 14 will be about the thickness of the chamber's inner and outer walls.

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As shown in Figure 3, the chamber material is sufficiently flexible at the rim area 40 that it can be folded back upon itself. Thus the inner wall 34 is folded back so that wall portions, such as 34a and 34b, contact each other and there is no space therebetween. The folded wall portions form the rim edge 34c.

As the bowl fills and empties, the rim edge 34c advances and retracts, and in a sense rolls, while retaining an edge. In Figure 3, the bowl is shown in an expanded position by the dashed lines with the inner wall 34 flattened against itself as it rolls axially upwardly and downwardly. Thus one of the inherent characteristics of the material selected for the inner wall is that it be capable of being folded flat against itself so as to define a rim area and rim edge and roll upwardly and downwardly without tearing or leaking.

Referring now to Figure 4, there are situations in which it is desirable to begin processing with an initial liquid volume in the chamber and/or to leave some liquid in the chamber at the end of the processing cycle. In such situations, the mandrel and rotor are arranged to permit the inner wall portions 34a and 34b to be spaced from each other in the rim area while still forming the rim edge 34c. The rim edge 34c advances upwardly and downwardly, but with the inner and outer walls spaced from each other. Again, the rim edge will not tear or leak.

In the simplest form, shown in Figure 1, only a single fluid port 38 is provided. Depending upon how the system is used, all fluid flow and separation can be accomplished through the port 38. Since the port is located on the spin axis, the port is referred to as the low-G (low-gravity) port. Alternatively, a single port could be provided at the greatest radial distance from the spin axis and this would be referred to as the high-G (high-gravity) port. In Figure 1, that position would be at the flange line 36. Other single port systems can be envisioned.

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For some applications, multiple port systems are desirable. Referring now to Figure 2, the low-G port is shown as 38 and the high-G port as 42.

The high-G port is formed by bonding tubing between the inner and outer walls at the flange 36. The tubing connects the port to a Y-connector 43 or to a harness which holds the tubing connecting the low-G port 38. The connection between the rotating parts and stationary parts external of the rotor and chamber may be made in the manner disclosed in U.S. Patents Re. 29,738; 3,986,442; and 4,108,353.

A number of different processing techniques can be used for separating the therapeutic components using the rate of the spin, the mandrel and either one or two ports.

In some situations a three-port system may be desirable. In such a system a third port 44 is provided through the outer wall 32 at a position intermediate the low-G port 38 and high-G 42. The third port could be used as a blood inlet, so that blood entering at port 44 would immediately begin to separate with high density components (such as red blood cells) moving toward the high-G port 42 and the low density components (such as plasma) separating toward the low-G port 38.

This is but one technique to be used, and it is important to note that blood inlet port 44 can be provided through the side wall 32. If such a port were added, it could be connected via tubing to the Y-connector 43 adjacent port 38 in the same manner as the tubing from the high-G port 42.

The embodiment previously described is fabricated by the vacuum forming of two sheets and inclusion of molded ports and tubing. Another technique by which such a system can be prepared is by blow-molding in which, for example, the high-G port and return tubing are molded into the side wall.

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One mode for operating the flexible volume reservoir is shown in diagrammatic form in Figures 5-12. Here for ease of consideration the variable-volume chamber is shown without the mandrel and rotor. It is understood that the chamber is held against the rotor wall and has assumed the shape of the rotor wall and mandrel.

In the system shown in Figure 5, the chamber 50 includes a low-G port 52 and line 53, and a high-G port 54 and line 56. The lines 53 and 58 are shown connected to a multiple-lumen umbilicus, which connects the low-G and high-G ports to external points. Various valves, clamps and pumps can be provided external of the chamber for controlling flow through the ports 52 and 54. One such system is described hereinafter.

As shown in Figure 5, the mandrel has compressed the chamber so that the chamber's inner and outer walls are compressed together.

Initially a small amount of anticoagulant is metered into the processing chamber (or is provided at the time of manufactured), and as shown in Figure 6, whole blood is delivered to the chamber and enters via low-G port 52. The blood fills the chamber and mixes with the anticoagulant. As the blood enters the chamber, the rotor rotates slowly and the mandrel retracts so as to fill the chamber with about 525 milliliters of whole blood.

Thereafter, the processing apparatus spins the rotor, chamber and mandrel in a first spin so as to separate the blood into red blood cells (RBC) and platelet-rich plasma (PRP). This spin is sometimes referred to as a soft spin and the specific spin conditions, as is known in the art, depend on factors such as rotational velocity, bowl surface area, time, initial blood hematocrit, and the like.

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Referring now to Figure 7, the red blood cells (RBC) move radially outwardly along the sides of the chamber, and the platelet-rich plasma collects in the center portion of the chamber and is identified as PRP. Red blood cells may be collected by closing the low-G port 52, opening the high-G port 54, and moving the mandrel downwardly so that the volume of the processing chamber is reduced, and red blood cells are forced from the chamber through the high-G port 54 and line 58 for harvesting and collection. This leaves the platelet-rich plasma (PRP) in the flexible bowl as shown in Figure 8.

Referring now to Figure 9, the bowl is than subjected to a second spin which separates the platelets from the platelet-rich plasma by driving the platelets along the outer wall, which leaves the platelet-free plasma at the center. This is sometimes known as a hard spin. Thereafter, the high-G port 54 is closed, the low-G port 52 is opened, the mandrel is moved downwardly, and the platelet-free plasma (PRP) is expressed from the chamber, as shown in Figure 10.

The mandrel is then retracted, which draws a small amount of air into the system from an empty but sterile and closed transfer pack or collection bag. Agitation resuspends the platelets into a small volume of carrier plasma. Under a third spin, or soft spin, as shown in Figure 12, the mandrel expresses the platelet concentrate out of the chamber and into a collection bag for transporting. Alternatively, the platelets can be transported in the processing bowl rather than being collected and transported in a separate bag.

As can be seen from these drawings, the volume of the chamber varies as blood is introduced into the chamber and in accordance with the separation procedure which is being used. In so doing, the rim edge 34c moves upwardly and downwardly, and thus that area must be flexible as previously described.

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In an alternative embodiment, the outer wall of the chamber may be rigid and a predetermined portion of the inner wall may be rigid. But the rim area and the rim edge must remain flexible.

A complete, integral, disposable, sterile and sealed collection and separation system is shown in Figure 13. This entire system is sterilely sealed upon manufacture and, as such, can be used to store and transport whole blood and components for times greater than those permitted by regulation when the system is open or pierced in the field.

In this system the flexible, variable-volume processing chamber 60 includes a high-G port 62 and tubing 64 and a low-G port 66 and tubing 68. The tubing may be threaded through peristaltic roller pumps 70 and 72 and then connected at a Y-junction 74. It will be recalled that the chamber 60 is rotating while the pumps 70 and 72 are fixed in place.

The rotating chamber and stationary pumps are connected via tubing 64 and 68. This connection is made in accordance with the teaching of U.S. Patents Re. 29,738; 3,986,442; and 4,108,353, which permit a sealless connection between rotary and stationary members. This fluid communication is established without rotary seals or the like.

The tubing 76 leading from junction 74 connects to a standard red blood cell collection bag 78, a standard plasma collection bag 80, a special breathable platelet collection bag 82, a saline-containing bag 84, an anticoagulant bag 85, and a catheter 86. Anticoagulant can be provided from a separate bag as shown or may be initially provided in the processing chamber 60 in which case an anticoagulant bag, such as 85, is not included the system.

With this system the saline solution may be drawn from bag 84 and anticoagulant from bag 85, through line 76, and into the chamber 60 for priming. Thereafter, blood is taken from the patient

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via catheter 86 and delivered via line 76 to chamber 60, preferably through low-G port 62. During this phase, the collection bags may be clamped using external clamping means, such as forceps or hemostats.

Various separation procedures have been described above, and as can be seen, red blood cells, for example, may be drawn from the high-G port 62 utilizing roller pump 70 and delivered to the red blood cell collection bag 78. Next, platelet-free plasma may be drawn from the low-G port 66 using pump 72 and delivered to the plasma collection bag 80. Then platelet concentrate may be collected via high-G port 62, pump 70 and delivered to the special platelet collection bag 82.

It will be understood that the entire system is disposable and sterilely sealed at the plant. Thus, it may be removed from the centrifuge, from the roller pumps 70 and 72, from the patient 86 and delivered to the processing site.

A preferred embodiment of the processing chamber is shown in Figures 14 through 17, being therein identified by reference numeral 112. As shown, the chamber 112 includes an inner wall 116 and an outer wall 118. These walls form a bowl-shaped chamber having a generally cylindrical bottom section 120 and a generally annular upstanding side wall section 122.

Referring now to Figure 15, it is seen that the bottom section 120 is formed by the transverse bottom wall portions of the inner wall 116a and of the outer wall 118a. The side wall portions are formed by the upstanding side wall 116b of inner wall and upstanding side wall 118b of the outer wall.

The inner wall 116 and outer wall 118 form a flexible rim area 124 which flexes and appears to roll as the chamber volume increases and decreases, thereby permitting changes without tearing or rupturing. The walls are each formed from a flexible

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polyvinylchloride sheet which is vacuum formed and the sheets are then heat sealed along a peripheral flange 126 so as to form the sealed chamber.

As shown in Figure 14, a high-gravity port 128 is formed in the flange at the radially outermost point and a low-gravity port 130 is formed in the bottom wall at the intersection of the spin axis A-A. Conduits 132 and 134 connect the ports 128 and 130 to external blood sources and collection containers. The chamber 112 is fitted into the bowl cover 110 and tubing from the chamber ports its within slot 129. A chamber engaging mandrel 114 is also provided as heretofore described. Stationary seal connections are made to the external blood sources and collection points as shown in U.S. Patents 4,151,844; 4,285,464; and 4,389,207.

Referring again to Figure 15, when the chamber is filled, it expands and the inner bottom wall portion 116a moves upwardly away from the bottom wall portion 118a, the inner side wall 116b moves inwardly from the outer wall 118a, and the rim area 124 moves axially upwardly.

The space between the bottom walls forms a cylindrical or disc-like plasma processing volume (Vp) 36, which has an outer cylindrical surface 138. The space between the side wall forms an annularly shaped red blood cell processing volume (Vbc) 40.

The interface between the blood volume and plasma volume is along the cylindrical surface 138, which forms at the transition from the bottom to the side wall. The bowl is shaped so that when blood having a hematocrit between 40-60 (ie., volume percent red blood cells) is processed, the red blood cell volume 40 and plasma volume 36 are approximately equal whether the bowl is fully filled as in Figure 15 or partially filled as in Figure 16.

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The bowl is also constructed such that the red blood cell sedimentation surface area (S_1) 118b is greater than the interface surface area (S_2) 132. For example, when the bowl is fully filled, the red blood cell sedimentation surface area 118b may be about four times that of the interface 138.

When the bowl is partially filled, as seen in Figure 16, the red blood cell area (S_1) 118b is clearly greater than the interface surface area (S_2) 138.

In operation, whole blood is introduced into the chamber through the low-G port 130, for example, and the apparatus is spun about the axis A-A in a first or hard spin. During this first spin the heavier red blood cells are driven toward or sediment against the outer wall 118b and red blood cells fill the blood cell volume 40. Platelet-rich plasma in the volume 40 is displaced inwardly toward the plasma volume 36. Eventually the red blood cells, which are experiencing high gravity forces, sediment or "pack out", thus filling the volume 40. Using this procedure, platelet separation from the red blood cells is maximized as is red blood cell purity.

The plasma volume 36 fills with the platelet-rich plasma initially in the volume and with the platelet-rich plasma displaced into the volume. The platelet-rich plasma in the plasma volume 36 experiences low-G forces as compared to the forces experienced by the red blood cells. The plasma at the axis A-A experiences almost no centrifugal forces, and the plasma at the interface 138 experiences some centrifugal forces.

Due to displacement and centrifugal forces some platelets will separate from the plasma and form a buffy layer at the interface 120. However, the amount of platelet separation and buffy layer formation is minimized and is related to the spin rate, plasma viscosity, interface position, and the like. The intent is to minimize platelet separation and buffy layer formation during red blood cell separation.

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In one example, the chamber was fully filled with about 500 milliliters of whole blood which has a hematocrit of about 40 (ie., 40 volume per cent red blood cells).

After the first or hard spin, the red blood cells formed a bed of packed cells in the volume 40, platelet-rich plasma collected in volume 36, and a thin buffy layer formed at interface 138. The packed cell volume was about 250 milliliters and the plasma volume was about 250 milliliters.

It will be appreciated that due to the higher G forces and larger surface area, the red blood cells separated or sedimented faster than the platelets at the interface 138.

After separation, the red blood cells can be collected through the high-G port 128 with minimal platelet contamination. Thereafter, the chamber can be utilized for platelet/plasma separation.

Since the volume relationships remain substantially constant (ie., about equal) and the red blood cell sedimentation area is greater than the buffy layer area, small or large quantities of whole blood can be processed.

Figure 16 shows the variable volume chamber set to process less than 525 milliliters of whole blood. As in Figure 15, the volumes are about equal and the red blood cell surface area is greater than the interface area. Processing is performed in substantially the same manner and the same type of separation is effected.

In Figure 17, an enclosed, rigid, fixed volume processing bowl 150 is shown. The housings, drives and controls for operating a rigid bowl system are known in the art. The bowl 150 may be blow-molded or fabricated from plastic members and includes rigid inner and outer walls 152 and 154 which define a fixed internal volume that includes a red blood cell volume 56 in the side wall and a plasma volume 58 in the bottom wall. The bowl includes a red

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blood cell sedimentation surface 160 and is structured to permit a buffy layer or interface 162 to form and be defined. High-G and low-G ports 164 and 166 and related conduits are also provided. Separation of therapeutic components using this bowl is similar to separation using the variable volume bowl except that no volume variation occurs.

It will be appreciated that numerous changes and modifications can be made to the embodiments disclosed herein without departing from the spirit and scope of this invention.

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CLAIMS:

1. A flexible, variable-volume, bowl-shaped chamber for use in centrifugal apheresis for receiving whole blood, separating blood into therapeutic components, and selectively collecting therapeutic components of blood, said chamber comprising:

an enclosed bladder-like casing which is formable into said bowl-shaped chamber, said chamber having a bowl-shaped outer wall, and a bowl-shaped inner wall positioned within said outer wall which defines a blood processing cavity therebetween and a flexible rim area connecting said inner wall and outer wall, which area defines a rim edge;

said flexible rim area being adapted to fold against itself to form a rim edge which is adapted to advance and retract as said chamber volume changes; and

said outer wall having at least one port extending therethrough for fluid communication with the blood-processing space.

2. A variable-volume chamber as in Claim 1, wherein a pair of ports are provided, with one port passing through the outer wall at the central spin axis to form a low-gravity port and the other port passes through the casing at a radially outermost point so as to form a high-gravity port.

3. A variable-volume chamber as in Claim 2 wherein a third port is provided, which passes through the outer wall at a point intermediate the low-gravity and high-gravity ports.

4. A variable-volume chamber as in Claim 1, wherein said inner and outer walls at said rim area are spaced from each other and are constructed to move in axially opposite directions as said chamber is filled and emptied so that the rim edge appears to roll axially.

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5. A variable-volume chamber as in Claim 1, wherein said inner and outer walls at said rim area contact each other and slide against each other in opposite directions as said chamber is filled and emptied so that the rim edge appears to roll axially.

6. A variable-volume chamber as in Claim 1, wherein said chamber forms a part of a disposable blood collection and component separation system which comprises said chamber, at least one therapeutic component collection container integrally and sterilely connected to at least one port of said bowl-shaped chamber, and catheter means integrally and sterilely connected to said bowl-shaped chamber to at least one port of said bowl-shaped chamber.

7. A system as in Claim 6, wherein there is provided three component collection containers, each adapted and constructed to receive a therapeutic component; one of said containers adapted to receive red blood cells; a second to receive platelets; and a third for receiving platelet-free plasma, each of said collection containers being constructed to be selectively opened and closed to receive a component from said processing chamber.

8. An enclosed processing bowl for use in centrifugal apheresis, said bowl having inner and outer walls which define a bottom section, a side wall section, and a blood-receiving cavity between said walls and at least one port for fluid communication with said cavity, and said bowl having a spin axis extending centrally through said bowl;

the bottom section of the bowl defining a cylindrically-shaped plasma processing volume between the inner and outer walls of said bottom;

the side wall section of the bowl defining an annularly-shaped red blood cell processing volume between the inner and outer walls of said side wall;

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said plasma processing volume and red blood cell processing volume being adjacent each other at the transition from the bottom wall to the side wall to form a generally cylindrical interface;

said outer wall of said annularly-shaped red blood cell processing volume forming a red blood cell sedimentation surface; and

the surface area of the red blood cell sedimentation surface being greater than the area of the cylindrical blood cell plasma interface.

9. A centrifugal processing bowl as in Claim 8, wherein the bowl is substantially symmetric about said spin axis.

10. A centrifugal processing bowl as in Claim 8, wherein the volume of the red cell processing volume and volume of the plasma processing volume are substantially equal.

11. A centrifugal blood processing bowl as in Claim 8, wherein the red cell processing sedimentation surface area is at least twice the surface area of the interface.

12. A centrifugal blood processing bowl as in Claim 11, wherein the red cell processing sedimentation surface area is about four times greater than the surface area of the interface.

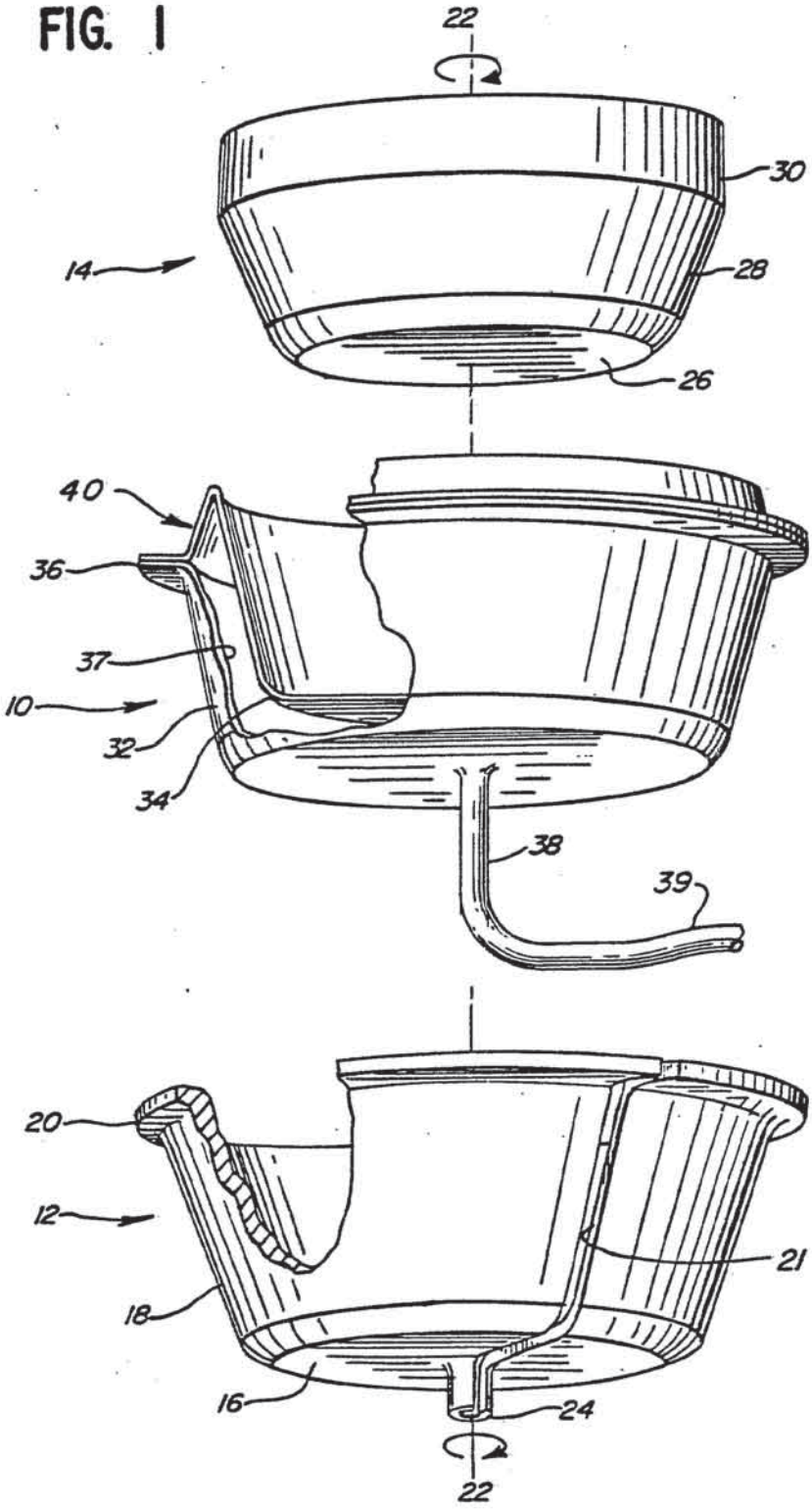
13. A centrifugal blood processing bowl as in Claim 8, wherein said bowl is of a fixed volume and the inner and outer walls are fixed and rigid.

14. A centrifugal blood processing bowl as in Claim 8, wherein said bowl is of a variable volume and the inner and outer walls join at a rim area and at least the rim area of said bowl are flexible so as to accommodate changes in bowl volume.

15. A centrifugal blood processing bowl as in Claim 14, wherein the red cell processing volume and plasma volume are approximately equal and said volumes remain equal to each other throughout the range of chamber column changes from empty to full.

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FIG. 1



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FIG. 2

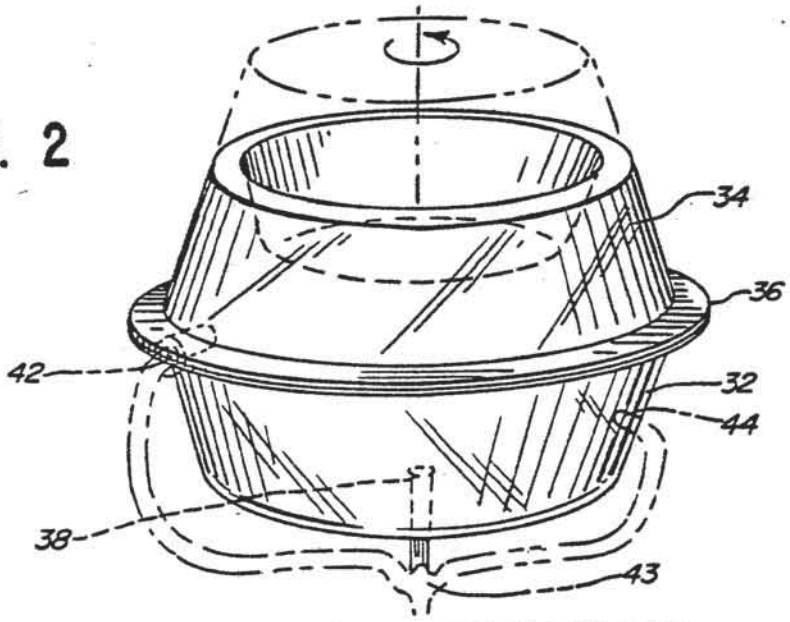


FIG. 3

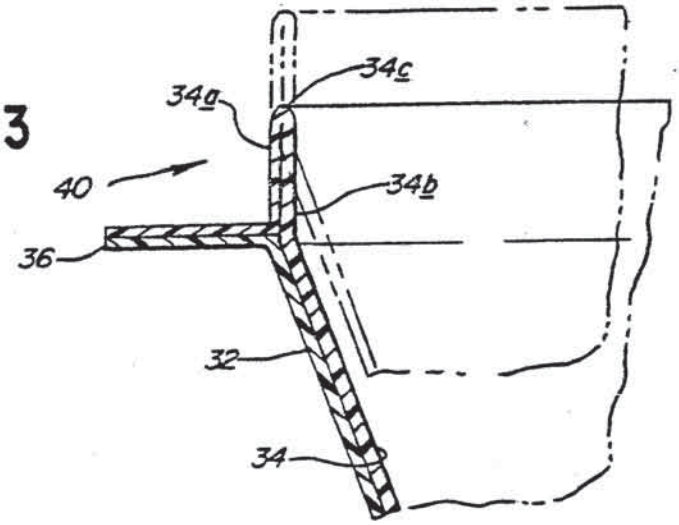
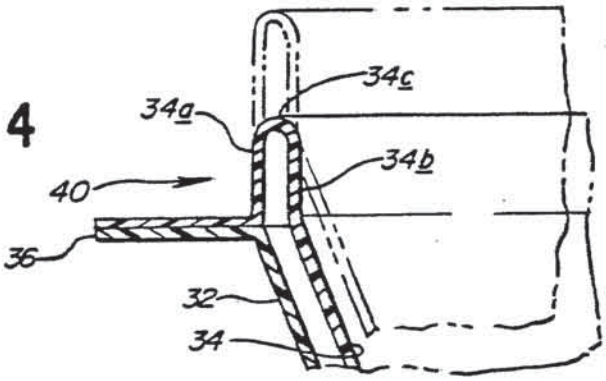


FIG. 4



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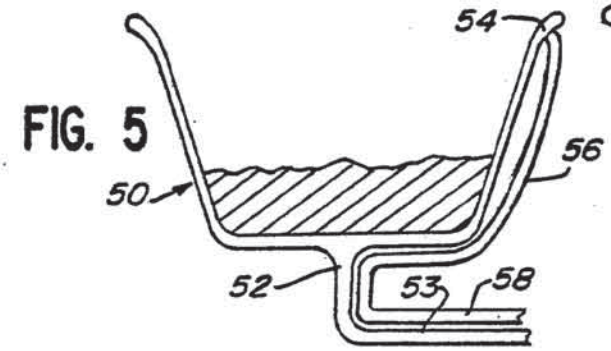


FIG. 5

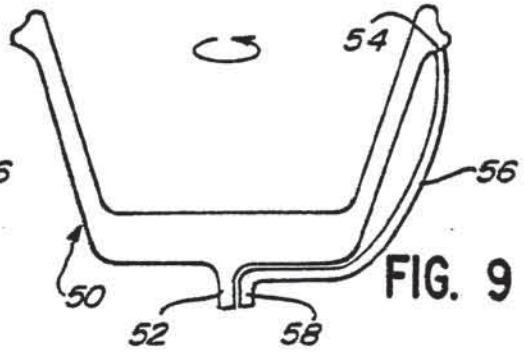


FIG. 9

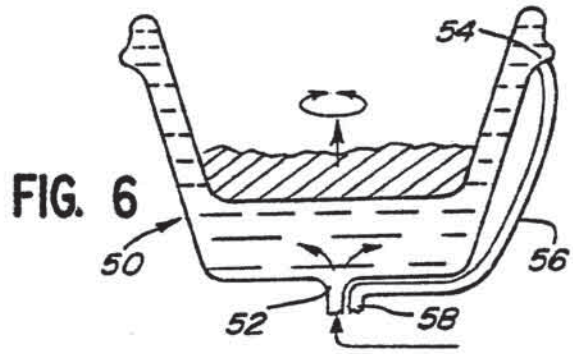


FIG. 6

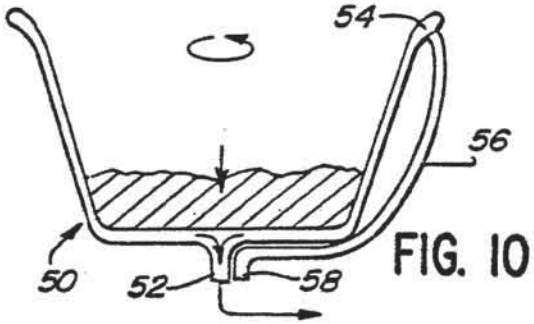


FIG. 10

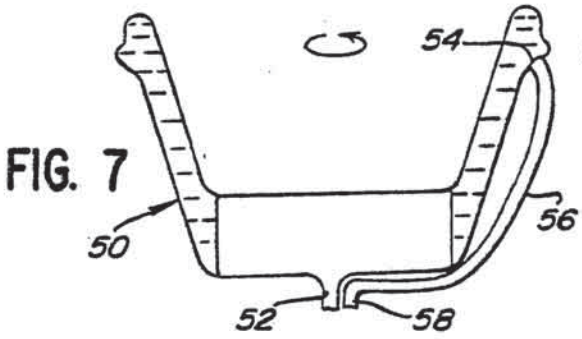


FIG. 7

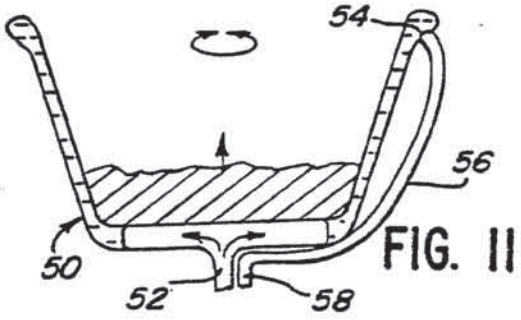


FIG. 11

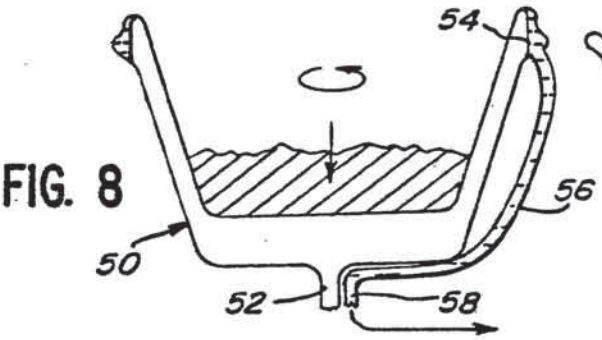


FIG. 8

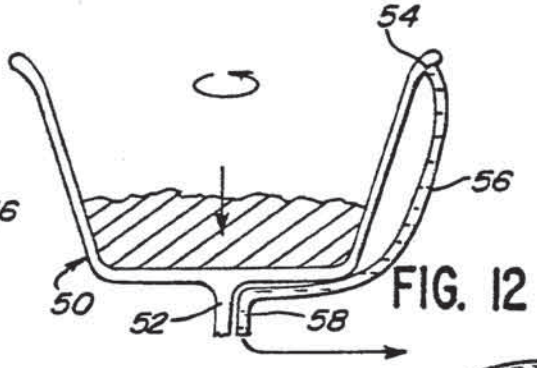
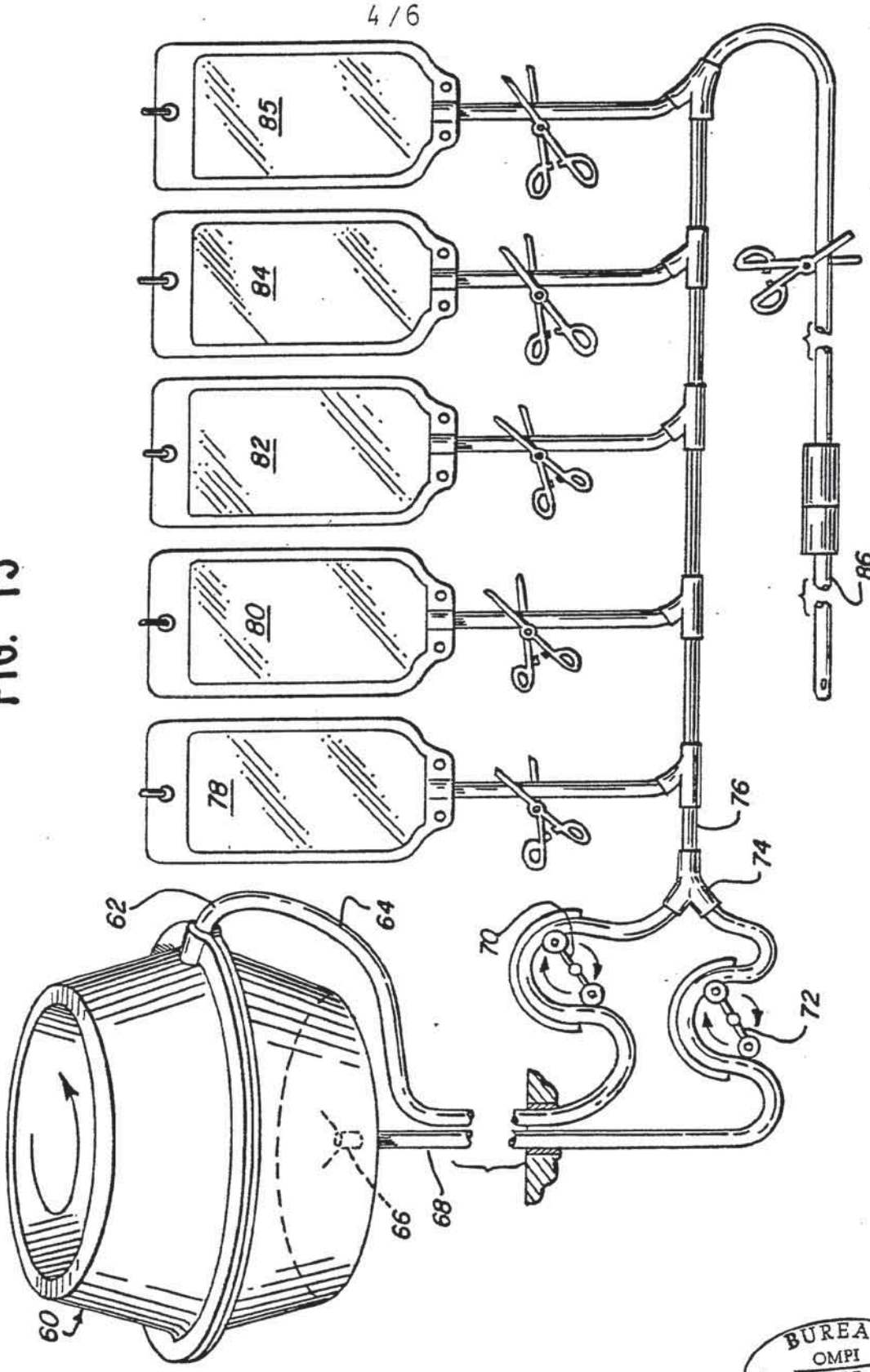


FIG. 12

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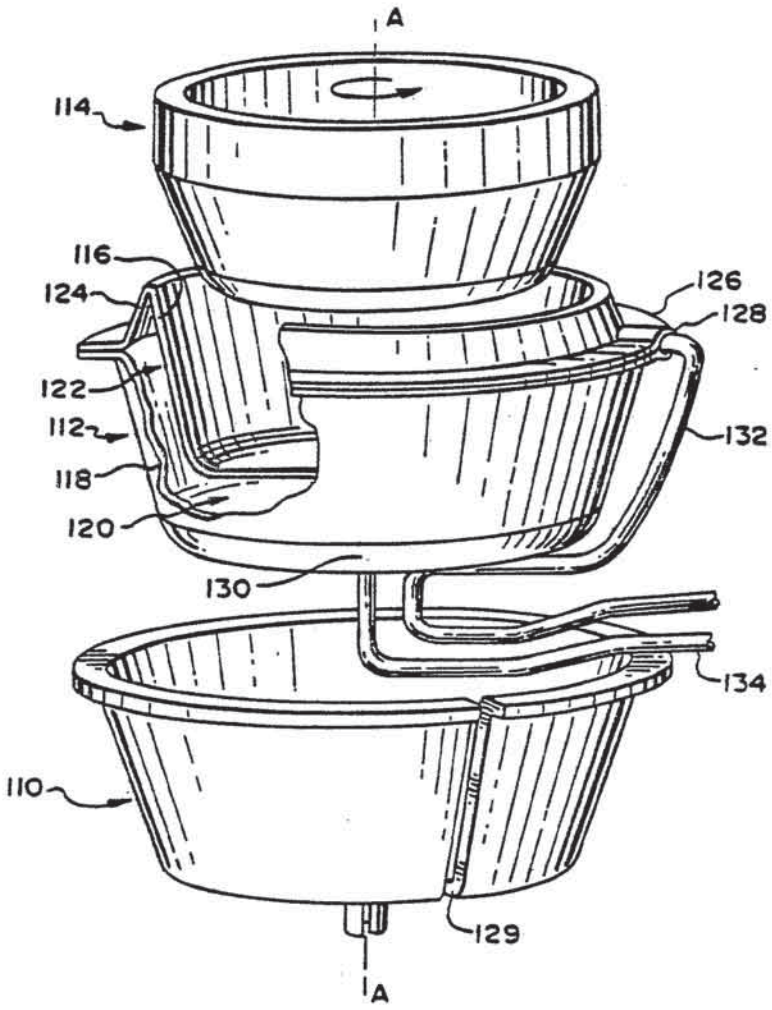
FIG. 13



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FIG. 14



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FIG. 15

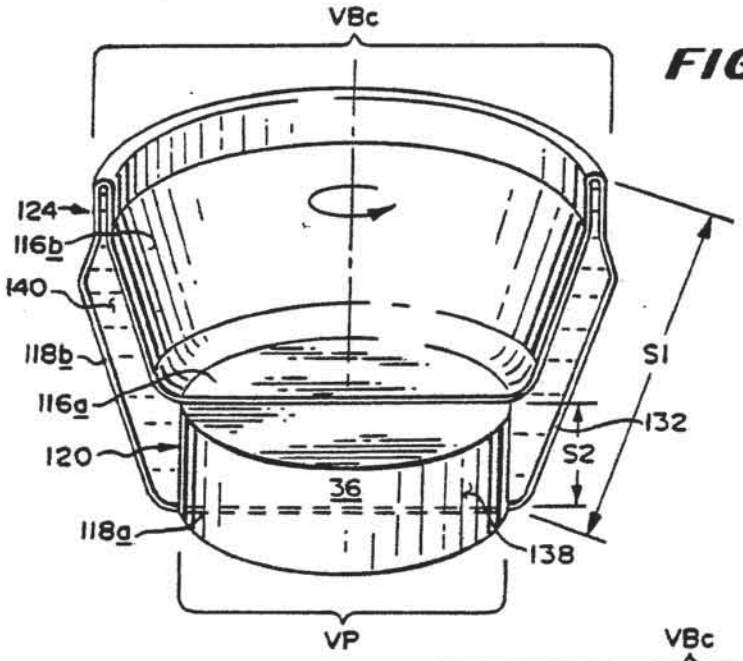


FIG. 16

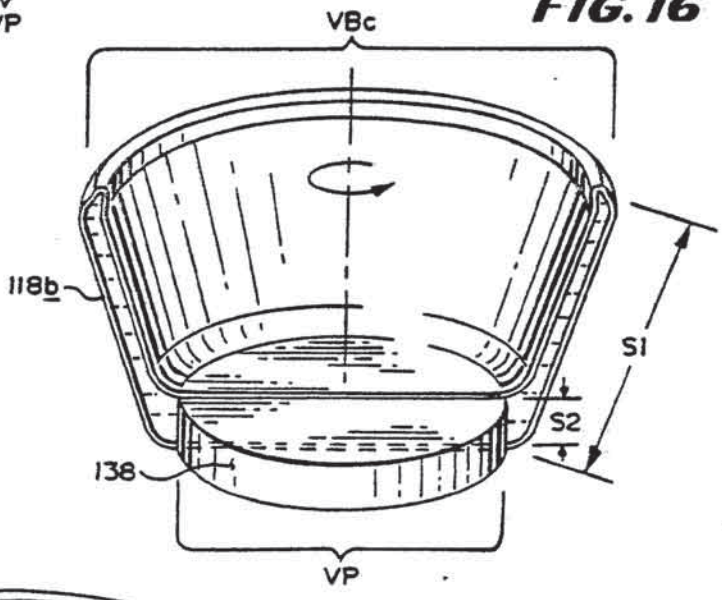
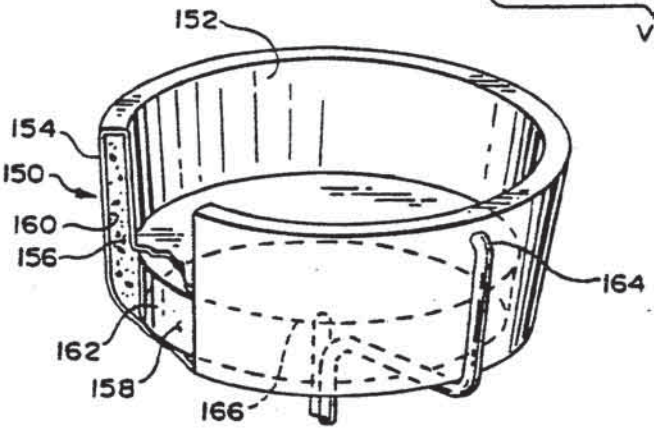


FIG. 17



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INTERNATIONAL SEARCH REPORT

PCT/US84/01796

International Application No

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [3]

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL.[4] B04B 1/10, 1/12, 11/02
U.S. CL. 494/45,65 210/512.1, 787,927

II. FIELDS SEARCHED

Minimum Documentation Searched [4]

Classification System	Classification Symbols
U.S.	494/18,20,21,45,65,84 210/512.1,787,927 604/4-6,408

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [5]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [14]

Category *	Citation of Document, [16] with indication, where appropriate, of the relevant passages [17]	Relevant to Claim No. [18]
Y	US, A, 4,413,771, PUBLISHED 08 NOVEMBER 1983, ROHDE ET AL.	1-7, 14,15
Y	US, A, 4,413,772, PUBLISHED 08 NOVEMBER 1983, ROHDE ET AL.	1-7, 14,15
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* Special categories of cited documents: [15]

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IV. CERTIFICATION

Date of the Actual Completion of the International Search [2]	Date of Mailing of this International Search Report [2]
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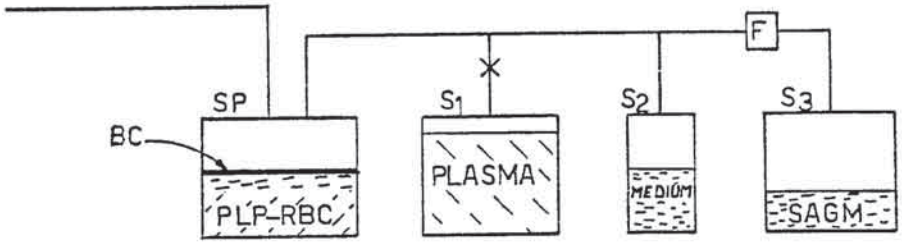
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(54) Title: PROCEDURE AND CONTAINER FOR THE PREPARATION AND STORAGE OF PLATELET CONCENTRATES



(57) Abstract

A procedure for the routine preparation in closed system and storage in a medium made of natural colloid (plasma) and crystalloid solution of PC deprived of leukocytes, which is based on a quadruple blood bag (PB) containing CPD anticoagulant, an empty satellite bag (S1), a satellite bag (S2) containing a synthetic crystalloid solution, a satellite bag with SAGM (or similar) additive solution for red blood cells (RBC), consisting in collecting the blood in the primary bag (PB), in centrifuging the blood bag at high speed, in expressing the supernatant plasma into bag (S1), in collecting 15-20 mL of the buffy-coat (BC) into bag (S2), in adding the SAGM solution of bag (S3) into bag (PB) containing the RBC concentrate, in disconnecting bags (PB) and (S1) from bags (S2) and (S3), in centrifuging bag (S2) at soft spin and in transferring the supernatant platelet concentrate (PLP-PC) formed after this centrifugation into the empty bag (S3), through a cotton wool filter (F) inserted along the tube line so as to remove residual leukocytes which contaminate the PC.

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Procedure and container for the preparation and storage of platelet concentrates.

This invention relates to a procedure for the routine preparation in closed system of platelet concentrates (PC) deprived of leukocytes and stored in a medium consisting of a mixture of natural colloid (plasma) and of crystalloid solution (called thereafter "medium"), and in particular for PC storage.

Standard RBC concentrates and PC, prepared by serial centrifugation from multiple bags and storage in a natural colloid medium (plasma), are contaminated with plasma and leukocytes, which can determine acute and chronic side-effects in transfusion recipients.

The transfusion of platelet concentrates (PC) is necessary for preventing the risk of hemorrhage in patients with low platelet count (thrombocytopenia).

Routine production of blood components (RBC and PC) with higher purity is hampered by technical difficulties concerning particularly the separation and storage of blood cells.

Presently available methods for preparing PC are based on soft spin of whole blood donations, the collection of platelet-rich-plasma, and the concentration of platelets in 50 mL plasma by high speed centrifugation. Such PC can be stored for a maximum of 5 days. A different approach is the collection of buffy-coats (BC) of whole blood donations (the BC is the layer formed at the red blood cell-plasma interface after whole blood high-spedd centrifugation), followed by soft spin of the BC and collection of platelets in the supernatant. The principal untoward effect of PC transfusion is the production of alloantibodies by PC recipients, caused by leukocytes which contaminate the PC. Moreover, allergic reactions to plasma proteins can occur.

To prevent these complications and to improve the quality of platelet transfusion the invention described below was developed.

The aim of this invention is to remove this difficulty by means of a procedure for blood fractionation allowing the routine

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production and storage in closed system of plasma- and leukocyte-poor RBC concentrates (PLP-RBC, ie RBC containing less than 10% of donated plasma and less than 30% of donated leukocytes), and of plasma- and leukocyte-poor platelet concentrates (PLP-PC, ie PC in a medium containing about 15-40% plasma, and free of leukocytes detectable by microscope counting).

In the procedure reported in this invention an additive RBC solution is used (SAGM or similar), in addition to a synthetic crystalloid solution which is added to the platelets so as to improve their quality and prolong storage to about 10 days.

The above crystalloid solution is preferably made (considering, for example, a volume of 40 mL) of 5.26 g sodium chloride; 2.22 g sodium acetate; 5.02 g sodium gluconate; 0.37 g potassium chloride; 0.14 g magnesium chloride; H_2O for IV use qs to 1,000 mL, pH 7.4 $\pm$ 0.1. It must be emphasized that this solution is very similar to one of the crystalloid solutions reported in the patents issued under the names of Gail Ann Rock and George Adams (Canada, Plasma-free medium for platelet storage, application, Nov 1, 1982, 414,583; USA, Plasma-free medium for platelet storage, Pat 4,447,415; Europe, Plasma-free medium for platelet storage, Granted May 16, 1984 - 0108588, Oct 31, 1983, 83306631.9; Canada, Improved plasma-free medium for platelet storage, application, July 20, 1984, 459,369); however, in the invention described here the quality of platelets is improved since the crystalloid solution is fortified with an amount of plasma derived from the BC; this amount is between 10 and 40% of the final medium, preferably 20-30%.

The procedure is carried out with a multiple bag, preferably a quadruple bag consisting of a primary bag and 3 satellite bags.

After high speed centrifugation, the blood contained in the primary bag is separated into a red blood cell button and supernatant plasma; this latter is transferred into one of the

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satellite bags, while the SAGM solution is added to the primary bag for red blood cell storage, after removing an amount of the buffy-coat (BC) layer, which is the layer between red blood cells and plasma, a layer enriched of platelets. The buffy-coat is transferred into a second satellite bag containing the crystalloid solution and, after a soft spin, the supernatant platelet concentrate is transferred in the third, empty satellite bag, through a cotton wool filter inserted along the tubing, which is capable of removing residual leukocytes which contaminate the platelet concentrate. A platelet concentrate prepared according to this method can be stored for about 10 days in this bag, which is made of plastic material with gas exchange characteristics similar to those of polyolefin.

The above procedure and bag system for the preparation of platelet concentrates from buffy-coats (BC) and their storage in a crystalloid colloid medium can be used also with BC prepared with standard blood bag systems, by mixing 6-8 BC in a transfer bag containing an appropriate amount of the above crystalloid solution. After a soft spin, the supernatant, containing the platelets, is transferred through a cotton wool filter into a new transfer bag where it is stored.

The procedure derived from this invention is now described, just for the sake of example, and with no limitation to its implementation, with the aid of enclosed fig. 2 through 5, which describe the procedure steps, as performed with a quadruple blood bag, for the preparation and storage of PLP-PC and PLP-RBC from a blood donation.

The multiple blood bag consists of a primary bag PB and of 3 satellite bags S1, S2, S3, integrally connected to each other with flexible plastic tubes.

The primary bag PB contains CPD (citrate-phosphate-dextrose) anticoagulant, the satellite bag S1 is empty, the satellite bag

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S2, which is cylinder-shaped and has a volume of 40-60 mL, contains 40 mL of crystalloid solution, the satellite bag S3 contains the SAGM red blood cell additive solution, and is made of plastice material with gas permeability characteristics similar to polyolefin. Along the tube connecting bags S2 and S3 a small (2-3 g) cotton wool filter is inserted.

The procedure regarding this invention is carried out as described below.

The blood donation is collected in the primary bag PB through a collection line I, at one end of which the blood collection needle is attached, and mixed with the CPD anticoagulant (fig. 1). The blood collected in the primary bag PB is centrifuged at high speed, e.g. 3,800 rpm for 4 min in a Sorvall RC-3B centrifuge. After this centrifugation, plasma- and leukocyte-poor red blood cells are concentrated in the lower part of the primary bag PB, the supernatant plasma is contained in the higher part of the bag, and in the layer between plasma and red blood cells the vast majority of platelets are concentrated. This small layer, enriched of platelets, which separated red blood cells from supernatant plasma is defined "buffy-coat" (BC)(fig. 2).

The supernatant plasma (except for about 30 mL) is expressed into and stored in satellite bag S2, which is diconnected from the other bags (fig.2).

A total of 25-50 mL of BC are then collected, which contain about 5 g hemoglobin, 80% of donated platelets, 50% of donated leukocytes and 20-40 mL plasma, and expressed into satellite bag S2, which contain the crystalloid medium (fig. 3).

Preferably, the crystalloid solution contained in satellite bag S3 has the following composition (reference to a volume of 40 mL): 5.26 g sodium chloride; 2.22 g sodium acetate; 5.02 g sodium gluconate; 0.37 g potassium chloride; 0.14 g magnesium chloride; H_2O for IV use qs to 1,000 mL, pH 7.4 $\pm$ 0.1.

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The SAGM solution contained in satellite bag S3 is added to the red blood cell concentrate PLP-RBC in the primary bag PB for its storage. The primary bag, containing the PLP-RBC and the satellite bag S1 containing the plasma are disconnected from satellite bags S2 and S3, which are stored, integrally connected to each other, in a platelet tumbler (a rotating machine for platelet resuspension during storage) (fig.4).

The buffy-coat (containing the platelets) contained in satellite bag S2 can be stored at room temperature for a maximum of 48 h. If platelet concentrates are needed the buffy-coat is centrifuged at low speed, so as to concentrate the red blood cells and the leukocytes in the lower part of the bag S2, and to collect the leukocyte-poor platelet concentrate in the higher part of satellite bag S2. The cylinder shape of satellite bag S2 favors a good separation between the 2 layers above after the soft spin.

The supernatant PLP-PC is transferred from satellite bag S2 to satellite bag S3 (which had been previously emptied of the SAGM solution), through filter F, which removes residual leukocytes present in the platelet concentrate (fig. 5).

Filter F can be much smaller than traditional cotton wool filters for leukocyte removal (2-3 g instead of 17 g) because leukocyte contamination of platelet concentrates prepared from buffy-coats is much lower than that of platelet concentrates prepared with traditional methods, in which centrifugation is carried out on platelet-rich-plasma instead of platelet-rich-buffy-coat.

Experimental data indicate that the platelet concentrate PLP-PC prepared with the above method can be stored in the crystalloid/colloid medium for at least 10 days in a bag made of polyolefin, or of a plastic material capable of providing a gas permeability similar to that of polyolefin, with a final pH of about 7.0, hypotonic shock response of 50% and morphology score according to Kunicki of 220. Moreover, PC prepared with this

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method and invention have the following parameters after 7 days of storage: glucose consumption 1.5 mmol/L/10^9 platelets (compared to 2.8 of PC prepared in the medium of G. Rock), and lactate production of 3.56 mmol/L/10^9 platelets (compared to 6.09 of PC prepared in the medium of Rock). Both parameters suggest better platelet quality in our medium. In addition, platelet aggregation is better in our medium compared to that in the medium of Rock.

These excellent results are mainly due to the crystalloid/colloid medium, of which a preferential composition has been given above, in which a crystalloid solution is mixed with a small amount of plasma (natural colloid) present in the buffy-coat, from which the platelet concentrate is prepared.

The above procedure for the preparation of platelet concentrates from buffy-coats (BC) and their storage in crystalloid/colloid medium can be also used with buffy-coats prepared from traditional blood collection bags, e.g. by using a triple bag made of a primary bag and 2 satellite bags, in which the red blood cell concentrate, the plasma and the buffy-coat are collected, respectively.

In this case 6-8 buffy-coats prepared with the methods above or similar are collected in a transfer bag of about 600 mL volume, containing about 350 mL of the previously described crystalloid solution. After soft spin, the platelet-rich supernatant is transferred through a small (2-3 g) cotton wool filter F into a transfer bag of about 1000 mL volume, with the same characteristics of previously described bag S3, where it is then stored.

The procedure described in this invention offers the following advantages, in addition to those already reported, in comparison to traditional procedures:

- leukocyte contamination of platelet concentrates is below detectable limits in all platelet concentrates, which implies a

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series of outstanding advantages for the patients;

- platelet metabolism can be conditioned by modifying the storage medium with the addition of possible additives;

- there is no need to follow ABO compatibility between donor plasma and recipient red cells, due to the small amount of plasma present in the platelet concentrates;

- more plasma can be recovered from standard blood donations;

- it is possible to prepare platelet concentrates only upon request, so reducing the workload;

- the procedure favors the routine production of buffy-coat deprived red blood cell concentrates (which are of better quality than standard red blood cell concentrates), since it is based on the avalability of buffy-coats.

Moreover, the crystalloid solution does not contain glucose, thus reducing the potential risk of bacterial contamination of PLP-PC.

The above advantages are supported by a series of in-vitro and in-vivo evaluations of platelet concentrates prepared from buffy-coats and stored in medium. A set of these evaluations is reported below.

We compared platelet concentrates prepared from pools of buffy-coats removed from standard blood donations and stored in the crystalloid solution described above (BCS-PC), with standard platelet concentrates, prepared from platelet-rich-plasma (PRP-PC). Total cell counts (median and range, n=43) in BCS-PC units were: platelets 3.6×10^{11} (2.2-5.5), leukocytes 21×10^{6} (4-79); values of PRP-PC units (n=23) were: platelets 0.64×10^{11} (0.47-0.83); leukocytes 148×10^{6} (3-611). Since one BCS-PC unit was prepared from 7 blood donations, a meaningful comparison of PRP-PC and BCS-PC data can be made by multiplying PRP-PC data by 7. Both platelet and leukocyte counts of BCS-PC were significantly lower than those of 7 PRP-PC. Platelet yield in BCS-PC and PRP-PC was 59 and 75 percent of donated platelets, respectively. Median number

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of total leukocytes in 1 BCS-PC unit, prepared from a pool of 7 buffy-coats, was 50 times lower than that of 7 PRP-PC. In vitro parameters of adequate platelet quality were maintained for 10 days in BCS-PC stored in 1000 mL polyolefin bags. Prolonged bleeding times were reduced or corrected in 3 of 3 thrombocytopenic leukemic patients evaluated before and after transfusion of stored BCS-PC. Pretransfusion, 1-h and 24-h posttransfusion median platelet counts of 57 leukemic recipients during 4 months of routine transfusion of BCS-PC (n=93) were 14, 35, and 27 x 10^9/L, compared with 13, 37 and 31 x 10^9/L of PRP-PC (n=246), respectively (p=ns). No reactions to BCS-PC were reported, compared with a reaction rate of 1.3 percent for PRP-PC transfusions. The median (and range) titer of ABO agglutinins in BCS-PC and PRP-PC was 8 (2-8) and 64 (32-128), respectively. A detailed description of the results is reported in tables 1-3.

In vitro evaluation of BCS-PC and PRP-PC during storage is reported in table 1.

It can be seen (section A) that in vitro parameters of adequate platelet quality (pH above 6.0, morphology score above 200) were maintained in BCS-PC for at least 10 days of storage in 1000 mL polyolefin bags; at this time the platelet response to hypotonic shock (HSR), a parameter related to platelet recovery and survival in normal volunteers, was still above 80 percent of values at day 1. This was not so for BCS-PC stored in 1000 mL PVC bags (section B), in which the median pH value was below 6.0 at day 3. This was associated with a complete loss of HSR and a marked deterioration of platelet morphology. Similarly to other reports, PRP-PC stored in PVC satellite bags of 400 mL volume showed adequate quality preservation for at least 5 days (section C). On day 1, PO_2 values of BCS-PC in 1000 mL bags were about 2 times higher than those of PRP-PC in 400 mL bags, as expected on the basis of both a larger bag and a smaller platelet concentration in the former. Platelet

quality during storage in PVC deteriorated more rapidly in BCS-PC than in PRP-PC. A contributory cause could have been the smaller ratio between bag surface area and PC volume in the former, determining a less efficient gas transport during storage. Oxygen consumption for aerobic metabolism, which is more favorable than anaerobic for PC preservation during storage, was maintained longest in BCS-PC stored in polyolefin, as indicated by the slowest PO_2 rise.

Results of in-vivo study are reported in Table 2 and 3.

Pilot phase. Pretransfusion, 1-h and 24-h posttransfusion platelet counts and percent recovery values obtained in "stable" leukemic recipients are reported in table 2. It can be seen that values of BCS-PC stored for 1-8 days were similar to those of PRP-PC stored for 1-3 days. Bleeding time (reference values 2-7 min) was reduced after BCS-PC transfusion in 3 of 3 patients evaluated, dropping from more than 30 to 9 min (6-day old BCS-PC containing 3.0×10^{11} platelets), from 25 to 5 min (4-day old BCS-PC containing 2.8×10^{11} platelets), and from 22 to 6 min (8 day old BCS-PC containing 3.1×10^{11} platelets). On these 3 occasions pre- and 1-h posttransfusion platelet counts were 17-43, 16-56 and 16-39 $\times 10^9$/L, respectively.

Routine phase. A total of 448 and 129 platelet transfusions were issued as 1-3 day-old PRP-PC and 1 day-old BCS-PC, respectively, to 57 leukemic patients. This group included all hematological patients transfused with platelet concentrates in the study period. Pretransfusion, 1-h and 24-h posttransfusion platelet count and percent recovery, available on 55 percent (PRP-PC) and 72 percent (BCS-PC) of occasions, are reported in table 3. Increments of BCS-PC were not significantly different from those of PRP-PC. No reactions were reported for BCS-PC, compared with 6 for PRP-PC; of these, 2 were febrile and 4 allergic.

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Table 1 storage.

Day	pH	PO_2 (mm Hg)	PCO_2 (mm Hg)	HSR (%)	Morphology score	Platelet count (% of day 1)
A) BCS-PC units stored in 1000 mL polyolefin bags (n=8)						
1	6.9 (6.7-6.9)	87 (70-109)	23 (20-31)	62 (39-68)	311 (250-333)	100
3	6.9 (6.4-6.9)	73 (61-115)	26 (19-36)	64 (46-67)	273 (230-306)	95 (75-100)
5	6.8 (6.4-6.9)	93 (40-123)	28 (19-39)	62 (42-70)	266 (215-297)	88 (73- 96)
10	6.7 (6.3-7.0)	101 (76-145)	25 (20-36)	51 (33-69)	203 (185-260)	81 (71- 93)
15	6.9 (5.8-7.2)	122 (65-175)	17 (9-27)	31 (0-60)	180 (105-280)	76 (68- 81)
B) BCS-PC units stored in 1000 mL PVC bags (n=8)						
1	6.8 (6.7-6.9)	90 (82-124)	27 (18-31)	50 (42-67)	312 (270-329)	100
3	5.9 (5.8-6.5)	148 (71-161)	37 (24-69)	0 (0-69)	160 (142-231)	92 (88- 97)
C) PRP-PC units stored in 400 mL PVC bags (n=10)						
1	7.0 (6.7-7.1)	40 (28-149)	56 (19-90)	55 (30-69)	260 (210-331)	100
3	7.0 (6.2-7.2)	47 (16-81)	46 (34-77)	51 (36-56)	226 (122-331)	100 (100-100)
5	7.0 (5.6-7.1)	58 (13-154)	42 (16-48)	47 (0-60)	208 (92-263)	100 (81-100)
10	6.6 (5.5-7.0)	86 (50-199)	35 (13-42)	21 (0-40)	167 (71-195)	94 (88- 97)
15	6.1 (5.7-6.8)	181 (123-201)	14 (6-28)	0 (0-9)	107 (73-154)	72 (60- 94)

Table 2. In vivo study: pilot phase. Median (and range) platelet counts and percent recovery in 11 "stable" leukemic patients receiving both BCS-PC and PRP-PC.

Type of PC	Storage Days	Storage Bag	Platelet count ($\times 10^9$/L) Pre-	Posttransfusion 1-h	Posttransfusion 24-h	Platelet in vivo recovery (% of expected) 1-h	24-h
BCS-PC n=8	1	1000 mL PVC	13 (9-20)	42 (23-56)	34 (28-46)	59 (19-81)	44 (28-62)
BCS-PC n=8	4- 8	1000 mL polyolefin	17 (9-21)	43 (16-56)	33 (12-40)	50 (0-102)	36 (0-54)
BCS-PC n=5	9-12	1000 mL polyolefin	10 (5-21)	43 (13-91)	21 (12-28)	73 (17-161)	11 (7-40)
PRP-PC n=15	1- 3	400 mL PVC	16 (4-29)	50 (10-92)	37 (14-79)	49 (0-102)	30 (0-92)

Table 3. In vivo study: routine phase. Median (and range) platelet counts and percent recovery in 57 hematologic patients receiving platelet transfusion during 4 months of routine use of both BCS-PC and PRP-PC.

Type of PC	Storage Days	Storage Bag	Platelet count ($\times 10^9$/L) Pre-	Posttransfusion 1-h	Posttransfusion 24-h	Platelet in vivo recovery (% of expected) 1-h	24-h
BCS-PC n=93	1	1000 mL PVC	14 (2-40)	35 (7-83)	27 (3-64)	40 (0-103)	22 (0-98)
PRP-PC n=246	1- 3	400 mL PVC	13 (1-69)	37 (4-114)	31 (1-137)	31 (0-110)	20 (0-124)

It is emphasized that the invention is not limited to the particular description reported above and in the enclosed figures, but it can me modified in several minor parts within the scope of the invention.

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CLAIMS

1. A method for the preparation and storage of plasma- and leukocyte-poor platelet concentrates from buffy-coats, which comprises the transfer of at least 1 buffy-coat into a bag (S2) containing a synthetic crystalloid solution (which is diluted with the plasma contained in the buffy-coat so as to constitute a colloid/crystalloid medium for platelet storage), the soft spin of the bag (S2) and the transfer of the supernatant PLP-PC formed after centrifugation into a (S3) bag made of polyolefin or of plastic material with gas permeability similar to polyolefin, through a cotton wool filter (F) of 2-3 g, so as to remove residual leukocytes contained in the platelet concentrate.

2. A method as claimed in claim 1, wherein the above bag S2 has an elongated, cylinder shape.

3. A process according to claim 1, wherein 1000 ml. of said synthetic crystalloid solution contain 5.26 gr sodium chloride, 2.22 gr sodium acetate, 5.02 gr sodium gluconate, 0.37 gr potassium chloride, 0.14 gr magnesium chloride, H_2O for I.V. use qs to 1000 ml and wherein said crystalloid solution has a pH of 7.4 ± 0.1.

4. A process according to claim 1, wherein 6-8 BC obtained from as many donations are transferred into the bag (S2).

5. A process according to claim 1, wherein the PLP-PC are stored in a synthetic crystalloid / natural colloid solution, comprising the crystalloid medium of bag (S2) and the plasma of each BC (about 20-40 ml of plasma in a BC volume of 25-50 ml).

6. A process according to claim 1, wherein the BC are separated in a multiple bag for the preparation and storage of PLP-PC and PLP-RBC (plasma- and leukocyte- poor RBC concentrates), e.g. in a quadruple blood bag comprising a primary bag (PB) and three satellite bags (S1), (S2), (S3).

7. A process according to claim 6, comprising:

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collecting the blood in a primary bag (PB) containing CPD anticoagulant, centrifuging at high speed said primary (PB) bag, tranferring the supernatant plasma into the bag (S2) containing tha crystalloid solution, and tranferring the SAGM solution of bag S3 into the (PB) bag containing PLP-RBC.

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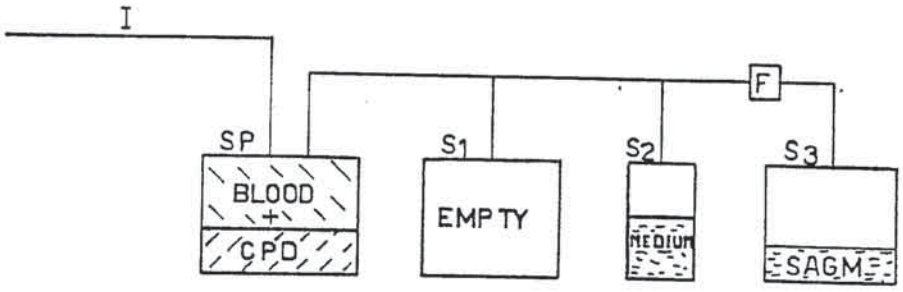


FIG_1

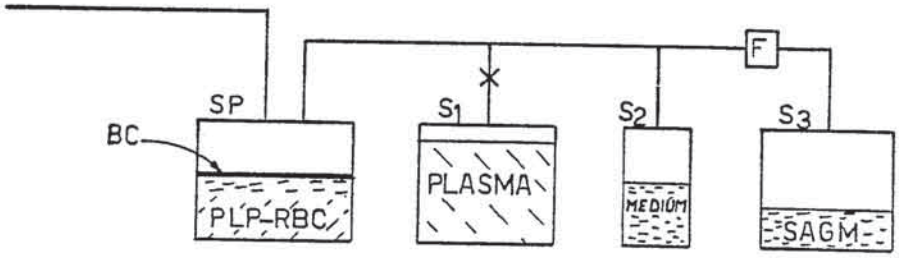


FIG_2

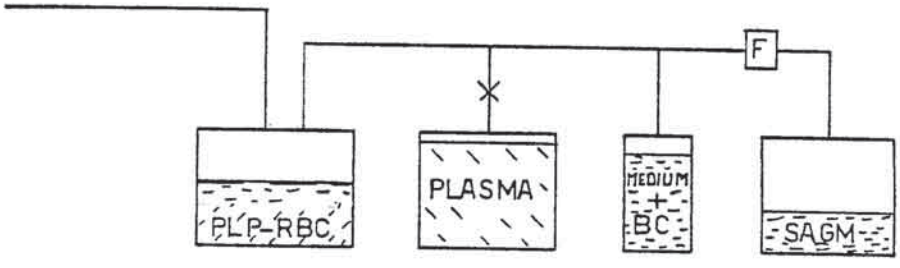


FIG_3

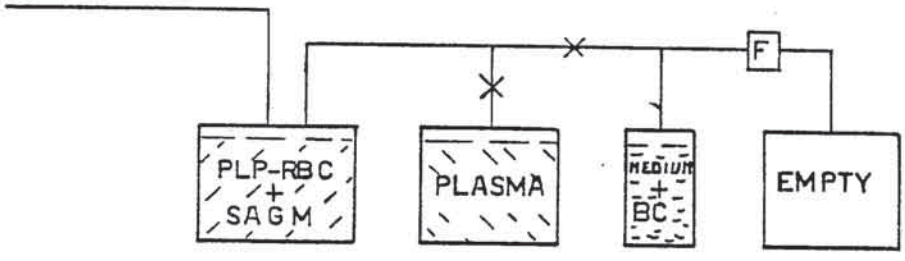


FIG_4

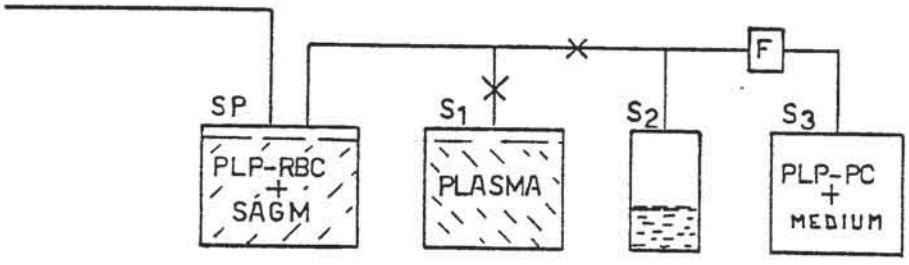


FIG_5

INTERNATIONAL SEARCH REPORT

International Application No PCT/IT 89/00048

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[5]: A 61 K 35/14, A 61 M 1/36

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[5]	A 61 K, A 61 M

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
A	EP, A, 0233112 (TERUMO K.K.) 19 August 1987 see page 4, lines 32-36; page 11, lines 31-36; page 12, lines 22-29; page 20, lines 28-34 --	1
A	US, A, 4639373 (B.M. BABIOR) 27 January 1987 see column 2, lines 18-19 --	1
A	US, A, 4447415 (G.A. ROCK) 8 May 1984 see claims 1,8 cited in the application --	1
A	WO, A, 86/03122 (CURATECH INC.) 5 June 1986 see claim 1 --	1
A	US, A, 4344936 (G. SOSLAU) 17 August 1982 see claim 1	1

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* Special categories of cited documents: [10]

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"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
13th September 1989	09. 10. 89

International Searching Authority	Signature of Authorized Officer
EUROPEAN PATENT OFFICE	T.K. WILLIS

Form PCT/ISA/210 (second sheet) (January 1985)

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. IT 8900048 SA 29644

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 29/09/89 The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A- 0233112	19-08-87	AU-A-	1885688	06-10-88
		AU-B-	578554	27-10-88
		AU-A-	6794387	06-08-87
		JP-A-	62258322	10-11-87
US-A- 4639373	27-01-87	None		
US-A- 4447415	08-05-84	CA-A-	1216518	13-01-87
		EP-A,B	0108588	16-05-84
		US-E-	RE32874	21-02-89
WO-A- 8603122	05-06-86	AU-A-	5094985	18-06-86
		DE-T-	3590594	29-01-87
		EP-A-	0202298	26-11-86
		JP-T-	62501628	02-07-87
		NL-T-	8520384	29-11-84
		SE-A-	8603228	25-07-86
US-A- 4344936	17-08-82	None		

EPO FORM P0479

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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(71) Applicant: HAEMONETICS CORPORATION [US/US]; 400 Wood Road, Braintree, MA 02184 (US).

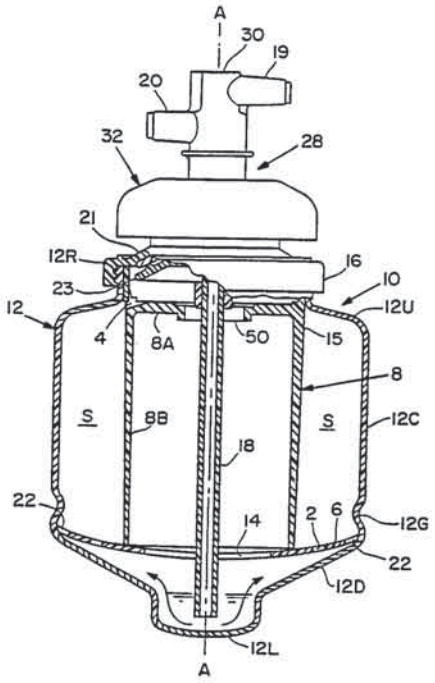
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(74) Agents: REYNOLDS, Leo, R. et al.; Hamilton, Brook, Smith & Reynolds, Two Militia Drive, Lexington, MA 02173 (US).

(81) Designated States: AT (European patent), BE (European patent), CH (European patent), DE (European patent), ES (European patent), FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent).

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With international search report.

(54) Title: DISPOSABLE CENTRIFUGE BOWL FOR BLOOD PROCESSING



(57) Abstract

An improved disposable blood processing centrifuge bowl is described comprising a rotary seal (28) enclosing an aperture in a bowl body (12) through which a two-piece core assembly (8, 6) is inserted.

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DISPOSABLE CENTRIFUGE BOWL FOR BLOOD PROCESSING

Description

Related Applications

This application is a continuation-in-part of U.S. Patent Application Serial No. 07/232,544 filed 8/15/88 entitled "Plasmapheresis Centrifuge Bowl" to Thomas D. Headley, which is a continuation of U.S. Patent Application Serial No. 06/888,764 filed 7/22/86 entitled "Plasmapheresis Centrifuge Bowl" to Thomas D. Headley.

Technical Field

This invention relates to blood processing and, more specifically, centrifuge bowls for blood processing.

Background of the Invention

Disposable centrifuge bowls have been developed for processing anticoagulated whole blood in pheresis and cell washing procedures. Prior to about 1986, commercially available disposable blood processing centrifuge bowls were of the type generally shown in Figs. 1 or 6 of U.S. Patent No. 4,300,717 (hereinafter "Latham bowl"), or U.S. Patent No. 4,086,924 (hereinafter "Grenade bowl"). The overall bowl construction in each case was similar and consisted of three essential units. The first was a multi-piece feed tube and seal assembly, which enable anticoagulated whole blood and/or wash

solution to be introduced to the interior of a rotating bowl body from a fixed location, and processed blood component to be removed from the bowl body and returned to a patient or donor, or stored. The second unit comprised a two-piece bowl body welded together at a peripheral seam.

The third unit was a core body usually of fairly solid construction. The core body served a number of functions. In the Latham bowl, it provides a narrow bottom fluid channel between the base of the core and the bottom of the bowl, through which fluid admitted through a central feed tube was passed to the outer periphery of the bowl body interior. In passing through this narrow channel, "impeller" vanes, formed on the bottom of the bowl, impart rotational velocity to the incoming feed fluid. With the core design shown in the Latham bowl, fluid feed is forced to pass to the outer separation region between the inner peripheral bowl body wall and the outer peripheral wall of the core. Without this core design, it would be possible for fluid admitted at the bottom of the bowl to by-pass the separation region and pass directly from the feed tube upwardly through the space between the inner core wall and the feed tube out the effluent port formed between the skirts of the seal assembly. The rigid core body was considered essential to avoid or dampen fluid wave vibrations which might occur between the rotating sterile air in the central region between the core and the feed tube

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and the fluid processed in the outer separation region.

The Grenade bowl construction is similar, except that the middle bowl body side walls are not tapered and the bottom of the core is not flared.

In addition to the above designs, a pheresis bowl, which was never commercialized, is described in U.S. Patent No. 4,059,108. This bowl was of two-piece construction, formed of a lower red cell reservoir and a plasma with a core baffle system (shown in Fig. 18) for the red cell reservoir.

Sometime during 1986/87, a new centrifuge bowl became commercially available. The construction of this bowl is shown in the Fig. 4-6 embodiment of co-pending U.S. Patent Application Serial No. 07/232,544 filed 8/15/88, which is a continuation of Serial No. 888,764 filed 7/22/86. This new bowl differed from the prior art bowl by the use of a one-piece integral blow molded bowl body. Among other things, this construction (hereinafter "integral bowl") eliminated the need for a weld about the periphery of the bowl; a possible source of bowl failure at high centrifugal speeds.

The Fig. 4-6 embodiment of the integral bowl utilized a one-piece core body with an outer diameter is equal to or smaller than the opening into the bowl. The small core size is insufficient to enable the core to force feed fluid, entering the bottom of the bowl through the feed tube, to be diverted to the extreme outer periphery of the separation region between the core body and the bowl

wall. This diversion is extremely important for cell washing procedures.

In cell washing systems, shed blood from a patient is filtered, collected and washed with saline in a disposable centrifuge bowl. Anticoagulated, filtered shed whole blood enters at the bottom center of the bowl and is separated by centrifugal forces into more dense red cells and less dense other components. The red cells fill the outermost portion of the rotating centrifuge bowl. As more shed blood enters the bowl, the red cells remain in the bowl displacing the supernatant (saline, plasma, contaminants, etc.) out of the mid-central region of the bowl. This concentrates the red blood cells in the bowl. Next, saline is directed into the bottom of the bowl, instead of shed blood. Saline, entering the Latham bowl, is directed by the lower extended skirt portion of the core to the outermost radius of the bowl and through the bed of packed red blood cells. In this way, the supernatant is diluted and displaced by the saline until a satisfactory "washout" efficiency is obtained.

The term "washout" efficiency, sometimes referred to as merely "washout", denotes the percentage of non-red blood cell fluid, i.e., plasma and saline and contaminants, originally entering the bowl and which are removed by the wash process. A 90% or greater efficiency is typically the goal of the wash process. At the end of the "wash" cycle,

the contents of the bowl are red cells suspended in saline. The centrifugal washing procedure in conjunction with filtration concentrates the red blood cells and removes contaminants, such as blood clots, bone chips, fatty tissue and activates clotting factors. The patient can then be reinfused with his or her own washed red blood cells.

The Fig. 4-6 embodiment of the integral bowl body bowl of the parent application does not disclose a diverter structure, as in the Latham type bowl. Therefore, some of the saline wash solution may not be forced to travel through the packed red cells before exiting the bowl through the effluent skirts on the rotary seal. This substantially decreases the washout efficiency and, hence, the time it takes to complete a cell washing procedure. As might be expected, time is an extremely critical factor in cell washing procedures, both from the point of view of cost and patient comfort and safety.

Disclosure of the Invention

In alternate embodiments of the integral bowl patent application, two core structures are disclosed which permit use of an integral bowl body, yet enable the core diameter to exceed the diameter of the bowl body opening. In one embodiment, the core is formed of one-piece construction using semi-rigid plastic material with a flared core and a wall body which can be deflected to allow the flared core to be inserted through the smaller diameter opening. This one-piece core construction, shown in

cross-section in Fig. 7 of the parent application, is complex and would be difficult and expensive to fabricate. Also, since it is unsecured along its length, it is susceptible to lateral movement in the event of vibrations which could occur as fluid in the bowl is rotated. Such lateral movement may result in blockage of the channel between the bottom flange of the core and the angled bottom wall of the bowl.

In the Fig. 9-10 embodiment of the parent application, the core is of two-piece construction. One piece is comprised of a generally cylindrical hollow walled core. The other piece is a disc-like member with a flared wall portion adapted to be located adjacent the diagonal wall of the bowl body.

The disc-like member is made of semi-rigid plastic and can be compressed to allow it to pass through the top opening in the bowl body. Circular grooves are formed around protrusions on the member to permit the bottom of the cylindrical core wall to made with the member after the walled core is inserted into the bowl body. The circular grooves form a press-fit, holding the two pieces together during rotation of the bowl. A central aperture in the disc-like member permits whole blood from a feed tube stem to enter the bottom of the bowl body.

This two-piece embodiment is difficult to assemble in the bowl body, relies on a press fit with very little penetration between the mating

members, and is also subject to vibrational displacement since the length of the core is essentially suspended from the top without lateral support.

The above summary of the development of centrifuge bowls over a long period of time reveals a need for a core body for blood processing centrifuge bowls which can be used in integral bowl bodies or non-integral bowl bodies, yet retain the features of the Latham style bowl, especially in connection with cell washing protocol. It would also be desirable to have a core body which could be constructed such that the same core body could be utilized for bowls of various volumetric sizes.

The method and apparatus of the present invention comprises, in general, a disposable centrifuge rotor or bowl formed of a combination of three basic items. The first is a rotary seal and header assembly; the second, a bowl body, preferably of seamless, integral, one-piece construction and the third is a two-piece core assembly capable of being rigidly retained against a bowl wall and used in standard bowl bodies of different internal volumetric capacity. The seal and header assembly is as described in the above-referenced parent application. The bowl body is preferably adapted to be manufactured by blow molding or injection blow molding, as also described in the parent application.

The core assembly consists of two plastic pieces made by injection molding or similar processes. The first piece is a generally cylindrical rigid hollow-walled core, similar to the walled core in the parent application. The second piece is a diverter in the form of a semi-rigid donut-like member, scalloped at its peripheral edges and having an outer diameter greater than the bowl opening and about equal to the inner diameter of the mid-section of the bowl.

An inner hole is provided on the donut-like member. This hole has a diameter slightly smaller than the diameter of the effluent header.

The core assembly is assembled inside the bowl by first bending the diverter to permit it to fit inside the bowl and then bending it back to its original flat aspect to fit laterally and horizontally across the bowl body. The walled core is then inserted through the bowl opening. The longitudinal length of the core is sized to be just long enough so that when the core is pushed downwardly in the bowl, it pushes the diverter downwardly into the bowl, also, until the diverter is laying in a generally horizontal, slightly bowed, rigid, compressed position opposite that portion of the bowl body which begins to incline radially inwardly and downwardly and become conical.

Optionally, a ring of holes are provided on the diverter with the ring concentric to the inner hole in the diverter and the diameter of the ring and hole size such that the holes in the ring are

located slightly radially outwardly from the core wall. These holes enable subsequent feed fluid to be introduced to the separation region at a radially inward bottom location after the initial introduction of fluid has occurred and separated component begins to block the peripheral scalloped openings.

The vertical location of the diverter can be adjusted for different volumetric bowl capacities simply by changing the length of the core wall. The semi-rigid diverter is held in compression against the inner circumferential side wall of the bowl body and is, therefore, less susceptible to movement caused by vibration or turbulence when the bowl is rotated at high speeds.

The above and other features and advantages will now be described in detail in connection with the drawings.

Brief Description of the Drawings

Fig. 1 is a cutaway side view showing a centrifuge bowl of the present invention with the core construction shown in cross-section.

Fig. 2 is a top view of the diverter 10 of Fig. 1 in accordance with the invention.

Fig. 3 is a view as in Fig. 1 except that a smaller volume bowl body and shorter length core is employed.

Best Mode of Carrying Out the Invention

Referring now to Figs. 1-2, the apparatus of the invention will now be described in detail in connection with an integral bowl body cell washing process. It is emphasized that the method and apparatus of the invention is capable of general applicability to other blood processing methods, such as pheresis, and to other bowl body structures.

As shown therein, the centrifuge rotor or bowl 10 of the invention, comprises a seal and header assembly, shown generally at 28; a one-piece integral bowl body, shown generally at 12; and a core assembly comprising core body 8 and diverter 6.

The seal and header assembly 28 is substantially identical to the seal and header assembly utilized in the parent application referenced above. Therefore, it need not be described in detail herein. Briefly, the assembly 28 is comprised of a non-rotatable header 30, an effluent tube (not shown), a feed tube assembly (not shown) and a rotary seal formed beneath secondary shield 32 comprising a seal ring, a flexible member (also not shown) and an outside seal member or crown 16.

The header 30 has a transverse inlet bore 19 extending transverse the longitudinal axis "A" of the bowl and then into a longitudinal passageway coupled to the inner bore of the feed tube assembly. The passageway leads to stem 18 forming an inlet fluid communication path for feed fluid, i.e., whole blood or saline, to enter the interior of centrifuge

bowl body 12 at the lower longitudinally axial portion 12L of the bowl body 12.

Header 30 is also provided with a transverse outlet bore 20, which extends transversely into a peripheral channel extending in parallel relationship with the feed tube assembly and into an outlet coaxial passageway (not shown). A secondary shield 32 is formed on header 30 and extends over the rotary seal. A pair of complementary skirts 21 and 23 provide an effluent passageway, therebetween, connecting the outlet passageway to the outlet bore 20.

Internal screw threads, on seal crown 16, secure the seal and header assembly to complementary threads on the bowl body.

The bowl body 12 is preferably an integral body adapted to be manufactured by blow molding or injection blow molding and may be formed of a suitable plastic, such as transparent styrene or equivalent.

The bowl body is formed of an upper ring portion 12R, an upper diagonal portion 12U extending radially outwardly and inclined downwardly, a straight middle central portion 12C extending vertically downward, a lower diagonal portion 12D extending radially inwardly and downward, and a lower cross portion 12L. Screw threads are formed on the outer surface of ring portion 12R and an opening extends longitudinally from the inner surface of the ring portion 12R into the main

portion of the bowl body 12. An optional groove is formed about the periphery of the bowl at 12G to form a holding surface for a centrifuge rotor chuck (not shown).

Prior to inserting the header and seal assembly 28 into the bowl body, a core assembly consisting of core body 8 and diverter 6 is inserted into the interior of the bowl.

The core body is adapted to be inserted into the bowl body 12 through the opening in ring portion 12R. Core body 8 is an integral member formed of a suitable rigid, or semi-rigid, blood compatible transparent plastic and has a cylindrical outer wall 8B extending longitudinally downward and coaxial to the axis A of bowl body 12. An upper transverse ring portion 8A of core body 8 is adapted to abut the inner wall of the ring portion 12R of the bowl body 12 when the core body is inserted into the upper opening of the bowl body 12.

Four L-shaped reinforcing tabs (not shown) are formed on the top wall of core body 8 to reinforce the ring portion 8A. Four peripheral slots (one of which is shown at 4) extend along the periphery of the core body at the juncture between the ring portion 8A and the cylindrical outer wall 8B. These slots provide a passageway for the exit of effluent, such as supernatant or plasma, which has been separated from the packed red blood cells by the operation of the centrifuge cell washing or pheresis process within the bowl body 12.

A coaxial opening 50 is provided in the transverse ring 8A of core body 8B to enable feed tube stem 18 to pass unimpeded into the lower portion 12L of the bowl body.

Diverter 6 is a donut-like member formed of blood-compatible semi-rigid transparent plastic material. The diverter has an outside diameter greater than the diameter of the opening in the top of the bowl body 12 and is provided with scalloped openings 22 at the peripheral edge thereof. The outer diameter of the diverter is about equal to the inner diameter of the bowl body at the mid-section 12C, so that when the diverter is folded and inserted into the bowl body through the top opening and unfolded into its flat aspect horizontal position, it extends across the entire cross-section of the bowl at the mid-section 12C. The core body is then inserted through the opening. The length of the cylindrical longitudinal wall 8B is just sufficient so that when the core body 8 is fully inserted and cover 16 is screwed in place, the diverter 6 is pushed into a horizontal position vertically aligned with the start of the lower radially inwardly diagonal or inclined portion 12D of the bowl.

In this manner, the diverter 6 is retained in a slightly bowed compressed rigid position at the precise vertical location preferred for introduction of fluid to the separation region "S" between the mid-section bowl wall 12C and the core body wall 8B.

Optionally, a ring of openings 2 are provided intermediate central opening 14 and the peripheral scalloped openings 22 at the periphery of the diverter 4. As fluid, such as anticoagulated shed blood, is first introduced to the bowl, it enters at the bottom region adjacent wall 12L and under the influence of centrifugal force, flows outwardly and upwardly in the direction of the arrows and enters the separation region S at the periphery thereof through scalloped openings 22.

Eventually, a layer of more dense packed red blood cells accumulates at the outermost radius of the separation region, covering the peripheral openings 22.

As wash fluid is next introduced, it is easier for this fluid to enter the separation region S at the radially inward openings 2 than at the peripheral openings 22. In this way, a desirable cell washing cross-flow is established with cell washing fluid flowing generally upwardly from openings 2 while whole blood particulate is in suspension sediment travelling in a radially outward direction.

Fig. 3 shows an alternate embodiment of the disposable centrifuge bowl 10' of the invention in which a smaller volumetric size bowl 12' is utilized in conjunction with a shorter length core body 8'. The bowl body is substantially as described in co-pending design patent application, Serial No. 07/102,646 filed September 30, 1987 to Thomas D. Headley entitled "Bowl Body".

In this bowl body, the outer diameter of the mid-section of the bowl 12' is stepped from a relatively large diameter equal to the diameter of the mid-section in Fig. 1 to a lesser diameter at a point about halfway along the length thereof. The length of the core 8' is similarly foreshortened, so that when the core is inserted against diverter 6', the diverter is compressed at the beginning of the first diagonal inwardly inclined region 12I of the bowl body.

The diverter 6' may be identical in size and shape to the above previously described diverter 6, in all respects, yet function in a similar manner in the smaller size bowl.

Equivalents

Those skilled in the art will recognize that there are many equivalents to the specific embodiments shown herein. Accordingly, the invention is not to be limited except as may be required by the scope of the claims herein.

CLAIMS

1. A disposable blood processing centrifuge rotor comprising:

a) a rotatable bowl body having at least one straight section and upper and lower inclined diagonal sections connected to one of said straight sections; said body being rotatable about an axis and having a single aperture therein concentric with said axis through an outer wall of the bowl body; and

b) a rotary seal assembly affixed to said bowl body and covering said aperture and having input and output ports for fluid communication with the interior of said bowl body;

c) a core assembly comprising:

(i) a walled core body having a transverse ring portion which mates with the bowl body at the aperture thereof and a cylindrical portion longitudinally extending from said ring portion; and

(ii) a diverter member having a donut-like shape with an inner opening coaxial to said axis and a diameter smaller than the outer diameter of said cylindrical portion and an outer apertured periphery with a diameter

about equal to the inner diameter of said straight section and larger than the diameter of the bowl aperture and sufficiently non-rigid as to be capable of being inserted through said bowl aperture and be rigidly retained in a horizontal position against an inner wall of the bowl body by compression as the bottom of the cylindrical portion of said core body abuts the diverter.

2. A disposable blood processing centrifuge rotor comprising:

a) a bowl body rotatable about its longitudinal axis and having a single closeable bowl body aperture concentric with said axis at one end thereof;

b) a core assembly concentric with said axis and having an open center extending within said bowl from said aperture about said axis formed of a longitudinally extending cylindrical wall member and an apertured disc-like diverter held in compression across said bowl body at a location corresponding to the length of said wall member when fully inserted in the bowl body; and

c) a rotary seal assembly having a cover for sealing said seal assembly to the outer body wall about the periphery of said single aperture.

3. The rotor of Claim 2 wherein the diverter is at least partly flexible at portions having an outer diameter greater than the bowl body aperture.

4. A disposable centrifuge blood processing rotor comprising:

a) a bowl body adapted for rotation about its longitudinal axis and having a bowl body aperture, through an outer wall, to the interior of said bowl body and concentric with said axis at one end of the outer wall of the bowl body;

b) a core assembly comprising a core body and a disc-like diverter with a central opening, and peripheral apertures, said assembly being insertable in said bowl body aperture and said diverter being retained by said bowl body in compression horizontally across the interior of said bowl body; and

c) a rotary seal assembly affixed to the outer wall about the periphery of said aperture and having an effluent port and an input port in fluid communication with the interior of said bowl body.

5. The rotor of Claim 1 wherein the aperture is on the top of the bowl body and the upper section of the bowl body inclines radially outwardly from top to bottom while the lower section of the bowl body inclines radially inwardly from

top to bottom and the diverter member is retained against the bowl body at a region where the bowl body begins to incline radially inwardly.

6. The rotor of Claim 5 wherein the bowl body has upper and lower straight sections and the diverter is retained between the upper and lower straight sections.

7. The rotor of Claim 1 wherein the outer apertures at the periphery of the diverter member are in the form of scalloped edges.

8. The rotor of Claim 1 wherein a plurality of openings are formed in said diverter member radially intermediate said apertured periphery and said inner opening to permit fluid from below said core body to enter the interior of said bowl body between said cylindrical portion and said straight section.

9. The rotor of Claim 4 wherein the diverter has an outer diameter when flat which exceeds the diameter of the bowl body aperture and is sufficiently flexible as to be capable of insertion through said aperture, yet sufficiently rigid as to be retained, by longitudinal force of said core body, across the interior of said bowl body at a region where said bowl body inclines radially inwardly from top to bottom.

10. The rotor of Claim 9 wherein the diverter has a ring of openings intermediate the central opening and peripheral apertures.

11. A method of forming an integral continuous flow blood processing centrifuge rotor comprising the steps of:

a) providing a one-piece bowl body having at least one straight section and upper and lower inclined diagonal sections connected to one of said straight sections; said body being rotatable about an axis and having a bowl aperture therein concentric with said axis through an outer wall of the bowl body; and

b) inserting through said bowl aperture a semi-rigid diverter member having a donut-like shape with an inner opening coaxial to said axis and an outer apertured periphery with a diameter about equal to the inner diameter of said straight section and larger than the diameter of the bowl aperture;

c) inserting a walled core body through said bowl aperture having a transverse ring portion which mates with the bowl body at the bowl aperture and a cylindrical portion longitudinally extending from said

ring portion and pushing said diverter member with said cylindrical portion until said diverter member is rigidly retained by compression against an inner wall of said bowl body; and

d) covering said aperture with a rotary seal assembly affixed to said bowl body and having input and output ports for fluid communication with the interior of said bowl body.

12. A method of forming a disposable blood processing centrifuge rotor comprising:

a) providing a seamless bowl body having a closeable aperture at one end thereof;

b) inserting a semi-rigid diverter into said bowl body through said aperture;

c) inserting a cylindrical wall member into said aperture to compress said diverter across said bowl body at a location corresponding to the length of said wall member when fully inserted in the bowl body; and

d) covering said aperture with a rotary seal assembly.

13. The method of Claim 12 wherein the diverter is at least partly flexible at portions having an outer diameter greater than the bowl body aperture.

14. The method of forming a disposable centrifuge blood processing rotor comprising:

a) providing a bowl body adapted for rotation about its longitudinal axis and having a bowl body aperture concentric with said axis at one end of an outer wall of the bowl body;

b) inserting a core assembly into said bowl body through said aperture by first inserting a disc-like diverter with a central opening, and peripheral apertures, and next inserting a core body into said aperture to retain said diverter in compression horizontally across the interior of said bowl body; and

c) covering said aperture with a rotary seal assembly affixed to the outer wall about the periphery of said aperture and having an effluent port and an input port in fluid communication with the interior of said bowl body.

15. The method of Claim 14 including forming a plurality of openings in said diverter radially intermediate said apertured periphery and said central opening to permit fluid from below said core body to enter the interior of said bowl body between said core body and said bowl body.

1/2

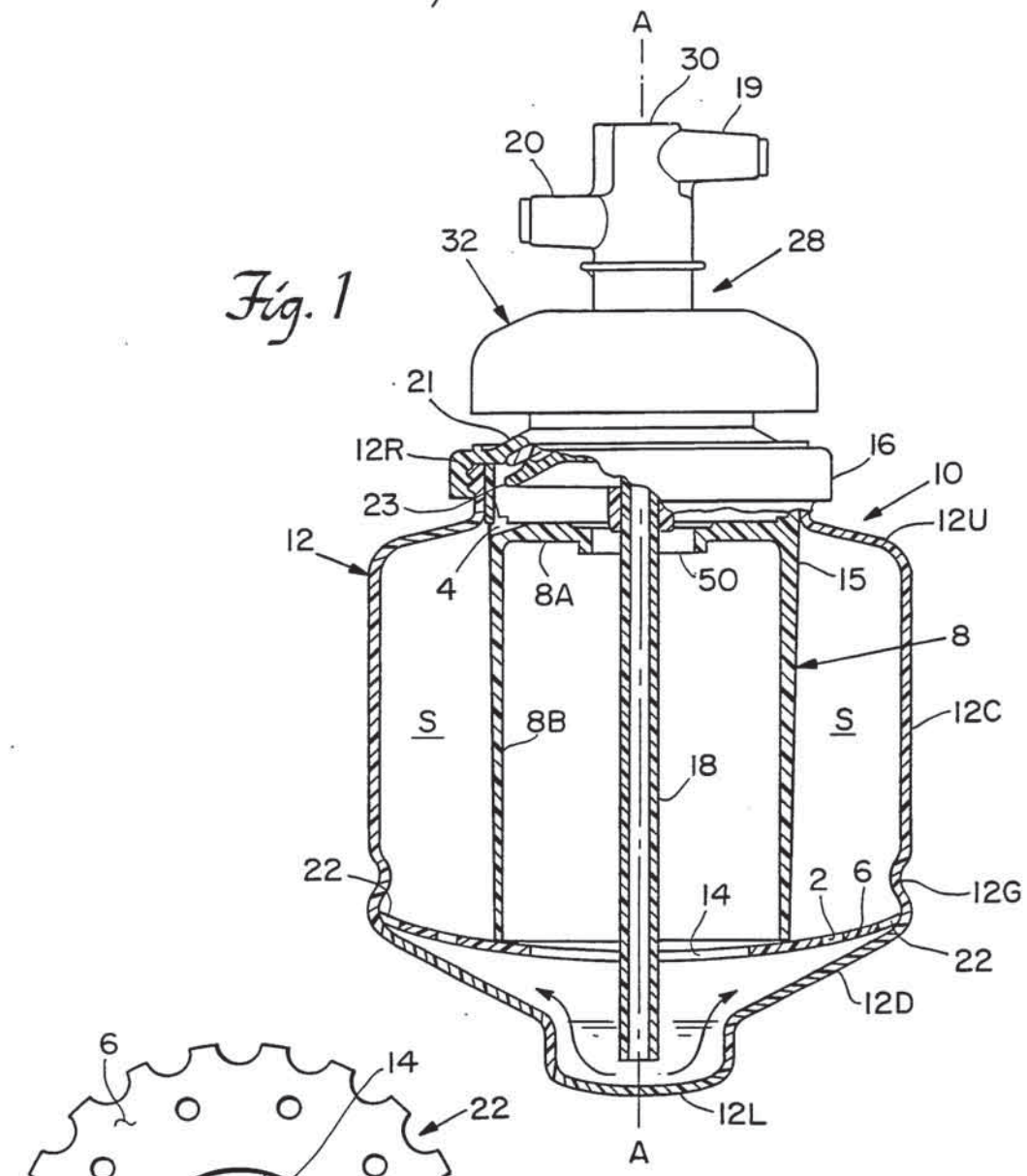

A
30
19
20
32
28
21
12R
16
10
23
12U
12
4
8A
50
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22
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A

Fig. 1

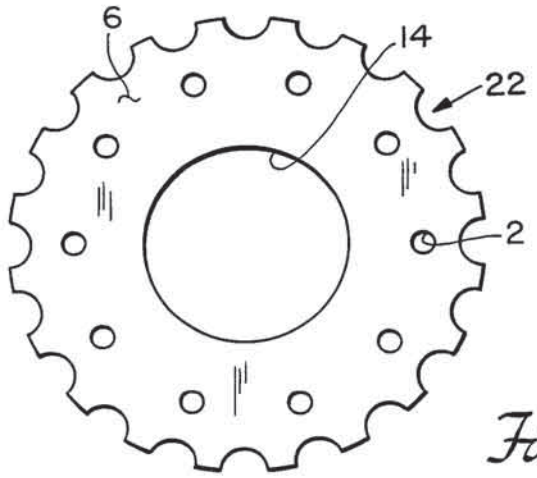

6
14
22
2

Fig. 2

2/2

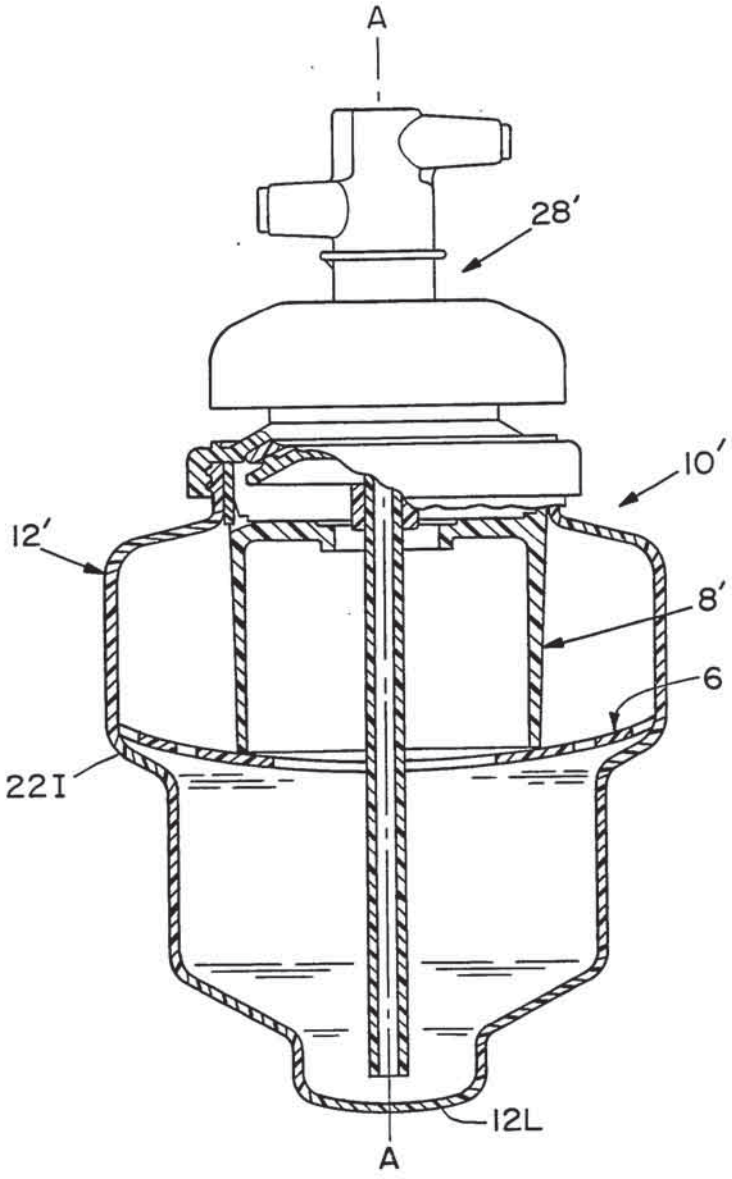


Fig. 3

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 89/05730

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[5]: B 04 B 7/08

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[5]	B 04 B

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category *	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
A	EP, A, 0257755 (HAEMONETICS CORP.) 2 March 1988, see abstract	1,2,4,5, 11,12,14

* Special categories of cited documents: [10]

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
27th March 1990	23 APR 1990
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	Mme N. KUIPER

Form PCT/ISA/210 (second sheet) (January 1985)

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. US 8905730 SA 33409

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 17/04/90 The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A- 0257755	02-03-88	JP-A- 63065873	24-03-88

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

Espacenet

Bibliographic data: WO9406535 (A1) — 1994-03-31

APPARATUS AND METHOD FOR FRACTIONATING A LIQUID MIXTURE

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Applicant(s): FISCHEL HALBERT [US]; FISCHEL RICHARD J [US] ± (FISCHEL, HALBERT, ; FISCHEL, RICHARD, J)

Classification: - international: ***A61M1/36; B01D63/16; B04B5/04;*** *A61M1/26;* (IPC1-7): B01D33/00; B01D61/00
- cooperative: **A61M1/262; A61M1/3692; A61M1/3693; A61M1/3696; B01D63/16; B04B5/0442;** A61M2202/0415; B04B2005/0464; B04B2005/0478

Application number: WO1993US08523 19930909 Global Dossier

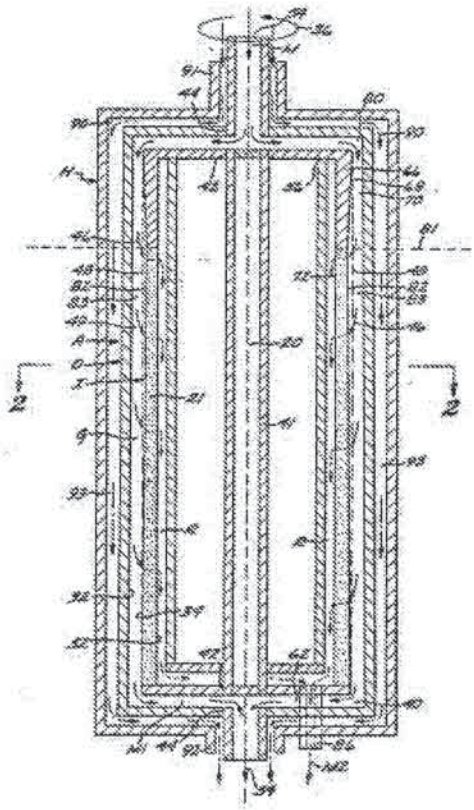
Priority number (s): US19920943731 19920911

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Abstract of WO9406535 (A1)

Apparatus and method for fractionating a liquid mixture into a plurality of liquid fractions whose components have different velocities. A rotating cylindrical assembly (A) has inner and outer shells (I, O) defining therebetween a tubular gap (G). One shell includes a porous structure (21) for permeation therethrough of one or more of the liquid fractions and to resist radial inward flow of the remainder. The cylindrical assembly (A) is rotated at a speed effective to impart sufficient centrifugal force to the liquid fractions to maintain one such fraction within the gap (G) while compelling flow of the other liquid fraction radially inwardly through the porous structure. The invention includes a porous structure (21) in both the inner and outer shells (I, O) to allow for levitation of one fraction of the mixture between such structures while a wash of solution bearing beneficial components is flowed radially inwardly therethrough.

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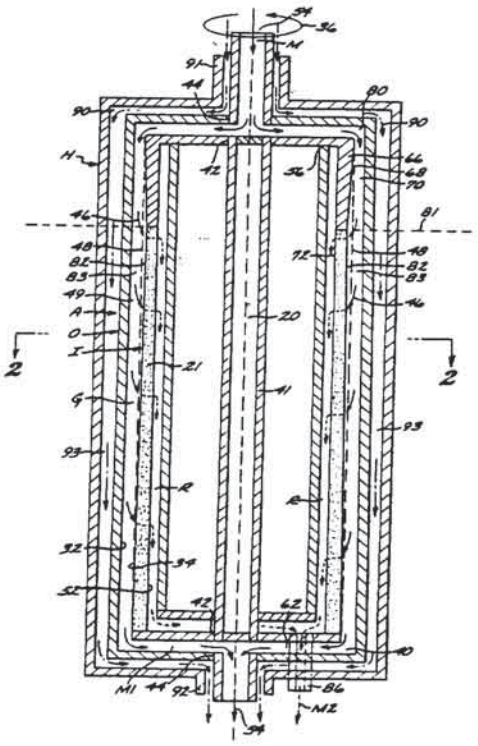
(81) Designated States: AU, CA, JP, KR, European patent (AT BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC NL, PT, SE).

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(54) Title: APPARATUS AND METHOD FOR FRACTIONATING A LIQUID MIXTURE

(57) Abstract

Apparatus and method for fractionating a liquid mixture into a plurality of liquid fractions whose components have different velocities. A rotating cylindrical assembly (A) has inner and outer shells (I, O) defining therebetween a tubular gap (G). One shell includes a porous structure (21) for permeation therethrough of one or more of the liquid fractions and to resist radial inward flow of the remainder. The cylindrical assembly (A) is rotated at a speed effective to impart sufficient centrifugal force to the liquid fractions to maintain one such fraction within the gap (G) while compelling flow of the other liquid fraction radially inwardly through the porous structure. The invention includes a porous structure (21) in both the inner and outer shells (I, O) to allow for levitation of one fraction of the mixture between such structures while a wash of solution bearing beneficial components is flowed radially inwardly therethrough.



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APPARATUS AND METHOD FOR FRACTIONATING A LIQUID MIXTURE

FIELD OF THE INVENTION

The present invention relates to centrifugation apparatus and methods for separating liquid mixture components, as for example, blood, having different sedimentation rates.

BACKGROUND OF THE INVENTION

Prior centrifugal separation systems, either continuous or batch, generally form layers of substantial thickness. The spin axis defines the rotation that produces the centrifugal force, which force causes the eventual separation of components according to differing densities. Greater densities occupy comparatively greater depths when sufficient time is allowed to permit the effective completion of the sedimentation process. The depth of a layer refers to its distance from the spin axis. As some components have a distribution of densities which overlap the density distribution of other components, separation of such components by this means is necessarily incomplete. Even with no overlap of component density distributions, separation may not be complete or as perfect as desired due to instabilities in the suspending media under rotation making it particularly difficult to extract material from thin intermediate layers. Such instabilities tend to increase as total liquid thickness increases, especially when the material is caused to flow for the purpose of decanting various components.

Parameters, such as the time required to produce useful separation by density layering, rotation rates, layer thickness, decanting geometry, volume processing capacity, and component purity have, heretofore,

required undesirable trade-offs in which one was compelled to compromise purity as against separation time or volume processing capacity. In most cases, limitations are imposed by the decanting geometry, method and rate which may introduce disturbances in the formed layers especially when the latter are very thin as in the case of "white" cells of blood, i.e., the "buffy coat".

Regardless of the many and diverse techniques utilized by prior art centrifugal separators for dealing with the various problems just described, they all require the separated material to form layers which closely approximate the end point of the sedimentation process. The loci of separation as between the several layers can be used to define a surface normal vector that would be substantially perpendicular to the spin axis at all points of the layer. Generally, the decantation of any particular layer requires at least some component of flow transverse to the layer's "surface normal" vector. See, for example, U.S. Patent No. 4,086,924. It is easily seen that one layer is required, at least in part, to "flow" in a shearing fashion over other layers in order to be decanted. This necessarily introduces stress on the interface between layers, which can contribute to contamination between layers. Viscous shear flow between fluid layers is anathema to centrifugal separation by density selective layering due to the instabilities it introduces under a rotational force field. Nevertheless, at least one component of shear flow along separation interfaces has always been involved at some stage of separation in prior centrifugal separators.

Other prior art techniques deliberately utilize shearing of suspensions flowing over membranes to separate components by what is understood to be cross-

flow filtration (see A.L. Zydney and C.K. Colton, Continuous Flow Membrane Plasmapheresis: Theoretical Models for Flux and Hemolysis Prediction,. Trans ASAIO, Vol 28 (1982), p. 408.). However, membranes become clogged over time.

Efforts to prevent clogging of the membrane have included increasing the membrane area (see B.A. Solomon, et al, U.S. Patent No. 4,212,742), the shear rate of the flowing blood so as to delay the clogging effect (see R.J. Fischel, et al, U.S. Patent No. 4,755,300), or the pressure differential across the membrane (see F. Castino, et al, The Filtration of Plasma from whole Blood: A Novel Approach to Clinical Detoxification, In: Chang, T.M., et al., Artificial Kidney, Artificial Liver, and Artificial Cells, New York: Plenum Press, 1978, pp. 259-266).

Another technique that has long been used for cell separation is usually referred to as centrifugal elutriation or CE (see M.L. Meistrich. Experimental Factors Involved in Separation by Centrifugal Elutriation. Cell Separation Methods and Selected Applications, Ed: Pretlow, T.G., Academic Press, New York, V.2, PP: 33-61 (1983)). The basic principle involved in various embodiments of this technique is separation by differences in particle settling rates. In some instances, a counter-flowing fluid is introduced against the centrifugal force field (see R.L. Berkow et al Purification and Functional Evaluation of Human Polymorphonuclear Leukocytes. Cell Separation: Methods and Selected Applications, Ed: Pretlow, T.G., Academic Press, New York, V.4, PP: 147-170 (1987)), and is referred to as counterflow CE or CCE. These methods are intended as experimental sample batch processes. They are not suitable for rapid processing of large volumes on a continuous basis.

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The blood cell washing procedure of the present invention uses much less costly sterile washing solution than required by prior apparatus employed for this purpose. The speed and thoroughness of blood component separation without the unacceptable blood priming volumes or harsh treatment of the fragile blood elements, not otherwise achieved heretofore, is now possible with particular embodiments of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic central vertical section of a apparatus embodying the present invention showing the basic method of operation thereof;

FIG. 1A is broken, fragmentary, schematic and enlarged view of the right-hand portion of FIG. 1 demonstrating the behavior of fluid components relative to the porous element;FIG. 2 is a horizontal sectional view taken along line 2-2 of FIG 1;

FIG. 3 is a broken foreshortened central, vertical sectional view showing the major components of the form of apparatus of FIG. 1 embodying the present invention;

FIGS. 4 and 5, are horizontal sectional views taken along lines 4-4, and 5-5, of FIG.3;

FIG. 6 is a foreshortened central vertical sectional view showing major components of a second form of apparatus embodying the present invention;

FIG 6A is a fragmentary central vertical sectional view of the apparatus of FIG. 6 showing the parts thereof arranged for a washing function;

FIG. 7 is a horizontal sectional view taken along line 7-7 of FIG. 6.

FIG. 8 is a central vertical sectional view showing major components of a third form of apparatus embodying the present invention.

FIG. 9 is a horizontal sectional view taken along line 9-9 of FIG. 8.

FIG. 10 is a graph demonstrating one principle of the invention relating to the separation of the components into separate fractions;

FIGS. 11 and 12 are schematic views demonstrating the relationship between rotational speed of the centrifugation unit and movement of the liquid components during operation of the apparatus embodying the present invention;

FIGS. 13, 14 and 15 are plots of diameter, density and settling rate, respectively, of various blood components in terms of population distribution, with FIG. 15 referring to Stokes settling velocity per unit of centrifugal force;

FIG. 16 is a schematic illustration showing how two devices embodying the present invention can be operated as two simultaneous stages for collection of platelet concentrate;

FIGS. 17-20 are schematic illustrations showing various functions which may be obtained employing the method and apparatus of the present invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

There are several important principles applicable to the design and operation of the method and apparatus of the present invention. Critical to the preservation of stability of centrifugal settling is the concept of spinning a "thin", as opposed to a "thick", film. The parameters which distinguish the two will be computed for blood and presented hereinafter. Initially, it is important to understand

that continuous operation of the method and apparatus requires that blood, or other liquid mixture, enter the spinning "film" at one end, preferably the top, and move axially, downwardly in laminar stream flow, i.e., viscous boundary layer flow, approximately parallel to the spin axis toward an exit from the "film". This flow would not be stable, in the sense that various types of secondary flows would be triggered, thus upsetting the preferred radial convective flow and particle settling geometry, if the film were not sufficiently thin. Thicknesses available to blood under this restriction lead to practical and useful designs.

Referring now to FIGS. 1 and 2, a preferred method and apparatus for separating a liquid mixture, e.g., blood plasma, and a blood component or components in that liquid with the liquid and blood component or components forming a flowable mixture is schematically illustrated. The apparatus includes a cylindrical assembly A adapted for rotation about a central vertical axis 20 and having inner and outer generally cylindrical shells I and O, respectively, defining therebetween an axially extending tubular gap G. The inner shell includes a porous cylindrical structure 21 for at least a part of its axial extension for a purpose to be described hereinafter. The cylindrical assembly A is shown disposed within a fixed housing H, for rotation relative to the housing about axis 20. The flowable liquid mixture which is to be fractionated into first and second liquid fractions, containing components having settling velocities which are higher and lower respectively than a selected value, enters the upper end of the gap G between the inner and outer shells. Fractionation is effected within this gap between spaced apart generally axially concentric and rotationally

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symmetric surfaces 32 and 34 of the inner and outer shells, such surfaces forming boundaries as defined by walls of the inner and outer shells. The boundaries 32 and 34 are shown as concentric tubular boundaries extending about the axis of rotation 20 of the cylindrical assembly A, and may either be cylindrical or variously, somewhat differently tapered, i.e., inclined to the rotational axis of the assembly at particular axial locations, as described hereinafter. The direction of rotation of the cylindrical assembly is indicated by arrow 36, and the liquid mixture, or fractions, in various states of localized concentration of particular components flow generally downwardly, i.e., axially from the top of gap G to the bottom of gap G between the vertically orientated boundary surfaces 32 and 34.

A vertical support tube 41 rigidly interconnects and carries the inner and outer shells I and O at 42 and 44. Power operated means (not shown in FIGS. 1 and 2) are interposed between housing H and the cylindrical assembly A to spin the inner and outer shells and their confronting surfaces 32 and 34 about the common axis of rotation 20 at the same angular velocity. The liquid mixture to be fractionated M may be fed into the axial portion of gap G above an imaginary reference horizontal plane 81 and also pressurized by means not shown in FIGS. 1 and 2, as via a feed stream indicated by flow path 46. Liquid mixture components in the gap more dense than the liquid mixture continuous phase migrate radially outwardly during rotation of the cylindrical assembly due to centrifugal force which is exerted on all elements of the liquid mixture whereby concentration of the said more dense components in the liquid flowing axially (shown) downwardly in FIG. 1 in the gap G becomes greater and less near surfaces 32 and

34, respectively. If the process of liquid component migration were allowed to proceed to completion in the gap, a boundary marking the separation of the liquid continuous phase from the settled discontinuous liquid components could, in some cases, become visibly well defined and is depicted by an imaginary reference boundary 48 which need not actually form as shown in the drawings. Boundary 48 is an imaginary cylindrical surface essentially parallel to the vertical axis of rotation 20 having a radius which can be controlled by mass balance of the liquid mixture and fraction flows into and out of the apparatus as described more fully hereinafter.

Controlled radially inward flow from gap zone 49, i.e., the axial portion of gap G below horizontal plane 81 of the second liquid fraction consisting of at least the continuous liquid phase of mixture M or a continuous phase including one or more discontinuous components in that zone is enabled in a pressure-drop direction operating to compel flow out of the gap zone 49 and through the porous surface 34 and the porous element 21 of the inner shell I into an inner region R defined between the inner surface of inner shell I and a cylindrical barrel element 50 coaxial with tube 41. Such enablement is effected as a function of the static pressure difference between gap G and interior region R, the effect of angular velocity of rotation ω of the zones defining boundaries, subjecting the liquid to centrifugation pressure opposing inward radial flow, and the porosity of porous structure 21 which resists flow. The thickness of the gap G will vary depending upon the nature of the liquid mixture being fractionated. In the case of blood, the preferred gap thickness is between about 5 to 150 mm.

As noted, the fluid mixture progresses axially and downwardly as it encounters the porous structure 21 of

the inner shell, the primary purpose of which is to act as a flow distributor. In order to serve this function, the porous structure must have certain properties. First, of course, the pores must be large enough to freely pass without sensible restriction, the discontinuous or formed constituents to be decanted. The pores may offer no restriction to constituents or particles that are intended to remain behind in the gap with the original medium because "filtration", understood as a sieving effect, plays no part in the operation of the method and apparatus of the present invention.

On the other hand, the porous structure must offer flow resistance to that portion of the suspending medium carrying the decanted constituent in the sense of creating a "pressure gradient". The preferred operative requirement is that the Trans Porous Pressure (TPP) drop substantially exceed the pressure loss required to move fluid from its entrance to the spinning film (mixture M) to its exit from the film (first liquid fraction M_1). Consequently, the porous structure means can act as a largely "uniform" flow distributor in accordance with the invention. In practice, this is not a serious restriction in, for example, generally useful blood flow rates, given that the thin film flow cross-sections possible in accordance with the invention, do not lead to significant axial blood flow pressure losses. Furthermore, as discussed in more detail within, there are very effective ways to increase the flow resistance of the porous means so that TPP is always sufficiently greater than the axial pressure gradient to cause substantial uniformity of decanting, i.e., uniform convective radial velocity over the entire porous surface.

The uniform decanting velocity referred to here is defined by dividing the volumetric decanting rate, of second liquid fraction, M_2 (ml/sec) by the porous area (cm^2). The uniform decanting rate is adjusted by controlling input and output volumetric pumping rates of incompressible fluids.

Centrifugation of the axially (here downwardly) flowing liquid mixtures in gap G tends to move discontinuous components throughout the mixture and separating fractions, which are more dense than the suspending continuous medium, in an outward radial direction generally opposite the inward radial flux through porous surface 34 and away from axis 20. Components which are less dense than the suspending continuous medium (i.e., buoyant particles) move in an inward radial direction under the influence of centrifugal force and are carried with the inward radial flux in all cases. Absent inward radial flux, the velocity of movement of discontinuous components in the radial direction due to centrifugation characterizes their effective settling rate.

Velocities vary among the individual specie of components and tend to retard as concentration of all components taken together increases. In dilute concentration the settling velocity, V_s, of a particular species of component, tends to be narrowly distributed and predicted by the Stokes equation. It is effectively proportional to centrifugal force, density difference, $\Delta\rho$ over that of the suspending medium and the square of particle diameter, D, (or dimension characterizing particle size) and inversely proportional to suspending medium viscosity, μ. Centrifugal force is proportional to the distance from the rotation axis 20 and the second power of the angular velocity, ω.

Consequently, centrifugation may be controlled, as for example by control of angular velocity, given radial dimensions of boundaries 32 and 34, to allow permeation of any component or components having radially outward characteristic settling velocities below a selected value, in the inward radial direction, along with the liquid, i.e., controlled permeation through the porous boundary 34 and porous cylindrical structure 21, the porosity of the latter in general allowing such components in the mix to pass through unobstructed. In one example, the porosity may be such as to allow all components (of different sizes and settling rates) to pass, i.e., including those of a relatively greater settling rate, but which are not allowed to permeate, due to the angular rate ω of centrifugation tending to retain them in the gap zone 49.

Flow path 54 in FIG. 1 indicates removal from gap G of modified mixture M_1, in the form of, or consisting of, the initial liquid mixture M less any liquid which has flowed radially inwardly through porous structure 21, and less any particle component or components carried with the liquid permeating porous structure 21. In particular, the difference between the rate or amount of feed of mixture M into the gap along path 54 at the top and the rate or amount of removal of M_1 from the gap along path 54 at the bottom is necessarily the net rate or amount of permeation, i.e., decantation for an incompressible liquid such as blood along flow path 46. In practice, static pressure is actually controlled by controlling the feed flow and removal flow rates using positive displacement pumps (not shown in FIGS. 1 and 2). FIGS. 11 and 12 illustrate vectorally the forces on the particles due to centrifugation and decantation.

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With continued reference to FIG. 1, it is important to note, that the upper portion of the inner shell is formed with a impervious inverted cup-shaped entrance member 66, the sides 68 of which are tapered downwardly and inwardly away from boundary 48 towards the center of the cylindrical assembly A. The lower end of entrance member 66 abuts the top of porous element 21 at horizontal plane 81.

Outer surface, 34 of porous element 21 forming the interior surface of the gap G is either parallel to or preferably tapered outward from axis 20 relative to boundary 48. The outer cylinder O also preferably tapers outward from axis 20 at an angle usually similar to that of surface 34, for reasons more fully explained below. Surface 68 is seen to resemble an inverted frusto-conical surface while surfaces 32 and 34 are seen to resemble upright frusto-conical surfaces, respectively. The angle of taper and special shaping, if any, of surfaces 68, 32 and 34 may best be understood by treating boundary 48 as a downward axially moving surface which matches the velocities at boundary 48 associated with the axial flow of liquid in gap regions 82 and 83, respectively. Gap regions 82 and 83 are radially inward and outward of cylindrical boundary 48, respectively. The purpose is to minimize shear, i.e., axial velocity gradient, as between regions 82 and 83 at boundary 48. By limiting shear between fluids of substantially different viscosities in a rotational field subject to strong Coriolis forces, laminar stream viscous boundary flow can be preserved as more fully explained within.

As less highly concentrated fluid (i.e., much of the suspending medium of the original mixture M) is drawn away from that part of region 82 below horizontal plane 81, the axial flow cross-section of

that region must be reduced in order to maintain matching axial velocity between fluids in regions 82 and 83, respectively at boundary 48. As more concentrated fluid forms in regions 83 below horizontal plane 81, the opposite must obtain. Consequently, solid surface 32, and porous surface 34 have the appearance of frusto-conical sections tapering (downward) away and toward cylindrical boundary 48, respectively. The outward taper of surface 32 further assists the downward (outward) axial flow of concentrated material by providing a resolved component of centrifugal force tangent to surface 32 in an axial direction toward the exit region 40 for the first fraction. The portion of total centrifugal force assignable to the outward axial component is the sine of the angle surface 32 makes with rotational axis 20. Even at one part in one hundred the axial component of force which must be added to one gravity in vertically oriented apparatus can be considerable and always advantageous to the movement of thickened viscous material.

The radial position of boundary 48, to the extent it actually forms, is best understood in relation to the lower extremity of surface 34. If most of the continuous phase contained in the original mixture M is decanted as suspending medium for the second fraction M2 or is itself M2 then boundary 48 will closely approach the lowest extremity of interior surface 34 because very little axial flow cross-section is required for the remainder of M2 to enter zone 62 where it re-mixes with the concentrated material leaving the lower end of gap G to become the final formulation of M1. In the limit where all available M2 is decanted and concentrated material is well formed, that is, boundary 48 is well defined, the latter will just intersect the extreme lower corner of

surface 34. Even more aggressive decantation of M2 will cause some of the concentrated material to enter M2 and boundary 48 intersects surface 34 at some axial position above the latter's extreme lower corner. Thus, the radial position of a well formed boundary 48 is very sensitive to the fraction of $_{M2}$ decanted through porous surface 34. Boundary 48 is merely a convenient reference for purposes of illustrating the process, however, the permeation of what is, at first, a very minuscule amount of concentrated material into M2 can be used as an observable indicator of conditions within the apparatus in most cases. Nephelometry or hemoglobin detection means placed at the output 86 of M2 will detect the very first permeation of cells or RBC, respectively, in the case of blood, whereby decantation flows may be adjusted at will. Similar techniques are available for most mixtures having concentrated separable components.

The above described liquid fractionating phenomena can be more fully understood by reference to FIG. 1A, when taken in conjunction with FIG. 1.

Referring now to FIG. 1A, there is shown a broken, fragmentary schematic enlarged view of the right-hand portion of the cylindrical assembly A as it is rotated, depicting the flow pattern of the first and second liquid components M1 and M2, respectively, relative to the porous cylindrical structure 21. For purposes of illustration, the space within gap G has been divided into zones RA, RB, RC, and RD. Zone RA is the space radially inward of boundary 48 radially outwardly of the cup-shaped entrance member 66. Zone RB is the space radially outwardly of boundary 48 adjacent zone RA toward which all of the mixture components (more dense than the suspending liquid medium and thus subject to centrifugal force) move. Zone RC is disposed below the imaginary horizontal

plane 81 adjacent the outer surface 34 of porous element 21 within boundary 48. Zone RD is disposed adjacent zone RC, but radially outwardly thereof and the porous element surface 34. Within zones RA and RB, all of the said more dense components that are subject to centrifugal force move radially outwardly, and there is no opportunity for radially inward flow. The purpose of including these zones is to provide an opportunity for the concentration of otherwise concentrated particles nearest the spinning outer surface of the cup-shaped element 66 to be lowered so as to create dilution of such particles radially inwardly of boundary 48. Within zone RB, increasing concentration of particles is taking place which tends to make boundary 48 more visible. Such boundary could, in fact, become readily visible when the liquid mixture is blood, since the red blood cells, as they start collecting within zone RB become quite dense. As plasma thins out, it begins to appear yellow and clear, even though plasma may be full of platelet particles. Zone RC is the zone which is most proximate to the outer surface 34 of the porous element wherein the separation of component M2 is occurring.

Within zone RC, a predictable or characteristic radially outward settling of particles takes place, since zone RC now contains a diluted mixture of particles. Because a known radially inward flow of liquid, possibly including certain particles and a known outward radial settling velocity of all particles is established in dilute concentration, it is possible to decide whether or not particular particles will be carried with the liquid leaving zone RC through the porous element 21. In zone RD, the particles are becoming more heavily concentrated due to centrifugal force, and accordingly, will not flow

radially inwardly through the porous cylindrical element 21. The fact that the liquid within zone RA is becoming more dilute means that it is becoming less viscous. The amount of dilute liquid is increasing in volume as the mixture flows axially downward so that the liquid in zone RA is increasing in volume.

Within zone RB, the liquid is becoming more concentrated, and accordingly, becomes more viscous. In zone RC, the liquid is less viscous, as in zone RA, but is also being removed radially inwardly through the porous element, and is accordingly, losing volume as the volume increases in zone RA. In zone RD, the liquid is becoming thicker and is substantially increased in viscosity so as to require more space within which to flow. The aforedescribed tapering of the outer and inner facing surfaces of the outer and inner cylinders is designed to take into account the fundamental physical fact that the division between the liquid portion and the concentrated portion follows a surface that is essentially parallel to the axis of rotation 20, and it should be understood that such cylinder is indicated by boundary 48. Boundary 48 is located radially within the gap depending upon the volumes that are flowing in and out of the cylindrical assembly. Because of the axial downwardly flow of the liquid, in combination with the radially inward flow of liquid component M2, the axial flow and the radial flow are vectorially independent as noted hereinabove. The aforedescribed tapered surfaces insures approximately the same axial velocity for the concentrated and non-concentrated liquid components at boundary 48. If such approximately matched axial velocity is not obtained, there would be a tendency for one or the other liquid component to have a shearing effect that would tend to create vortices in

the high energy rotational field generated by rotation of the cylindrical assembly A.

One of the most important criteria for a device dedicated to the collection of blood components is the ability to isolate all surfaces and environments that could be exposed or accessible to the blood or its separated products. These must be sterilizable by means approved in the industry (e.g., Gamma, ETO, etc.) and must be capable of retaining sterility under ordinary conditions of use. This is extremely difficult and expensive to achieve when attempting to seal a moving part from the external environment. The solution of the problem in connection with the present invention as disclosed herein is not, in principal, restricted to the present invention, rather it is believed it constitutes a significant contribution to the practical embodiment of devices incorporating, moving, sterile parts.

The basic concept provided by the present invention is to immerse the entire rotating cylindrical assembly A in a bath of sterile solution, compatible with blood, e.g., saline, or anticoagulant, indicated by flow arrows 90, which is contained within the stationary housing H. Access to the interior of the housing H is made through upper and lower conduits 91 and 92, to be described fully hereinafter, which lead into and out of the housing from or to sterile containers respectively. The entire sterile path, including the rotating cylindrical assembly, and the several sterile containers which may be permanently attached to the assembly housing prior to sterilization comprise a closed sterile system. Conventional peristaltic pumps, not shown in FIG. 1, engaging conduits in communication with the interior of the assembly can be used to move fluids to and from the containers and the assembly without invading the

sterile environment which includes, in part, the extracorporeal blood path and the vessels in which the separated concentrated blood components are stored. See FIG. 18. As indicated by flow path 90 which begins at the upper portion of the rotating assembly and its stationary housing H, a sterile or wash solution is urged downwardly between the space 93 separating the exterior surface of the outer cylinder O and the inner surface of the stationary housing H. Such sterile or wash solution is discharged at the bottom of the rotating assembly and housing combination. Fluid seals (not shown in FIGS. 1 and 2) are interposed between the upper and lower elements of the rotating assembly and its stationary housing H. A portion of the sterile solution flows through these seals.

It is important that the sterile bath is maintained at a higher static pressure than the fluid flowing through paths within the rotating assembly. With this arrangement, the entire rotating assembly is surrounded by the sterile bath and the seals which need not function as bearings, are provided to operate between that bath and the fluid flow paths of the rotating assembly. The criteria governing the design of the seals (preferably rotating seals) are less critical than the criteria normally required for sterility barriers. For example, although these rotating seals (as between the sterile bath and the blood) can be impervious to fluids without detracting from the operation of the apparatus and method of the present invention, because the sterile bath is maintained at a higher static pressure than the blood, or, in the alternative view, caused to flow at a pre-determined rate across the seal by means of positive displacement into the blood, as long as the leakage rate is small, the dissolution effect is harmless, and

the direction of flow operates to protect the fragile components of the mixture by preventing them from entering the seals. As described hereinafter, however, as in cell washing, the sterile bath may also be the wash solution and a high leakage rate is intended.

The advantages of such a rotating seal concept are significant in connection with high spin rates. First, high sealing and bearing pressure is not required, which mitigates the heating effect. Second, the sterile fluid crossing the sealing surfaces at their interface forms a fluid film that reduces friction, further mitigating the heating effect while absorbing and carrying away what heat is generated. The same concept may be employed in separate load bearing bearings between the housing H and cylindrical assembly A, except that flow through the bearings is much higher and does not represent a "leak" from one fluid into another. The cooling effect of the sterile bath can be enhanced by maintaining a circulation of this bath around the rotating mechanism and through the rotating bearings and seals exposed to the circulating bath. The same sterile bath can be continuously recirculated by providing fluid entrance and exit routes on the stationary containment vessel, as shown in FIG. 1 for that purpose.

It should be noted that not maintaining a positive flow across the rotating seal from sterile bath into the blood path does not result in a critical difficulty. There is no loss of sterility and, contamination of the sterile bath with blood or blood components is not crucial since this material is disposed of, following the procedure. Nevertheless, it is not desirable because blood components, particularly RBC, will inevitably be damaged in transit across the nominal seal. The damaged

components carried into the sterile bath are of no particular importance, but the material they generate (e.g., free hemoglobin) can and usually does leak back into the primary blood path. This is to be avoided in the manner previously described in keeping with the highest quality blood separation. Heretofore, systems using rotating seals against blood without a protective leakage component, as described herein, have invariably caused measurable contamination with hemoglobin released by RBC damaged within the seals.

Referring now to FIGS. 3, 4, and 5, there is shown the major components of a first form of apparatus embodying the present invention constructed in accordance with the principles of the invention described hereinabove and shown in FIGS. 1, 1A, and 2. Like parts bear the same reference numerals. The power-operated means for rotating the cylindrical assembly A within housing H may take the form of a conventional electro-magnetic armature drive utilizing a stator 100 affixed to the upper part of housing H which cooperates with an armature assembly 102 which is keyed to an upper coaxial drive tube 104 that extends downwardly with its lower end affixed to the upper portion of the support tube 41. An upper bearing member 115 is interposed between the upper portion of drive tube 104 and a drive support member 105 that extends upwardly from a neck 107 formed on housing H. The upper end of drive support member 106 is provided with an inlet fitting 110 which is connected with the upper end of drive tube 104 to conduct the liquid M downwardly therethrough. An upper combination bearing and O-ring assembly 112 is interposed between the upper portion of drive tube 104 and the drive support member 106. A sterile solution conduit 91 is affixed to the neck 107 of the stationary housing H to conduct sterile solution

upwardly through a first sleeve 113 formed on the neck along the inner surface thereof, radially inwardly and downwardly through vertical passages 114 of upper bearing 115, then radially outwardly below bearing 115 and downwardly along the inner surface of a second sleeve 116 below drive support member 105 and exterior of armature assembly 102. From the space below the armature assembly 102, the sterile solution flows downwardly through a main bearing assembly 118 through vertical passages 119 formed through the intermediate bearing assembly. Main bearing 118 is carried by neck 107.

Thereafter, the sterile solution flows downwardly into space 93 between the interior of the housing H and the exterior of the outer shell O. Next, the sterile solution flows downwardly through the lower confines of the space 93 underneath the outer shell O to flow downwardly out of a discharge conduit 92. It should be noted that additional sterile solution is introduced into the base portion 120 of the housing H through a conduit 130, such sterile solution being indicated by flow arrows 132. The sterile solution entering through conduit 130 flows upwardly through vertical passages 133 formed in a lower bearing assembly 142 to mix with the sterile solution entering through the upper conduit 91, and then flows outwardly through discharge conduit 92. This second flow of sterile solution also moves downwardly through a lower top combination bearing and O-ring seal assembly 140 and upwardly through a lower combination bearing and O-ring seal assembly 142. The sterile solution may serve as a coolant for the bearings and seal assemblies.

Referring to the upper portion of FIG. 3, the liquid component M designated by flow arrows 54 is moved downwardly through drive tube 104 and radially

oriented in passages 141 formed in the common top wall of the inner and outer cylinder, then into the upper portion of gap G to flow downwardly therethrough to be separated as described herebefore into the first liquid component M1. As indicated by flow arrows 144 liquid M1 flows radially inwardly through passages 145 formed in the common bottom wall of the inner and outer shells, and then downwardly through lower tube 150 to be finally discharged through discharge conduit 86 which is coaxial with the tubes and the cylindrical assembly. It will be seen that the lower tube 150 extends through bearing O-ring seal assemblies 140 and 142 and a bottom combination bearing O-ring assembly 154. The sterile solution entering through lower conduit 130 cools the lower bearing and combination bearing and O-ring seal assemblies.

With continued reference to FIG. 3, liquid component M2 which flows through the porous cylinder 21, as indicated by flow arrows 46, moves radially inwardly from the bottom of inner region R through passages 160 formed in the lower portion of the inner and outer cylinders I and O to be collected in chamber 164 formed between the lower portion of the vertical support tube 41 and the lower drive tube 150 for ultimate discharge through fitting 87.

Shock absorbing pads 156 may be interposed between the horizontally facing surfaces of housing H and outer cylinder O.

It should be understood that the sterile solution entering through the respective upper and lower conduits 91 and 130 follows a sterile path which includes the exterior of the rotating cylindrical assembly A and is maintained at a higher static pressure than the fluids M, M1, and M2 so as to protect the fragile components of these fluids by preventing them from entering the seals as described

in detail hereinbefore. It should also be understood that it is possible to force a saline solution into the gap G, as hereinbefore described, should it be necessary to re-liquify or otherwise render fluid any packed cells of the liquid component M1 within the lower portion of gap G.

The principles of operation of the separator apparatus shown in FIG. 3 may be seen by reference to the schematic illustration of FIG. 18. Referring thereto, the housing A4 of the separator apparatus receives blood from a donor at its upper end. Upon rotation of the cylindrical assembly, the concentrated blood cells of the donor are returned to the donor, as indicated by the directional arrows. Plasma is transferred to a suitable receptacle from the lower right side of the housing as shown by the directional arrows. The volumetric pumping rate of the blood-handling upper pump P11 is greater than that of the lower pump P12 so as to provide the pressure differential required to effect permeation of the plasma through the walls of the porous cylinder element 21. Saline sterile solution forced by pump P13, enters the upper and lower left-hand portions of the housing A4 and such saline solution is metered out of the lower portion of the housing by pump P14 as shown by the directional arrows. Saline pumps P13 and P14 maintain the saline solution at a higher pressure than the pressure maintained in the separator apparatus and the conduits leading to and from such separator for the reasons set forth hereinbefore.

Referring now to FIGS. 6, 6A, and 7, there is shown the major components of a second form of apparatus embodying the present invention. This form of the invention is similar to the form of the invention shown in FIGS. 3, 4, and 5, with the exception that the inner shell I' is formed at its

lower portion with a second porous structure in the form of a porous ring 170 disposed below the main porous cylinder 21'. It should be understood that the upper part of the apparatus of this second form of the invention is also provided with a electro-magnetic armature drive (not shown) disposed within a drive support member 106' of the type utilized in the apparatus of FIG. 3 for rotating the cylindrical assembly A as a liquid M to be fractionated is caused to flow downwardly within drive tube 104'. During such rotation, component migration, particularly described in conjunction with the description of FIG. 1 and 1A hereinbefore takes place whereby an imaginary boundary 48' is formed in general alignment with the upper and lower peripheries of the inner shell I' as the liquid fraction M2 flows radially inwardly through the main porous element 21'.

In this form of the apparatus, however, a third liquid fraction M3 is harvested from the lower portion of the fluid within the radially inner lower zone E portion of the boundary 48'. Such liquid component fraction M3 is forced through the lower porous ring 170 by the excess of fluid pressure within the gap G over that maintained in an inner region RR interior of porous ring 170. Such liquid, after passing through the lower porous ring 170 continues to move radially inwardly through the lower region RR which is defined by passages 174 formed in the lower walls of the inner and outer shells. This M3 liquid fraction is collected within a space 176 disposed outwardly of lower tube 150' to be ultimately discharged through an outlet conduit 178 formed in the lower right-hand portion of the stationary housing base 120'.

With continued reference to FIG. 6, 6A, and 7, the lower portion of the outer shell O', generally radially outwardly of the porous ring 170, is formed

with a cylindrical opening 180 over which is disposed a vertically movable cylindrical valve ring 182. Such valve ring 182 is seated on a pair of O-ring seals 183 mounted in the outer portion of opening 180. The lower portion of the valve ring is formed with a plurality of circumferentially spaced holes 186. A porous diffusion ring 184 is disposed within the reduced diameter opening 185 inwardly of and aligned with opening 180. Valve ring is normally arranged in its lowered position of FIG. 6, however, such valve ring may be moved upwardly into its raised position of FIG. 6A by suitable electro-magnetic means (not shown) in a conventional manner. Steps 188 limit movement of the valve ring. In the raised positions of the valve ring 182, the holes 186 of the valve ring are disposed radially outwardly of the openings 180 and porous diffusion ring 184. With the valve ring is arranged in its normal lowermost position, saline solution entering through upper and lower conduits 91' and 130' flows outwardly through an outlet conduit 190 attached to the left-hand lower portion of housing H' from the space between the outer surface of the outer shell O' and the inner surface of stationary housing H'. The saline wash solution entering lower conduit 130', additionally, flows through the lower bearing and bearing O-ring seal members, just as in the apparatus of FIG. 3 and for the same purposes. When the valve ring 182 is moved to its raised position of FIG. 6A, however, saline wash solution is introduced radially inwardly through valve ring holes 186, as indicated by flow arrows 194, whereby such saline solution will flow radially inwardly from space 93' through the porous rings 184 and then ring 170 at a rate of flow effective to enable an inward radial velocity of controllable and uniform value within the gap G'. Diffusion ring 184 may be somewhat displaced axially

upward (i.e., toward the entrance zone of the gap) relative to porous ring 170 in order to accommodate downward axial displacement of wash solution in the time required for the latter to cross the gap. After the saline wash solution enters and crosses porous outer ring 184 and gap G', it enters and crosses porous ring 170, and enters inner region R', as noted above. The inward radial convective velocity associated with wash solution flow should be higher than that of prior flow across surface 34' of porous element 21' in order to take full advantage of a sequential concentrating followed by a washing step intended to remove contaminants not otherwise permitted to follow with flow across surface 34'.

Forced inward convection of wash solution into and across the concentrated cell mass tends to displace the cellular material radially inward away from the interior surface of porous outer ring 184, i.e., floated or "levitated" off the surface. Each cell that remains with the first fraction finds a new point of equilibrium (at some radial position within the gap) where convective drag on the cell (a force which is controlled by wash solution flux) is in balance with centrifugal force on the cell. Any particle which cannot find new equilibrium, e.g., broken cell stroma, will be washed out. It should be understood that the portion of boundary 48' between the facing porous surfaces of rings 170 and 184 will become somewhat displaced radially inward from its position as shown in FIG. 6A and less clearly defined because the population of cells has a distribution of settling velocities. Some perturbation of reference boundary 48' must occur in zone E due to the change in equilibrium conditions previously established in zones RC' and RD'.

Liquid component M2 which flows through the porous cylinder 21', as indicated by flow arrows 46', moves radially inwardly into inner region R' and then upwardly through such region and into passages 199 formed in the upper common walls 198 (Fig. 6) of the inner and outer shells and then upwardly through a space 201 between the outer surface of drive tube 104' and the inner surface of support tube 41' into a collection chamber 202 between combination bearing and O-ring seals 203 and 204 to be discharged through a conduit 205. It should be understood that during operation of this form of the apparatus, sterile solution is forced through conduit 91' into the housing neck 107' so as to cool the bearings and seals disposed in the drive support member 106' and the housing neck in the same manner described hereinbefore with respect to the apparatus of FIG. 3. It should also be understood that the sterile solution entering through conduits 91' and 130' follows a sterile path which includes the interior of the housing H' and the exterior of the rotating cylindrical assembly A, and is maintained at a higher static pressure than the fluids M, M1, M2, and M3 so as to protect the fragile components of these fluids by preventing them from entering the seals as described in detail hereinbefore. Moreover, the introduction of sterile solution through porous element 184 makes it possible to re-liquify or otherwise render axially flowable any packed cells of the liquid component M1 within the lower portion of gap G'.

Reference may now be made to FIGS. 13 - 15 for a description of the general mode of operation of the present invention as applied to previously described separator apparatus.

It is important to note:

a) the separation of particles is occurring as a result of differences or changes in "settling rate", see FIG. 15, i.e., a dynamic condition; and not due to separation after the particles have arrived at their static bands, as shown in the classical separation bands of FIG. 14.

b) Settling rate in a given medium is a function of particle size, shape, concentration, and density. It is also a function of fluid viscosity and is generally proportional to the term $r\ \omega^2$, where r = distance of particles from spin axis; ω = spin angular velocity, which is selected to achieve dynamic settling rate separation of different particles. FIG. 15 is a plot of the population distribution for several formed elements of blood with respect to their settling rates divided by the multiplier $r\ \omega^2$. Dilute concentrations are assumed and the Stokes approximation is used for these plots. There is good agreement with observation for all blood particles except concentrated red blood corpuscles (RBC).

Note that in FIG. 15, the separation of platelets from other particles, as a function of settling rate, is much greater than in FIG. 14, which is a plot of the population distribution as in FIG. 15 but, in this case, with respect to particle density only, wherein the platelet band overlaps (i.e., is not spaced from) the lymphocyte particle band. The density bands of FIG. 14 illustrate the end point distribution of essentially fully settled particles.

c) In accordance with the present invention, decanting occurs while particulate is settling out, and not after settling is completed into bands as shown in FIG. 14.

d) Further, in accordance with the present invention, decanting can occur after some particles

have settled out according to density to form distinct bands, however prior art centrifugal separators employ means to extract material from these formed "layers", which is radically different from and inferior to that which is used in the present invention partly due to the fact that in the present invention, decanting occurs in a direction parallel to the force field (i.e., in the direction of vector 300 in FIG. 11), and not at an angle to the force field, thereby eliminating otherwise obligatory and destabilizing shear to achieve decanting. The latter effect reduces the effectiveness of all known prior art devices; and

e) particles separate even while they are still physically mixed in suspension not otherwise possible when separating particles from "formed" layers.

As a consequence of these novel principles, it is possible to separate platelets from lymphocytes, RBC, and granulocytes in apparatus designed in accordance with the present invention by selecting the appropriate operating parameters as described above. Separation is in accordance with differences in settling rate, (FIG. 15) not density, (FIG. 14). Decanting flow velocity and spin rate determine which components follow the several possible liquid fractions. These are fully selectable for many diverse applications as hereinafter described.

Application of these inventive principles to important blood component separation problems may be illustrated by first referring to FIGS. 13, and 14 which show a summary of published data on the population distribution of effective diameters and densities, respectively, of four important classes of human blood components, namely, red blood corpuscles (RBC), platelets, lymphocytes, and granulocytes. Except in regions of high concentration of components,

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the settling rate of that component in human plasma may be computed or at least characterized from these data using the Stokes drag equation:

$$V_s = \frac{D^2 \Delta\rho}{18 \mu} r \omega^2$$

V_s - settling velocity (cm/sec);

D - equivalent particle diameter (cm);

$\Delta\rho$ - density difference, particle minus medium

μ - viscosity, medium

$\frac{r \omega^2}{g}$ - g's of centrifugal force if g = acceleration of gravity.

Equivalent particle diameter refers to that diameter that gives the experimentally observed or "correct" settling velocity according to the Stokes equation which is more useful to show how settling velocity varies with design and operating parameters r and ω, respectively. To this purpose calculations based on the Stokes equation are plotted in FIG. 15 as velocity per unit of centrifugal acceleration. Note that granulocytes, due to size as well as density, settle much faster than other particles, and the lot settles at least eight times faster than platelets.

Consequently, platelets which could not be separated from lymphocytes by density (see FIG. 14), which is a very significant problem in achieving the desired lymphocytes-free platelets required for therapy, can be separated by settling rate using the teachings of the present invention.

In the operation of the apparatus of FIGS. 3, 4, and 5, as a separator for blood components, liquid mixture M is blood which enters the upper portion of the rotating cylindrical assembly A through drive tube 104 and enters gap G. This form of the apparatus is particularly adapted for use as a collector of cell free or platelet rich plasma.

In the usual blood-bank setting a typical donor can be "bled" at a rate of about 100 ml/min. At an average hematocrit (Hct) of 45% (i.e., percent of whole blood by volume comprising cellular material), 55 ml/min of the 100 ml/min is plasma, the suspending medium, which, incidentally, is over 90% water, the rest being dissolved complex organic molecules, lipids, and salts. Because the device illustrated in FIG. 3 is capable of decanting as much as 90% of the plasma, leaving the remainder to support fluidity of the concentrated portion, one can use, for purposes of this example, the removal, i.e., decanting, of 50 ml/min of plasma uniformly distributed over 50 cm^2 of porous flow distributing surface. Hence, the inward radial convective decanting velocity is 1.0 cm/min or 0.0167 cm/sec, that is, 50 ml/min divided by 50 cm^2.

For operating and design purposes, one might pick a settling rate for red blood corpuscles to be 0.02 cm/sec which exceeds the convective velocity by enough

to prevent red blood corpuscles from approaching the porous surface. Referring to FIG. 15, one has

$$0.8 \times 10^{-7} \times r\,\omega^2 = 0.02 \text{ or } r\,\omega^2 = 2.5 \times 10^5.$$

A practical example for the diameter of a blood film could be 1.5 inch. With an $r\,\omega^2$ of 2.5×10^5 the r.p.m. would be 3486 giving 255 g's of centrifugal force. Inserting these values into the Stokes equation and solving for V_s, the corresponding settling rate of the fastest platelets is only

$$0.2 \times 10^{-7} \times 2.5 \times 10^5 = 0.005 \text{ cm/sec}$$

or far less than the convective velocity of 0.0167 by a factor of 0.30. Hence platelets are easily carried with the plasma to yield what is referred to as platelet rich plasma (PRP) but without, it should be noted, the presence of any leukocytes.

This calculation assumes a relatively low concentration of red blood corpuscles near the porous surface for the Stokes equation or, more to the point, a narrow well defined range of settling velocities to apply. The initial impregnable zone makes this possible as follows:

Suppose the blood film thickness is nominally 0.1 cm, which, as will be shown herein, is well within the allowable range. When the red blood corpuscles and lymphocytes travel about 0.05 cm, they are nearly fully settled out as together they comprise nearly half the volume of the initially whole blood. They

travel nearly this entire distance, or about 0.04 cm in 2 seconds, in the absence of a radial convective velocity such as obtains over the initial impregnable zone. Since the feed rate of 100 ml/min is 1.667 ml/sec, a hold-up volume of 3-1/3 ml of blood film over this zone (which may, for example, be obtained by using a gap G thickness of 0.1 cm and a first encountered impregnable surface area of 33-1/3 cm^2) will cause the blood to have a residence time of 2 seconds over the impregnable area and 6 seconds over the 50 cm^2 of porous surface 21. The latter value is due to the fact that half of the 100 ml/min is withdrawn resulting in an effective axial flow of 50 ml/min through a hold-up volume of 5.0 ml over 50 cm^2 of porous surface. The total residence time is 8 seconds in the operative blood film.

As just seen, the red blood corpuscles are nearly settled out before they even get to the porous surface 21 and settle even further thereafter. It is therefore reasonable to conclude that throughout the proximity of the porous surface, the concentration of red blood corpuscles is low and the Stokes settling rate is obeyed.

On the other hand, in 2 seconds, the platelets move away from the surface by, at most, 0.005 cm or barely 1/10th of the distance they would otherwise travel to their settled position absent convective

decanting. They retrace this entire displacement in less than 1/3rd second after encountering radial inward convective flow upon first reaching the porous surface 21 and continue to be drawn through the porous flow distributing surface for the remaining 5.67 seconds of residence time over that surface.

These simple calculations demonstrate a device that yields nearly all the available plasma completely rich in platelets and absent all other cellular material. The size of the device for the application example indicates that it could easily have been made smaller say 1.0 inch diameter, and ω increased to 4270 r.p.m. to achieve the same effect. On the other hand, there is another use for the device wherein the larger device can be used to advantage, that is, where one wants to either concentrate the collected platelet rich plasma in a second stage (see FIG. 12) or simply collect cell-free plasma.

In the latter case, assume again that the decantation rate is 50 ml/min over 50 cm^2 of porous surface or a convective velocity of 0.0167 cm/sec. For completely cell-free plasma the settling rate of platelets must exceed this value, say 0.02 cm/sec or greater. Then, because platelets are so sparsely concentrated to begin with, (i.e., their concentration has no affect on the validity of the Stokes calculation) one may use:

$r\ \omega^2 \times 0.5 \times 10^{-8} \geq 0.02$ or, for a 2.0 inch diameter blood film, the r.p.m. must be 12,077. This rotation speed can be achieved with proper bearing design and balancing of the apparatus.

By way of example, FIG. 16 illustrates the manner in which two separator apparatus A-1 and A-2 of the type shown in FIG. 3 may be operated simultaneously to produce platelet concentrate (PC) using positive displacement peristaltic roller pumps commonly available for the pumping of blood or other sterile fluids.

In the operation of the apparatus of FIGS. 6, 6A, and 7 as a separator for blood components, liquid M would be blood which enters the upper portion of the rotating cylindrical assembly A through drive tube 104' and enters gap G'. This form of the apparatus is particularly adapted for use as a rapid PC collector in certain surgical settings where high platelet loss is expected. If a fully therapeutic dose of platelets could be obtained from the surgical patient in the O.R. during surgical preparation and returned to that patient following surgery, significant clinical benefits (related to control of bleeding, i.e. clotting mechanisms) would be expected. Having reference to FIGS. 6, 6A, and 7, such a procedure can be carried out in one step in the apparatus shown. Because access to venous circulation is substantial in

this case it is possible to obtain, for example, about 300 ml/min of blood flow, at least half of which, 150 ml/min, will be plasma available for collection or processing. Of that, 30 ml/min will carry the concentrated platelets and 120 ml/min would be the cell-free plasma to be decanted first. Referring to FIG. 6, with blood entering gap G' at the top, such blood first encounters impervious entrance member 66' and then porous sections 21' and 170 in succession. For purposes of the present example, the area of porous surface 34' of porous element 21' is fixed at 200 cm^2. 120 ml/min of cell free plasma flowing radially inward through the porous element produces a radial convective velocity of 0.01 cm/sec, i.e. 2 ml/sec divided by 200 cm^2. In order to collect only cell-free plasma as the second liquid fraction M2, the Stokes velocity for platelets must exceed the convective velocity by at least 25%. In the present example $r\ \omega^2 x\ 0.5\ x\ 10^{-8} \geq 0.0125$ represents the required condition. See FIG. 15. For a 2.0 inch diameter blood film the r.p.m. is 9548. Larger diameters or more porous surface area would reduce the r.p.m. requirement.

The plasma remaining in zone E after decantation of cell free plasma from zone RC' contains PC which can, in sequential decantation across the outer surface of porous element 21' be largely removed from

zone E through porous ring 170 as third liquid fraction M_3, the remainder rejoining the concentrated material from zone 83' at passage 144' where the recombined material, now first fraction M_1, is led away at conduit 86'. In order to prevent RBC or lymphocytes from being decanted along with the platelets it is necessary to choose a convective radial velocity which exceeds the settling velocities of platelets but is less than those for RBC. Referring to FIG. 15 it is seen that such a velocity would be adequately represented by $r\ \omega^2 \times 2 \times 10^{-8}$ which, for the specified blood film and rotation rate, is 0.05 cm/sec. Given the decantation rate for M_3, (i.e. PC), that is, 30 ml/min or 0.5 ml/sec, the area of the exterior surface of porous ring 170 must be 10 cm^2 to enable the convective inward velocity of 0.05 cm/sec at that surface. Thus, the second porous element 170 is much smaller than the first porous element 21 in area and axial extension.

Referring again to Figs 6, 6A, and 7, yet another application of the invention has great utility in the washing and concentrating of red blood corpuscles either in connection with frozen blood storage or, perhaps more importantly, for application to blood cell salvage in what is termed auto-transfusion of the surgical patient's own blood during surgery. In the latter instance, it is the removal of excess heparin

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and return of concentrated protein and clotting factors for the purpose of clotting function regulation that has the greatest clinical importance. The processing of high volumetric rates can be useful. Cell washing should involve a concentration step followed by the simultaneous addition, separation and removal of wash solution, usually saline. If concentration precedes washing, the amount of wash solution required to displace cell stroma dispersed in the original suspending medium is minimized.

With particular reference to FIG. 6A, when cylindrical valve ring 182 is raised, a saline wash solution, indicated by flow arrows 189 from space 93' flows radially inwardly through porous rings 184 and 170, respectively, at a rate of flow effective to enable an inward radial velocity of controllable and uniform value across the gap and into passages 174, space 176, and through discharge conduit 178 (see FIG 6). The inward radial convective velocity associated with wash solution flow should be higher than that of prior flow across surface 34' of porous element 21' in order to take full advantage of a sequential concentrating followed by a washing step intended to remove contaminants not otherwise permitted to follow with flow across such surface. Using the criteria above described, assume the apparatus of the present invention is capable of removing 200 ml/min from a

blood flow that would be typically 300 to 400 ml/min. Also, assume surface 34' has an area of 200 cm^2 so that the inward radial convective velocity is 0.0166 cm/sec. In order not only to salvage most of the red blood corpuscles, especially the youngest and healthiest cells, which are generally the least dense, but further, to prevent smaller contaminants such as cell stroma which have settling velocities comparable to platelets, from following with the protein comprising the second liquid fraction, one would again consult FIG. 15 where the minimum Stokes velocity for platelets is about $5 \times 10^{-9} \times r \omega^2$ and set this value at or above 0.02. Using a 2.0 inch diameter blood film, the required r.p.m. is 12,080. It remains only to use a higher radial velocity than that used to decant liquid from zone RC' to decant wash solution, after deciding how much wash solution is required, bearing in mind it can always be adjusted to fit whatever operating conditions prevail and that the example here is for maximal conditions. The operative parameter is about 10 ml/min of wash solution for each 1.0 cm^2 of exterior and interior porous surface of porous elements 170 and 184, respectively, in order to maximize the washing effect (i.e. displacement of cell stroma) while still retaining all RBC in the first fraction. Because the pre-concentration step removed so much protein containing liquid which does not now

have to be displaced by an approximately equal amount of wash solution, it is estimated that 20 to 50 ml/min of wash solution would be sufficient to process about 100 ml/min of packed RBC. Using the upper value, the surfaces of porous elements 170 and 184 and could be as little as 5 cm^2. However, if one doubles the area and rate of wash solution flow, the design is virtually identical to that for the PC collector. It will be understood that operation of cylindrical valve ring 182 to block and unblock access of saline solution to porous elements 184, as shown in FIG. 6A, converts the FIG. 6 apparatus from PC collector to a cell washer and concentrator.

It is noted that the washing process operative in the example herein described displaces rather than mixes with the original suspending medium as in prior art cell washing methods. Consequently, washing is more thorough per unit volume of wash solution because, as in the comparison between a shower and a bath, the wash solution is not substantially diluted. It is further noted that the crystalloid portion of the first separated protein containing liquid (i.e. plasma) can be removed as by ultra filtration in separate apparatus so that protein concentrate can also be returned to the patient. See FIG. 17.

Figure 17 is a schematic illustration of the operation of separator apparatus embodying the present

invention which is convertible from a platelet concentrator to a cell washer/concentrator in accordance with principles of the invention. Whole blood or a solution containing blood components is delivered by pump P6. As a PC collector or cell washer/concentrator, pump P7 removes concentrated blood while pump P8 removes cell-free and stroma-free liquid. The difference, that is, the volumetric pumping rate of P6 less the sum of rates of P7 and P8 is a net flow which is PC or contaminated wash solution in the cases of platelet collector and cell washing/concentrating, respectively. In the former, cell-free plasma is recombined with concentrated blood to form reconstituted blood for return to the patient. In the alternate, cell-free liquid, containing plasma proteins and crystalloid material including water, follows a different path as indicated by the dotted lines at the left portion of FIG. 17 to a separate device incorporating membrane filtration to remove a large part of the water and crystalloid to form concentrated plasma protein. The latter is recombined with concentrated blood for return to the patient.

Saline circulation is handled in each case as follows: Pump P9 delivers saline to each end of the apparatus while pump P10 removes saline from the central port 190 simultaneously, and at a slightly slower volumetric rate, in the case of platelet

collection, in order to force some saline across the seals.

For cell washing, pump P10 is slowed further. Pump P10 removes saline from the apparatus A at a volumetric rate which is less than the volumetric rate of pump P9. The difference is the volumetric rate at which saline wash solution is delivered across the gap. It is understood that fluids other than saline may be used for the purpose described above. When the cylindrical valve ring 182 (FIG.6) is raised, saline solution enters the porous ring 170 and outlet conduit 178 to wash contaminants picked up by the saline solution for disposal, as indicated by the dotted lines at the right portion of FIG. 17.

Referring now to FIGS. 8 and 9, there is shown the major components of a third form of apparatus embodying the present invention. This form of the invention is similar to the form of the invention shown in FIGS. 3, 4, and 5, with the exception that the outer cylinder O is provided with a porous element 193 over a portion of its axial extension. Like parts bear double primed reference numerals. The upper part of the apparatus of the third form of the invention is provided with an electro-magnetic armature drive, like that shown in FIG. 3 arranged to effect rotation of the inner and outer cylinders I'' and O'' within stationary housing H''. A sterile solution is

introduced into the conduit 91'' at top of drive support member 104'', and is discharged through an outlet conduit 92'' at the lower right-hand portion of housing H''. The liquid component M to be fractionated enters through the upper end of drive tube 104'' and flows downwardly through the lower end of the drive tube into the entrances of radially outwardly extending passages 196 formed between the upper walls of the inner and outer cylinder members. The radially outer ends of these passages empty into the upper end of gap G''. The lower end of the gap G'' is in communication with the radially outer ends of radially extending passages 209 found between the lower walls of inner and outer cylinders I'' and O''. The radially inner ends of these passages are connected to the upper end of lower tube 150'' to discharge liquid fraction M1 through the lower end of the housing H''. A circular baffle 210 is arranged coaxially between support tube 41'' and inner cylinder I'' to define inner region R''. Inner region R'' receives liquid fraction M2 which permeates through porous element 21'' of the inner cylinder I'' by a pressure differential created between the gap G'' and inner region R'', as fully described hereinbefore. Passages 211 formed in the lower portion of the cylindrical assembly A'' transfer liquid component M2 into a space 212 from which the liquid is discharged

through the lower portion of housing H''. The lower portion of the housing H'' is provided with bearings and O-ring bearing seals (not shown) through which a sterile, cooling solution is circulated as with the apparatus of FIGS. 3 and 6.

Assuming the liquid mixture is blood, for cell washing purposes, blood entering drive tube 104'' at the top of the apparatus usually consists of concentrated cells (i.e., 90+% cells in a liquid medium or "carrier"). The blood cell concentrate is led via flow path 207 to a gap entrance region 208 at the upper end of the separation gap G''. The gap is defined by interior surfaces of the inner and outer shell's axial sections. Sterile solution, such as a saline wash solution, enters the upper and lower ends of housing H'' by means of positive displacement volumetric pumping, follows a flow path through conduits designed to cool the bearings and seals and prevent blood component leakage and enters exterior region space 93'' between housing H'' and outer cylinder O'' at a substantially uniform pressure throughout the exterior region. It further enters and crosses (i.e., permeates) porous element 193 of the outer cylinder under the influence of the uniform pressure at a uniform volumetric rate over the entire exterior surface of such porous element, thus establishing an inward radial flow velocity of wash

solution across the axial extent of gap G" enclosed by porous element 193, as described hereinbefore. The flux velocity is determined by the volumetric rate at which wash solution crosses porous element 193 divided by the inner surface area 213 of such porous element. The portion of wash solution that enters space 93'' in excess of that which crosses porous element 193 leaves the apparatus via port 92''.

Wash solution which crosses porous element 193 nearest the top of the gap enters the concentrated blood cell mixture at gap region 218 and operates to dilute the mixture (provided wash solution is miscible with carrier fluid) even as the cells migrate radially outwardly under the influence of centrifugal force. The cells form a concentrated cell mass exterior to imaginary boundary 48''. Wash solution accumulates in gap region 219 and flows axially downwardly along with the concentrated cell mass in gap region 218. Gap region 219 is formed by impervious entrance element 216 which comprises an axially extending portion of the inner shell at the latter's top, which portion is tapered radially inwardly or away from boundary 48'' in the downward direction. Consequently, gap region 219 increases in thickness downwardly to accommodate the addition of wash solution to the mixture.

Wash solution enters gap region 220 at a flux velocity identical to that at which it enters region

218. However, wash solution is simultaneously crossing the outer surface of porous element 21'' at the same rate thus removing wash solution from gap region 221 as fast as it enters. The net effect is that wash solution crosses the gap in a radially inward direction with no net accumulation of wash solution in the gap for the axial extent of the gap which is defined and enclosed by the common axial overlap (i.e., axially co-extensive portions) of porous elements 21'' and 193 acting together. The axial extensions of porous elements 21'' and 193, where they do not face each other, serve purposes described separately herein. The gap-defining surfaces of the porous elements, where they face each other, remain concentric and parallel to boundary 48'' and to each other. The latter is the principal washing region of the gap.

The washing method is practiced by causing the wash solution flux velocity to be greater and less than the settling velocities of particles and/or cells to be washed out and cells to be retained in the gap, respectively. Clearly, continuous phase will be washed out and virtually replaced with wash solution, provided the two liquids are miscible. If they are not, it is not possible to predict with certainty the behavior just described.

Wash solution that was added to gap regions 218 and 219 is an excess volume not removed from gap region 221 and must flow axially toward exit region 209. However, the bottom portion of the outer cylinder is comprised of an impervious element 222 having an inner gap defining surface 223 for approximately the same axial extent as the impervious upper element 216 of the inner shell. Impervious surface 223 is a continuation of porous element 193 wherefore wash solution flows out of gap region 224 without simultaneous replenishment from gap region 225. Consequently, porous surface 226 of element 21'' is tapered outwardly and downwardly toward boundary 48'' to account for the diminishing amount of continuous phase. Cells in gap region 225 become more concentrated until they reach the level of concentration at which they entered, thus canceling the dilution introduced in gap regions 218 and 219. Surface 226 is tapered outwardly and downwardly to boundary 48'' to aid in the flow of concentrated cells toward exit region 209.

The described method of dilution and re-concentration has the effect of increasing the distance between imaginary boundary 48'' and the inner shell's porous outer surface 226. The additional distance operates to maintain dilute concentration of cells in the mixture most proximate the porous

"separation" surface 226. The main concentration of cells is radially exterior of boundary 48''.

The "environment" in which biologically valuable cells exist in gap regions 220 and 221 is unique in the present invention and, being sustainable indefinitely, has not been so achieved in apparatus heretofore. The opposing forces on a biological cell, operative in the gap, are centrifugal force urging the cell to seek the inner porous surface of the outer shell and the drag force of radially inwardly flowing media tending to carry the cell toward the outer porous surface of the inner shell. All cells remaining in the gap find a point of balance between these forces or "rest" on the inner surface of the outer shell which contains pores through which the cells cannot pass, not necessarily because the pores are too small in "size" for cells (some of which are sufficiently deformable to enter pores smaller than their normal cross-section) to enter but, rather, because the pore-open to pore-matrix solid volume is sufficiently low to substantially increase the wash solution inward radial flux velocity obtaining within the porous element volume to overcome the outward radial migration velocity of all relevant cells. Again, "filtering", understood as a sieving process, is not the operative feature here, nor does the outer porous element operate as a physical barrier, absent

the radially inward flow of wash solution, to effect separation of components.

For every collection of cells there exists a wash solution flow rate corresponding to an inward radial flux velocity in the gap in combination with a centrifugal force, determined in the apparatus by rpm, that can easily be found experimentally to produce a cell concentration gradient most dilute near the inner shell and most concentrated near the outer shell wherein every cell is surrounded by wash solution flowing continuously over its surface and wherein every cell no longer moves radially in either direction. In effect, the cells can be levitated and maintained in suspension even while the suspending phase is being continuously ex changed. The cell mass exists under conditions which are analogous to a "liquified bed". Such apparatus can superimpose a controlled axial flow or operate without axial flow by deleting gap regions 218, 219, 224, and 225 along with the associated impervious elements. Once stasis is achieved, it can be maintained indefinitely. Wash solution can carry nutrients and oxygen to the cells and simultaneously remove CO_2 and other waste products. It can be used to control temperature, enzymes and drug delivery to the cell. It is clearly a novel cell culturing method that does not subject the cell to the damaging effects of mechanical shear and filtration or

substrate interaction as used in some prior cell culturing methods.

Furthermore, given the indefinitely extended time scale, separation as between cells with very closely matched sedimentation properties could be carried on very gradually over long periods of time. These novel techniques suggest promising new possibilities for further biological and medical research involving in vitro cell studies.

As a more immediate practical application of the cell washing method of the present invention, FIG. 19 illustrates a simple pumping arrangement for washing stored blood using the separator apparatus of FIGS. 8 and 9. Blood is pumped via pump P15 while washed cell concentrate is pumped via pump P16 into a separate washed-blood bag. Because of the normal time delay required for some chemicals such as ethylene glycol (typically used to store frozen blood) to leave the red blood corpuscles (RBC) one would allow the first washed blood to re-enter the original storage bag, after all blood is cycled through the cell washer, by opening a valve between the two bags. After a period of time, the cycle is repeated for as many cycles as may be required to rid the stored blood of objectionable chemical. The last cycle leaves the clean blood in the washed-blood bag. Pumps P18 and P19 provide circulation and positive pressure on the

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seals of the apparatus A5 for controlled leakage as described hereinbefore, but the difference in their volumetric rates, i.e., the pressure of pump P18 minus the pressure of pump P19 is now also used to provide the positive definite flow of wash solution. The volumetric rates of pumps P15 and P16 match at all times so that there is never any difference in blood volume. Consequently, all excess flow, i.e., flow from pump P18 minus flow from pump P19 must leave the separator apparatus A5 via the waste wash path.

Another use of the cell washing method and apparatus of FIGS. 8 and 9 permits a major departure in extracorporeal blood oxygenation not possible heretofore. FIG. 20 illustrates such general method. The first stage employs a plasma separator apparatus A6 of the type shown in FIGS. 8 and 9 yields two outlet streams, one being highly concentrated RBC bearing de-oxyhemoglobin, that is, red cells poor in oxygen and saturated with carbon dioxide, RBC-D, the other being most (90% to 95%) of the plasma which is returned to the patient. The concentrated RBC-D (not pumped in order to minimize hemolysis), is led to a mixing chamber 400 through conduit 402 where it is thoroughly mixed with concentrated oxygen rich artificial blood particles, AB-O. The resulting mixture contains RBC bearing oxyhemoglobin, RBC-O, and spent AB saturated with CO_2 or AB-D. The mixing

chamber output rate of flow is determined by the rate of pump P20 (PR1) minus the rate of pump P21 (PR2) plus the rate of pump P25 (PR6), which flow enters the cell washer A7 through conduit 403. The difference of pump rates, PR1 minus PR2 is determined by the hematocrit of the patient blood (i.e., cell volume fraction, Hct.). The rate of pump P25 (PR6) will necessarily be related to that difference which correlates with the mass flow of hemoglobin, Hb., that is:

$$PR6 = f\ (PR1 - PR2)$$

where f is some factor depending upon the AB product used.

The wash solution flow rate is the rate of pump P23 (PR4) minus the rate of pump P24 (PR5) even though the wash solution is led serially through the plasma separator A6 (which draws off very little wash solution) before entering the cell washer A7, as shown in FIG. 20. Again, the concentrated RBC-O is not pumped in order to protect the cells but pump P22 draws waste wash solution out of the system. So long as PR3 = PR6 + (PR4 - PR5) or PR3 = (PR4 - PR5) + f (PR1 - PR2), the cellular output of RBC-O from the cell washer A7 will match that of the plasma separator A6, i.e., PR1 - PR2. This preserves the RBC cell mass. The wash rate PR4 - PR5 is controlled to provide the necessary wash-out of AB particles and

suspending medium. In order to prevent repeated dilution of plasma protein with each pass of blood through the oxygenator, the wash solution in this example should be the patients own plasma or donated plasma. This is both possible and practical because very little wash solution is required per pass to remove AB particles from the concentrated RBC cell mass in accordance with the method of the present invention. Finally, the RBC-O is recombined with the plasma from the plasma separator to reconstitute the blood, i.e., plasma with, now, oxygen-rich, CO_2-regulated, RBC. The reconstituted whole blood must flow into sufficient positive pressure so that neither pumps P21 nor P22 apply suction to the fluids. This provision is important to prevent fluid outgassing or cavitation. The suction side of pump P22 is the lowest pressure in the system, but it need not be below atmospheric if there is adequate resistance in the patient return line 404.

Having described the system, it is important to note that there are many varieties of artificial blood generally consisting of particles of extraordinary solubility relative to gases such as O2 and CO_2. Many are very compatible with blood and organ tissues. A typical example is Perfluorooctyl Bromide, PFOB, sold by Nippon Mektron Ltd. The ability of these particles to rapidly transfer oxygen and remove CO_2 from the body

tissues and blood cells, with no apparent toxicity, is well established. Consequently, direct mixing of PFOB with concentrated RBC-D converts the latter immediately to RBC-O. The problem has always been separating the spent PFOB from the blood before returning the latter to the patient. Wholesale injection of PFOB into the patient is not approved.

Complete separation of entrained PFOB particles by filtration has not been possible because such particles are only about 0.1 micron in diameter. Separating them by prior centrifugation techniques is equally difficult because the particles have a specific gravity approaching 2.0 and would form a thin dense layer under the RBC which would defeat any reasonable method of skimming. On the other hand, the settling velocities of the particles are a small fraction of the settling velocity of RBC due to their small size. The settling velocity of a PFOB particle is about 0.006 the settling velocity of an RBC. Consequently, they are easily washed out using the present invention.

In summary, the oxygenator system of the present invention as described immediately hereinabove includes a plasma separating step (so as not to require separating PFOB particles from plasma) followed by a step which mixes RBC with AB, followed by a step which washes AB and any other stroma out of

the RBC and finally recombination of clean, oxygenated RBC with the plasma for return to the patient. These steps run continuously and simultaneously in a closed extracorporeal circuit as will be clear from FIG. 20.

With reference to porous elements disposed in the inner shells I, I', and I" of FIGS. 1 through 9, their necessary properties may be summarized as follows. They should have:

1) pore diameters of sufficient size to pass formed or particulate supernatant constituents without restriction, but not substantially larger than that size; and

2) resistance to flow of the supernatant fluid <u>medium</u> so that pressure loss experienced by supernatant crossing the porous barrier is substantially greater than pressure loss experienced by the remaining suspension as the latter flows from entrance to exit of the device; and

3) because axial movement of the blood within the blood film must be under conditions of viscous boundary flow in order to remain stable, the outermost layer of the porous cylinder or outer diameter surface must be "wettable" by

the suspending medium, hydrophilic in the case of blood.

Examples of how these properties can be achieved in a practical device are as follows:

First, it should be noted that the porous flow distributors are essentially tubular and can be comprised of multi-layers of concentric cylinders of various properties which, acting in combination, achieve the desired results.

Once the outer surface is "wetted", the interior remainder of the porous structure need not obey this condition (i.e., hydrophobia) which is one way of significantly increasing flow resistance.

It is further desirable, although not as fundamentally required, that the outer diameter of the porous cylinder have a high "open" to "solid" volume ratio or stated in other terms, a high concentration of pores per unit surface area. This condition should exist for a depth of at least several pore diameters in order to prevent local concentration of supernatant flow velocity at a microscopic level. Once the supernatant becomes trapped within the porous structure and removed from the bulk blood film, the high open to solid ratio need not be maintained. Consequently, inner layers of the continuously open porous structure can be comprised of lower open to solid ratios or lower concentration of pores. This

further adds to flow resistance without affecting the requisite blood contact surface properties of the porous flow distributor. Of course, simply adding layers, or pore structure thickness, further adds to flow resistance.

In summary, three ways to establish the desired flow resistance of the porous flow distributor are:

1. Decreasing the open to solid volume toward the interior of the pore structure.
2. Increasing the depth or thickness of the pore structure.
3. Changing the "philic" nature of the surface in contact with the suspension to a "phobic" condition toward the interior.

In practice, one may achieve these alterations of pore structure properties by employing concentric multi-layers.

It should be understood with respect to the aforedescribed apparatus and method of the present invention, that the fluid film, (e.g., blood) being separated must be thin enough that secondary flows which would disturb settling may not arise. The only flows permitted are the bulk rotation of the fluid film trapped between two surfaces rotating at the same angular velocity, the axial laminar streamline viscous boundary layer flow within that film from top entrance to bottom exit, and the forced convective radial

inward flow through one or more porous flow distributing surfaces.

In general, flow in a rotating system is characterized by very strong secondary flows that arise as a consequence of the rotational effects. Briefly, the Coriolis force balances the centrifugal pressure force in any regions of the fluid flow that are unaffected by viscosity such as would obtain sufficiently distant from a wall or surface containing the flow. In these regions where the flow is termed "geostrophic", the fluid velocities are nearly zero because the force results in no driving forces to move the fluid. Thus, if there is a global flow occurring in the system, the flow must occur in a region where viscosity can upset the geostrophic force balance to allow a fluid velocity. In many systems, viscosity is important only near the walls of the rotating container and, as a result, the bulk of the flow occurs only in thin layers near the wall. The layer where viscosity is important is called the Ekman layer when the wall surface normal vector is approximately parallel to the axis of rotation, and the Stewartson layer when the wall surface normal vector is nearly perpendicular to the axis of rotation.

A non-dimensional parameter that can be used to measure the importance of these boundary flows is the Ekman number given by

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$$\epsilon_k = \upsilon/\omega L^2$$

where υ is the kinematic viscosity of the fluid medium, ω is the rotational angular velocity, and L is a system characteristic length measured along the rotation axis. The Ekman number is a ratio of the viscous force to the Coriolis force in a rotating system. In systems rotating at high speed, ϵ_k, is typically very small, suggesting that geostrophic flow dominates the character of the flow. Using the viscosity of blood plasma and the approximate dimensions of a device suitable for separating platelets, the Ekman number is tabulated below for several rotation speeds.

TABLE I

Speed (rpm)	Ekman Number (ϵ_k)
5,000	1.71×10^{-7}
10,000	8.56×10^{-8}
15,000	5.70×10^{-8}
20,000	4.28×10^{-8}

It is evident that geostrophic flow will dominate in a typical centrifugal separator used heretofore with blood because the Ekman number is so small. Consequently, all significant fluid flow will occur in a region very close to the walls of the processing volume which goes to the heart of the reason for keeping the blood film "thin" in the instant invention. Incidentally, this problem plagues all

prior continuous centrifugal separators attempting to decant formed layers during rotation in a bulk or batch separator. Estimates of the thickness of the boundary layers where the flow actually occurs can be made based upon the Ekman number and the length scale. The thickness of the Ekman layer (on walls perpendicular to a vertical axis of rotation, i.e., horizontal surfaces) is estimated by:

$$t_{\epsilon k} = (\epsilon k)^{0.5} L$$

The thickness of the more important Stewartson layer (on walls parallel or at some small angle to a vertical axis of rotation, i.e., vertical or nearly vertical walls) is estimated by:

$$t_{st} = (\epsilon k)^{0.25} L$$

Using these formulas, the estimated thickness of the layers are indicated in Table II below:

TABLE II

speed (rpm)	$t_{\epsilon k}$ (horizontal)	t_{st} (vertical)
5,000	0.0019 inch	0.096 inch
10,000	0.0014 inch	0.081 inch
15,000	0.0011 inch	0.073 inch
20,000	0.0010 inch	0.068 inch

Clearly the blood film perpendicular to the rotation axis, that is, blood flow along horizontal surfaces in a vertically oriented device, are subject to instabilities and geostrophic flow. More important, however, is the fact that the operative

separation chamber, namely, the "thin" blood film flowing parallel to the vertically oriented rotation axis is within the Stewartson boundary layer thickness provided the blood film is limited to those thicknesses listed in Table II under t_{st}. These values define maximum claimed blood film thickness, at least for the entering whole blood.

As the blood becomes more concentrated and viscosity increases toward the blood exit, dramatically in some cases, one may wish to permit a thickening of the blood film by as much as 20% to 30%, relative to the entrance value. It is noted that film thickness varies only as the 1/4th root of viscosity.

For most applications a blood film thickness of 0.060 inch at the whole blood entrance is adequate for the purpose of limiting axial pressure gradients, even for flows on the order of 1 to 2 liters/min.

Provided that the blood film thickness for the entire volume, where layering and separation is intended to occur, is within the Stewartson layer, as defined herein, no geostrophic region with zero flow velocity will exist. Consequently, undesirable secondary flows are very unlikely. In short, the radial thickness of the processing chamber is so small that the entire region can be thought of as a boundary flow.

As a check on the potential for instabilities due to the forced convective flow radially inward toward the porous flow distributor, it is appropriate to examine the influence of inertial effects in rotating systems. This can be estimated by computing the Rossby number given by:

$$R_o = \upsilon / \omega L$$

where υ is a characteristic velocity in the plane perpendicular to the axis of rotation. Using the estimated convective velocity of 0.0167 cm/sec, the Rossby number was calculated for radial plasma flow in whole blood as shown in Table III below:

TABLE III

speed (rpm)	R_o
5,000	6.4×10^{-7}
10,000	3.2×10^{-7}
15,000	2.1×10^{-7}
20,000	1.6×10^{-7}

Even at 20 times the convective velocity, as may obtain in surgical cell salvage and concentration, and as is evident in Table III, the Rossby number is very small indicating that inertial effects are much smaller than Coriolis effects in this flow. Hence, the convective velocity does not contribute instabilities even approaching those which limit the thickness of the Stewartson layer. Other instabilities which might give rise to inertial waves

could occur at the entrance to the processing chamber but are quickly damped due to supporting vanes which separate walls defining entry to the blood film, and to the stabilizing influence of the initial impregnable zone which quickly establishes the Stewartson viscous boundary flow.

Finally, it is important to consider the influence of rotation on the settling of the particles in question. This will be done for platelets and red blood corpuscles.

The first issue is the particle Taylor number, T_ϱ. This parameter is a measure of the ratio of the size of the particle compared to the thickness of the Ekman layer, or, alternatively, the ratio between the Stokes drag force on the particle and the Coriolis force. The particle Taylor number is given by:

$$T_\varrho = 0.2 \frac{a^2 \omega}{\upsilon}$$

where a is the particle radius. The particle Taylor numbers for platelets and red corpuscles are listed below in Table IV.

TABLE IV

speed (rpm)	t_ϱ (platelets)	t_ϱ (RBC)
5,000	1.09×10^{-4}	7.08×10^{-4}
10,000	2.18×10^{-4}	1.41×10^{-3}
15,000	3.27×10^{-4}	2.12×10^{-3}
20,000	4.36×10^{-4}	2.83×10^{-3}

If the particle Taylor number is large, which is not the case here, rotational effects can strongly influence the Stokes drag on the particle. This would have introduced error in the calculation of settling rates presented in FIG. 5(c), which can now be safely relied upon. In the case of red blood corpuscles, the Stokes drag is strongly dependent upon particle concentration, such as hematocrits typical of whole blood. However, it will be seen in specific examples to follow that red corpuscles sediment very quickly leaving only platelet rich plasma for which particle concentration effects on the Stokes drag is minimal due to very low concentration of platelets on a volume percentage basis.

A second non-dimensional parameter related to the settling of a particle is the time ratio λ. The time ratio is the ratio of separation time for a particle to the spin-up time for that particle. The spin-up time is the time for the particle to reach the system rotational speed after it enters the rotating system. The time ratio is given by:

$$\lambda = \epsilon_k^{0.5}/\epsilon T_\varrho \ (L/r)$$

ϵ is the density ratio defined by:

$$\epsilon = (\varrho_d - \varrho_c)/\varrho_c$$

where ϱ_c is the density of the continuous phase, in this case, plasma, and ϱ_d is the density of the dispersed phase, namely, platelets or red blood

corpuscles. Table V below lists the time ratios for these particles:

TABLE V

speed (rpm)	λ (platelets)	λ (RBC)
5,000	13.0	1.20
10,000	4.6	0.43
15,000	2.5	0.22
20,000	1.6	0.15

This indicates that the separation of either red blood corpuscles or platelets is a relatively fast process. In fact, it may happen so quickly that the cells are not up to the rotational speed of the device (for $\lambda << 1.0$). This would be a problem for red corpuscles at very high speeds. Potentially, red blood corpuscles could sediment to the outer wall before they have reached approximately the same rotational speed as the wall. This could tend to cause high shear on the red blood corpuscles with the possibility of hemolysis which must be avoided. Therefore, conduits and vanes at the blood entrance to the device serve not only to space and support the walls defining the blood film but are indeed crucial in the design to force, especially the red blood corpuscles to spin-up to match device rotational speeds. Supporting vanes are both shaped and angled in such a manner as to accomplish the imparting of system rotational speed to the red blood corpuscles

with a minimum of trauma, i.e., shearing of the red blood corpuscles among the spin-up surfaces. As seen in Table V, the time ratio for platelets is about 10 times that for red blood corpuscles and, consequently, red blood corpuscles sediment about 10 times faster than platelets as was seen in the several examples previously presented.

In summary:

1) The appropriate blood film thickness has been computed and must be limited by viscous boundary flow or the Stewartson layer.

2) Inertial instabilities are small, particularly in connection with the forced convection which decants the supernatant, i.e., the Rossby number is very small.

3) Turbulence is not an issue because the Reynolds number is less than 10 in this system.

4) The particle Taylor number indicates that, apart from concentration effects which influence only red blood corpuscles, the Stokes model for the drag on a particle is valid.

5) The time ratio is such that the settling of particles can be relatively fast in comparison with their spin-up time so that entry vanes are essential to force particle spin-up and should be designed with a minimum of turbulence and shearing of the particles.

In practicing the present invention, the details

may be replaced with other technically equivalent elements; furthermore, the materials used, and the shapes and dimensions, may be any selected ones to meet individual requirements without departing from the scope of the present invention.

WE CLAIM:

1. Apparatus for fractionating a liquid mixture substantially into first and second liquid fractions whose components have settling velocities which are under identical conditions of centrifugal force, higher and lower, respectively, than a selected value, said apparatus comprising:

a rotary assembly for rotation about a central axis and including inner and outer shells defining therebetween an axially extending tubular gap and an inner region radially inwardly of said inner shell;

said inner shell including a flow resistive porous structure to provide for permeation therethrough of said second fraction at a radially inward entrance velocity below said selected value and to restrict flow of the residual of said fluid mixture therethrough;

an inlet for introducing said liquid mixture into said gap at one axial end thereof;

a frame for mounting said frame for rotation about said axis;

a drive for rotating the assembly at a predetermined fractioning speed effective to impart centrifugal force to said liquid mixture within said sufficient gap to cause said second fraction to flow radially inwardly through said porous structure and to prevent said first liquid fraction from permeating said porous structure; and

an outlet for drawing said first fraction from said inner region.

2. The apparatus of Claim 1 that includes:

a residual outlet at one axial end of said gap for withdrawing said second fraction therefrom.

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3. The apparatus of Claim 1 that includes:

a pump for controlling pressure in said gap to control the pressure differential across said first porous structure.

4. The apparatus of Claim 3 wherein:

said pump is operative to maintain the pressure of said liquid in said gap at a predetermined pressure and wherein said apparatus includes:

a tank enclosing said assembly and cooperating therewith to form a pressure chamber;

encapsulating fluid in said pressure chamber; and

means for maintaining the pressure of said encapsulating fluid in said pressure chamber at a selected pressure higher than said predetermined pressure.

5. The apparatus of Claim 4 for use in fractioning a said mixture including blood components and wherein:

said encapsulating fluid is sterile.

6. The apparatus of Claim 1, wherein:

said inner shell includes an impervious cap between said inlet and said inner porous structure, the outside surface of said cap being tapered gradually radially inwardly and away from said inlet to gradually increase the annular flow area in said gap.

7. The apparatus of Claim 1 for fractionating a liquid mixture of the type having a predetermined ratio of first to second fractions and which, during rotation of said assembly at said predetermined fractioning speed, builds up an inner

layer on the outer surface of said porous structure leaving an outer layer including said first fraction and wherein:

said assembly is axially elongated; and

said inner shell adjacent said mixture inlet tapers radially inwardly and away from said inlet at an angle to reduce said outer surface thereof sufficiently so that as said drive rotates said assembly at said predetermined fractionating speed said inner and outer layers will flow axially at substantially the same axial velocity.

8. The apparatus of Claim 1 for fractionating a blood mixture and wherein:

said inner and outer shells are concentric to form said gap with a radial thickness of between at least 5 and 150 millimeters.

9. The apparatus of Claim 1 for treating a blood mixture including plasma and wherein:

said porous structure is constructed for, at said predetermined fractioning speed, permeation therethrough of said plasma.

10. The apparatus of Claim 1 for treating said second fraction with a selected fluid and wherein:

said porous structure is constructed for, at said predetermined fractioning speed, permeation therethrough of said selected fluid; and

said outer shell includes an inlet for introduction of said selected fluid for flowing through said second fraction.

11. The apparatus of Claim 1 for fractionating a liquid mixture of blood with plasma

defining said second fraction and red blood cells defining said first fraction and wherein:

said porous structure is constructed for, at said predetermined fractioning speed, permeation therethrough of said plasma.

12. The apparatus of Claim 11 for drawing blood from a patient and which further includes:

an inlet conduit for connecting said inlet to a patient's blood circulatory system for drawing said blood therefrom.

13. The apparatus of Claim 11 wherein:

said rotary assembly includes a residual outlet for withdrawing said red blood cells as said second fraction from said gap; and

a blood outlet conduit connected to said residual outlet for withdrawing said red blood cells therefrom for infusion back into said patient's blood circulatory system.

14. The apparatus of Claim 1 for fractionating a liquid mixture, including blood components susceptible to forming packed components which are reliquefiable by a selected fluid and that includes:

rotary seal means configured to allow for some fluid seepage of said selected fluid;

an encapsulating housing around said outer shell to be pressurized by said selected fluid to a pressure sufficient to cause said selected fluid to seep through said seals into said gap to reliquefy said packed components which might form in said assembly.

15. The apparatus of Claim 1 wherein:

said porous structure is axially elongated and said apparatus includes, and is configured to, and has a thickness and pore diameter effective to, when said fluid mixture fully covers the surface thereof and a predetermined pressure drop is formed radially across said porous structure, establish a predetermined rate of permeation; and

a pump coupled with said fluid mixture inlet for maintaining said predetermined pressure drop across said porous structure.

16. The apparatus of Claim 1 that includes:

a tank enclosing said assembly and cooperating therewith to form a pressure chamber;

bearings mounting said assembly from said tank;

cooling fluid in said pressure chamber; and

circulation means for circulating said cooling fluid in heat exchange relationship with said bearings.

17. The apparatus of Claim 1, wherein:

said rotary assembly is axially elongated, said inlet disposed at one end of said gap and that includes:

a residual outlet at the opposite end of said gap; and

inlet and outlet pumps connected with the respective said inlet and residual outlet to control the rate of fluid flow through said gap.

18. The apparatus of claim 1 for fractionating said fluid mixture of the type having a predetermined ratio of said first to second fractions

and predetermined viscosity characteristics and wherein:

said gap is axially elongated, said inlet disposed at one end thereof and that includes a residual outlet disposed at the opposite end thereof;

said inner shell and porous structure is so configured that, at said predetermined fractionating speed, said assembly is operative to form an outer layer including said first fraction in said gap surrounding an inner layer including said second fraction on the outer surface of said inner shell; and

a pump connected with said inlet for controlling flow of said mixture at a predetermined steady flow rate axially through said gap to cause said inner and outer layers to flow axially at substantially the same velocity.

19. The apparatus of Claim 1 for treating said second fraction with a treatment solution and wherein:

said assembly is axially elongated with said inlet disposed at one end of said gap and that includes:

an outlet disposed at the opposite end of said gap;

a porous treatment structure in said inner shell spaced axially toward said outlet from said inner porous structure for flow of said first fraction axially in said gap past the outer surface thereof; and

a treatment solution tank surrounding said outer shell and formed with a treatment port for introducing said treatment solution into said gap adjacent said porous treatment structure whereby said treatment solution may be introduced to said tank to

flow radially inwardly over said second fraction of said liquid mixture to pass radially inwardly through said porous treatment structure.

20. The apparatus of Claim 19 that includes:

valve means for controlling flow of said treatment solution to said wash port.

21. Apparatus of Claim 1 for use with an encapsulating fluid compatible with said fluid mixture and that includes:

a pump for maintaining the pressure in said gap at a predetermined pressure;

seals for sealing said assembly against uncontrolled escape of said fluid mixture and constructed to, upon application of said encapsulating fluid at a selected pressure, provide for seepage inwardly therethrough to flow said fluid mixture away from said seals;

an encapsulating tank surrounding said assembly for receipt of said encapsulating fluid; and

a pump connected with said tank for applying said encapsulating fluid at said selected pressure thereto.

22. The apparatus of Claim 1 that includes:

means for pressurizing the liquid mixture within said gap during such rotation of said rotary assembly to positively compel flow of said second fraction radially inwardly through said porous structure into said inner region.

23. The apparatus of Claim 1 for fractionating a liquid mixture containing red blood cells and plasma and wherein:

said porous structure at said fractionating speed provides flow resistance to radial inward flow of said red blood cells while allowing said plasma to flow freely therethrough.

24. A method for fractionating a liquid mixture into first and second liquid fractions and including the following steps:

selecting an assembly of the type including inner and outer shells constructed for equal angular velocity rotation about a common central axis, said inner shell including a porous structure for at least a part of its extent and a space interior of said porous structure;

introducing said liquid mixture into said gap between facing surfaces of said inner and outer shells;

compelling flow of said second fraction through said porous structure; and

rotating said shells at a speed effective to prevent the first liquid fraction from inclusion in said flow causing said first and second fractions to form on opposite sides of said porous structure.

25. The method of claim 24 that includes:

distributing the flow of said mixture substantially uniformly over the outer surface of said porous structure.

26. The method of claim 25 that includes:

distributing said flow over said porous structure to cause the radial inward velocity of entry of said flow into said porous structure to be substantially uniform over its outer surface.

27. A method for fractionating a liquid mixture substantially into first and second liquid fractions whose components have settling velocities which are, under identical conditions of centrifugal force, higher and lower, respectively, than a selected value, which includes the steps of:

selecting an assembly of the type having inner and outer shells defining therebetween an axially extending tubular gap, and a radially inward inner region, the inner shell including an axially extending porous structure disposed radially outward of said inner region for permeation therethrough of said second fraction at a radially inward entrance velocity substantially equal to said selected value and to resist radial inward flow of the residual of said fluid mixture;

introducing said liquid mixture at a predetermined rate into said gap at one end thereof;

rotating said assembly at a predetermined fractioning speed effective to impart sufficient centrifugal force to said liquid mixture within said gap to apply a radially outward velocity to said first liquid fraction to resist permeation of said porous structure; and

pressurizing said liquid mixture within said gap during such rotation of said assembly to compel flow of said second liquid fraction radially inwardly through said porous structure into said inner region while retaining said first fraction in said gap.

28. The method of Claim 27 that includes:

rotating said assembly at a sufficient speed and pressurizing said gap with sufficient pressure to maintain a portion of said fluid mixture, including said first fraction, flowing along the exterior

surface of said inner shell in a substantially uniform flow pattern.

29. The method of Claim 28 that includes:

rotating said assembly at a sufficient speed and maintaining said pressure in said gap at a sufficient level to maintain said residual of said fluid mixture flowing along said inner shell in a sufficiently thin layer to maintain laminar axial flow throughout the depth thereof.

30. Fractionating apparatus for treating a selected fraction suspended in a suspension medium of a liquid mixture with a selected treatment solution, said treatment solution and selected fraction formed by respective components having settling velocities which are, under identical conditions of centrifugal force, higher and lower, respectively, than a selected value, said apparatus comprising:

an axially elongated rotary assembly adapted for rotation about a central axis, said assembly having inner and outer shells defining therebetween an axially extending tubular gap and an inner region disposed radially inwardly of said inner shell;

said inner shell including a flow resistant porous structure for at least a part of its axial extension to provide for permeation therethrough of said treatment solution and to present resistance to radially inward flow of said suspension fluid;

a liquid mixture inlet to one end of said gap;

a treatment solution inlet for introducing said treatment solution into the radially outward portion of said gap;

a frame rotatably supporting said rotary assembly for rotation about said axis;

a drive coupled with said rotary assembly to rotate said assembly at a predetermined fraction speed sufficient to, when said mixture is introduced to said gap through said mixture inlet and said treatment solution is introduced through said solution inlet, apply a settling velocity to said predetermined fraction sufficient to hold it suspended within said gap while said treatment solution is introduced through said treatment solution inlet causing it to flow radially inwardly through said suspension fluid and second fraction.

31. The apparatus of Claim 30 for use in washing a mixture of the type including red blood cells with a saline wash solution and that includes:

a saline tank encapsulating said rotary assembly and formed with said treatment solution inlet port; and

a treatment pump to pump said saline treatment solution into said tank and through said treatment solution inlet port.

32. The apparatus of Claim 30 wherein:

said inner shell is formed adjacent said fluid mixture inlet with a frusto-conical shape to slope gradually radially inwardly and away from said fluid mixture inlet to gradually increase the radial thickness of said gap.

33. The apparatus of Claim 30 that includes:

bearings interposed between said housing and assembly; and

circulation means connected with said treatment solution inlet for flowing said treatment

solution in heat exchange relationship with said bearings.

34. Fractionating apparatus for fractionating a first fraction suspended in a suspension medium of a liquid mixture including a second fraction, said fractions formed by respective components having settling velocities which are, under identical conditions of centrifugal force, higher and lower, respectively, than a selected range of settling velocities, said apparatus comprising:

an axially elongated rotary assembly adapted for rotation about a central axis, said assembly having inner and outer shells defining therebetween an axially extending tubular gap and an inner region disposed radially inwardly of said inner shell;

said inner shell including a flow resistant porous structure for at least a part of its axial extension to provide for permeation therethrough of said first fraction and to present resistance to radially inward flow of the remainder of said fluid mixture;

a liquid mixture inlet to one end of said gap;

a frame rotatably supporting said rotary assembly for rotation about said axis; and

a drive coupled with said rotary assembly to rotate said assembly at a predetermined fractioning speed sufficient to, when said mixture is introduced to said gap through said mixture inlet, apply settling velocities in said selected range of settling velocities to hold said second fraction in said gap while flowing said first fraction through said flow resistant porous structure into said inner region.

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AMENDED CLAIMS

[received by the International Bureau on 17 February 1994 (17.02.94);
original claims 1,2,15,18,24,27-30,32 and 34 amended;
other claims unchanged (13 pages)]

1. Apparatus for fractionating a liquid mixture substantially into first and second liquid fractions whose components have settling velocities which are under identical conditions of centrifugal force, higher and lower, respectively, than a selected value, said apparatus comprising:

a rotary assembly for rotation about a central axis and including concentric inner and outer shells having a common axis defining therebetween an axially extending tubular gap and an inner region radially inwardly of said inner shell;

said inner shell including a flow resistive porous structure to provide for permeation therethrough of said second fraction at a radially inward entrance velocity substantially uniform over the outer surface of said inner porous structure and below said selected value and to restrict flow of the residual of said fluid mixture therethrough;

an inlet for introducing said liquid mixture into said gap at one axial end thereof;

a frame for mounting said frame for rotation about said axis;

a drive for rotating the assembly at a predetermined fractioning speed effective to impart centrifugal force to said liquid mixture within said sufficient gap to cause said second fraction to flow radially inwardly through said porous structure and to prevent said first liquid fraction from permeating said porous structure; and

an outlet for drawing said second fraction from said inner region.

2. The apparatus of Claim 1 that includes:

a residual outlet at one axial end of said gap for withdrawing a residual liquid fraction.

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3. The apparatus of Claim 1 that includes:

a pump for controlling pressure in said gap to control the pressure differential across said first porous structure.

4. The apparatus of Claim 3 wherein:

said pump is operative to maintain the pressure of said liquid in said gap at a predetermined pressure and wherein said apparatus includes:

a tank enclosing said assembly and cooperating therewith to form a pressure chamber;

encapsulating fluid in said pressure chamber; and

means for maintaining the pressure of said encapsulating fluid in said pressure chamber at a selected pressure higher than said predetermined pressure.

5. The apparatus of Claim 4 for use in fractioning a said mixture including blood components and wherein:

said encapsulating fluid is sterile.

6. The apparatus of Claim 1, wherein:

said inner shell includes an impervious cap between said inlet and said inner porous structure, the outside surface of said cap being tapered gradually radially inwardly and away from said inlet to gradually increase the annular flow area in said gap.

7. The apparatus of Claim 1 for fractionating a liquid mixture of the type having a predetermined ratio of first to second fractions and which, during rotation of said assembly at said

predetermined fractioning speed, builds up an inner layer on the outer surface of said porous structure leaving an outer layer including said first fraction and wherein:

said assembly is axially elongated; and

said inner shell adjacent said mixture inlet tapers radially inwardly and away from said inlet at an angle to reduce said outer surface thereof sufficiently so that as said drive rotates said assembly at said predetermined fractionating speed said inner and outer layers will flow axially at substantially the same axial velocity.

8. The apparatus of Claim 1 for fractionating a blood mixture and wherein:

said inner and outer shells are concentric to form said gap with a radial thickness of between at least 5 and 150 millimeters.

9. The apparatus of Claim 1 for treating a blood mixture including plasma and wherein:

said porous structure is constructed for, at said predetermined fractioning speed, permeation therethrough of said plasma.

10. The apparatus of Claim 1 for treating said second fraction with a selected fluid and wherein:

said porous structure is constructed for, at said predetermined fractioning speed, permeation therethrough of said selected fluid; and

said outer shell includes an inlet for introduction of said selected fluid for flowing through said second fraction.

11. The apparatus of Claim 1 for fractionating a liquid mixture of blood with plasma defining said second fraction and red blood cells defining said first fraction and wherein:

said porous structure is constructed for, at said predetermined fractioning speed, permeation therethrough of said plasma.

12. The apparatus of Claim 11 for drawing blood from a patient and which further includes:

an inlet conduit for connecting said inlet to a patient's blood circulatory system for drawing said blood therefrom.

13. The apparatus of Claim 11 wherein:

said rotary assembly includes a residual outlet for withdrawing said red blood cells as said second fraction from said gap; and

a blood outlet conduit connected to said residual outlet for withdrawing said red blood cells therefrom for infusion back into said patient's blood circulatory system.

14. The apparatus of Claim 1 for fractionating a liquid mixture, including blood components susceptible to forming packed components which are reliquefiable by a selected fluid and that includes:

rotary seal means configured to allow for some fluid seepage of said selected fluid;

an encapsulating housing around said outer shell to be pressurized by said selected fluid to a pressure sufficient to cause said selected fluid to seep through said seals into said gap to reliquefy

said packed components which might form in said assembly.

15. The apparatus of Claim 1 wherein:

said porous structure is axially elongated and said apparatus includes, and is configured to, and has a thickness and pore diameter effective to, when said liquid mixture fully covers the surface thereof and a predetermined pressure drop is formed radially across said porous structure, establish a predetermined rate of permeation; and

a pump coupled with said fluid mixture inlet for maintaining said predetermined pressure drop across said porous structure.

16. The apparatus of Claim 1 that includes:

a tank enclosing said assembly and cooperating therewith to form a pressure chamber;

bearings mounting said assembly from said tank;

cooling fluid in said pressure chamber; and

circulation means for circulating said cooling fluid in heat exchange relationship with said bearings.

17. The apparatus of Claim 1, wherein:

said rotary assembly is axially elongated, said inlet disposed at one end of said gap and that includes:

a residual outlet at the opposite end of said gap; and

inlet and outlet pumps connected with the respective said inlet and residual outlet to control the rate of fluid flow through said gap.

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18. The apparatus of claim 1 for fractionating said liquid mixture of the type having a predetermined ratio of said first to second fractions and predetermined viscosity characteristics and wherein:

said gap is axially elongated, said inlet disposed at one end thereof and that includes a residual outlet disposed at the opposite end thereof;

said inner shell and porous structure is so configured that, at said predetermined fractionating speed, said assembly is operative to form an outer layer including said first fraction in said gap surrounding an inner layer including said second fraction on the outer surface of said inner shell; and

a pump connected with said inlet for controlling flow of said mixture at a predetermined steady flow rate axially through said gap to cause said inner and outer layers to flow axially at substantially the same velocity.

19. The apparatus of Claim 1 for treating said second fraction with a treatment solution and wherein:

said assembly is axially elongated with said inlet disposed at one end of said gap and that includes:

an outlet disposed at the opposite end of said gap;

a porous treatment structure in said inner shell spaced axially toward said outlet from said inner porous structure for flow of said first fraction axially in said gap past the outer surface thereof; and

a treatment solution tank surrounding said outer shell and formed with a treatment port for

introducing said treatment solution into said gap adjacent said porous treatment structure whereby said treatment solution may be introduced to said tank to flow radially inwardly over said second fraction of said liquid mixture to pass radially inwardly through said porous treatment structure.

20. The apparatus of Claim 19 that includes:

valve means for controlling flow of said treatment solution to said wash port.

21. Apparatus of Claim 1 for use with an encapsulating fluid compatible with said fluid mixture and that includes:

a pump for maintaining the pressure in said gap at a predetermined pressure;

seals for sealing said assembly against uncontrolled escape of said fluid mixture and constructed to, upon application of said encapsulating fluid at a selected pressure, provide for seepage inwardly therethrough to flow said fluid mixture away from said seals;

an encapsulating tank surrounding said assembly for receipt of said encapsulating fluid; and

a pump connected with said tank for applying said encapsulating fluid at said selected pressure thereto.

22. The apparatus of Claim 1 that includes:

means for pressurizing the liquid mixture within said gap during such rotation of said rotary assembly to positively compel flow of said second fraction radially inwardly through said porous structure into said inner region.

23. The apparatus of Claim 1 for fractionating a liquid mixture containing red blood cells and plasma and wherein:

said porous structure at said fractionating speed provides flow resistance to radial inward flow of said red blood cells while allowing said plasma to flow freely therethrough.

24. A method for fractionating a liquid mixture into first and second liquid fractions and including the following steps:

selecting an assembly of the type including inner and outer shells constructed for equal angular velocity rotation about a common central axis, said inner shell including a porous structure for at least a part of its axial extent to resist radial inward flow of said liquid mixture substantially uniformly over the outer surface of said porous structure;

introducing said liquid mixture into said gap between facing surfaces of said inner and outer shells;

compelling flow of said second fraction through said porous structure; and

rotating said shells at a speed effective to prevent the first liquid fraction from inclusion in said flow causing said first and second fractions to form on opposite sides of said porous structure.

25. The method of claim 24 that includes:

distributing the flow of said mixture substantially uniformly over the outer surface of said porous structure.

26. The method of claim 25 that includes:

distributing said flow over said porous structure to cause the radial inward velocity of entry of said flow into said porous structure to be substantially uniform over its outer surface.

27. A method for fractionating a liquid mixture substantially into first and second liquid fractions whose components have settling velocities which are, under identical conditions of centrifugal force, higher and lower, respectively, than a selected value, which includes the steps of:

selecting an assembly of the type having inner and outer shells defining therebetween an axially extending tubular gap, and a radially inward inner region, the inner shell including an axially extending porous structure disposed radially outward of said inner region for permeation therethrough of said second fraction at a radially inward entrance velocity substantially uniform along said axial extension equal to said selected value;

introducing said liquid mixture at a predetermined rate into said gap at one end thereof;

rotating said assembly at a predetermined fractioning speed effective to impart sufficient centrifugal force to said liquid mixture within said gap to apply a radially outward velocity to said first liquid fraction to resist permeation through said porous structure; and

pressurizing said liquid mixture within said gap during such rotation of said assembly to compel flow of said second liquid fraction radially inwardly through said porous structure into said inner region while retaining said first fraction in said gap.

28. The method of Claim 27 that includes:

rotating said assembly at a sufficient speed and pressurizing said gap with sufficient pressure to maintain a portion of said liquid mixture, including said first fraction, flowing along the exterior surface of said inner shell in a substantially uniform flow pattern.

29. The method of Claim 28 that includes:

rotating said assembly at a sufficient speed and maintaining said pressure in said gap at a sufficient level to maintain said residual of said liquid mixture flowing along said inner shell in a sufficiently thin layer to maintain laminar axial flow throughout the depth thereof.

30. Fractionating apparatus for treating a selected fraction suspended in a suspension medium of a liquid mixture with a residual and a selected treatment solution, said treatment solution and selected fraction formed by respective components having settling velocities which are, under identical conditions of centrifugal force, higher and lower, respectively, than a selected value, said apparatus comprising:

an axially elongated rotary assembly adapted for rotation about a central axis, said assembly having inner and outer shells defining therebetween an axially extending tubular gap and an inner region disposed radially inwardly of said inner shell;

said inner shell including a flow resistant porous structure for at least a part of its axial extension to provide for permeation therethrough of said treatment solution and to present flow resistance to said residual of said liquid mixture substantially

uniformly along the outer surface of said porous structure;

a liquid mixture inlet to one end of said gap;

a treatment solution inlet for introducing said treatment solution into the radially outward portion of said gap;

a frame rotatably supporting said rotary assembly for rotation about said axis;

a drive coupled with said rotary assembly to rotate said assembly at a predetermined fraction speed sufficient to, when said mixture is introduced to said gap through said mixture inlet and said treatment solution is introduced through said solution inlet, apply a settling velocity to said predetermined fraction sufficient to hold it suspended within said gap while said treatment solution is introduced through said treatment solution inlet causing it to flow radially inwardly through said suspension liquid and second fraction.

31. The apparatus of Claim 30 for use in washing a mixture of the type including red blood cells with a saline wash solution and that includes:

a saline tank encapsulating said rotary assembly and formed with said treatment solution inlet port; and

a treatment pump to pump said saline treatment solution into said tank and through said treatment solution inlet port.

32. The apparatus of Claim 30 wherein:

said inner shell is formed adjacent said liquid mixture inlet with a frusto-conical shape to slope gradually radially inwardly and away from said

fluid mixture inlet to gradually increase the radial thickness of said gap.

33. The apparatus of Claim 30 that includes:

bearings interposed between said housing and assembly; and

circulation means connected with said treatment solution inlet for flowing said treatment solution in heat exchange relationship with said bearings.

34. Fractionating apparatus for fractionating a first fraction suspended in a suspension medium of a liquid mixture including a second fraction, said fractions formed by respective components having settling velocities which are, under identical conditions of centrifugal force, higher and lower, respectively, than a selected range of settling velocities, said apparatus comprising:

an axially elongated rotary assembly adapted for rotation about a central axis, said assembly having inner and outer shells defining therebetween an axially extending tubular gap and an inner region disposed radially inwardly of said inner shell;

said inner shell including a flow resistant porous structure for at least a part of its axial extension to provide for permeation therethrough of said first fraction and to present flow resistance to said residual of said liquid mixture substantially uniformly along the outer surface of said porous structure;

a liquid mixture inlet to one end of said gap;

a frame rotatably supporting said rotary assembly for rotation about said axis; and

a drive coupled with said rotary assembly to rotate said assembly at a predetermined fractioning speed sufficient to, when said mixture is introduced to said gap through said mixture inlet, apply settling velocities in said selected range of settling velocities to hold said second fraction in said gap while flowing said first fraction through said flow resistant porous structure into said inner region.

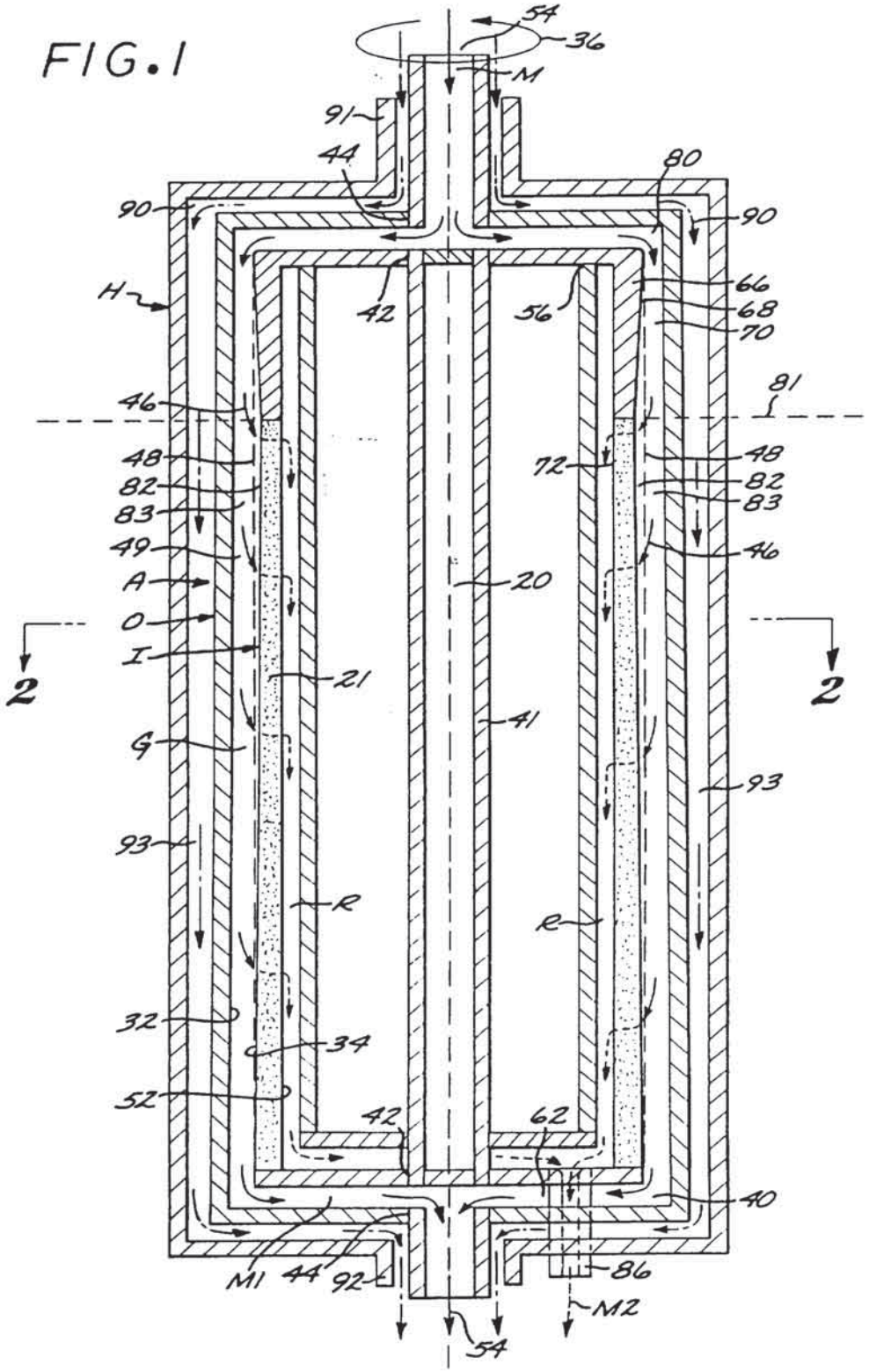
STATEMENT UNDER ARTICLE 19

Claims 1, 2, 15, 18, 24, 27, 28, 29, 30, 32 and 34 have been amended to more particularly claim the matter for which protection is sought and are being submitted in accordance with PCT Article 19.

The amended claims are fully supported by the description and do not go beyond the disclosure in the international application as filed. None of the references in the International Search Report, alone or in combination, suggest the present invention as now claimed.

In conclusion, the amended claims more specifically claim the present invention disclosed in the international application. The present invention as now specifically claimed is not suggested by the international search authority references, alone or in combination.

FIG. 1


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FIG. 1A

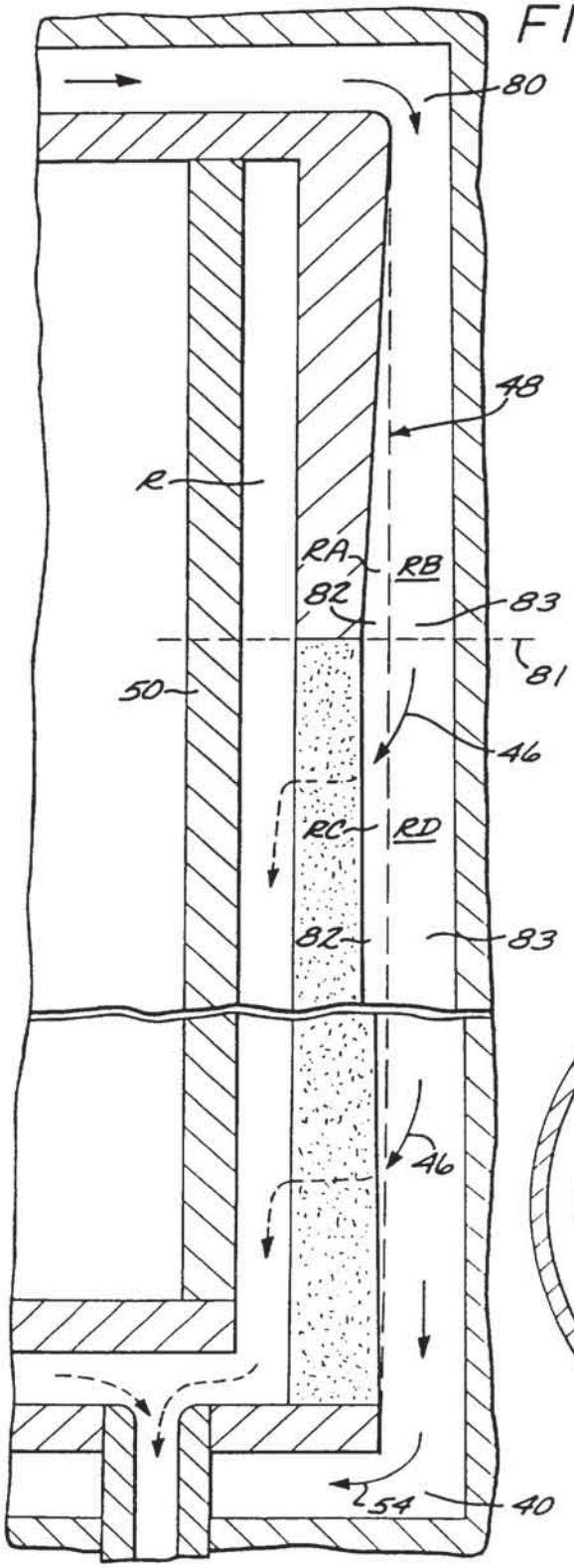


FIG. 2

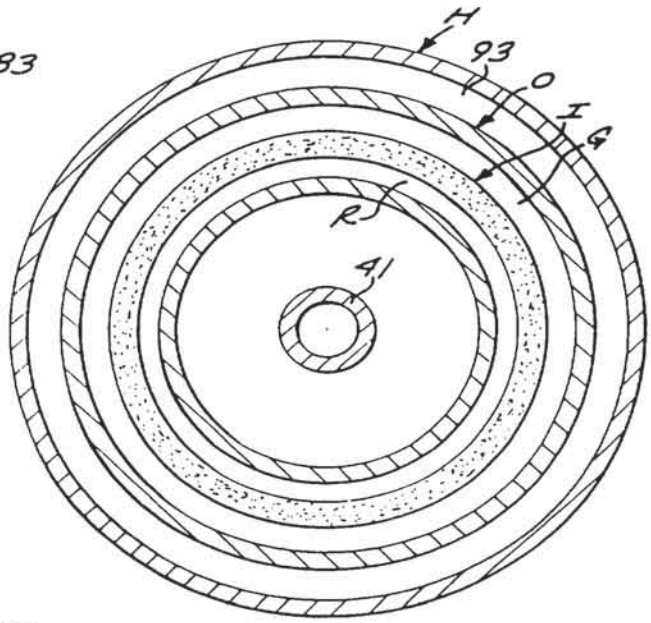


FIG. 3

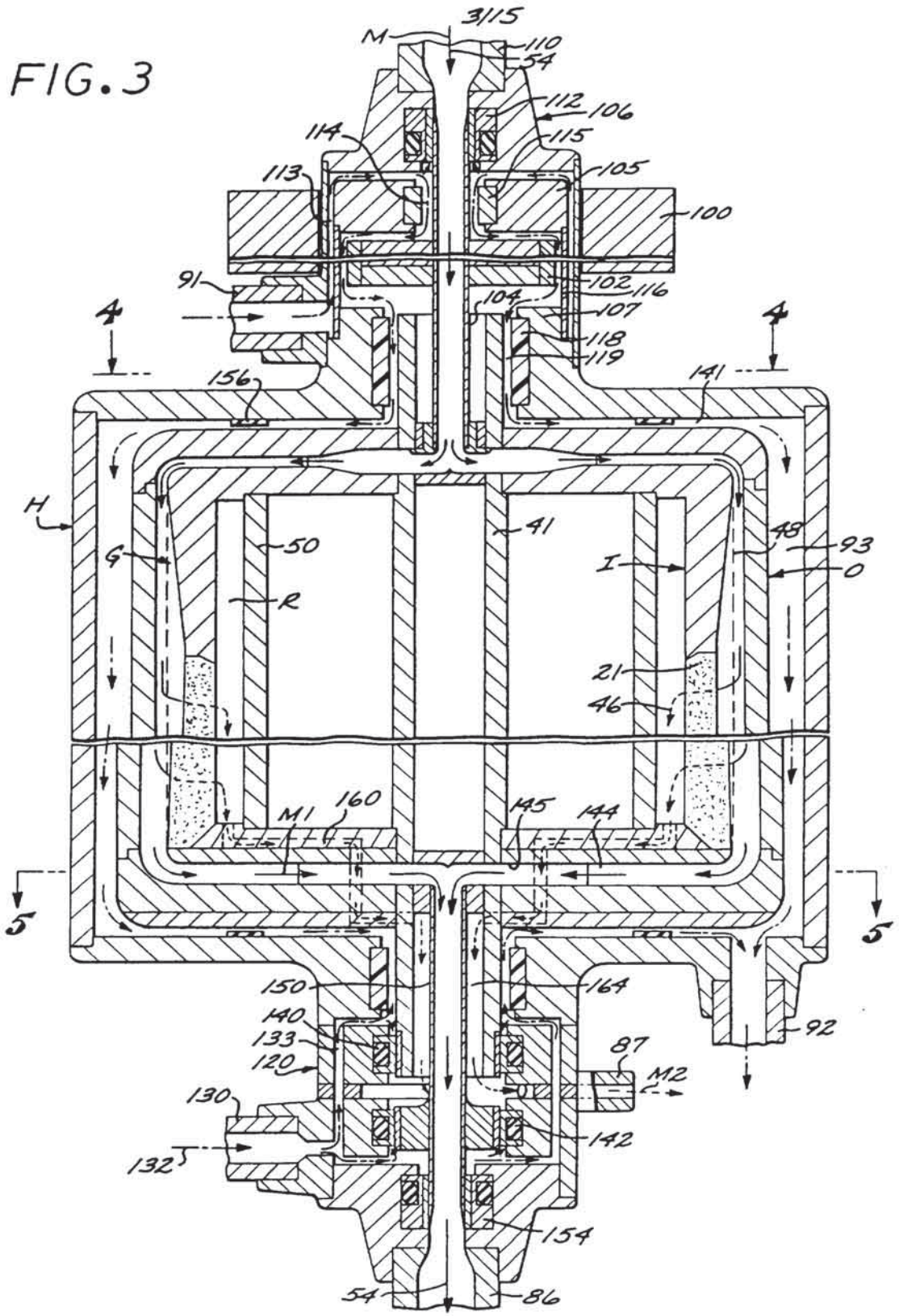

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FIG. 4

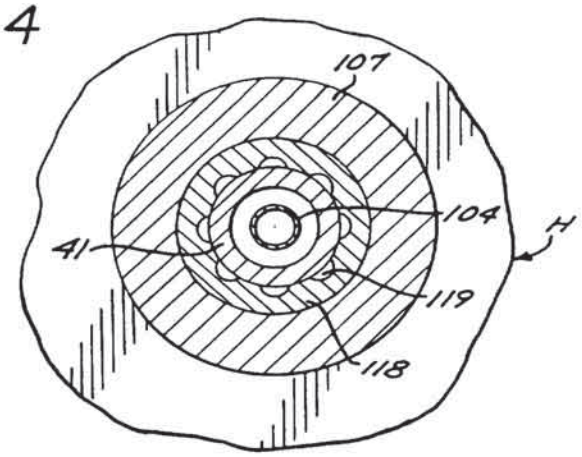


FIG. 5

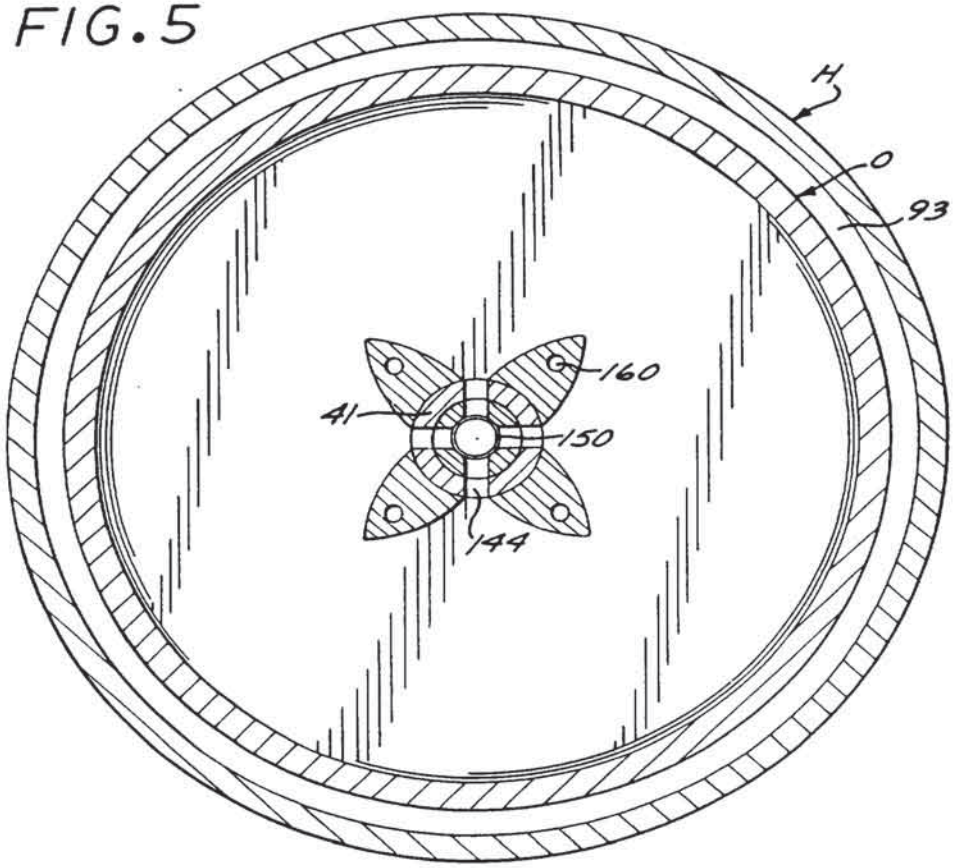


FIG. 6

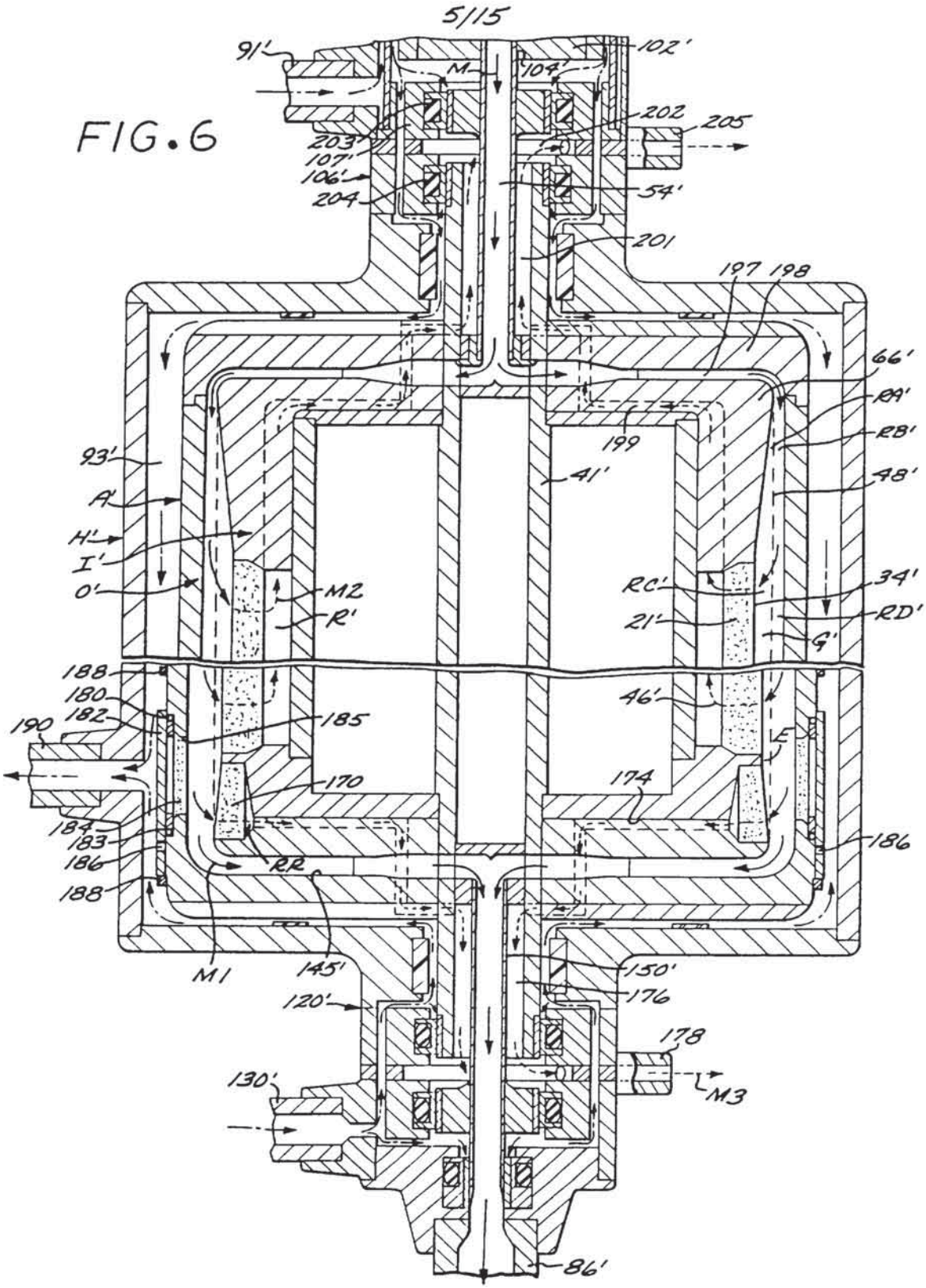

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170
174
184
183
186
188
RR
186
M1
145'
150'
176
120'
178
130'
M3
86'

FIG. 6A

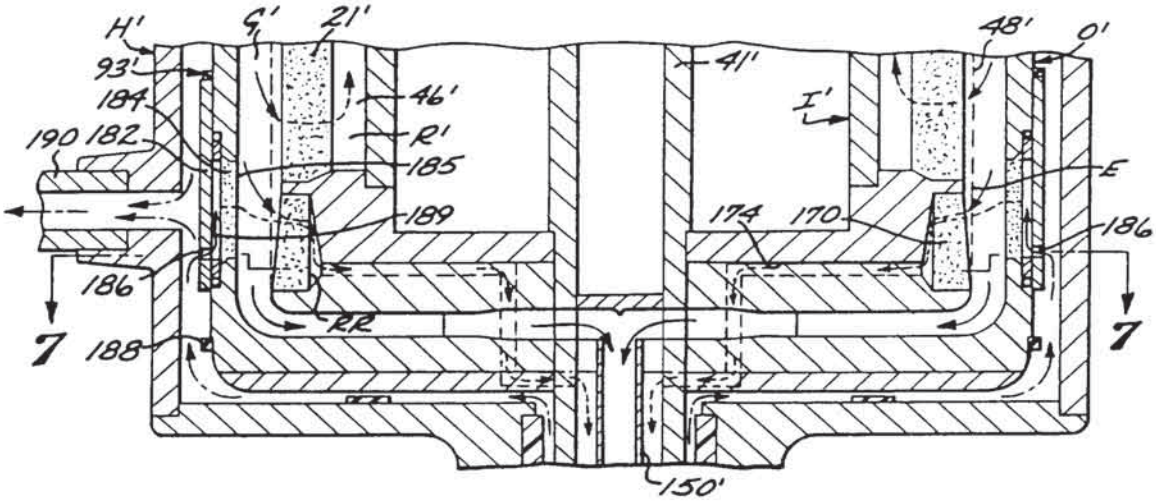

H'
G'
21'
93'
184
190
182
46'
R'
185
189
186
7
188
RR
41'
48'
O'
I'
E
174
170
186
7
150'

FIG. 7

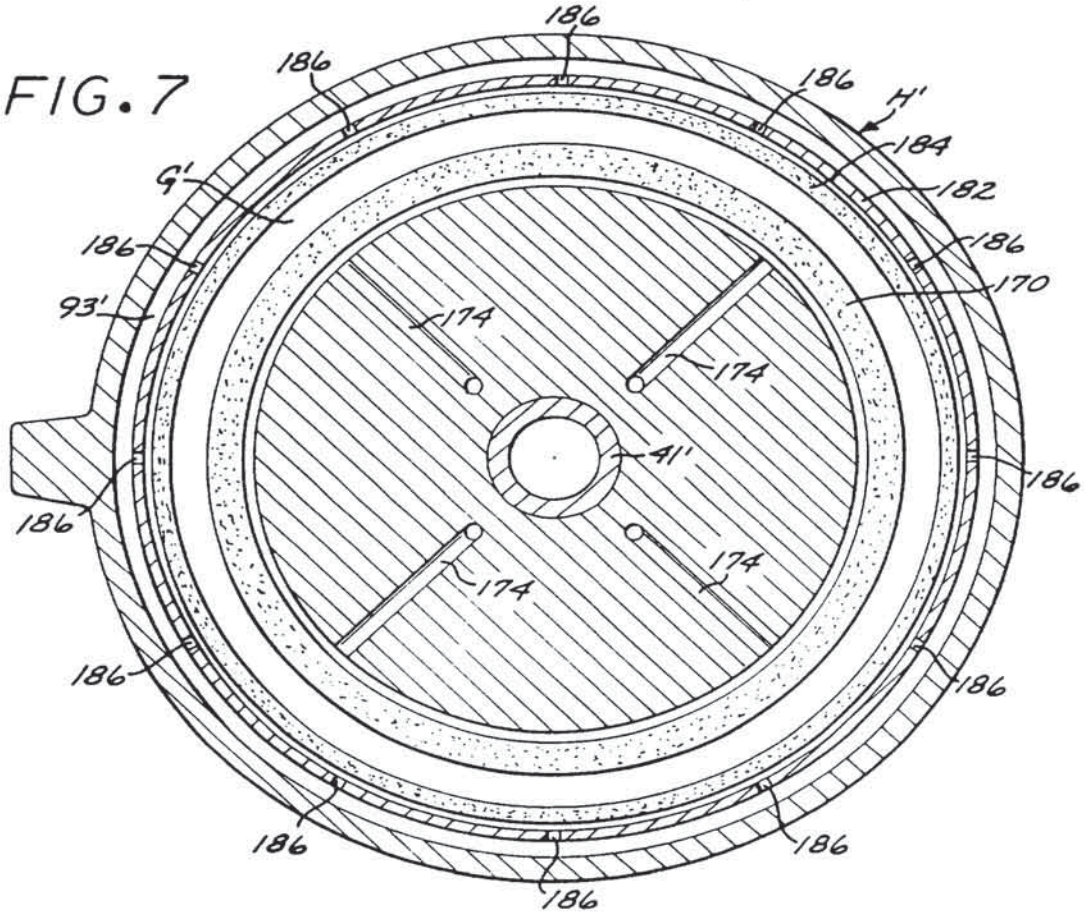

186
186
186
H'
184
182
G'
186
186
93'
170
174
174
41'
186
186
174
174
186
186
186
186
186

FIG. 8

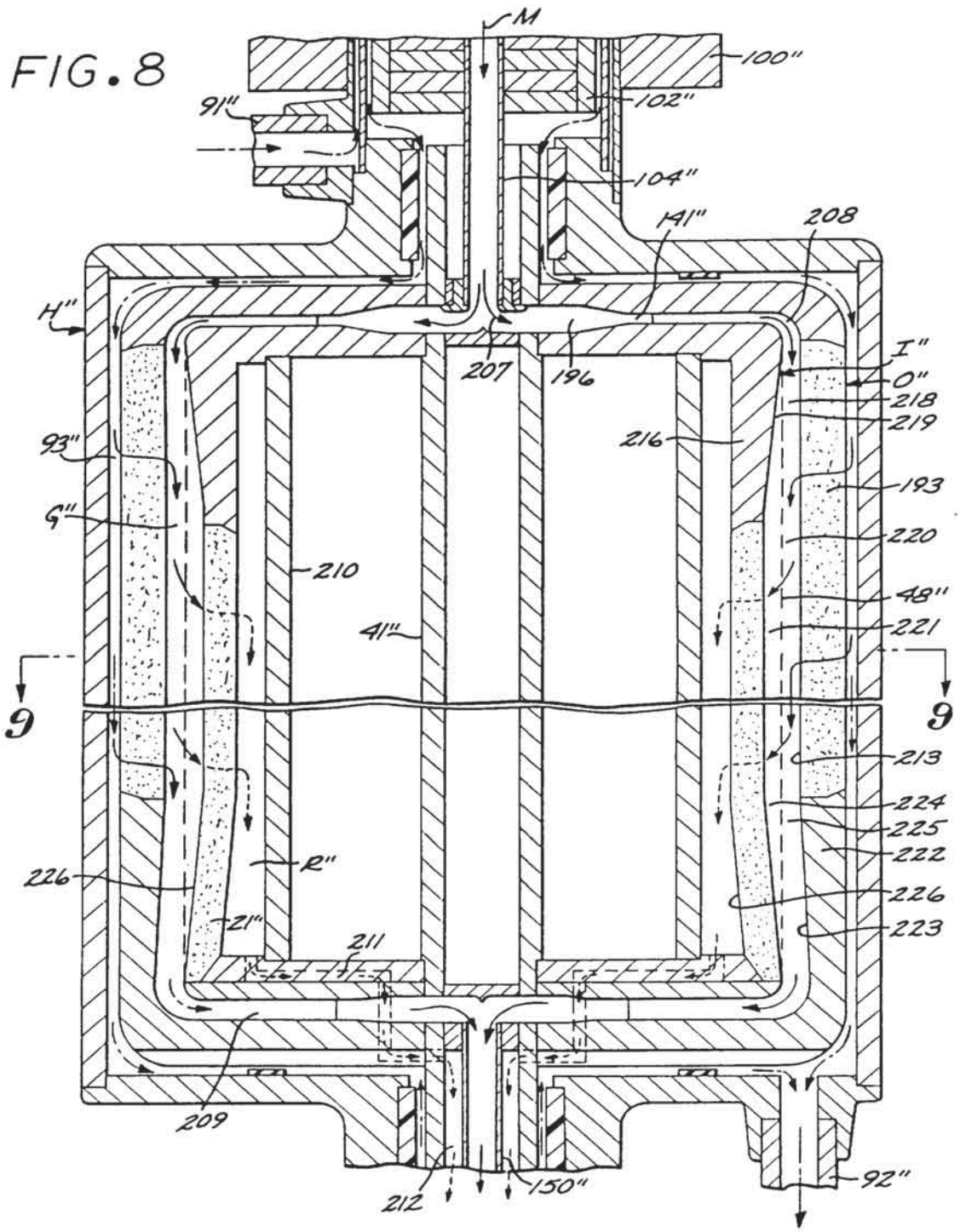

M
100"
102"
91"
104"
141"
208
H"
207
196
I"
O"
218
219
216
93"
193
G"
220
210
48"
41"
221
9
9
213
224
225
222
226
R"
226
21"
211
223
209
212
150"
92"

FIG.9

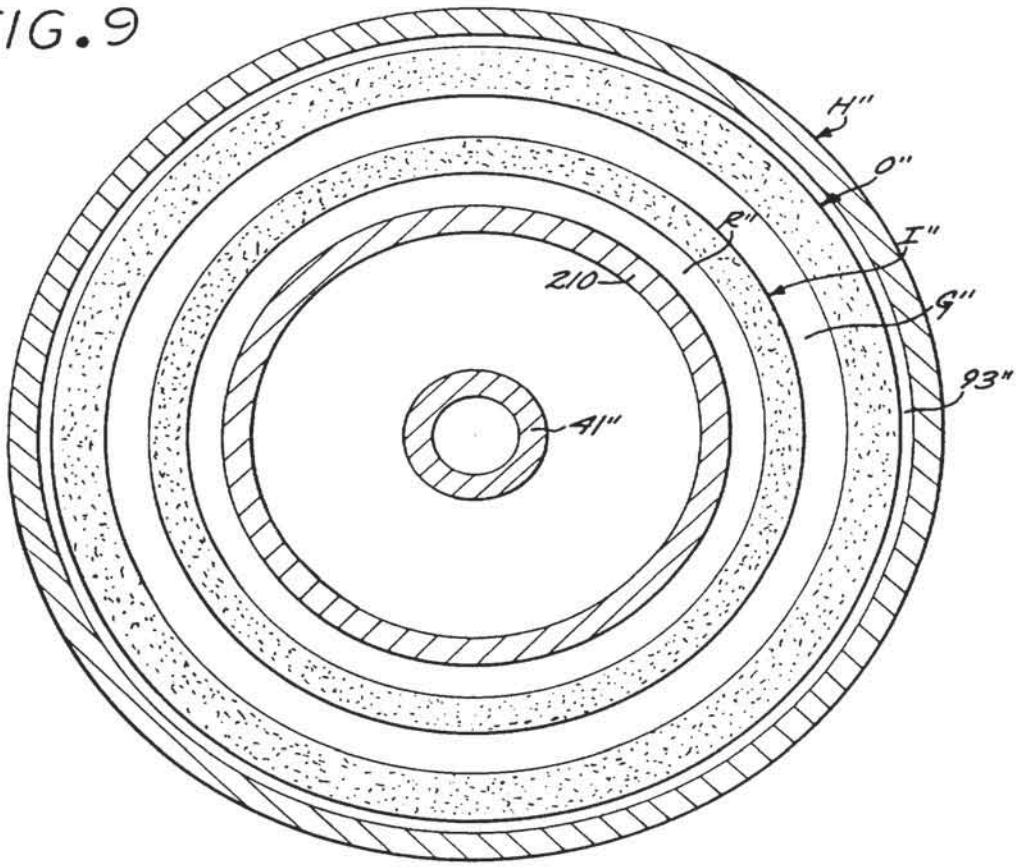
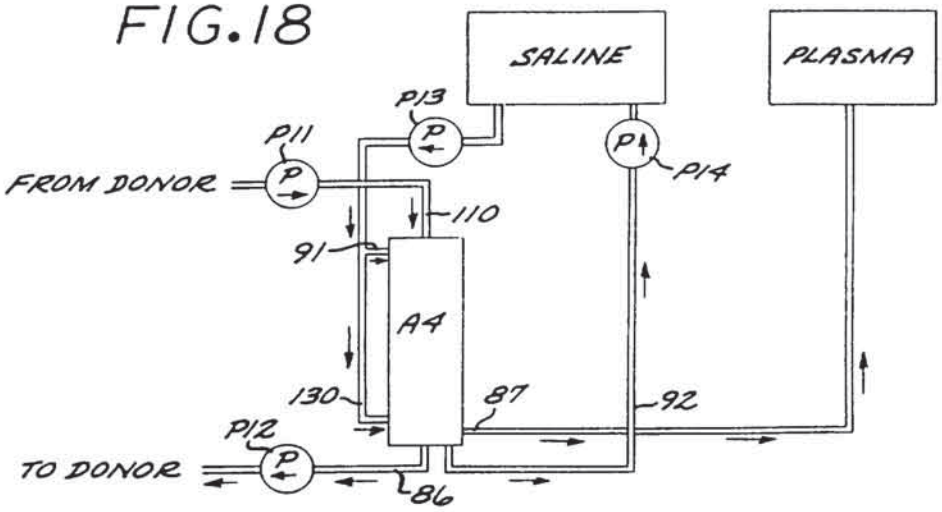

H"
O"
R"
I"
210
9"
93"
41"

FIG.18


SALINE
PLASMA
P13
P11
P14
FROM DONOR
110
91
A4
130
87
92
P12
TO DONOR
86

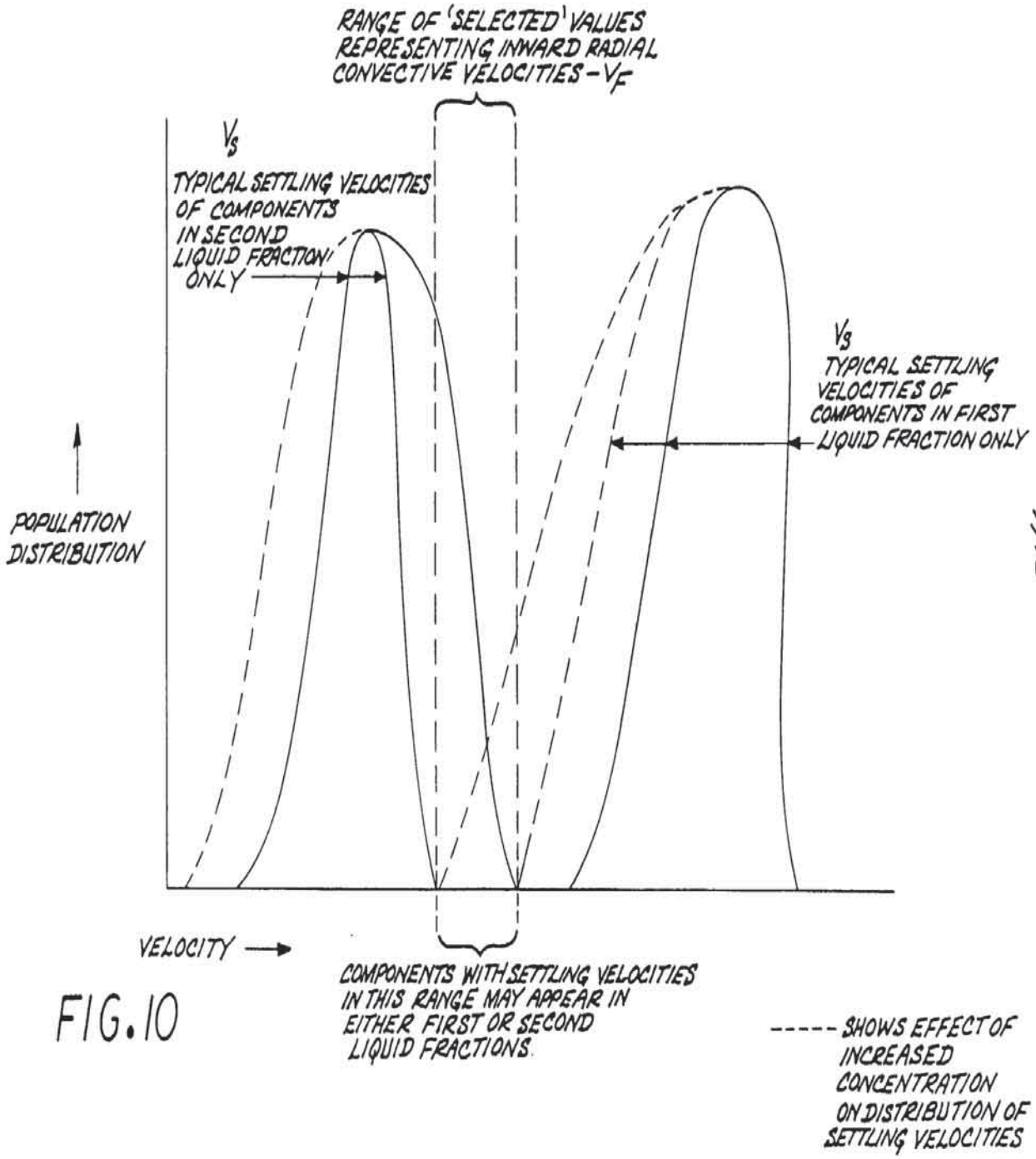

RANGE OF 'SELECTED' VALUES REPRESENTING INWARD RADIAL CONVECTIVE VELOCITIES - V_F
V_S
TYPICAL SETTLING VELOCITIES OF COMPONENTS IN SECOND LIQUID FRACTION ONLY
V_S
TYPICAL SETTLING VELOCITIES OF COMPONENTS IN FIRST LIQUID FRACTION ONLY
POPULATION DISTRIBUTION
VELOCITY
COMPONENTS WITH SETTLING VELOCITIES IN THIS RANGE MAY APPEAR IN EITHER FIRST OR SECOND LIQUID FRACTIONS.
----- SHOWS EFFECT OF INCREASED CONCENTRATION ON DISTRIBUTION OF SETTLING VELOCITIES

FIG. 10

FIG.11

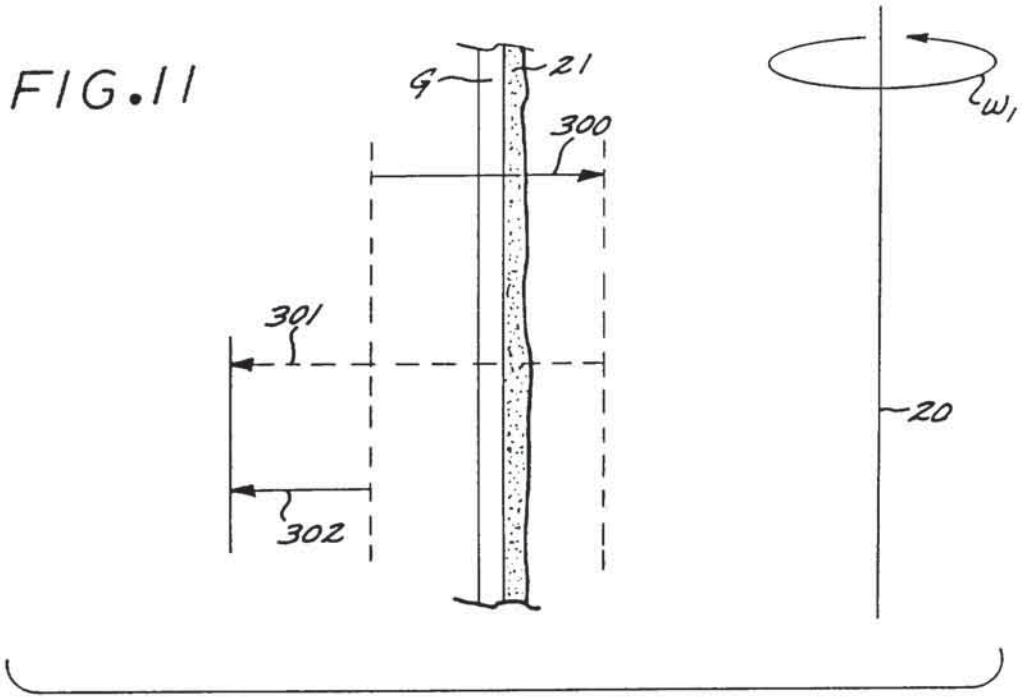
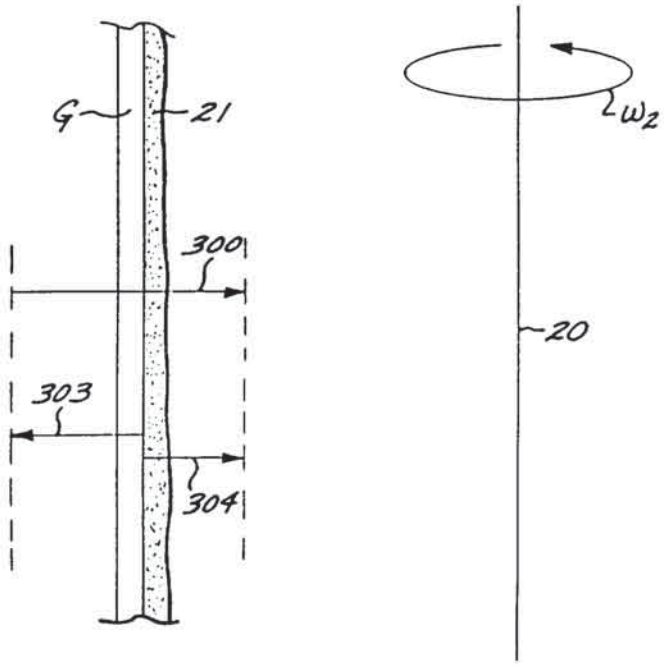


FIG.12



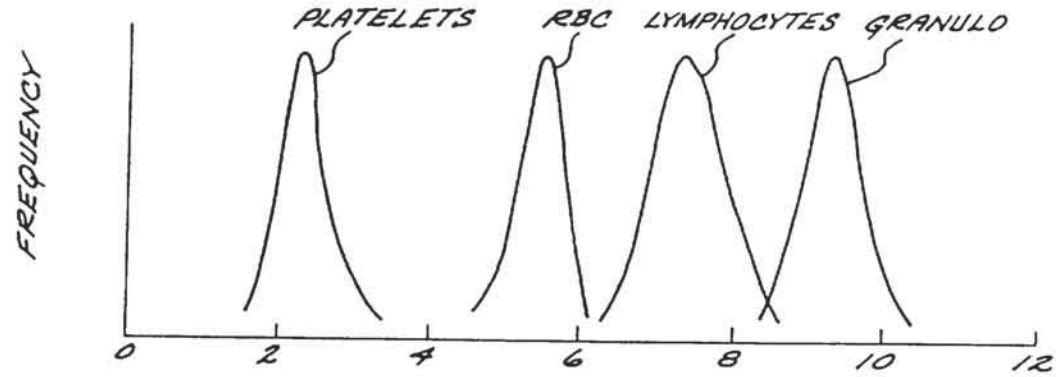


FIG.13

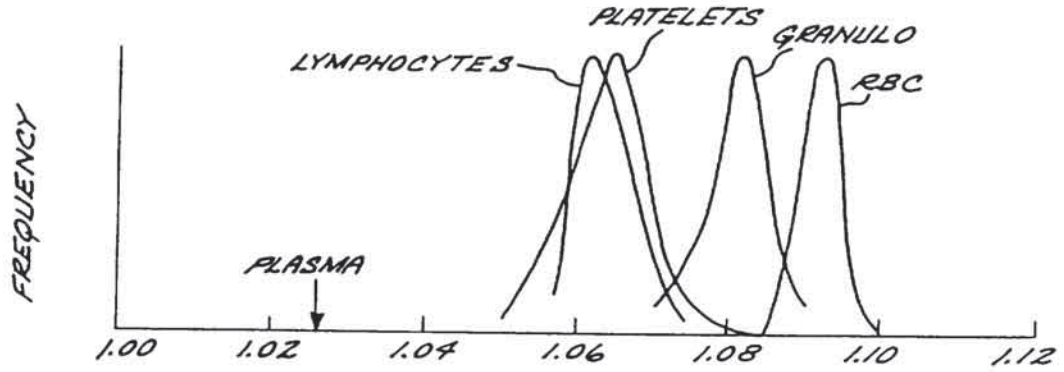


FIG.14

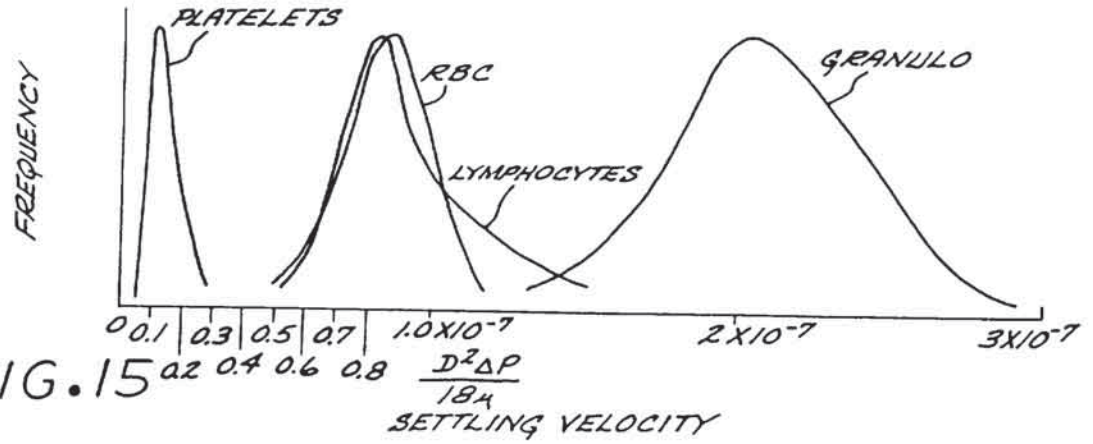


FIG.15

FIG.16

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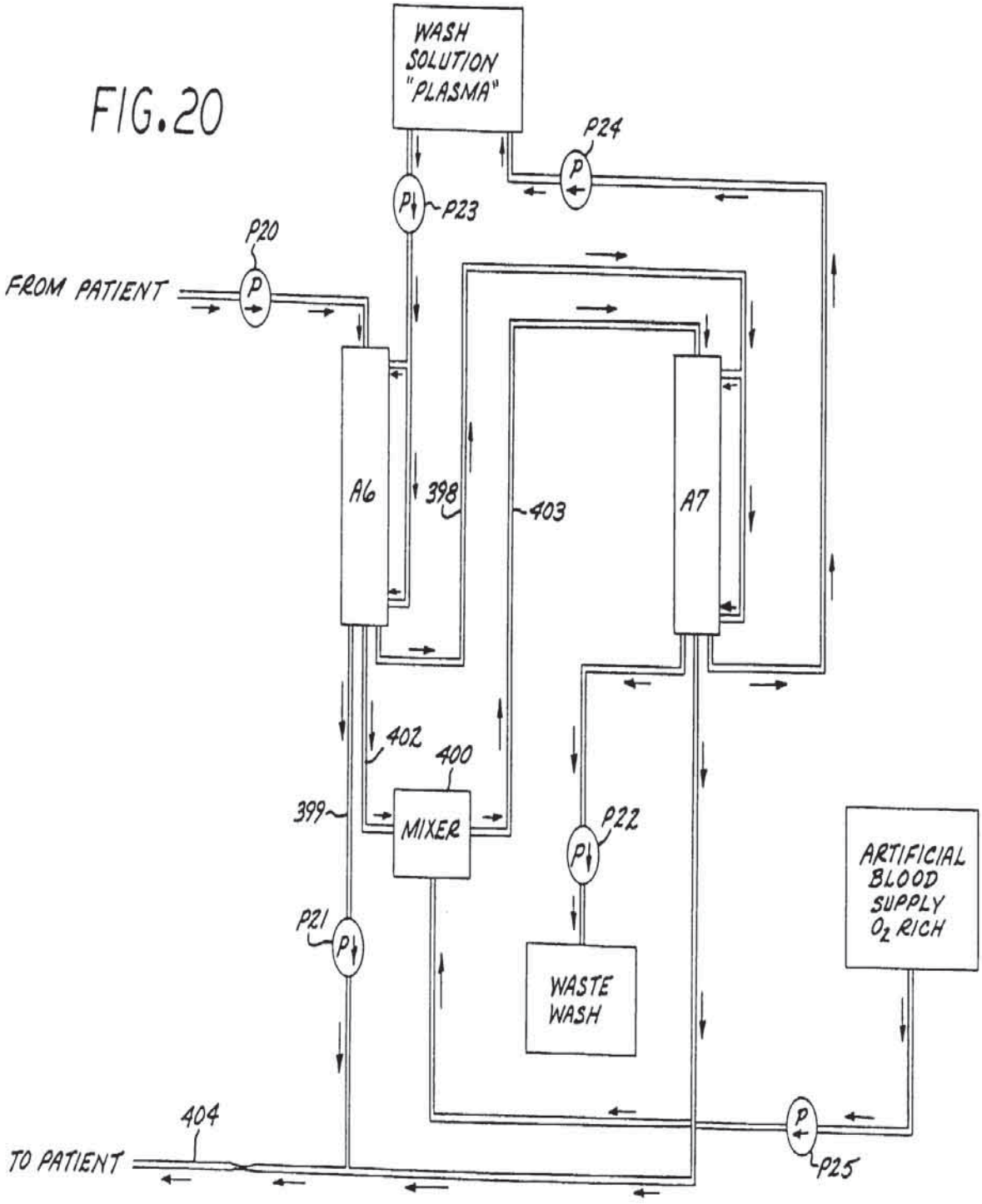
FIG.17

SALINE
PC
CONTAMINATED WASH
P9
P10
P6
FROM PATIENT
P8
A3
190
TO PROTEIN CONCENTRATOR
P7
TO PATIENT

FIG.19

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FIG.20



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Page #792

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/08523

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :B01D 33/00, 61/00
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US, A, 5,034,135 (Fischel) 23 July 1991 See entire document	1-5,8-19,21-31,33-34 --- 20
X -- Y	US, A, 4,871,462 (Fischel et al.) 3 October 1989 See entire document	1-3,6-7 --- 32

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

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Date of the actual completion of the international search 03 DECEMBER 1993	Date of mailing of the international search report 16 DEC 1993
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. NOT APPLICABLE	Authorized officer SUN UK KIM Telephone No. (703) 308-2350

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/08523

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

210/87, 90, 97, 134, 177, 178, 195.2, 216, 252, 258, 321.67, 321.68, 321.87, 324, 359, 360.1, 483, 497.01, 497.3, 512.1, 650, 651, 782, 787; 436/177, 178; 604/4, 5, 6

B. FIELDS SEARCHED
Minimum documentation searched
Classification System: U.S.

210/87, 90, 97, 134, 177, 178, 195.2, 216, 252, 258, 321.67, 321.68, 321.87, 324, 359, 360.1, 483, 497.01, 497.3, 512.1, 650, 651, 782, 787; 436/177, 178; 604/4, 5, 6

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Page #794

Espacenet

Bibliographic data: WO9611747 (A2) — 1996-04-25

BLOOD PROCESSING SYSTEM

Inventor(s):

Applicant(s): TRANSFUSION TECHNOLOGIES CORP [US]; HEADLEY THOMAS D [US]; POWERS EDWARD T [US] + (TRANSFUSION TECHNOLOGIES CORPORATION, ; HEADLEY, THOMAS, D, ; POWERS, EDWARD, T)

Classification:
- **international:** ***A61M1/02; A61M1/36; B04B5/04;*** *A61M1/00; A61M5/148;* (IPC1-7): A61M1/36; B04B5/04
- **cooperative:** **A61M1/3692; A61M1/3693; A61M1/3696; A61M1/3698; B04B5/0428; B04B5/0442;** A61M1/0009; A61M1/0011; A61M2205/3306; A61M2205/331; A61M2205/3393; A61M5/1483

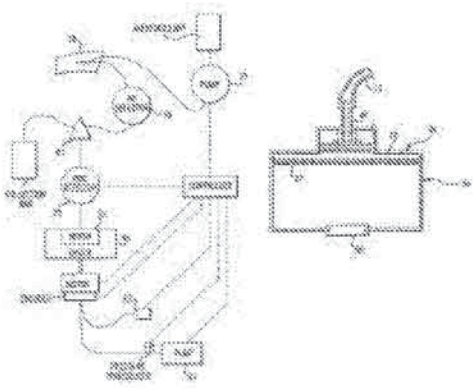
Application number: WO1995US13447 19951010 Global Dossier

Priority number(s): US19940322601 19941013

Also published as: WO9611747 (A3) AT234157 (T) AU4132296 (A) AU699141 (B2) CA2202284 (A1) more

Abstract of WO9611747 (A2)

A rotor (2a-2e) for collecting and centrifuging biological fluids in a range of volumes. The rotor includes an elastic impermeable diaphragm (31) which defines at least a portion of a variable-volume processing chamber (30), where the fluid is centrifuged. The rotor includes a rigid mounting member (28), to which the diaphragm is mounted and which is held and spun by a chuck. Preferably, this rigid mounting member includes a boundary wall (10) which together with the elastic diaphragm defines the



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chamber. The boundary wall may be a substantially imperforate circular wall which extends to the periphery of the processing chamber but defining one opening, preferably near the axis of rotation, permitting a conduit (13) or conduits (83, 93, 163, 165, 188) to pass therethrough so as to be in fluid communication with the processing chamber. The rotor may include a separate structure (40, 190, 244) for controlling the flow of liquid out of the chamber into the conduit. In a preferred embodiment, this outlet-control structure is a perforate, substantially rigid wall or plate (40), located within the processing chamber and mounted adjacent the rigid boundary wall. In an alternative embodiment, the outlet-control structure for controlling flow from the processing chamber to the conduit may include at least one tube or preferably a set of tubes (190), wherein each tube provides fluid communication between the chamber and the conduit. In one preferred embodiment, grooves (244) in the boundary wall may be used as the outlet-control structure.

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PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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A2

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(30) Priority Data:
08/322,601 13 October 1994 (13.10.94) US

(71) Applicants: TRANSFUSION TECHNOLOGIES CORPORATION [US/US]; 9 Erie Drive, Natick, MA 01760 (US). HEADLEY, Thomas, D. [US/US]; 83 Westgate Road, Wellesley, MA 02181 (US). POWERS, Edward, T. [US/US]; 8 Nason Road, Hampton Falls, NH 03844 (US).

(74) Agents: SUNSTEIN, Bruce, D. et al.; Bromberg & Sunstein, 11th floor, 125 Summer Street, Boston, MA 02110-1618 (US).

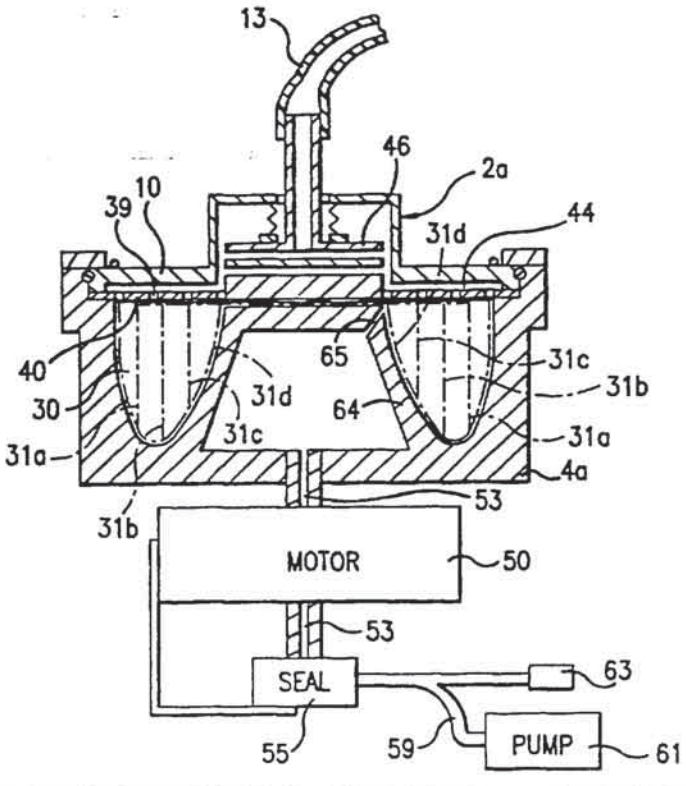
(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
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(54) Title: BLOOD PROCESSING SYSTEM

(57) Abstract

A rotor (2a-2e) for collecting and centrifuging biological fluids in a range of volumes. The rotor includes an elastic impermeable diaphragm (31) which defines at least a portion of a variable-volume processing chamber (30), where the fluid is centrifuged. The rotor includes a rigid mounting member (28), to which the diaphragm is mounted and which is held and spun by a chuck. Preferably, this rigid mounting member includes a boundary wall (10) which together with the elastic diaphragm defines the chamber. The boundary wall may be a substantially imperforate circular wall which extends to the periphery of the processing chamber but defining one opening, preferably near the axis of rotation, permitting a conduit (13) or conduits (83, 93, 163, 165, 188) to pass therethrough so as to be in fluid communication with the processing chamber. The rotor may include a separate structure (40, 190, 244) for controlling the flow of liquid out of the chamber into the conduit. In a preferred embodiment, this outlet-control structure is a perforate, substantially rigid wall or plate (40), located within the processing chamber and mounted adjacent the rigid boundary wall. In an alternative embodiment, the outlet-control structure for controlling flow from the processing chamber to the conduit may include at least one tube or preferably a set of tubes (190), wherein each tube provides fluid communication between the chamber and the conduit. In one preferred embodiment, grooves (244) in the boundary wall may be used as the outlet-control structure.



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BLOOD PROCESSING SYSTEM

DESCRIPTION

Technical Field

This invention generally relates to systems for processing blood and other biological fluids.

Background Art

Centrifugal biological-fluid-processing systems have been in existence for some time. Some are used to collect high concentrations of certain components of a person's blood while others are used to further process blood components by washing, concentrating or otherwise purifying the blood component of interest. Some of these systems are used to process biological fluids other than blood. Filtration systems are also used for processing blood and other biological fluids.

The centrifugal systems (hereinafter called blood-processing systems) generally fall into two categories, continuous-flow devices and discontinuous-flow devices.

In continuous-flow systems, whole blood from the donor or patient flows through one conduit into the spinning rotor where the components are separated. The component of interest is collected and the unwanted components are returned to the donor through a second conduit on a continuous basis as more whole blood is being drawn. Because the rate of drawing and the rate of return are substantially the same, the extracorporeal volume, or the amount of blood that is out of the donor or patient at any given time in the procedure, is relatively small. These systems typically employ a belt-type rotor, which has a relatively large diameter but a relatively small (typically 100 ml or less) processing volume. Although continuous-flow systems have the advantage that the amount of blood that must be outside the donor or patient can be relatively

small, they have the disadvantage that the diameter of the rotor is large. These systems are, as a consequence, large; furthermore, they are complicated to set up and use. These devices are used almost exclusively for the collection of platelets.

In discontinuous-flow systems, whole blood from the donor or patient also flows through a conduit into the rotor where component separation takes place. These systems employ a bowl-type rotor with a relatively large (typically 200 ml or more) volume that must be filled with blood before any of the desired components can be harvested. When the bowl is full, the drawing of fresh blood is stopped, and the unwanted components are returned to the donor or patient through the same conduit intermittently, in batches, rather than on a continuous basis. When the return has been completed, whole blood is again drawn from the donor or patient, and a second cycle begins. This process continues until the desired amount of component has been collected.

Discontinuous-flow systems have the advantage that the rotors are relatively small in diameter but have the disadvantage that the extracorporeal volume is large. This, in turn, makes it difficult or impossible to use discontinuous systems on people whose size and weight will not permit the drawing of the amount of blood required to fill the rotor. Discontinuous-flow devices are used for the collection of platelets and/or plasma, and for the concentration and washing of red blood cells (RBCs). They are used to reconstitute previously frozen RBCs and to salvage RBCs lost intraoperatively. Because the bowls in these systems are rigid and have a fixed volume, however, it is difficult to control the hematocrit of the final product, particularly if the amount of blood salvaged is insufficient to fill the bowl with RBCs.

One RBC-washing system marketed by Cobe Laboratories is made almost entirely of flexible PVC. It has the advantage of being able to vary the volume of the rotor to control the final hematocrit but has the disadvantage of being limited

to a rather flat, wide pancake-like shape due to manufacturing constrictions. The Cobe system controls the rotor volume by pumping a hydraulic fluid--a liquid--in or out of a bladder that rotates with and squeezes the blood out of rotor. The Cobe system takes up a fairly large amount of space, and its flexible pancake-shaped rotor is awkward to handle. The Cobe system does not permit blood to flow into and out of its rotor at the same time. The Cobe system also does not permit blood to be pulled into the rotor by suction. The Cobe rotor is usually filled with blood by gravity, although the blood may be pumped into the rotor. After the blood has been separated, it is squeezed out of the rotor by pumping hydraulic fluid into the bladder.

Haemonetics Corp. and others have provided systems to collect blood shed during surgery, concentrate and wash the RBCs, and return them to the patient. Existing systems typically use a 3 liter reservoir to collect and coarse filter the blood vacuumed from the surgical site and a separate processing set including a special centrifugal processing chamber to wash and concentrate the red blood cells in order that they may be safely reinfused to the patient. Because of their cost and complexity of use, these systems are used only in operations where relatively large blood loss is expected. The prior-art rotors used for processing blood collected during an operation, made by Haemonetics Corp. and others, must be completely filled with RBCs before any processing can occur, and thus the process takes more time and is not appropriate for use with small people or for an operation with low blood loss. Because the volume of the processing chamber is fixed, the final concentration of the RBCs in the last cycle of the process cannot be easily controlled.

Solco Basel AG makes a filter-based system for wound drains. This wound-drain system has the disadvantage that the blood returned to the patient contains, in addition to the RBCs, substances that may be deleterious to the patient.

There exists the need, therefore, for a centrifugal system for processing blood and other biological fluids, that is compact and easy to use and that does not have the disadvantages of prior-art discontinuous-flow systems. There is also a need for improving the way that blood is processed in a variety of applications, such as apheresis, intraoperative blood-salvage systems, and wound drains, so that the blood processing takes less time, requires less cumbersome equipment, and/or reduces harmful side effects in the patient or donor.

Summary of the Invention

The present invention provides a container, referred to herein as a rotor, which may be used for collecting and centrifuging biological fluids in a range of volumes. The rotor includes an elastic impermeable wall (diaphragm) which defines at least a portion of a variable-volume processing chamber, where the fluid is centrifuged. The rotor includes a rigid mounting member, to which the diaphragm is mounted and which is held and spun by a chuck. Preferably, this rigid mounting member includes a wall which together with the elastic diaphragm defines the chamber.

This diaphragm and rigid wall are both referred to herein as boundaries, since each defines a portion of the boundary of the variable-volume processing chamber and each has one side which does not come into contact with the biological fluid. In some embodiments, the diaphragm may be located inside other walls on the exterior of the rotor, such as the rigid boundary wall or an exterior shell.

The rigid boundary wall may be large enough to surround the maximum volume that may be taken up by the chamber, or the rigid mounting member may be only large enough to provide a place where the diaphragm may be mounted and where a chuck can hold and spin the rotor. In a preferred embodiment, the rigid boundary wall is a substantially imperforate circular wall which extends to the periphery of the processing chamber, so as to define the top of the

processing chamber; the diaphragm is attached to the perimeter of the wall and defines the remainder of the processing chamber.

As noted above, the rigid wall in one embodiment surrounds the chamber, and the diaphragm is located inside a portion of the rigid boundary wall. In one version of this embodiment, the rotor includes a core located inside the rigid boundary wall and the chamber, and the diaphragm is mounted about the core.

In a preferred embodiment, the rigid boundary wall is substantially imperforate but defines one opening, preferably near the axis of rotation, permitting a conduit or conduits to pass therethrough so as to be in fluid communication with the processing chamber. In another alternative embodiment, the rigid boundary wall has a plurality of openings for controlling the flow into and/or out of the rotor while the rotor is being spun.

Preferably, the rotor includes a separate structure for controlling the flow of liquid out of the chamber into the rotor's (outlet) conduit. In a preferred embodiment, this outlet-control structure is a perforate, substantially rigid wall or plate, located within the processing chamber and mounted adjacent the rigid boundary wall. Since it is located within the processing chamber, and both of its sides come into contact with the biological fluid, this perforate wall is referred to as an interior wall. The perforate interior wall preferably extends substantially to the periphery of the chamber, although in other embodiments it may have a smaller diameter. Although in a preferred embodiment the perforate wall has many holes, in alternative embodiments the perforate wall may have holes located only at a discrete radius or at discrete radii from the axis of rotation. The interior wall may also serve the purpose of protecting the elastic membrane from being abraded from a non-rotating portion of the rotor while the body of the rotor is spun.

In an alternative embodiment, the outlet-control structure for controlling flow from the processing chamber to the conduit includes at least one tube or preferably a set of tubes, wherein each tube provides fluid communication between the chamber and the conduit. The tubes used as the outlet-control structure may have holes along their length to provide additional points of entry for fluid from the processing chamber. In some versions of the rotor, the tube or tubes provide fluid communication from a variety of radii within the chamber; in other versions, the tube or tubes provide fluid communication from a discrete radius or discrete radii within the chamber.

In another preferred embodiment, the outlet-control means may include vertical walls that define channels. These channels may be grooves formed in the interior surface of the rigid boundary wall. As long as the vertical channel walls are spaced close enough to each other (i.e., as long as the grooves are narrow enough), the channels (grooves) will remain open even though the processing chamber is at its lowest volume and the elastic membrane is pressed against the bottom of the vertical walls. Such channels can provide fluid communication to the rotor's outlet conduit from the periphery of the processing chamber to the innermost radius of the processing chamber and all the points in between. The grooves can be shortened so as to provide fluid communication to the outlet conduit from just those points between two radii within the chamber.

In one embodiment of the rotor, a single conduit passes through a portion of the rotor that does not rotate during centrifugation--i.e., the rotor's fixed portion. The fixed portion passes through the rigid boundary wall, and the rigid boundary wall is rotatably mounted around the fixed portion. In another embodiment, two or more conduits pass through a portion of the rotor that does not rotate during centrifugation. This embodiment permits unseparated fluid to flow into the spinning rotor through one conduit, while separated fluid can flow out of the rotor through the other

conduit. This embodiment of the rotor may further include a substantially imperforate interior wall, mounted between the boundary wall and the perforate interior wall and around the fixed portion, so as to provide a channel permitting fluid to flow from the rotor's input conduit to the chamber's periphery. This substantially imperforate interior wall does define a center hole through which the rotor's fixed portion passes. The substantially imperforate interior wall may be considered an inlet-control structure which controls the flow of fluid into the rotor--in this case directing the fluid to the rotor's periphery.

Alternative embodiments of the rotor do not have a fixed portion. The conduits extending from these embodiments of the rotor thus spin with the rest of the rotor during centrifugation. A rotary seal may be located at some point in the tubing connecting the rotor with the rest of the processing set. Alternatively, a skip-rope system may be used in lieu of a rotary seal.

The embodiments of the rotor having a fixed portion preferably include a rotary seal that has a base, a spring member, first and second seal faces, which spin in relation to each other, and a flexible seal member. The spring is mounted on the base, and the first seal face is mounted on the spring member so that the spring member presses the first seal face against the second seal face. The seal member prevents flow between the first seal face and the base. Preferably, the flexible seal member and the first seal face are disposed so that the force with which the spring member presses the first seal face against the second seal face is not adversely affected by pressure within the rotor. In a preferred embodiment, the flexible seal member and the spring member are separate members, although they may be made out of different portions of the same piece of material. Alternatively, if the flexible seal member is resilient and rigid enough to apply the proper force between the first and second seal faces, a separate spring member may not be necessary.

In one embodiment, the rotary seal's base is part of the rotor's fixed portion, and the rotary seal's second seal face is attached to the rigid mounting member, which is part of the rotating portion of the rotor. Alternatively, the rotary seal's base may be part of the rotor's rigid mounting member, and the rotary seal's second seal face is attached to the rotor's fixed portion.

The rotor may be spun in a centrifuge system that includes a chuck for holding and spinning the rotor and a pressurized fluid supply for supplying a pressurized control fluid--preferably gas--adjacent the rotor's diaphragm, while the rotor is being spun. The pressurized gas may be used to force fluid out of the rotor's processing chamber. The system preferably includes means for applying a vacuum to the exterior side of the diaphragm (i.e., the side that does not come into contact with the fluid being processed), so as to draw fluid into the processing chamber. In one embodiment, for use with a rotor where the diaphragm is mounted along the bottom of a substantially flat, circular boundary wall, the chuck has extending from a rotatable base an outer peripheral wall, so as to define a cylindrical cavity into which the diaphragm may expand. In one version of this chuck embodiment, the chuck also has extending from its base a core, so that the chuck defines an annular cavity into which the diaphragm may expand. In another embodiment, for use with a rotor that has a core in the rotor's interior, the chuck has extending from a rotatable base a nozzle, through which the pressurized gas is provided through the rotor's core to an area adjacent the rotor's diaphragm. Another embodiment of the chuck holds the rotor from inside a rigid core in the rotor.

In order to make the rotor more portable while biological fluid is being collected in the rotor, a rigid, airtight exterior shell may be attached and sealed to the rigid boundary wall. In one embodiment, the shell may be removably attached to the rotor. The shell permits a vacuum to be applied to the exterior side of the diaphragm when the

rotor is not in a chuck. Thus, fluid may be drawn into the processing chamber when the rotor is not in a chuck. A spring bellows may also be used to create a vacuum against the diaphragm.

The system may also include a control system for controlling the rotational speed of the chuck and the gas pressure provided by the gas supply to achieve the most advantageous combination of centrifugal force for separation and gas pressure against the diaphragm required to force fluid out of the rotor. The control system may be programmed to determine the volume of the processing chamber based on the rotational speed of the chuck and the air pressure provided by the chuck.

The rotor and centrifuge systems of the present invention may be used in many different processes involving biological fluid. A method for using the rotor would generally include the steps of introducing an unseparated fluid into the rotor's processing chamber, spinning the rotor so as to separate the fluid into denser and lighter components, and applying pressure to the diaphragm's exterior side so as to force a fluid component--usually the lighter fluid components--through the conduit.

Further aspects of the present invention will be apparent from the following description of specific embodiments, the attached drawings and the appended claims.

Brief Description of the Drawings

FIG. 1 is a top plan view of a rotor according to the present invention.

FIG. 2 shows a cross-section of the rotor shown in FIG. 1.

FIG. 3 shows a cross-section of the FIG. 2 rotor and a chuck for holding and spinning the rotor.

FIG. 4 shows a cross-section of the rotor and chuck system of FIG. 3 showing the shapes of the diaphragm with varying volumes of blood in the rotor.

FIG. 5 is a perspective view of a system that may use the rotor in post-operative salvage (i.e., with a wound drain).

FIG. 6 is a schematic of a system to utilize the rotor as a donor-connected apheresis system for the collection of plasma or RBC.

FIG. 7 shows a cross-section of a rotor with an exterior shell.

FIG. 8A shows a cross-section of a rotor with an alternative exterior shell.

FIG. 8B shows a cross section of the rotor shown in FIG. 8A mounted on a chuck located within the core of the rotor's shell.

FIG. 9 shows a cross-section of the FIG. 2 rotor in an alternative chuck.

FIG. 10 is a top plan view of a two-conduit rotor.

FIG. 11 shows a cross-section of the FIG. 10 rotor.

FIG. 12 shows the FIG. 11 rotor mounted in a chuck.

FIG. 13 shows a cross-section of the FIG. 12 rotor and chuck system showing the shapes of the diaphragm with varying volumes of blood in the rotor.

FIG. 14 is a perspective view of a system used in RBC apheresis.

FIG. 15 is a schematic of a system for RBC apheresis.

FIGS. 16-18 show cross-sections of several alternative rotors having varying configurations of interior walls and fixed portions.

FIGS. 19A-19D show how an alternative rotor may be used to collect platelets.

FIG. 19E shows a rotor that may be used to collect the separated fluid component with the greatest density.

FIG. 20 shows a cross-section of an alternative rotor having a balloon-shaped diaphragm mounted around a core.

FIG. 21 shows a cross-section of the FIG. 20 rotor mounted in a chuck.

FIG. 22 shows a cross-section of the FIG. 21 system centrifuging blood.

FIG. 23 shows a cross-section of an alternative two-conduit rotor.

FIG. 24 shows a cross-section of a modified version of the FIG. 23 rotor.

FIG. 25 shows cross-section of the FIG. 24 rotor mounted in a chuck.

FIG. 26 shows a cross-section of the FIG. 25 system centrifuging blood.

FIG. 27 shows a cross-section of the FIG. 25 system after centrifuging blood.

FIG. 28 is a schematic showing how an alternative rotor may be used to process blood.

FIG. 29 is a cross-section of the rotor shown in FIG. 28 and a portable device for applying a vacuum.

FIG. 30 shows an alternative rotor having a set of tubes, in lieu of a perforate interior wall, for controlling the flow from the processing chamber.

FIG. 31 shows a variation of the rotor shown in FIG. 30, wherein the tubes leading from the processing chamber remain separate.

FIG. 32 is a top plan view of a rotor having a set of radially mounted tubes in lieu of a perforate interior wall.

FIG. 33 shows a cross-section of the FIG. 32 rotor.

FIG. 34 shows a cross-section of a rotor having a fixed portion and a set of radially mounted tubes in lieu of a perforate interior wall.

FIGS. 35 and 36 show respectively a cross-section and a top plan view of a rotor having a fixed portion, a set of radially mounted tubes and a diaphragm that covers most of the top of the rotor.

FIG. 37 shows a cross-section of a rotary seal representative of prior-art rotary seals.

FIG. 38 shows a cross-section of an improved rotary seal, which may be used in the rotors disclosed herein that have fixed and rotating portions.

FIG. 39 shows a detail of an alternative rotary seal, wherein the spring and the flexible seal member and the

spring are formed out of different portions of the same piece of material.

FIG. 40 shows an alternative rotor having a hemispherical boundary wall.

FIG. 41 shows a bottom view of a preferred rotor embodiment without its diaphragm.

Fig. 42 shows a cross-section of the FIG. 41 rotor with its diaphragm.

Description of Specific Embodiments

FIGS. 1 and 2 show a version of the centrifuge rotor **2a** according to the present invention. The rotor **2a** has an elastic boundary, i.e., an impermeable diaphragm **31**, which is sealed to a rigid, imperforate boundary wall **10** by an O-ring **35** or other means. The diaphragm **31** is preferably made of an elastic, stretchable and resilient material, such as latex or silicone rubber. A perforate interior wall **40**--also referred to as a plate--having holes **39** is attached under the rigid boundary wall **10**. Preferably, the boundary wall **10** and the interior wall **40** are made out of a rigid thermoplastic. The perforate interior plate **40** is held a short distance away from the imperforate boundary wall **10** by standoffs (not shown), thereby forming a passage **44**.

The rotor **2a** also has a collector assembly **46**, which is attached to tube **13**, and a rotary seal **48**, which maintains the sterile environment in the rotor **2a** but allows the rotor to turn even while the collector assembly is held stationary. The rotary seal **48** provides a seal between the collector assembly **46** and that portion **28** of the boundary wall **10** that surrounds the collector assembly **46**, while permitting the boundary wall **10** to spin around the collector assembly **46** while the collector assembly **46** is held in place.

Tube **13** is attached to the rest of the disposable processing set (tubing set), which may include a cassette (see item **15a** in FIG. 5). The tube **13** and the collector

assembly **46** are held fixedly in place, while the rest of the rotor **2a**--the rigid boundary wall **10**, the diaphragm **31**, the plate **40** and any fluids in the variable-volume processing chamber--is spun. Although otherwise imperforate, the boundary wall **10** does of course define a central opening through which the collector assembly **46** can extend to connect with the tube **13**.

A variable volume is defined in the rotor **2a** between the boundary wall **10** and the diaphragm **31**. This variable volume is the processing chamber where the blood is centrifuged and separated. The processing chamber is sealed in by the boundary wall **10** and the diaphragm, so that during centrifugation the only fluid communication between the interior of the processing chamber and outside of the rotor **2a** is through the conduit leading to tube **13**--or in the embodiments of the rotor having multiple conduits into and out of the rotor (such as those shown in FIGS. 11, 16-18, 19A-19D and 23) through the multiple conduits. The conduit or conduits providing fluid communication with the processing chamber pass through the rotor's fixed portion, which includes the collector assembly **46**.

The plate **40** is located within the processing chamber. It is desirable to minimize the volume of the processing chamber above the plate **40** (including the channel), so that as much fluid as possible can be forced out of the processing chamber when the diaphragm **31** is forced against the plate **40**. Nevertheless, the passage **44** needs to be wide enough so as to permit sufficiently unrestricted flow from the periphery to the center of the passage **44**, even when the diaphragm **31** is forced against the plate **40**.

The interior plate's holes **39** allow fluid communication between the areas of the chamber above and below the plate **40**. The holes **39** should be small enough to prevent the diaphragm **31** from protruding too far into the passage **44**. If they are too large, protrusions of the diaphragm **31** through the plate's holes **39** could restrict flow from the

processing chamber's periphery to the center of the channel. The size and placement of the holes **39** may be varied in order to regulate the flow out of the rotor **2a** as the rotor **2a** is emptied.

If the holes **39** are too large and too close to the collector assembly **46**, the portions of the diaphragm could touch the fixed portion's collector assembly **46**. Allowing the diaphragm **31** to touch the collector assembly **46** can cause abrasion of the diaphragm if the body of the rotor **2a** is being spun while the collector assembly **46** is being held in place, and continual abrasion may cause the diaphragm **31** to eventually rupture. Thus, the plate **40**, as well as the top wall **10**, separate the spinning diaphragm **31** from the non-spinning tube **13** and the collector assembly **46**.

In use, the rotor **2a** is placed in a centrifuge chuck **4a** and held in place by clamp **8**, as shown in FIG. 3. O-ring **35** is pressed against an inside wall of the chuck **4a** to form an air tight seal. Of course, different configurations may be used in order to create a seal between the rotor **2a** and the chuck **4a**, such as the use of a lip seal **36** shown in FIG. 12.

In one preferred embodiment, the chuck **4a** has a core **64** which limits how far the diaphragm **31** can expand towards the rotor's axis of rotation. Holes **65** in the interior core portion **64** of the chuck **4a** allow a control gas, preferably air, to flow from a compressor/vacuum pump **61** to the area of the chuck **4a** exposed to the elastic wall **31** of the rotor **2a**. Channels extending from the holes **65** may be provided on the inner surface of the chuck, so as to allow air to flow from the holes **65** to various points adjacent the diaphragm **31** when the diaphragm is fully extended (as shown by line **31d** in FIG. 4). The chuck **4a** is turned by a motor **50** and shaft **51**. The shaft **51** has an axial through hole **53** and protrudes below the motor **50**. A rotary pneumatic seal **55** is attached to the shaft **51** and is held stationary by a brace **57**. The pneumatic rotary seal **55** is connected by tubing **59** to the

compressor/vacuum pump **61** and to a controllable exhaust valve **63**.

Instead of a rotary pneumatic seal, the tubing **59** may be connected to a compartment attached and sealed to the bottom of the motor **50**, so that the bottom of the shaft **51** extends into the compartment; if the motor forms a substantially air-tight barrier enclosing the compartment, this arrangement can be used instead of the rotary pneumatic seal. Instead of using a dual-purpose pump to provide both positive and negative pressure, a separate compressor and vacuum pump may be used to create positive and negative pressures respectively. Alternatively, the negative pressure may be provided by the hospital's vacuum source, which may be supplied to the housing by a vacuum line, while the pump **61** creates the positive pressure.

In the rotor shown in FIG. 2, the imperforate, rigid boundary wall **10** has a diameter substantially equal to the largest diameter of processing chamber, i.e., the space defined by the chuck **4a**. In an alternative embodiment, the diameter of the rigid boundary wall **10** may be as small as the collector/rotary-seal area **28**. In a rotor having an imperforate wall **10** with a smaller diameter than the perforated interior plate **40**, the elastic diaphragm **31** is bent around the periphery of the plate **40** in order to cover that portion of the top of the plate **40** not covered by the imperforate wall **10**. (See for example FIG. 35, which shows a rotor that uses tubes to control the flow out of the processing chamber instead of a perforate interior wall.) The chuck for holding and spinning such a rotor should have a lid in order to keep the portion of the diaphragm **31** above the interior plate **40** in the proper shape when the rotor is spun and in order to maintain an air-tight seal. It is desirable that the rigid rotatable portion of the rotor be large enough so that the diaphragm **31** may be mounted on it and so that the chuck **4a** may grasp the rigid rotatable portion in order to spin the rotor. In rotors having small-

diameter boundary walls, the perforate interior wall **40** or other structure for controlling the flow out of the processing chamber may be modified to fold out of the way when the rotor is being built or stored. During centrifugation, the perforate interior plate **40** should--in a preferred embodiment--extend to the periphery of the processing chamber in order to ensure that fluid can flow from the periphery of the processing chamber to the collector assembly **46**, even when the processing chamber is at its smallest volume.

It will be appreciated that using a rotor having a rigid boundary wall extending all the way to the largest diameter of the processing chamber, like that shown in FIG. 2, has the advantages of being easier to use and not requiring the use of a lid on the chuck.

FIG. 4 shows the rotor **2a** while it is spinning and while blood flows into the rotor **2a** from the rest of the disposable set. While the body of the rotor **2a** is spun by the chuck **4a**, the collector assembly **46**, including the conduit connected to tube **13**, is held in place by a brace (such as brace **11** shown in FIG. 5). When the blood touches either the boundary wall **10** or the interior plate **40**, it is propelled by centrifugal force towards the perimeter of the rotor **2a**. As more blood enters, it continues to be propelled to the perimeter eventually flowing through the holes in the interior plate **40**. As the volume of the blood and the processing chamber **30** increases, the diaphragm stretches to allow the blood to reach the furthest diameter and at some point takes on a shape shown by line **31a**. As blood enters the rotor, the air in the chuck **4a** that is displaced by the blood escapes through hole **65**, down the shaft hole **53** and out exhaust valve **63**. If necessary, the blood flow rate can be increased by a vacuum in the chuck **4a** generated by the pump **61** or a separate vacuum supply (such as a separate vacuum pump or the hospital vacuum provided through a vacuum line). As more and more blood enters the

rotor **2a**, the diaphragm changes shape to accommodate the blood. As it is filled further, the diaphragm takes on the shapes shown by line **31b** and line **31c** and finally, when the rotor is full, takes on the shape of the chuck interior, as shown by line **31d**.

As the diaphragm stretches to accommodate the expanding size of the processing chamber **30**, it comes into contact with the chuck in a sequential manner. As successive portions of the diaphragm come into contact with the chuck, they may become immobilized and cease to stretch, while those portions of the diaphragm that have not yet come into contact with the chuck continue to stretch, with the consequence that portions of the diaphragm may be subjected to greater stretching than other portions. In order to avoid rupturing of the diaphragm when the processing chamber **30** is filled with blood, the chuck **4a** may be shaped so as to minimize variations in the amount of stretching between different portions of the diaphragm.

FIG. 5 shows a system, according to the present invention, for recovering blood drawn by vacuum into a tube **17** from a wound drain. A filter **26** may be provided in the tube **17**. This type of system is known as post-operative salvage. A preferred embodiment of the system includes a housing **6**, having a small footprint of approximately 8 inches by 11 inches and a height of only about 10 inches. For some applications, even smaller systems, with smaller rotors, may be used. The rotor **2a** is held in the chuck, such as the chuck shown in FIGS. 3 and 4, by chuck clamp **8**. A vacuum is provided through the chuck to the exterior side of the diaphragm. Because the diaphragm is pulled downward by the vacuum in the chuck, fluid is drawn into the rotor **2a** through the rotor tube **13**. The blood is thus drawn from the wound-drain site through the tube **17** then through a cassette **15a**, which provides valving to control the flow of fluids through the various lines, and then through the rotor tube **13** to the rotor **2a**. Standard valves or valving techniques

(e.g., pinching a tube) may be used to control fluid flow in the system instead of a cassette **15a**. Anticoagulant may be added to the drained blood at some point during the process.

An intermediate wound-drain canister may be placed in the line **17** between the patient and the cassette **15a**. The filter **26** may be located adjacent to or in this canister, and anticoagulant may be added to the blood in the canister. Such a canister can hold the whole blood pulled from the patient until the blood is to be processed; at that time, the vacuum generated in the chuck or a pump may be used to pull the blood from the canister to the rotor **2a**.

When it is desired to separate the blood in the rotor **2a**, the chuck spins the body of the rotor **2a**. In a preferred version of the post-operative salvage process using the present invention, blood flow to the rotor **2a** is stopped when the desired or the available amount of blood has entered the rotor, or when it is full. Since, in the rotor of the present invention, the processing chamber has a variable volume, the rotor **2a** does not have to be filled to its capacity with blood for the process to be done properly. After the flow into the rotor is stopped, the blood is then subjected to centrifugal force as long as is appropriate to separate the various components. The portion of the rotor **2a** where the rotor tube **13** enters the rotor **2a** (i.e., the fixed portion, which as noted previously in connection with FIG. 4 includes the collector assembly **46**) is held and prevented from spinning by a brace **11**.

Referring to FIG. 4, when the separation is complete, the compressor begins to pump compressed air into the chuck **4a**. When the air pressure acting on the diaphragm's exterior (i.e., the side that does not come into contact with blood) exceeds the fluid head between the collector assembly and the inner vertical face of the diaphragm (lines **31a**, **31b**, **31c** and **31d**), fluid begins to flow from the processing area in the rotor through the holes **39** in the interior plate **40** into the area around the collector

assembly **46**, through the collector assembly and out of the rotor **2a** into the rotor tube **13**. The fluid head between the collector assembly and the inner vertical face of the diaphragm is created by the centrifugal force acting on the fluid in the channel **44**. In order to minimize the amount of air pressure needed to overcome the centrifugal force of the rotor, the rotational speed of the rotor **2a** may be reduced--at some point during the process--to a level that is high enough simply to keep the blood components separated.

It should be noted that while the use of air is described herein to apply pressure to the diaphragm **31**, other fluids could be used as well. Preferably a gas is used, since a gas will have a lower specific gravity than the lightest separated fluid in the processing chamber and therefore will stay between the liquid being centrifuged and the rotor's axis of rotation. Air is preferred since it is readily available and easily disposed of. Nitrogen or carbon dioxide may be used instead.

The compressed air first pushes the blood element with the lightest specific gravity out of the processing area. the lighter fluid passes through those holes **39** in the plate **40** at the smallest radius not sealed by the diaphragm **31**. Each blood element in turn by specific gravity flows through the holes **39** in the plate **40** at the smallest radius not yet sealed by the diaphragm **31** and then out of the rotor.

Referring to FIG. 5 again, the blood elements exiting the rotor can be diverted as desired by the cassette **15a**. The fluid flowing out of the rotor's processing chamber may be diverted to a specific container (e.g., a waste bag or an RBC bag) or returned to a donor depending on the purpose of the process, on how the system is configured and on how the cassette **15a** or other tubing directs the fluids.

In a typical post-operative salvage process using the present invention, the lighter elements--most of the plasma and platelets--are considered waste and are sent through the cassette **15a** (or other valving mechanism) and the tube **24** to

a waste bag. The remaining blood elements--mostly concentrated RBCs--may then be further processed in the rotor **2a** and then forced out of the rotor **2a** through the cassette **15a** and the tube **22** to an RBC bag. After a sufficient amount of RBCs are sent to the RBC bag, the RBC bag is disconnected from the cassette **15a** and may then be attached to the patient in order to return the patient's RBCs.

The emptying of the processing chamber **30** of the rotor **2a** can be stopped at any time by stopping the increase in the air pressure inside the chuck **4a**, while maintaining the rotational speed of the chuck. If the rotor is processing blood, one likely place to stop might be when the RBC layer begins to exit the rotor and another might be when the rotor is empty.

The cycle of sending fluids into the rotor, centrifuging and forcing fluids out of the rotor **2a** can be repeated, for instance for further processing of the blood components left in the rotor (for instance, washing the RBCs or ficol-hypaque separations). Other fluids can be allowed to flow into the rotor and back out again by inflating or deflating the diaphragm **31** and appropriately actuating the cassette **15a** (shown in FIG. 5). At the end of the last cycle in the post-operative salvage process, the air pressure in the chuck **4a** can be adjusted to the proper level to obtain the desired hematocrit in the final product.

The rotor speed may be changed at different times while the rotor is emptying, in order to achieve the most advantageous combination of centrifugal force for separation and air pressure inside the chuck required to force fluid out of the rotor. It is desirable to avoid applying too much air pressure against the outside of the diaphragm **31**, for safety considerations, and for reducing the size of the system components and the power consumed by the system.

Thus, in a preferred embodiment the rotor is emptied in the following manner, with reference to FIG. 4. Initially,

the rotor **2a** is spinning at full processing speed--say for instance 5000 rpm. The gas in the chuck **4a** is positively pressurized, thereby causing fluid to flow out of the rotor's chamber **30** until an equilibrium is reached between the gas pressure in the chuck and the centrifugal force acting on the fluid in the channel **44** above the plate **40** between the outer edge of the collector assembly **46** and the inner vertical face of the diaphragm (lines **31a**, **31b**, **31c** and **31d**. The gas may continue to be pressurized until it reaches 2 psi--or whatever pressure limit is chosen. Then, the rotational speed of the rotor **2a** is reduced. The rotational speed may be reduced without affecting the separation of the fluids in the rotor if the speed is reduced smoothly and slowly, and as long as the rotational speed does not fall below the minimum speed necessary to maintain separation, which may for example be as low as 500-1500 rpm. Reducing the speed lowers the centrifugal force on the fluid in the channel **44**. Thus, additional fluid is forced out of the rotor until a new equilibrium is reached. By continuing to reduce the rotor's rotational speed, additional fluid is forced out of the rotor even though the gas pressure in the chuck **4a** is kept constant.

Alternatively, fluid may be forced out of the rotor **2a** with low gas pressure by first reducing the rotational speed of the rotor **2a** to the desired level--for instance, the lowest speed which will maintain separation--and then increasing the pressure in the chuck **4a**. It is also possible to reduce the rotational speed and increase the gas pressure at the same time. An advantage of this technique of emptying the rotor--namely, reducing the rotational speed of the rotor to assist in emptying--is that less gas pressure in the chuck is needed to force liquid out of the rotor.

The chuck's gas pressure and rotational speed may be controlled by a controller (preferably, a digital data processor located in the system housing **6**, which housing is

shown in FIG. 5), which receives information from a pressure transducer for measuring the gas pressure in the chuck **4a** and from an encoder for measuring the rotational speed of the chuck **4a** and the rotor **2a**. The controller may control the compressor **61** and the motor **50**, in addition to valves in the rest of the disposable set. The controller may also be programmed to calculate the volume of liquid in the rotor's processing chamber based on the chuck's gas pressure and the rotational speed.

In order to avoid excessive vibration of the system as the rotor is being spun, the speed of rotation may be varied. For instance, instead of trying to maintain a constant speed of rotation of 5000 rpm, the motor may cycle through a range of speeds around 5000 rpm. This cycling will help avoid the motor staying at a rotational speed that puts the system into a resonant vibration. The rotational speed should be changed quickly enough so that the system does not have an opportunity to resonate at a given speed, yet the speed should not be changed so quickly that the separation of the fluid components is upset.

At some point in the emptying, only one component will remain in the rotor, for instance red blood cells (or only components whose separation is not required will remain in the rotor). At that point, the foregoing process may continue until the rotor **2a** is empty or, preferably, the spinning of the rotor **2a** may be stopped. The gas pressure necessary to push the remaining liquid out of the rotor **2a** when it is stopped must only be greater than the fluid head from the rotor **2a** to the highest point in the tubing between the rotor and the collection bag.

FIG. 6 is a schematic of a system to utilize the rotor **2a** described above in a donor-connected apheresis system for the collection of RBCs. A suitable anticoagulant is metered into the blood at the end of the needle which has been inserted into a vein in an arm of the donor **70**. The flow of anticoagulant is controlled by a pump or other metering

device **77**. The anticoagulated blood flows through the donor tubing and into the rotor by the combination of gravity and venous pressure and, if needed, vacuum from compressor/vacuum pump **61** or a peristaltic pump. At this point during the process, valve **81** closes off the component collection bag and permits flow to the rotor.

After sufficient blood enters the rotor, the rotor is spun quickly enough and long enough to cause adequate separation. The valve **81** remains in the position where the donor tubing is open and the tubing to the collection bag is closed. While the chuck continues to spin the rotor in order to maintain separation (although the rotational speed may be reduced), the compressor **61** pumps air into the chuck forcing plasma to flow back to the donor. The plasma flowing back to the donor is checked for air bubbles by the air detector **79**. As the RBCs start to emerge from the rotor, as detected by RBC detector **75**, the valve **81** opens the tubing to the collection bag and closes the tubing to the donor. When the rotor is empty, the compressor stops and the pressure in the rotor is vented through vent **63**. The process can be repeated as desired.

If plasma is to be collected instead of RBCs, the valve **81** would first shunt the plasma exiting the rotor to the collection bag. Then, when RBCs were detected by the RBC detector **75** the valve **81** would open the donor tubing and permit the RBCs to be sent to the donor. The valve **81** may be placed in a cassette, like cassette **15a** (shown in FIG. 5), which may provide chambers for detecting RBCs and air bubbles and which may further provide supplemental pumping means.

FIG. 6 shows a controller regulating the anticoagulant pump **77**, the valve **81**, the chuck's motor, the vent **63** and the pump **61**. The controller is connected to an encoder or tachometer to monitor the motor's speed, and is connected to a pressure transducer to measure the gas pressure being applied to the exterior side of the rotor's diaphragm. The

controller also monitors the air detector and the RBC detector. As discussed above in relation to FIG. 5, the controller may increase the gas pressure in the chuck and/or reduce the rotational speed of the chuck in order to force the blood components out of the rotor.

In this embodiment, no separate pump is required to move blood to or from the rotor (although pumps may be used). Standard peristaltic blood pumps can create a large amount of pressure or suction and therefore require special devices to protect the donor from excessive suction while drawing blood and from excessive pressure when returning blood. In this system, the draw and return pressures can be controlled exclusively by the air pressure from the chuck and therefore can be controlled and monitored much more safely and with less cost for both the equipment and the disposables. The potential for runaway blood pumps is also reduced by the system above.

The FIG. 2 rotor **2a** may also be used for recovering blood suctioned from the surgery site on a patient during an operation. This type of system is known as intraoperative salvage. A suction canister, which is attached to a hospital's wall vacuum (or which utilizes a vacuum pump in the system housing), draws blood from the patient's surgery site through a suction tube. Anticoagulant may be provided to the canister in order to prevent the blood from clotting. Normally, in the intraoperative salvage process, the suctioned blood has been diluted with saline which was used to irrigate the surgery site.

The blood that has collected in the canister is drawn from the canister through a cassette or other valving mechanism to the rotor tube **13** and finally to the rotor **2a**. Blood flow to the rotor is stopped when the desired or the available amount of blood has entered the rotor, or when it is full. (As noted above, since, in the rotor of the present invention, the processing chamber **30** has a variable volume, the rotor **2a** does not have to be filled to its capacity with blood for the process to done properly.) The

rotor **2a** is spun so as to separate the blood into its components. When the separation is complete, like the post-operative process discussed above in relation to FIG. 5, the compressor (item **61** in FIGS. 3, 4 and 6) may begin to pump compressed air into the chuck, and the rotational speed of the rotor **2a** may be reduced to a level that is high enough simply to keep the blood components separated. As discussed above in relation to FIG. 4, when the air pressure acting on the exterior of the diaphragm **31** exceeds the fluid head from the inner radius of the diaphragm **31** to the skirt of the collector **46**, fluid begins to flow from the processing area in the rotor **30** through the holes **39** in the plate **40** into the area around the collector assembly **46**, through the collector assembly **46** and out of the rotor **2a** into the rotor tube **13**.

Like the post-operative salvage system discussed above in connection with FIGS. 4 and 5, in an intraoperative salvage process, the lighter components--primarily the saline and the plasma--are the first components to be pushed out of the rotor **2a** through the rotor tube **13**. In a typical intraoperative process, these components are considered waste and are shunted by the cassette to a waste bag. After the waste components are pulled from the rotor **2a**, the remaining blood components, which now have a higher concentration of RBCs, are pushed through the rotor tube **13** and then shunted by a cassette (or other valve means) to an RBC bag. After a sufficient amount of RBCs are sent to the RBC bag, the bag is disconnected from the cassette and connected to the patient in order to return the patient's RBCs. Alternatively, a tube may be connected directly between the patient and the bag so that blood may be returned directly to the patient by gravity without removing the bag.

FIG. 7 shows the rotor **2a** of FIG. 2 with an airtight exterior shell **3a** attached and sealed to the boundary wall **10**. The use of an exterior shell makes the FIG. 2 rotor **2a**

especially convenient for use as a wound drain. In one embodiment, the shell **3a** may be removably attached to the rotor **2a**. The shell **3a** permits a vacuum to be applied to the exterior side of the diaphragm **31** (i.e., the side that does not come into contact with the blood) without placing the rotor **2a** in the chuck **4a**. A valve **68** is disposed in the shell **3a**. The valve **68** permits the shell **3a** to be attached to the hospital vacuum or a vacuum pump. A vacuum is thus introduced into the shell **3a**, and the vacuum in the shell **3a** draws blood from the wound drain. With the FIG. 7 configuration, the rotor **2a** can begin drawing blood from the wound drain as soon as the wound drain is placed in the patient--typically in the operating room--without mounting the rotor **2a** in the chuck **4a**. Later--when the patient is brought into the recovery room--the rotor **2a** can be placed in a chuck to process the drained fluid. If the shell **3a** is removable, it may be removed from the rotor **2a**, and the rotor **2a** may then be placed in the chuck **4a** shown in FIG. 3. If the shell **3a** is not removable, a different chuck may be used. Such a chuck would have means for opening valve **68** in order to permit fluid communication between the chuck and the interior of the shell **3a**. Preferably, such a chuck would provide a compressed gas in order to force fluid out of the rotor **2a**. In addition, such a chuck would also preferably be able to provide a vacuum to the interior of the shell **3a** in order to draw additional fluid into rotor **2a**. The shell **3a** also protects the diaphragm **31** from accidental abrasions.

An alternative shell **3b** is shown in FIG. 8A. This alternative shell **3b** has a core **66** that extends up from the bottom of the shell **3b** around the rotor's axis of rotation. Near the top of this core **66** is the valve **68**, which is normally closed but which may be opened for permitting either a vacuum or positive pressure to be introduced into the interior of the shell **3b**.

If the shell **3a**, **3b** remains attached to the rotor **2a** during centrifugation, the shell may be shaped so as to reduce variations in the stresses in the diaphragm **31** (like the chuck shown in FIG. 3 for example). Also, if the shell **3a**, **3b** remains attached to the rotor **2a** during centrifugation, the diaphragm **31** may be attached to the bottom of the shell and/or to the core **66**.

As shown in FIG. 8B, using a rotor having a shell **3b** with a core **66**--or a rotor like rotor **2c** shown in FIG. 20 (discussed below) having a core **116** which is part of the rigid boundary wall **10**--permits the use of a chuck **4'** that fits inside the core **66**, so that the rotor **2a** and shell **3b** may be held from the inside of the core **66**, instead of the outside of the rotor like the chucks **4a** and **4c** shown FIGS. 3 and 21. Such an arrangement permits a smaller system housing to be used, and the motor **50'** and perhaps even part of the pump **61'** may be located within the rotor's core.

FIG. 9 shows the addition of a secondary elastic wall **67** in the chuck. This secondary elastic wall **67** is held in place by clamp **69**. This secondary elastic wall is a barrier between the air in the chuck and the diaphragm **31** of the rotor and would prevent pressurized air entering the rotor's processing chamber in the event of a tear in the diaphragm **31**. Operationally, this configuration of the system would work in a manner very similar to that described above except that before blood was allowed to flow into the rotor, the pump would inflate the secondary elastic wall **67** until it completely filled the chuck. The air in the chuck would be forced out holes **71**, which are covered by one-way valves **73** to prevent air from re-entering the chuck.

FIGS. 10 and 11 show respectively a top plan view and a cross-section of a two-conduit, edge-loading rotor, which permits flow into and out of the rotor **2b** at the same time. Like the rotor **2a** shown in FIG. 2, the FIG. 11 rotor **2b** has an elastic diaphragm **31**, a plate **40** with holes **39**, and a boundary imperforate wall **10**. (Most of the boundary

imperforate wall, as in an alternative embodiment mentioned above in connection with rotor **2a**, can be substituted for with a portion of the diaphragm **31** extending over the top of the rotor and adapting the chuck to include a lid. See FIG. 35.) These portions of the rotor are spun by a chuck. Like the FIG. 2 rotor, the FIG. 11 rotor **2b** also has a collector assembly **46**, which is held in place while the rest of the rotor is spun. The FIG. 11 rotor may be modified so that the bottom rigid wall, i.e., the perforate interior wall **40**, is flat--like the perforate plate **40** shown in FIG. 2.

The FIG. 11 rotor further includes a second imperforate wall **87** (which is also referred to herein as an inlet-control structure or an imperforate interior plate) located between the top imperforate wall **10** and the perforate interior plate **40**, so as to form a channel **85** between the two imperforate walls. Like the rigid boundary wall **10**, the interior imperforate plate **87**, although otherwise imperforate, does define a central opening to permit the collector assembly **46** to pass through. This second plate **87** is also spun along with the perforate interior plate **40**, the top wall **10** and the diaphragm **31**. The rotor **2b** also has an umbrella deflector **91**, which directs the unseparated fluid along the top of the imperforate interior plate **87**. Instead of a single input/output tube **13** of the FIG. 2 rotor, the FIG. 11 rotor **2b** has an input tube **83** and a separate output tube **93**, which together with the collector assembly **46** are held in place during centrifugation while the rest of the rotor is spun.

In use, the rotor **2b** is placed in centrifuge chuck **4b**, as shown in FIG. 12. (The interior of chuck **4b** has a somewhat different shape from that of the FIG. 3 chuck **4a**. The shape of the chuck's interior may be varied depending on whether the rotor is usually filled while being spun by the chuck or while at rest.) The rotor **2b** is held in place by clamp **8**. Lip seal **36** interfaces with the rotor to form an air-tight seal. The centrifuge is turned by motor **50** and

shaft **51**. The shaft **51** has an axial through hole **53** and protrudes below the motor **50**. A rotary pneumatic seal **55** connects tubing **59** to the shaft **51** and is held stationary by fixture **57**. (Alternative means for providing substantially air-tight fluid communication between the tubing **59** and the axial through hole **53** as discussed above may be used in lieu of the rotary pneumatic seal **55**.) The tubing **59** connects the rotary pneumatic seal **55** to the compressor/vacuum pump **61** and to a controllable exhaust valve **63**. Holes **65** in the chuck core **64** allow air to flow from the compressor into the space between the chuck and the diaphragm. (As noted above in connection with the FIG. 3 chuck **4a**, channels emanating from the holes **65** may be provided in the chuck so that fluid may flow to various points adjacent the exterior of the diaphragm even when the diaphragm is fully extended.)

FIG. 13 shows the rotor **2b** spinning. Blood flows into the rotor through tube **83**, then the blood flows off umbrella deflector **91** and is channeled to the outside edge of the rotor through channel **85**. As the volume of the blood in the rotor **2b** increases, the diaphragm **31** stretches to allow the blood to fill the processing area and at some point will take on a shape shown by line **31a**. As blood enters the rotor, the air in the chuck **4b**, which is displaced by the diaphragm **31** and the blood, escapes through hole **65**, down the shaft hole **53** and out exhaust valve **63**. As more and more blood enters the rotor, the diaphragm changes shape to accommodate the blood. The diaphragm will in turn take on the shapes shown by lines **31b**, **31c** and **31d**.

In the FIG. 11 rotor **2b**, unprocessed blood or fluids can flow into the rotor **2b**, while the lighter blood elements can simultaneously flow out of the rotor **2b**. This flow pattern is similar to the flow pattern in rotors marketed by Haemonetics, Electromedics and Shiley. One distinction between those prior-art rotors and the present invention is that when it is time to harvest the heavier components from

the rotor **2b** (typically red blood cells) the compressor **61** turns on and increases the air pressure in the chuck **4b**, forcing any remaining lighter elements out of the rotor **2b** until the desired concentration of remaining products is achieved. Once the desired concentration is achieved, the remaining products can be harvested from the rotor **2b** by further increasing the air pressure in the chuck **4b**. Alternately, if the rotor **2b** is stopped, the remaining elements can be harvested with low air pressures in the chuck **4b** or even pumped out through either tube **93** or tube **83**.

A further distinction between the FIG. 11 rotor **2b** and prior-art rotors is that by controlling the air pressure in the chuck **4b** the increase in the volume of blood in the rotor **2b** can be stopped at any position such as **31a** in FIG. 13. At that time, the flow pattern of unprocessed fluids entering the rotor **2b** (via tube **83** and channel **85**) simultaneously with the lighter elements leaving the rotor **2b** (via channel **44**, collector assembly **46** and tube **93**) takes place but with a chosen rotor volume that is smaller than the rotor's maximum volume. One important advantage of this rotor **2b** and process described herein is that the variable volume of the rotor's processing chamber **30** makes it ideal for use for the intraoperative or post-operative salvage of shed blood. If the patient is small or if the blood loss has been gradual, it may be desirable to harvest the collected RBCs from the rotor **2b** before the rotor is completely full of RBCs. This cannot be done in the prior-art systems unless the operator is willing to accept a low hematocrit product. With the FIG. 11 rotor **2b**, the operator can keep the rotor's processing chamber **30** at the appropriate volume with air pressure in the chuck to suit the needs of the patient.

If the rotor **2b** is already fully expanded but there are not very many RBCs in the rotor when it is desired to harvest those RBCs, the compressor **61** is used to increase

the air pressure in the chuck **4b**, thereby forcing out the lighter waste products until the desired concentration of RBCs is achieved. The RBCs can then be harvested from the rotor **2b** by one of the means described above.

Another important advantage of this rotor **2b** and system is that its variable volume makes it ideal for use in blood apheresis. Some apheresis blood collections such as platelet and RBC collections work better or faster if blood entering the rotor is forced to the edge of the rotor. These apheresis blood collections can be performed with less extracorporeal volume and therefore on smaller donors and from donors who are sensitive to blood volume changes. The extracorporeal volume is controlled by keeping the rotor's processing chamber **30** at the appropriate volume with air pressure in the chuck **4b**.

The FIG. 11 rotor **2b** may be used in a system, such as that shown in FIG. 14 for performing RBC apheresis. With this system, whole blood is drawn from the donor through tube **17'**, preferably with the assistance of a pump **95** to the cassette **15b**, which directs the whole blood to the input tube **83**. With the introduction of fluid into the rotor **2b**, the diaphragm **31** is distended in much the same way as shown in FIG. 13. Usually, the rotor **2b** is spinning while it is being filled. After separation is complete, while the rotor is still spinning, and while blood is still being introduced into the rotor **2b**, the plasma--the lighter blood component--can be forced, by air pressure in the chuck, through the plate's holes **39** (see FIG. 13) to the collector assembly **46** to the output tube **93** to the cassette **15b** (see FIG. 14) and finally to the tube **101** for returning the plasma back to the donor. A pump **103** may be used to assist in the return of plasma to the donor. Thus, the plasma may be returned to the donor while whole blood is still being taken from the donor and introduced into the rotor.

Once the desired volume of the processing chamber is established, the air pressure may be used to keep the volume

constant; thus, the incoming whole blood will force out a corresponding volume of plasma. Preferably, however, the volume may be allowed to grow so that the volume of plasma exiting the rotor is the same as the volume of the plasma component of the whole blood entering the rotor. At some point the rotor's processing chamber may become filled with RBCs. At that point the pump **95** is turned off so that no more blood is drawn from the donor, and the RBCs are forced out of the rotor **2b** through the cassette into a line **22** connected to an RBC bag.

By using the FIG. 11 rotor **2b**--or the rotor **2d** shown in FIG. 23 and described below--for RBC apheresis, one does not have to wait for the rotor's processing chamber to be filled with whole blood before returning plasma to the donor. Likewise, the chamber does not have to be filled with RBCs before they can be forced out of the rotor's processing chamber through the cassette **15b** and into the RBC bag. This flexibility permits the plasma to be returned to the donor gradually, while the donor is still giving blood. This gradual return permits the plasma to be re-introduced to the donor over a longer period of time. This is desirable because the plasma contains most of the anticoagulant, for example, citrate. Citrate can cause an adverse reaction in some donors, especially if introduced into the donor too quickly. The rotor **2b**, **2d** also permits the processing of any given amount blood up to the maximum amount permitted by the rotor **2b**, **2d**. As noted previously, prior-art systems using fixed-volume rotors require that a fixed amount of blood be processed. With the variable-volume rotors **2b**, **2d**, a donor may be allowed to donate less than a standard unit of RBCs, which is advantageous in many situations, such as children and other donors with low body weight. These rotors **2b**, **2d** may also be used to minimize donor reactions caused by both the total amount of extracorporeal volume and the rate of change of extracorporeal volume.

FIG. 15 schematically represents a particular RBC apheresis process using rotor **2b**--or rotor **2d**. This process

permits the collection of up to two-units of RBCs from a donor quickly and safely. (Donor monitoring and safety systems, such as bubble detection, are not shown in the FIG. 15 schematic for clarity. Likewise, a controller is not shown in FIG. 15. A digital data processor is preferably used for monitoring and controlling the various components of the systems in all of the various processes set forth herein.) Anticoagulant is pumped by pump **105** from bag **B1** down to needle **N1** which has been inserted in the donor's vein. The anticoagulant mixes with the blood at the needle hub and both are pumped by pump **95** to the rotor **2b**--or alternatively rotor **2d**. The rotor's processing chamber volume is initially held small by air pressure in the chuck, say at a volume of 100 ml. When plasma starts to emerge into tube **93**, the air pressure in the chuck is slowly decreased (by venting air through vent **63** shown in FIG. 13) thereby allowing the rotor's processing chamber to expand at the rate that the RBCs are entering the rotor as part of the whole blood. As the anticoagulated plasma emerges from the rotor, it flows to bag **B2** and then is pumped back to the donor by pump **103** via needle **N2** inserted in a different vein.

This procedure keeps all the RBCs in the rotor but continues to force the anticoagulated plasma out of the rotor **2b** so it can be returned to the donor on a continuous basis. The process continues until the desired amount of RBCs have been collected or until the rotor is full of RBCs. The air pressure in the chuck can then be increased by turning on compressor **61** (see FIG. 13) to achieve the desired concentration of RBC's. The RBCs are then harvested from the rotor and stored in bags **B3** and **B4** by stopping the rotor, maintaining the proper air pressure to push the RBCs out of the rotor **2b** and switching valve **81** to open the passageway to the bags **B3** and **B4**. If desired, RBC preservative solutions can be provided in bags **B3**, **B4**. This procedure results in plasma being returned to the donor

sooner than is possible with the fixed-volume prior-art rotors and results in plasma being returned to the donor in a continuous stream. Therefore, the peak extracorporeal blood volume is lower and there is less extracorporeal volume fluctuation for the donor, thereby reducing the potential for adverse reactions.

One important factor in RBC apheresis is how long the donor is connected to the system. This factor is particularly important in mobile blood collections where donors are only available for a limited time, such as during blood drives at factories. The system shown in FIG. 15 is particularly fast because the plasma is being returned at the same time whole blood is being drawn and there are no stoppages to empty the rotor until the process is complete and the donor is disconnected from the system.

The plasma in the blood pathway of this FIG. 15 system is always in motion. In addition, the volume of the blood pathway filled with anticoagulated plasma is small, and the length of time any particular drop of plasma is out of the body is short and predictable. Therefore, since there is less propensity for the plasma to clot, the amount of citrate in the anticoagulant may be reduced from standard levels without danger of the plasma starting to clot. With less citrate in the system, the potential for donor citrate reactions is reduced further. (As noted above, the potential for citrate reactions is also reduced because, with the present invention, the anticoagulated blood may be returned to the donor over a longer period of time.)

Another advantage of this system is that it will allow the collection of RBCs from small donors and/or patients whose size or medical condition prevents them from donating with existing systems. Unlike the traditional bag systems and systems that use a fixed volume rotor, the FIG. 15 system causes only a low extracorporeal volume and can be stopped after any amount of RBCs have been collected. Further, the RBCs can be harvested as RBC concentrate. The operator simply stops the expansion of the diaphragm after

the appropriate amount of RBCs have been collected, increases the air pressure in the chuck slightly to concentrate the cells and then harvests the RBCs.

It is sometimes desirable to replace the blood volume given by the donor. This can be accomplished simply in this process by pre-filling bag **B2** with an appropriate amount of an acceptable solution, such as 500 ml of saline. This replacement fluid is then simply reinfused along with the plasma.

Alternatively, the citrate required for proper anticoagulation can be further reduced and the donor can be kept isovolemic simultaneously by putting the replacement fluid such as saline or another injectable solution in bag **B1** along with the anticoagulant and increasing the ratio of anticoagulant/saline to blood by adjusting the relative rates of pumps **105** and **95**. Adding saline to the blood path in this manner will dilute the plasma, and the saline will travel intermixed with the plasma through the system. Diluting plasma with saline extends the clotting time so that less total citrate is needed to keep the plasma from clotting in the short time the plasma is outside of the donor's body. The same saline thus performs two functions: first, by helping to anticoagulate the plasma and, second, by being the replacement fluid as well. This arrangement has the additional advantage of reducing the percentage of plasma trapped in the RBCs because the plasma is diluted by the saline before it is trapped by the RBCs. The amounts of white blood cells and platelets trapped in the packed RBCs are also reduced because the saline provides a type of elutriation to wash them out with the plasma.

A variation of the above system that requires only one needle but has a longer processing time is achieved by connecting the tube from pump **103** into the tubing between needle **N1** and pump **95**. With this tubing arrangement and safeguards to insure both pumps are never on at the same time, the system can alternate between drawing blood with

pump **95** and returning blood with pump **103** through the same needle **N1**.

In the FIG. 11 rotor **2b**, the spinning top wall **10** and interior plate **40**, as noted above, separate the spinning diaphragm **31** from the non-spinning input **83** and output **93** tubes and the top of the collector assembly **46**. It is important to keep rigid members that spin with the diaphragm **31** between the diaphragm and the non-spinning components of the rotor, so as to prevent the diaphragm **31** from touching a non-spinning component during centrifugation. (Some embodiments of the rotor do not have a fixed section and therefore do not have to use their interior walls to perform this function. See for example FIG. 28, discussed below.) In addition to preventing the diaphragm **31** from touching the rotor's fixed portion, the plate **40** also serves the important function of controlling flow out of the processing chamber to the collector assembly **46**. The interior walls **40** of the rotors **2a**, **2b** shown in FIGS. 2 and 11 (and of the rotors shown in FIGS. 20, 23, 28 and 39, which are discussed below) extend to the periphery of the processing chamber and thus keep a channel **44** open between the periphery of the interior wall **40** and the collector assembly **46**, no matter what the position of the diaphragm **31** is. If the interior wall **40** did not extend substantially all the way to the rotor's periphery and did not have holes **39** at the rotor's periphery, the fluid at the periphery of the spinning processing chamber **30** could be prevented from flowing to the collector assembly **46** by the diaphragm **31**.

FIG. 16 shows an example of a rotor with a perforate interior plate **40a** and a rigid imperforate interior plate **87a** that do not go all the way to the edge of the rotor. In the FIG. 16 rotor, the imperforate interior plate **87a** and the perforate interior plate **40a** shown extend about halfway to the edge of the FIG. 16 rotor as an example. These perforate and imperforate interior plates (walls) could extend to any desired radius, depending on the desired

application of the rotor. With this configuration of interior plates, the channel between the perforate interior plate **40a** and the imperforate interior plate **87a** remains open during centrifugation as long as the volume of the processing chamber is greater than a defined amount. Once the processing-chamber volume drops below that amount, the diaphragm **31** blocks off further flow out of the processing chamber into the channel. This may be desirable during certain processes involving biological fluids. The imperforate plate **87a** does not have to have the same radius as the perforate interior wall **40a**. For instance, the imperforate interior wall may extend all the way to the rotor's periphery while the perforate interior wall extends only halfway to the periphery. Such a configuration would allow the rotor to be filled from the outer edge of the imperforate interior wall.

FIG. 17 shows another alternative rotor with a different configuration of interior plates **87a**, **87b**, **40b** and **40c**. In this rotor, fluids enter the processing chamber at different radii depending on how full the rotor is; likewise, fluids leave the rotor at different radii depending on how empty the rotor is.

As shown in FIG. 18, the interior walls **87**, **87'**, **40**, **40'** can be stacked and connected to inlets **83**, **83'** or outlets **93**, **93'**, so that fluids can enter or leave the processing chamber at different points. In the FIG. 18 rotor, fluids can enter and leave the rotor's processing chamber from multiple radii at the same time. Imperforate plate **87** defines one radius--near the rotor's periphery--where fluid enters the processing chamber, and imperforate plate **87'** defines a second, intermediate radius where fluid enters the processing chamber. In the FIG. 18 rotor, like the FIG. 16 rotor, a perforate wall **40'** does not extend all the way to the periphery of the processing chamber. Thus, the FIG. 18 rotor, like the FIG. 16 rotor, can prevent further flow over the top of the interior wall **40'** to a

collector assembly at a particular point during emptying. The rotor in FIG. 18 has two inlets **83**, **83'** and two outlets **93**, **93'** allowing a multiplicity of flow patterns depending on how full the rotor is and which tubes connected to the inputs and the outputs are clamped or open.

Another way to use interior plates to accomplish the desired flow patterns is to strategically place holes in the plates. For instance, in FIG. 19A the fluid first exits the rotor in the middle through a set of holes **39'**, all of which are at a constant radius, even if the rotor is completely full. This configuration permits an intermediate-density fluid, such as platelets, to be emptied from the processing chamber while the lightest and heaviest fluids remain in the rotor.

FIG. 19B shows the FIG. 19A rotor mounted in a chuck **4b'**, which is similar to the chuck shown in FIG. 12. Anticoagulated whole blood may be pumped into the rotor through inlet **83**, while the chuck **4b'** and the rotor are being spun. Imperforate plate **87** directs the incoming whole blood towards the periphery of the rotor. The rotor is filled with blood, so as to occupy the entire space available in chuck **4b'**, causing plasma to be forced out of the rotor first, through holes **39'**. When a sufficient amount of RBCs is in the rotor, the platelet layer lines up with holes **39'**. One way for determining when the platelet layer lines up with holes **39'** is an optical detector, which detects the buff color of the platelet layer.

Once the platelet layer is lined up with holes **39'**, a valve (not shown) connecting the outlet **93** to a platelet-collection bag (also not shown) is opened. Compressor **61** then pumps air into the chuck **4b'**, causing the platelets to be forced through holes **39'**. As some of the platelets are forced out of the rotor, some of the plasma may be able to escape past the platelets through holes **39'**. However, the escaping plasma will entrain the platelets nearer the axis of rotation. If the platelet layer begins to move radially

outward, away from the axis of rotation and away from holes **39'**, more whole blood may be added to the rotor so as to reposition the platelet layer directly under the holes **39'**.

A significant advantage of this platelet-collection process is that the plasma used to push the platelets out of the rotor comes from the center of the rotor instead of the rotor's periphery. Thus, the plasma pushes out the lightest platelets, which are the youngest platelets and which have the least amount of white blood cells intermixed with them. Prior-art platelet collection processes use fixed-volume rotors and use plasma coming from the periphery of the rotor to push platelets out of the rotor.

The system shown in FIG. 19C is similar to the system shown in FIG. 19B, except that the rotor has additional holes **39"** located at a smaller radius than holes **39'**. In using this rotor in the platelet collection process, the plasma flows out of holes **39"** as the rotor fills with RBCs. When the platelets are lined up with holes **39'**, whole blood flow into the rotor is stopped. Air is pumped into the chuck **4b'** causing plasma to flow through holes **39"** until the diaphragm covers the holes **39"**. When holes **39"** are covered, the platelets, which are lined up with holes **39'**, are forced out through holes **39'**.

FIG. 19D shows a system that permits platelet collection at various extracorporeal volumes. Sets of holes **39a**, **39b**, **39c**, **39d** and **39e** are arranged in circles and are spaced by some distances, such as 0.1 to 0.2 inches. There may be more or fewer sets of holes as desired. All of the holes in each set are located at the same radius. Platelets may be collected when there are sufficient RBCs in the rotor to position the platelets at any of the sets of holes.

For example, once the rotor shown in FIG. 19D is filled so that the platelets are located directly under holes **39b**, air may be pumped into the chuck **4b'** to force the plasma, which is located inside the layer of platelets, out first through holes **39e** (assuming that the rotor was completely

filled before the platelets became located under holes **39b**), then holes **39d** and **39c** in turn. (The volume of the processing chamber may, of course, be set at less than its maximum volume by maintaining a positive air pressure in the chuck **4b'**; in such a case, the plasma would first be forced out through the holes at the smallest radius not covered by the diaphragm.) Once sufficient plasma has been forced out of the rotor so that all the holes located inside of the layer of platelets--holes **39c**, **39d** and **39e** in the example--are covered by the diaphragm, the platelets are forced out of the rotor through holes **39b**.

FIG. 19E shows a rotor that has as an outlet-control structure an imperforate interior wall **40"**, instead of a perforate interior wall (like plate **40** discussed above). This rotor has only one conduit **13**, which serves both as the inlet and outlet, at different times, to the rotor's processing chamber. This rotor may be used with a chuck, such as that shown in FIG. 3, or with an exterior shell, such as those shown in FIGS. 7 and 8A. Using an imperforate interior wall **40"** in this way permits the collection of separated fluid components having the greatest density first, before the collection of intermediate density and lighter density components. After the processing chamber has been filled with desired amount of blood (or other biological fluid) and the blood has been separated, the air pressure against the exterior of the diaphragm **31** is increased or the rotation of the rotor decreased so as to force the concentrated RBCs, which are located furthest away from the rotor's axis of rotation, past the outer edge of the imperforate interior wall **40"**. Since there may initially be separated blood components in the channel **44** between the boundary wall **10** and the interior wall **40"** after separation, there may be a small amount of lighter fluid components exiting the rotor before the concentrated RBCs. After this small amount of lighter blood components--plasma, platelets--are forced out of the channel **44**, all the RBCs

may be collected before the remaining lighter blood components reach the periphery of the interior wall **40"**.

Thus, different configurations of the inlet-control and outlet-control structures allow rotors to be optimized for different types of blood-component collection processes, such as plasma collection or platelet collection, or other biological-fluid-component collection processes. In general, the placement of holes in the interior plates and the diameter of the plates can be manipulated in order to accomplish the desired flow patterns out of and/or into the rotor. As is discussed below in connection with FIGS. 30-36, tubes may be used instead of plates (e.g., plates **40**, **40'**, **40"**, **87**, **87'**, **87a** and **87b**) to achieve the desired flow patterns into and/or out of the rotor's processing chamber. It will be appreciated that various types of outlet-control structures, including tubes and plates that permit fluid to flow out of the processing chamber at a selected radius or selected radii (like the plates **40** shown in FIGS. 19A-19E), may be used with other types of rotor designs, such as the rotors shown in FIGS. 20 and 23.

For some of the blood-processing procedures which have been discussed in this application, such as post-operative and intraoperative salvage, and RBC and plasma apheresis (see for example the processes represented in FIGS. 6 and 15), it is desirable that the interior plates **40** have holes **39** located at varying and closely spaced distances from the center of the plate **40** to its periphery. This placement of holes **39** ensures that all of a lighter fluid element (e.g., plasma) is forced out of the processing chamber **30**, before a heavier fluid element (e.g. RBCs) begins to be forced out.

FIG. 20 shows an alternative rotor **2c**, which may be used in much the same way as the rotor **2a** shown in FIG. 2. Like the FIG. 2 rotor **2a**, the rotor **2c** shown in FIG. 20 allows fluids to flow in or out of the rotor in only one direction at a time. The boundary wall **10** of rotor **2c** includes a top portion **108**, a circumferential portion **110**

and a bottom portion **112**, so that the boundary wall **10** forms a shell surrounding the processing chamber **30**. Note that the shell formed by the circumferential **110** and bottom **112** portions of the FIG. 20 rotor **2c** differ from the exterior shell **3a** shown in FIG. 7 and the shell **3b** shown in FIG. 8A. The FIGS. 7 and 8A shells **3a** and **3b** do not directly touch the blood in the processing chamber. The circumferential **110** and bottom **112** portions of wall **10** in FIG. 20 do touch the blood in the processing chamber **30**.

The top portion **108**, circumferential portion **110** and bottom portion **112** of the boundary wall **10** may be curved, so that the rotor is generally ovoid and the borders between the various wall portions are not distinct. Shaping the boundary wall **10** in this way may reduce the amount of stress on the diaphragm **31** (in much the same way that the shaping of the interior of chuck **4a** shown in FIG. 3 reduces stresses in the diaphragm, as discussed above).

The FIG. 20 rotor **2c** also includes central core **116**. The boundary wall **10** and the core **116** are preferably made of rigid plastic pieces joined together. At the top of the rotor **2c**, there is a collector assembly **46** attached to a tube **13** connected to the rest of the disposable blood processing set (e.g., a cassette and additional tubing). The collector assembly **46** also interfaces with a rotary seal **48**, like the rotary seals discussed in connection with the FIG. 2 and FIG. 11 rotors **2a**, **2b**. The rigid core **116** of rotor **2c** is covered by an elastic balloon-shaped diaphragm **31**, which is held in place with an air-tight seal by a clamp **122**. (In alternative embodiments, the diaphragm may be attached to any point on the bottom wall **112**, or even to the circumferential wall **110**. If the membrane is attached near the top of the circumferential wall, the rotor becomes very similar to the rotor **2a** and shell **3b** combination of FIG. 8A. In such a rotor, the circumferential and bottom walls would not be considered boundary walls, since they would no longer

come into contact with the blood being processed.) Between the diaphragm **31** and the collector assembly **46** is a plate **40**. As in the previously discussed rotors **2a**, **2b**, the plate **40** prevents the diaphragm **31** from touching the collector assembly **46**. The plate **40** is held away from the upper part **108** of the boundary wall **10**, so as to form a passage **44** between the boundary wall **108** and the plate **40**. The plate **40** preferably contains many, preferably small, holes to permit fluid to flow into the passage **44** from almost any point along the plate **40**. In a wall within the core **116** separating the core into interior and exterior portions is a pressure-supply port **120**, which is blocked by a frangible diaphragm during storage.

FIG. 21 shows the rotor **2c** being held in a chuck **4c**, which is turned by a motor **50**. As noted above in relation to the rotor/exterior-shell arrangement shown in FIG. 8A, the chuck and motor may be made small enough to fit inside core **116**, below pressure-supply port **120**; thus the chuck would hold the rotor **2c** from inside the core **116** instead of from outside the circumferential wall **110** as shown in FIG. 21. The collector assembly **46** is held stationary and in the proper alignment by brace **11**. The shaft **51** projects up past the chuck **4c** and narrows into a thinner section **126** (a nozzle), which penetrates the frangible diaphragm on the pressure-supply port **120** and makes an airtight seal. The shaft **51** has an axial through hole and protrudes below the motor **50**. A rotary pneumatic seal **55** is attached to the shaft **51** and is held stationary by fixture **57**. The pneumatic rotary seal **55** is connected by tubing **59** to the compressor/vacuum-source **61** and to a controllable exhaust valve **63**.

FIG. 22 shows the rotor **2c** spinning and partially full. In operation, the motor **50** spins the rotor **2c**. The diaphragm **31** is inflated by the compressor **61** until it fully occupies the cavity **114** defined by the plate **40**, the core

116 and the boundary wall's circumferential 110 and bottom 112 portions. The inflated diaphragm 31 thus expels all of the air previously in the cavity 114 into the passage 44 and collector assembly 46 and on through a filter in the disposable set out to the room atmosphere. This reduces to its minimum the volume of the processing chamber 30, which is defined by the boundary wall 10 and the diaphragm 31. Donor blood, shed blood or another type of biological fluid then is allowed to flow into the rotor from the rest of the disposable set through tube 13 and collector assembly 46. The blood is propelled by centrifugal force towards the perimeter of the rotor 2c. As more blood enters, it continues to be propelled to the perimeter eventually flowing through the holes in the plate into the cavity 114 defined by the boundary wall 10, the core 116 and the plate 40, thereby increasing the volume of the processing chamber 30. As blood enters the processing chamber 30, the diaphragm 31 slowly collapses around the core 116, and the air between the diaphragm 31 and the core 116 is allowed to escape through exhaust valve 63.

Blood flow into the rotor 2c is stopped when the desired or available amount of blood has entered the rotor 2c or when the cavity 114 is full. The blood is subjected to the centrifugal force as long as is appropriate to separate the various components. When the separation is complete, the compressor 61 begins to re-inflate the diaphragm 31.

The manner of processing blood in the FIG. 20 rotor 2c is very similar to that of the FIG. 2 rotor 2a. When the air pressure acting on the side of the diaphragm 31 opposite the blood exceeds the pressure from the radius of the diaphragm 31 to the skirt of the collector assembly 46, fluid begins to flow from the cavity 114 through the holes in the plate 40, into the passage 44 to the collector assembly 46 and out of the rotor 2c into the rest of the processing set. This fluid may be diverted to a specific container or returned to a donor depending on the intention

of the process and the specifics of the processing set. The blood element with the lightest specific gravity first flows out of the cavity **114** through the holes in the plate at the smallest radius not yet covered by the diaphragm **31**. Each blood element in turn by specific gravity will flow out of the rotor **2c** and can be diverted as desired. The process of emptying the rotor **2c** can be stopped at any time by stopping the compressor **61** from increasing the air pressure on the diaphragm **31** (while keeping the chuck's rotational speed constant).

If the rotor **2c** is processing blood, one likely place to stop might be when the diaphragm **31** touches the RBC layer and another might be when the rotor **2c** is empty. As noted with the FIG. 2 rotor **2a**, this cycle can be repeated as desired or, if washing of the blood components left in the rotor **2c** is desired, other fluids can be allowed to flow into the rotor **2c** and back out again by inflating or deflating the diaphragm **31** and manipulating valves and/or tubes in the processing set. At the end of the last cycle, the diaphragm **31** can be inflated to the proper position to obtain the desired hematocrit in the final product. As noted above, it may be desirable to change the rotor speed at different times while the rotor **2c** is filling or emptying in order to achieve the most advantageous combination of centrifugal force for separation and air pressure inside the diaphragm **31** required to overcome the current fluid head.

The core **116** of the FIG. 20 rotor **2c** serves a similar purpose to the chuck core **64** of the chuck **4a** shown in FIGS. 3-4, 9 and 12-13. The core **116** helps shape the diaphragm **31** when the processing chamber **30** is at its largest volume (which in the FIG. 20 rotor **2c** is when the diaphragm **31** is its relaxed position, unlike the FIG. 2 rotor **2a**, in which the diaphragm is in its relaxed position when the processing chamber **30** is at its lowest volume). The core **116** ensures that, when the processing chamber **30** is at its largest volume, there are holes **39** located at the innermost radius

of the processing chamber **30**. (It will be appreciated that by shaping the core **116** so that the top of the core **116** covers the plate's center **37**, and so that the diameter of the top of the core **116** is not greater than the diameter at any other point of the core **116**, one can ensure that all of the lighter fluid elements can be emptied out of the rotor **2c** first, even when the processing chamber **30** is at the greatest volume permitted by the boundary wall **10** and the core **116** of the FIG. 20 rotor **2c**.)

FIG. 23 shows an alternative rotor **2d**, which can be used in much the same way as the rotor **2b** shown in FIG. 11. Like the FIG. 11 rotor **2b**, the rotor **2d** shown in FIG. 23 permits fluids to flow in and out of the rotor at the same time. The rotor **2d**, like the FIG. 20 rotor **2c**, has a boundary wall **10** that surrounds the processing chamber **30** and that is preferably made of rigid plastic pieces joined together. At the top of the rotor **2d**, there is a collector assembly **46** attached to tubes **83**, **93** connected to the rest of the processing set. The collector assembly **46** interfaces with a rotary seal **48**. The passage between the skirts of the collector assembly **46** connect with tube **93**. The fixed portion of rotor **2d** has an extension tube **130**, which connects tube **83** with the bottom of the rotor **2d**. The rigid core **116** is covered by a sleeve-shaped elastic diaphragm **31**, which is held in place with a air-tight seal by the inner portion of a lower, imperforate interior wall **134** and the inner portion of the (upper) plate **40**. The lower interior wall **134** is shown in FIG. 23 as extending to the periphery of the cavity **114**, but in an alternative embodiment, a smaller-diameter lower interior wall **134** may be used, or the lower interior wall may be left out entirely except for the inner ring portion that is used to clamp the bottom of the diaphragm **31**, or a perforate plate, like item **134'** in FIG. 24, may be used.

The rigid core **116** is attached to the air-introduction area **136** and has one or more generally vertical holes in it that act as air conduits from the air-introduction area **136** to the space between the diaphragm **31** and the rigid core **116**. There are gaps in the rigid core **116** below the lower interior wall **134** and above the air-introduction area **136** that allow blood to flow from the extension tube **130** towards the perimeter of the rotor **2d**. The outer wall of the air-introduction area **136** has a pressure-source port **120** covered with a frangible diaphragm.

FIG. 25 shows the rotor **2d** being held in a chuck **4d**. The collector assembly **46** is held stationary and in proper alignment by brace **11**. The shaft **51** projects up past the chuck **4d** and narrows into a thinner section **126**, which penetrates the frangible diaphragm covering the pressure-source port **120** and makes an airtight seal with the port **120**.

FIG. 26 shows the rotor **2d** spinning and partially filled with fluid and with the diaphragm **31** partially inflated. The motor **50** spins the rotor **2d** at the proper rate. The process may be started with the diaphragm **31** deflated. Blood or other fluid flows into the rotor **2d** from the rest of the processing set through tube **83** and extension tube **130**. When the blood touches the bottom of the rotor **2d** it is propelled by centrifugal force towards the perimeter of the rotor **2d** and into the processing area. As blood enters the rotor **2d**, the air in the processing chamber **30** exits through the collector assembly **46** and tube **93** to a holding container in the processing set.

If it is not desired to process a full rotor of blood, the diaphragm **31** can be inflated by compressor **61** when the desired volume of blood has entered the rotor **2d**. The diaphragm **31** is inflated until it fills the unwanted rotor volume **138**. Operation of the rotor **2d** can then continue as normal but with a smaller-volume processing chamber **30**.

When the processing chamber **30** is full of blood (with or without the diaphragm **31** inflated), the flow of blood into the rotor can continue through tube **83** and extension tube **130**. This new blood simply displaces the elements of blood in the processing chamber **30** with the lowest specific gravity. The elements with the lower specific gravity flow out through the collector assembly **46** and tube **93** to be diverted as desired by the processing set.

The extension tube **130**, like the interior imperforate plate **87** of the FIG. 11 rotor **2b**, introduces the unprocessed whole blood into the processing chamber **30** at a point spaced away from where the separated blood components exit the chamber **30**. If the unprocessed whole blood was introduced into the chamber **30** at a point too close to the point where the separated blood components exit the chamber **30**, some unseparated whole blood may be drawn out of the chamber **30** with the separated blood components.

In order to wash RBCs, wash solution may be introduced through tube **83** and extension tube **130**. At the end of the process, the diaphragm **31** can be further inflated to push out remaining wash fluid thereby increasing the hematocrit of the final product.

At the end of the cycle, the air between the diaphragm **31** and the core **116** is vented to exhaust valve **63** and the rotor **2d** is stopped. As shown in FIG. 27, the blood remaining in the processing chamber **30** falls to the bottom of the rotor **2d** and is pumped out through the extension tube **130** and tube **83** and replaced by the previously collected air.

This cycle may be repeated as desired. As discussed above in connection with the other rotors, it may be desirable to change the rotor speed at different times in order to achieve the most advantageous combination of centrifugal force for separation and air pressure inside the elastic wall member required to overcome the current fluid head.

In the modified version of the FIG. 23 rotor shown in FIG. 24, the imperforate interior plate **40"** may be substantially imperforate so that fluid can only exit the processing chamber **30**, **114** at the periphery of the chamber. The lower interior wall may be perforate. Whole blood may be introduced into the processing chamber through an extension tube, so that the whole blood emerges into the processing chamber near the rotor's axis of rotation. Concentrated RBCs may be collected from the periphery of the processing chamber. The plate **40"** of the FIG. 24 rotor may be modified so that intermediate-density blood components, e.g., platelets, may be collected. (See the discussion above regarding FIGS. 19A-19D.)

FIG. 28 shows a rotor **2e** having a central port **163** that rotates with the body of the rotor during centrifugation. The rotor **2e** can serve both as the reservoir for collecting the blood collected by vacuum (e.g., from a wound drain, i.e., post-operative salvage) and as the centrifugal processing chamber. The rotor **2e** consists of a rigid boundary wall **10** and central core **116** made of rigid plastic pieces joined together. In the center at the top of the rotor **2e**, there is a port **163** attached to a tube **165** which terminates in a luer-type connector **167**. The rigid core **116** is covered by an elastic balloon-shaped diaphragm **31**, which is held in place with an air-tight seal by a clamp **122**. Between the diaphragm **31** and the central port **163** is a plate **40**. In the wall separating the inner and outer portions of the core **116** is a pressure-source port **120** covered with a frangible member. The pressure-source port **120** may be used to connect the rotor to a vacuum source, so that a vacuum may be applied to the diaphragm during the collection of blood. Pressurized gas may also be applied to the diaphragm through the pressure-source port **120** so as to force blood components out of the rotor.

Once the desired amount of blood has been collected in rotor **2e**, the vacuum pulling the blood into the rotor **2e** is

discontinued, and the collected blood may then be processed. The rest of a disposable processing set, such as that shown in FIG. 28, may be connected to the rotor's connector **167**. For washing or concentrating the collected blood, the rotor **2e** is placed in a chuck as shown in FIG. 28. As with the chuck **4c** shown in FIG. 21, a thin section **126** of the shaft **51** penetrates the frangible member on the rotor's pressure-source port **120** and makes an airtight seal with the port **120**.

In a variation of the systems discussed above (such as the systems shown in FIGS. 5 and 14), the tubing **170** leading from the rotor **2e** may contain the rotary seal **148**, instead of a rotary seal being incorporated into the rotor. Alternatively, a skip-rope system, such as those described in U.S. Patent Nos. 4,151,844 to Cullis et al., 4,283,004 to Lamadrid, 4,734,089 to Cullis, and 4,900,298 to Langley, may be used. (A skip-rope system has the effect of untwisting the tubing connected to the rotor as the tubing is being twisted by the spinning rotor. The skip-rope system results in the tubing having net zero twist, and thus the tubing can be directly attached to both the spinning rotor and the stationary portion of the processing set.)

The tubing **170** in the disposable processing set shown in FIG. 28 branches into three tubes, one of which leads to a bag of saline (which is the wash solution), while another tube leads to the waste bag and the third tube leads to the product bag (where the processed cells are stored). The rotary seal **148** is held stationary and in proper alignment by fixture **11b**. (Since the rotary seal **148** is separated from the body of the rotor **2e** by tube **165**, the outlet-control plate **40** in this rotor **2e** does not serve the purpose of protecting the diaphragm **31** from being abraded by a non-rotating portion of the rotor. The plate **40** still serves the purpose of ensuring the proper flow of the separated fluid elements out of the rotor **2e** when the rotor is being emptied.)

To process the blood in the rotor **2e**, the motor **50** spins the chuck and rotor **2e**. When separation of the blood components is complete, the compressor **61** begins to inflate the diaphragm **31**, so as to cause the fluid to flow through the holes in the plate **40**, through the passage **44** and out of the rotor **2e** into the rest of the disposable processing set. The blood element with the lightest specific gravity (the plasma, irrigation fluid, anticoagulant, etc.) is forced out of the rotor first and may be diverted to the waste bag by a valve **174**. Typically, the process of emptying will be stopped when the diaphragm **31** touches the RBC layer.

At this time, if the user wants to wash the RBCs before concentrating them, the speed of rotation of motor **50** and rotor **2e** is reduced to a slow speed. Saline from the saline bag is directed by valve **174** into the rotor **2e**. When the rotor **2e** is sufficiently full of the saline wash solution, the motor **50** alternately goes forward and backwards to mix the wash solution and the cells. After sufficient mixing, the motor **50** goes forward and gains speed up to its processing speed. In a manner similar to that described above, once the blood is fully separated, the diaphragm **31** is inflated, pushing the used wash solution out into the waste bag. When the diaphragm **31** touches the RBC layer or when sufficient wash solution has been removed to reach the desired final hematocrit, the final emptying process begins. As RBCs emerge from the rotor **2e**, they are diverted by valve **174** to the product bag. This process continues until the rotor **2e** is empty.

If the user does not want to wash the blood collected in the rotor, the steps of introducing saline into the rotor **2e**, washing the cells, centrifuging and forcing out the used saline may be omitted. As with the processes previously discussed, it may be desirable to change the rotational speed at different times while the rotor is emptying in order to achieve the most advantageous combination of

centrifugal force for separation and air pressure on the diaphragm **31** to overcome the current fluid head.

In order to draw fluid into the rotor **2e**, the elastic diaphragm may be used to create the vacuum. Prior to attaching the port **163** to the tubing leading to the patient, the diaphragm is inflated by a source of compressed air, such as pump **61**. (FIG. 29 shows the diaphragm in its relaxed position **31e** and in its inflated position **31f**.) A compressor may be used to inflate the diaphragm to position **31f**, and the air in the interior of the rotor **2e** is vented to atmosphere through port **163**. After the diaphragm **31** is inflated to its maximum diameter, port **163** is attached by means of a tube to a patient, and the compressor **61** is turned off. The air on the core **116** side of the diaphragm **31** is vented to atmosphere--through vent **63**, if the rotor is mounted in a chuck as shown in FIG. 28. The vacuum caused by the stretched, resilient diaphragm (shown by line **31f** in FIG. 29) trying to resume its natural shape (shown by line **31e** in FIG. 29) causes blood to flow from the patient into the rotor **2e**.

After a vacuum has been pulled on the diaphragm, the vacuum source can be turned off or even disconnected until sufficient blood has flowed into the rotor to reduce the vacuum below an acceptable level. This would allow the patient to be transported (for example between the operating room and the recovery room) without being attached to a vacuum source.

FIG. 29 shows an inexpensive and simple means of providing compressed air to inflate the diaphragm and a vacuum to assist deflating it. The rotor **2e** is attached to spring bellows **180** which incorporates a calibrated spring **182**. The bellows **180** and the rotor **2e** are supported by legs **184**. To inflate the diaphragm **31e**, the operator squeezes the spring bellows **180**. After the patient is connected to port **163** of rotor **2e**, the operator allows the spring bellows **180** to re-expand under the force of the spring **182** thereby

creating the vacuum assist for the inflated diaphragm **31f** for pulling blood into the rotor **2e** from the patient.

The rotor **2c** shown in FIG. 20 can also be used to collect blood from a wound drain, in much the same way as the rotor **2e** of FIGS. 28 and 29. A spring bellows similar to the one shown in FIG. 29 can also be adapted for providing a vacuum to the diaphragm of the rotors **2a** of FIG. 2, or for supplementing the vacuum in the rotor/shell combinations shown in FIGS. 7 and 8A.

FIG. 30 shows an alternative rotor according to the present invention using a set of tubes **190** extending from the top wall **191** of the rotor. This rotor, unlike all of the previously discussed rotors, does not have an interior wall--i.e., a wall (plate) both sides of which come into contact with the blood or other biological fluid being processed. The set of tubes **190** all join together into a common tube **165**, through which fluid both enters and exits the rotor. When this rotor is emptied, fluid first exits the innermost tube or tubes not covered by the diaphragm. Thus, if the processing chamber is at its maximum volume, the innermost tube or tubes **188** provide the first pathway for the exiting fluid. The common tube **165** may be attached to the rest of the processing set (which of course does not rotate) by means of a rotary seal, such as the rotary seal **148** shown in FIG. 28, or a skip-rope system.

FIG. 31 shows a rotor similar to the FIG. 30 rotor except that the various tubes connected to the rotor remain separate and attach through a skip-rope system or rotary seal to various parts of the stationary portion of the processing set. These tubes permit the addition of various fluids to the rotor at chosen radii and/or the removal of fluids from chosen points by controls such as pumps or clamps acting on the stationary portion of the processing set.

In an alternative rotor shown in FIGS. 32 and 33, the set of tubes **190** are located within the processing chamber--

between the boundary wall **10** and the diaphragm **31**. The common outlet tube **165** exits the rotor's top wall **10** at only one location, instead of several locations as shown in FIG. 30. The tubes of the FIG. 32 rotor are oriented radially and may be located adjacent the top wall **10**. The tubes may be formed by spot welding a sheet of material that is at least semi-rigid to the bottom of the boundary wall **10**. The tubes must be rigid enough to maintain open channels from one end of the tube to the other even when air pressure in the chuck is pressing the diaphragm **31** towards the boundary wall **10**. A set of tubes **190** having varying lengths, such as the tubes shown in phantom in FIG. 32, may be used to permit fluid communication between the outlet port **165** and points at various radii in the processing chamber. The set of tubes **190** includes tubes **196** extending substantially to the periphery of the rotor, tubes **198** not extending very far from the rotor's axis of rotation, and tubes **192** of varying intermediate lengths. Of course, more or fewer tubes may be used. In addition, the tubes may include holes to provide the separated fluid elements additional points of exit from the rotor's processing chamber.

In one alternative arrangement, all the tubes extend substantially to the rotor's periphery, and all the tubes have holes in order to provide fluid communication with different points in the rotor's processing chamber. In another alternative embodiment, a single tube having a plurality of holes along its length may be arranged in a spiral extending from the rotor's axis of rotation to its periphery. In all of these embodiments using tubes, the tubes perform the function of the outlet-control plates: they keep open passageways for fluid to flow to and from various points at various radii in the processing chamber. Thus, only tubes **192** of intermediate length may be used to draw fluid components of intermediate density from the rotor's processing chamber (like the plate **40** shown in FIG. 19A), and tubes **196** that extend to the rotor's periphery may

be used as an inlet-control structure to introduce unseparated fluid to the periphery of the rotor (like the imperforate plate **87** shown in FIG. 11).

FIG. 34 shows a rotor having tubes arranged in a manner similar to the rotor shown in FIGS. 32 and 33. The FIG. 34 rotor has a fixed portion with a collector assembly **46**, which is separated from the diaphragm **31** by a small-diameter wall **137**, to which all the tubes are attached and which spins with the tubes, the boundary wall **10** and the diaphragm **31**. A rotary seal **48** provides the seal between the collector assembly **46** and the collector/rotary-seal area **28** of the boundary wall **10**. The rotor's cross-section shown in FIG. 34 shows tubes **192** extending an intermediate distance between the rotor's axis of rotation and the rotor's perimeter. The rotor may also have additional tubes of different lengths. One of the tubes **192** shown in FIG. 34 has a hole **139** to permit flow into the tube **192** from a point closer to the rotor's axis of rotation. Instead of tubes (or an interior plate), grooves may be formed on the bottom of the top wall **10** in order to provide an outlet control means, as shown below in FIGS. 41 and 42.

The FIG. 34 rotor may also be adapted to function like the two-conduit, edge-loading rotor **2b** shown in FIG. 11, by adding an imperforate interior wall between the boundary wall **10** and the tubes, and adding a second conduit to the fixed portion. Instead of tubes, radial grooves (like those shown in FIGS. 41 and 42) may be formed on the bottom of the imperforate interior wall. In another alternative embodiment, imperforate tubes extending all the way to the periphery of the processing chamber may be used to introduce unseparated fluid to the edge of the processing chamber, instead of an imperforate interior wall.

FIGS. 35 and 36 show another alternative rotor. This rotor has a plurality of tubes **196** which extend from a small-diameter wall **137** all the way to the rotor's periphery. The tubes **196** have holes **139** in order to permit

flow from the chamber **30** to the collector assembly **46**. Instead of having a top wall, this rotor's diaphragm **31** bends around the tubes **196** so as to cover most of the top of the rotor. The rigid rotating portion **28** of the rotor covers the collector assembly **46** and the rotary seal **48**. The diaphragm **31** is attached to the circumference of the rigid rotating portion **28**. The rigid rotating portion **28** is capable of being held and turned by a chuck so as to cause the diaphragm **31**, the tubes **196** and any fluids in the chamber **30** to spin as well. The chuck should also have a lid to cover the top portion of the diaphragm **31** so as to limit how far the diaphragm **31** can expand upwards. The FIG. 35 rotor may also be adapted to function like the two-conduit, edge-loading rotor **2b** shown in FIG. 11, by adding a second conduit to the fixed portion, and adding an imperforate interior wall above the tubes **196** or imperforate tubes extending to the periphery of the processing chamber.

It will be appreciated that, during centrifugation in the systems shown in FIGS. 3, 9, 12 and 21, rigid portions of the chuck and/or rotor limit how far the diaphragm **31** can expand outwardly in a radial direction or in an axial direction. For instance, in the system shown in FIG. 3, the chuck **4a** limits how far the diaphragm can expand in a radial outward direction and in a downward axial direction. The rotor's rigid boundary wall **10** prevents fluid from flowing upwardly out of the chamber. In the system shown in FIG. 20, the top **108**, bottom **112** and circumferential **110** portions of the rotor's boundary wall **10** respectively limit the diaphragm's expansion in the upward and downward axial directions and in the outward radial direction. By limiting the expansion of the diaphragm **31**, stresses on the diaphragm during centrifugation may be limited, and better control of the volume of the processing chamber **30** may be maintained.

The rotors having a fixed portion and a rotatable portion (e.g., the rotors shown in FIGS. 2, 11, 16-18, 19A-19D, 19E, 20, 23, 34 and 35) all have a rotary seal **48**.

FIG. 37 shows a rotary seal **48** typical of the prior-art rotary seals made by Haemonetics and others. The fixed portion **204** is held in place by a rotor brace (such as item **11** shown in FIGS. 5, 21 and 25) and is thus restrained from vertical, horizontal and rotational movement. While the fixed portion **204** is held in place, the body of the rotor **10**, only part of which is shown in FIG. 37, may be spun by a chuck, which restrains the body of the rotor from vertical and horizontal movement while spinning the rotor body. The rotating body **10** of the rotor has rigidly attached and sealed to it an annular rotating seal face **209**, which is typically made of ceramic or carbon and is lapped to a very flat surface. The rotating seal face **209** interfaces with an annular non-rotating seal face **208**, which is also typically made of ceramic or carbon and lapped to a very flat surface. The non-rotating seal face **208** is held against the rotating seal face **209** by resilient seal member **206**. The resilient sealing member **206** is attached and sealed to the fixed portion **204**.

This rotary seal **48** is less effective when the pressure inside the rotor becomes greater than the ambient pressure, because the greater inside pressure tends to push up the resilient seal member **206** and thus reduces the force the non-rotating seal face **208** exerts against the rotating seal face **206**. The rotors shown hereinabove are subjected to greater internal pressures, especially during the emptying phase, when air pressure in the chuck pushes against the diaphragm in order to force fluid out of the rotor. If the pressure differential becomes large enough, the seal faces **208**, **209** will separate momentarily until the internal and external pressures equalize. This momentary separation permits gas to escape from the rotor. Alternately, when a vacuum is created in the interior of the rotor, greater force pushes the seal faces **208**, **209** together, thereby creating more heat from friction.

Although the rotary seal shown in FIG. 37, or another type of rotary seal, may be used in the rotors of the present invention, the improved rotary seal **48** shown in FIG. 38 is preferred. As in the prior-art rotary seal, the fixed portion **204** is held by a brace, preventing vertical, horizontal and rotational movement by the fixed portion **204**. The boundary wall **10** of the rotor body is spun by a chuck, which restrains the rotor body from horizontal and vertical movement. The annular rotating seal face **209**, preferably made from ceramic or carbon and lapped to a very flat surface is rigidly attached and sealed to the boundary wall **10**.

An annular non-rotating seal face **212** is pressed against the rotating seal face **209** by a spring **214**, one end of which is attached to the fixed portion **204** and the other end of which is attached to the non-rotating seal face **212**. The force applied by this spring **214** is not affected by changes in air pressure within the rotor. The non-rotating seal face **212** can move up and down with respect to the fixed portion **204**. The non-rotating seal face **212** is also preferably made of ceramic or carbon and lapped to a very flat surface. A seal is provided between the non-rotating seal face **212** and the fixed portion **204** by flexible seal member **216**. The flexible seal member **216** and the spring member **214** are separate members (unlike the prior-art rotary seals). Both seal faces **209**, **212**, the spring **214** and the flexible seal member **216** surround the rotor's axis of rotation.

It is important that the fixed portion and the rotor body be located an acceptable distance apart, otherwise the spring **214** may not exert the desired amount of force. If the spring is compressed too much (because the fixed portion and the rotor body are too close to each other), the rotary seal may generate excessive heat when the rotor is spun. If the spring is not compressed enough (because the fixed portion and the rotor body are too far from each other), the

rotary seal may not exert enough force to keep contaminants from entering the processing chamber between the seal faces **209**, **212**.

The flexible seal member **216** and the non-rotating seal face **212** may be designed so that any pressure differential between the inside and the outside of the rotor does not affect the force holding the non-rotating seal face **212** against the rotating seal face **209**. This may be accomplished by creating opposing surfaces of equal surface area on the flexible seal member **216** and the non-rotating seal face **212**, so any effect caused by pressure on one surface is canceled by the effect on the other equal and opposing surface. One way of accomplishing this is to use a flexible seal member **216** with a circular cross-section (as shown in FIG. 38) and to place a small step **218** in the non-rotating seal face **212** (as also shown in FIG. 38) to make up for the small gap in the circular cross-section of the flexible seal member **216**. In this design, increases or decreases in pressure act uniformly in all directions and therefore exert no net force. With this design, the seal strength is independent of any pressure differential between the inside and outside of the rotor and is determined solely by the spring constant and the amount of compression of the spring **214**.

The rotary seal may be configured so that the spring **214** is connected to and extends from the rotating body of the rotor to the rotating seal face, the flexible seal member **216** connects the rotating body and the rotating seal face, and the non-rotating seal face is rigidly attached to the rotor's fixed portion. Alternatively, two springs and two flexible seal members may be used, so that both seal faces are mounted on springs--one spring being attached to the rotor's fixed portion and the other spring being attached to the rotor's rotating body--and so that a flexible seal member forms a seal between each seal face and

its respective portion of the rotor (i.e., the rotating portion or the fixed portion).

The rotary seal shown in FIG. 38 may be modified in a number of ways. For instance, as shown in the detail view represented in FIG. 39, the spring **314** and the flexible seal member **316** of the rotary seal may be made out of the same piece of material **310**. In addition to manufacturing advantages, such a design has the advantage of providing a spring **314** that applies an even vertical force around the axis of rotation (whereas a coil spring may apply a greater force on some areas of the seal face **212** than on others). One end **303** of the integral spring/seal member **310** is attached to the fixed portion **204** of the rotor. Of course, as noted above with respect to the FIG. 38 rotary seal, the non-rotating seal face **212** can move up and down with respect to the fixed portion **204**. The middle **305** of the member **310** is attached and sealed to the seal face **212**. The spring portion **314** of the member **310** stretches between these two points of attachment **303**, **305**. The other end **307** of the member **310** is also attached and sealed to the rotor's fixed portion **204**. The flexible-seal-member portion **316** of the member **310** connects the two points of attachment **307** and **305**. FIG. 39 also shows the step **218** in the seal face **212** for negating the effects of internal rotor pressure on the force applied to the seal faces.

FIGS. 38 and 39 show the springs **214**, **314** located outside of the flexible seal **216**, **316**, so that the spring is in contact with ambient pressure but is not in direct contact with the rotor air, which air undergoes the rapid pressure variations. The spring may also be located inside the flexible seal. Thus, the spring may be mounted in the region of the step **218**, spanning the space between the fixed portion **204** and the non-rotating seal face **212**. If the spring is perforated, the changes in internal rotor pressure may pass through the spring to the flexible seal member, so that changes in internal pressure exert no net changes in

force between the rotating and non-rotating seal faces **209**, **212**.

If the flexible seal member **216**, **316** is resilient and rigid enough to maintain an adequate seal, it may function as the spring member as well, so that a separate spring member is not required. As long as the components of the rotary seal are shaped properly, changes in internal rotor pressure will exert no net changes in force between the rotating and non-rotating seal faces **209**, **212**. For example, since the seal portion **316** and the rotating seal face **212** in the rotary seal shown in FIG. 39 have opposing surfaces of equal surface area--so that any effect caused by pressure on one surface is canceled by the effect on the other equal and opposing surface--the separate spring portion **314** may be eliminated without causing the changes in internal rotor pressure to effect the effectiveness of the rotary seal as long as the seal portion **316** is resilient and rigid enough.

It will be appreciated that the rotors of the present invention can have shapes other than those described hereinabove. For example, FIG. 40 shows a rotor similar in function to the rotor of FIG. 11, but having a generally hemispherical shape.

Different types of outlet-control means may be used. For example, FIGS. 41 and 42 show top and cross sectional views of a preferred embodiment of the rotor. This rotor uses grooves **244**--preferably radially aligned--formed on the bottom of the top wall **10** as the outlet control means, instead of tubes or an interior perforate wall. The grooves **244** are defined by vertical channel walls **240**; if the vertical channel walls **240** are placed close enough to each other, they can keep channels--the grooves **244**--open from the holes **239**, which connect the processing chamber and the collector assembly **46**, to the periphery of the rotor, or to whatever radius it is desired to maintain a channel. The FIG. 42 rotor has a fixed portion (which includes the collector assembly **46** and which interfaces the rotating

portion of the rotor at a rotary seal **48**), and thus a small-diameter internal wall **237** is necessary to keep the spinning diaphragm **31** from coming into contact with the fixed portion and possibly being abraded.

Although the invention has been described with reference to several preferred embodiments, it will be understood by one of ordinary skill in the art that various modifications can be made without departing from the spirit and the scope of the invention, as set forth in the claims hereinbelow.

What is claimed is:

1. A rotor for use in a centrifuge system having means for holding and spinning the rotor, the rotor comprising:

a rigid mounting member for being held and spun by the spinning means; and

an elastic diaphragm mounted on the rigid mounting member so as to spin with the rigid mounting member, the diaphragm defining a chamber of varying volume, wherein the rigid mounting member defines a conduit in fluid communication with the chamber.

2. A rotor according to claim 1 further including a fixed portion, through which the conduit passes; and

a rotary seal located around the rotor's axis of rotation, the rotary seal providing a seal between the rigid mounting member and the fixed portion; wherein the rigid mounting member is rotatably mounted around the fixed portion and the rotor's axis of rotation, the mounting member capable of being held and spun by the spinning means.

3. A rotor according to one of claims 1 and 2, further including outlet-control means for controlling the flow of liquid out of the chamber into the conduit.

4. A rotor according to claim 3, wherein the outlet-control means includes channel walls, defining a channel from a point in the processing chamber to a point in fluid communication with the conduit, the channel walls being spaced close enough to each other so as to prevent the diaphragm from blocking the channel.

5. A rotor according to claim 3, wherein the rigid mounting member includes an imperforate boundary wall, and wherein the outlet control means includes channel walls on the interior side of the boundary wall, the channel walls defining channels on the interior of the imperforate boundary wall.

6. A rotor according to claim 3, wherein the outlet-control means includes a perforate, substantially rigid interior wall located within the chamber.

7. A rotor according to claim 6, wherein the rigid mounting member includes a boundary wall, the boundary wall being substantially rigid and substantially imperforate, and wherein the perforate interior wall is mounted adjacent to the boundary wall.

8. A rotor according to one of claims 5 and 7, wherein the outlet control means extends substantially to the periphery of the chamber.

9. A rotor according to claim 8, wherein the outlet control means provides fluid communication between a variety of points within the chamber and the conduit.

10. A rotor according to one of claims 5 and 7-9, wherein the boundary wall extends substantially to the chamber's periphery.

11. A rotor according to claim 10, wherein the boundary wall includes a circumferential portion, and wherein the chamber and the diaphragm are located inside of the circumferential portion.

12. A rotor according to one of claims 5 and 7, wherein the boundary wall defines the top of the chamber and the diaphragm is mounted near the perimeter of the boundary wall.

13. A rotor according to one of claims 10 and 12, further including an exterior shell mounted around the circumference of the boundary wall, such that the exterior shell and the boundary wall define a cavity and the diaphragm is located within the cavity.

14. A rotor according to claim 13, wherein the exterior shell includes a core.

15. A rotor according to claim 3, wherein the outlet-control means includes at least one tube, wherein the tube provides fluid communication between the chamber and the conduit.

16. A rotor according to claim 3, wherein the outlet-control means includes a set of tubes.

17. A rotor according to one of claims 3-16, further including a second conduit, so that uncentrifuged fluid may enter the chamber through the second conduit, while centrifuged fluid may exit the chamber through the first conduit.

18. A rotor according to claim 17, wherein the rotor further includes an imperforate interior wall mounted adjacent the outlet control means, so as to direct fluid entering the chamber from the second conduit towards the periphery of the chamber, the imperforate interior wall also defining the first conduit so that fluid may flow from the outlet-control means to the first conduit.

19. A rotor according to claim 18, wherein the imperforate interior wall extends substantially to the chamber's periphery.

20. A rotor according to claim 17, wherein the rotor further includes

a rigid core member fixedly mounted to the rigid mounting member and about the rotor's axis of rotation, the diaphragm being located around the core member, and

wherein one of the first and second conduits includes a tube extending through the core member to the bottom of the chamber.

21. A rotor according to claim 2, wherein the rotary seal includes

a base,

a spring member surrounding the rotor's axis of rotation and mounted on the base,

first and second seal faces, which surround the rotor's axis of rotation and which spin in relation to each other, the first seal face being mounted on the spring member so that the spring member applies a force pressing the first seal face against the second seal face, and

a flexible seal member surrounding the rotor's axis of rotation, and preventing flow between the first seal face and the base.

22. A rotor according to claim 21, wherein the spring member and the flexible seal member are different portions of a single piece of material.

23. A rotor according to one of claims 21 and 22, wherein the flexible seal member and the first seal face are disposed so that the force with which the spring member presses the first seal face against the second seal face is not substantially affected by pressure within the rotor.

24. A rotor according to one of claims 21-23, wherein the rotary seal's base is part of the rotor's fixed portion and the rotary seal's second seal face is attached to the rigid mounting member.

25. A rotor according to claim 21, wherein the spring member has an interior side and an exterior side, and the pressures on the interior and exterior sides is the same.

26. A rotor according to claim 2, wherein the rotary seal includes

a base,

first and second seal faces, which surround the rotor's axis of rotation and which spin in relation to each other, wherein a force presses the first seal face against the second seal face, and

a flexible seal member surrounding the rotor's axis of rotation, and preventing flow between the first seal face and the base, wherein the flexible seal member and the first seal face are disposed so that the force pressing the first seal face against the second seal face is not substantially affected by pressure within the rotor.

27. A rotor according to claim 2, wherein the rotor includes an interior wall fixedly attached to the rigid mounting member, wherein the interior wall separates the diaphragm from the fixed portion of the rotor.

28. A rotor according to claim 27, further including channel walls, defining a channel from a point in the processing chamber to a point in fluid communication with the conduit, the channel walls being spaced close enough to each other so as to prevent the diaphragm from blocking the channel.

29. A rotor according to claim 28, further including

a second conduit, so that uncentrifuged fluid may enter the chamber through the second conduit, while centrifuged fluid may exit the chamber through the first conduit; and

an imperforate interior wall attached to the rigid mounting member so as to spin with the rigid mounting member, and mounted with respect to the second conduit so as to direct fluid entering the chamber through the second conduit towards the periphery of the chamber, wherein the imperforate interior wall having the channel walls disposed thereon so as to permit flow from the chamber to the first conduit.

30. A system for separating a fluid having heavier and lighter components, the system comprising:

a rotor according to one of claims 1-29; and

means for holding the rigid mounting member of the rotor and for spinning the rotor around an axis; and

means, in fluid communication with the spinning means, for changing the pressure of a control fluid adjacent the rotor's diaphragm.

31. A system according to claim 30, wherein the pressure-changing means includes means for applying pressurized gas against the diaphragm, so as to force fluid out of the rotor.

32. A system according to one of claims 30 and 31, wherein the pressure-changing means includes means for applying a vacuum against the diaphragm, so as to draw fluid into the rotor.

33. A system for processing blood from a wound drain according to claim 32, further including

a wound drain placed in a patient, the wound drain being attached the rotor, wherein a vacuum is applied to the diaphragm so as to draw blood from the wound drain into the chamber; and

means for directing, after the rotor is spun, lighter blood components to a separate reservoir and returning concentrated red blood cells remaining in the rotor to the patient.

34. A system according to claim 33, wherein the directing means directs the concentrated red blood cells to a second separate reservoir, which may be connected to the patient.

35. A system for processing blood from a wound drain according to claim 31, further including

a wound drain placed in a patient;

canister means, in fluid communication with the wound drain and the rotor, for holding blood from the wound drain, wherein a vacuum is applied to the canister means so as to draw blood from the wound drain into the canister means;

means for moving blood from the canister means to the rotor; and

means for directing, after the rotor is spun, lighter blood components to a separate reservoir and returning concentrated red blood cells remaining in the rotor to the patient.

36. A system for processing blood from a patient's surgery site according to claim 31, further including

a suction tube leading from the surgery site, the suction tube being attached to the rotor, wherein blood drawn from the surgery site through the suction tube may be provided to the rotor; and

means for directing, after the rotor is spun, lighter blood components to a separate reservoir and returning concentrated red blood cells remaining in the rotor to the patient.

37. A system for processing blood from a patient's surgery site according to claim 36, further including

canister means, in fluid communication with the suction tube and the rotor, for holding blood from the suction tube, wherein a vacuum is applied to the canister means so as to draw blood from the wound drain into the canister means; and

means for moving blood from the canister means to the rotor.

38. A system for separating a fluid having heavier and lighter components, the system comprising:

a rotor according to one of claims15-17, 21 and 22; and

means for holding the rigid mounting member of the rotor and for spinning the rotor around an axis; and

means, in fluid communication with the spinning means, for changing the pressure of a control fluid adjacent the rotor's diaphragm;

wherein the first conduit permits into flow of unseparated fluid into the chamber, while the second conduit flow of separated fluid components out of the chamber.

39. A system for performing red-blood-cell apheresis on a donor according to claim 38, further including

means for drawing whole blood from the donor and introducing the whole blood into the chamber through the second conduit; and

control means for controlling the speed of rotation of the spinning means and the rotor, and for controlling the pressure-changing means so that the pressure being applied to the diaphragm allows the chamber to increase in volume at a rate substantially equal to the volume of the red-blood-cell component of the whole blood entering the chamber, so that the volume of lighter fluid components in the chamber is kept relatively low.

40. A system according to claim 39, wherein the means for drawing blood includes means for adding replacement fluid to the whole blood as the whole blood is drawn from the donor.

41. A system according to claim 39, further including means for adding replacement fluid to blood components being returned to the patient.

42. A system according to claim 30-41, further including control means for controlling the speed of rotation of the spinning means and the rotor, and for controlling the pressure-changing means.

43. A system according to claim 42, wherein the control means includes means for determining the chamber's volume

based on the speed of the spinning means and the pressure created by the pressure changing means.

44. A system according to claim 43, wherein the control means further includes means for controlling the volume of the chamber.

45. A system for processing biological fluids of different densities, the system comprising:

a rotor according to one of claims 3-22;

means for holding and spinning the rotor around the axis of rotation so as to separate the fluid into a denser component, a lighter component, and an intermediate-density component;

means for determining when the intermediate density component is located at the given radius; and

means for applying pressure radially outward from the axis of rotation, so as to force the intermediate-density component through the outlet-control means and the conduit.

46. A centrifuge system for accepting a rotor having a rigid mounting member and an elastic diaphragm attached to the mounting member, the system comprising:

means for holding the rigid mounting member of the rotor and for spinning the rotor around an axis; and

means for changing the pressure of a control fluid adjacent the rotor's diaphragm.

47. A system according to claim 46, wherein the spinning means includes a chuck and the pressure-changing means is in fluid communication with the chuck.

48. A system according to one of claims 46 and 47, wherein the pressure-changing means includes means for applying a vacuum against the diaphragm, so as to draw fluid into the rotor.

49. A system according to one of claims 46-48, wherein the pressure-changing means includes means for applying pressurized gas against the diaphragm, so as to force fluid out of the rotor.

50. A system according to one of claims 46-49, further including control means for controlling the speed of rotation of the spinning means, and for controlling the pressure-changing means.

51. A system according to claim 50, wherein the control means includes means for determining the volume of fluid in the rotor based on the speed of the spinning means and the pressure created by the pressure-changing means.

52. A system according to claim 51, wherein the control means includes means for controlling the volume of fluid in the rotor by controlling the speed of the spinning means and the pressure created by the pressure-changing means.

53. A system according to claim 52, wherein the control means causes the volume of the processing chamber to remain constant.

54. A centrifuge system for accepting a rotor, the system comprising:

means for spinning the rotor around an axis; and

control means for controlling the spinning means so as to cause the spinning means to continually cycle through a range of rotational speeds around a desired rotational speed, so as to prevent the system from vibrating excessively.

55. A method for processing biological fluids of different densities, the method comprising the steps of:

providing a rotor according to one of claims 1-29;

introducing an unseparated fluid into the chamber; and

holding the rotor by the rigid mounting member and spinning the rotor around an axis so as to separate the fluid into denser and lighter components, the denser component congregating away from the axis while the lighter component congregates closer to the axis.

56. A method according to claims 55 further including the step of applying pressure to the diaphragm so as to force a fluid component out of the chamber.

57. A method according to claim 56, wherein a lighter component is forced out of the chamber first.

58. A method according to claim 56, wherein a denser component is forced out of the chamber first.

59. A method of processing blood from a donor according to claim 56, wherein the step of introducing unseparated fluid into the chamber includes the step of introducing blood into the chamber; and

wherein the method further includes the steps of

storing lighter blood components, and

directing concentrated red blood cells remaining in the rotor to the donor.

60. A method of processing blood according to claim 56, wherein the step of introducing unseparated fluid into the chamber includes the step of introducing blood into the chamber; and

wherein the method further includes the steps of

directing lighter blood components to the donor, and

storing concentrated red blood cells.

61. A method of processing blood from a wound drain according to claim 56, wherein the step of introducing unseparated fluid into the chamber includes the step of

placing a wound drain in a patient,
attaching the wound drain to the rotor, and
drawing blood from the wound drain into the chamber; and

wherein the method further includes the steps of
directing lighter blood components to a separate reservoir, and
returning concentrated red blood cells remaining in the rotor to the patient.

62. A method of processing blood from a wound drain according to claim 56, wherein the step of introducing unseparated fluid into the chamber includes the steps of
placing a wound drain in a patient,
attaching the wound drain to a canister,
attaching the canister to the rotor, and
drawing blood from the canister into the chamber; and

wherein the method further includes the steps of
directing lighter blood components to a separate reservoir, and
returning concentrated red blood cells remaining in the rotor to the patient.

63. A method of processing blood from a patient's surgery site according to claim 56, wherein the step of introducing unseparated fluid into the chamber includes the steps of
drawing blood from the surgery site into the chamber; and

wherein the method further includes the steps of
directing lighter blood components to a separate reservoir, and
returning concentrated red blood cells remaining in the rotor to the patient.

64. A method according to claim 56, wherein the speed that the rotor is spun is reduced so as to force a fluid component out of the chamber.

65. A method according to claim 56, wherein the rotor is spun at a constant speed, while the pressure applied against the diaphragm is increased, until a predetermined pressure is reached, then while the pressure against the diaphragm is held constant, the speed of the rotor is reduced.

66. A system according to claim 56, wherein the pressure-changing means maintains a constant pressure against the diaphragm, while the speed of the rotor's spinning is decreased until a predetermined speed is reached, then the pressure against the diaphragm is increased.

67. A method according to claim 56, wherein the rotor is emptied by reducing the speed that the rotor is spun and increasing the pressure against the diaphragm.

68. A method according to claim 56, wherein the volume of the chamber is controlled by changing the pressure applied to the diaphragm and by controlling the speed of rotation of the rotor.

69. A method according to claim 56, wherein the rotor is stopped and pressure applied to the diaphragm so as to force the remaining fluid out of the rotor.

70. A method for processing biological fluids of different densities, the method comprising the steps of:

providing a rotor according to one of claims 15-17, 21 and 22;

introducing an unseparated fluid into the chamber;

holding the rotor by the rigid mounting member and spinning the rotor around an axis so as to separate the fluid into denser and lighter components, the denser

component congregating away from the axis while the lighter component congregates closer to the axis; and

applying pressure to the diaphragm,

wherein the first and second conduits permit the separated lighter components to be forced out of the rotor through the first conduit while unseparated fluid is introduced into the chamber through the second conduit.

71. A method according to claim 70, wherein the pressure being applied to the diaphragm is held constant so as to maintain the chamber at a constant volume, so that the volume of lighter components being forced out of the chamber is substantially equal to the volume of unseparated fluid entering the chamber.

72. A method of performing red-blood-cell apheresis on a donor according to claim 70, wherein the step of introducing unseparated fluid into the chamber includes the steps of

drawing whole blood from the donor, and

introducing the whole blood into the chamber through the second conduit while the rotor is being spun; and

wherein the step of applying pressure to the diaphragm includes the step of

forcing lighter blood components out of the chamber through the first conduit to the donor, while the rotor is being spun and while whole blood is being introduced into the chamber.

73. A method according to claim 72, further including the step of adding anticoagulant to the whole blood as the whole blood is drawn from the donor.

74. A method according to one of claims 72 and 73, further including the step of adding replacement fluid to the blood components being returned to the donor.

75. A method according to one of claims 72-74, wherein the pressure being applied to the diaphragm allows the chamber to increase in volume at a rate substantially equal to the volume of the red-blood-cell component of the whole blood entering the chamber, so that the volume of lighter fluid components in the chamber is kept relatively low.

76. A method of separating fluid into lighter and heavier components, the method comprising the steps of:

providing a rotor having an elastic diaphragm defining a variable-volume processing chamber, and having first and second conduits providing fluid communication to the processing chamber;

spinning the rotor; and

introducing the unseparated fluid into the processing chamber through the second conduit while the rotor is being spun and while separated fluid components are forced out of the processing chamber through the first conduit.

77. A method of performing red-blood-cell apheresis on a donor according to claim 76, the method further including the steps of

drawing whole blood from the donor;

adding replacement fluid to the whole blood before the whole blood is separated;

introducing the whole blood into the rotor through the second conduit while the rotor is being spun, so that the whole blood is separated into red blood cells and lighter fluids, including plasma and replacement fluid; and

returning the plasma and the replacement fluid to the donor while whole blood is still being drawn from the donor.

78. A method of collecting red blood cells from a donor, the method comprising the steps of:

providing a rotor having first and second conduits providing fluid communication to the processing chamber;

drawing whole blood from the donor;

adding replacement fluid to the whole blood;

after adding the replacement fluid to the whole blood, introducing the whole blood into the rotor through the second conduit;

spinning the rotor, so that the whole blood is separated into red blood cells and lighter fluids, the lighter fluids including plasma and replacement fluid; and

drawing plasma and replacement fluid out of the rotor through the first conduit.

79. A method according to claim 78, further including the step of:

returning the plasma and the replacement fluid to the donor.

80. A method according to claim 78, further including the step of:

returning the plasma and the replacement fluid to the donor, while whole blood is still being drawn from the donor.

81. A method according to 78, wherein the step of adding replacement fluid to the whole blood includes adding anticoagulant to the whole blood.

82. A method for processing biological fluids of different densities, the method comprising the steps of:

providing a rotor comprising:

an elastic diaphragm defining a chamber for holding the biological fluids,

a conduit leading from the chamber, and

outlet-control means for maintaining an open channel to the conduit for fluid at a given radius in the chamber;

spinning the rotor around an axis so as to separate the fluid into a denser component, a lighter component, and an intermediate-density component;

determining when the intermediate density component is located at the given radius; and

applying pressure radially outward from the axis of rotation, so as to force the intermediate-density component through the outlet-control means and the conduit.

83. A rotary seal comprising:

a base;

a spring member surrounding the rotary seal's axis of rotation and mounted on the base;

first and second seal faces, which surround the axis of rotation and which spin in relation to each other, the first seal face being mounted on the spring member so that the spring member applies a force pressing the first seal face against the second seal face; and

a flexible seal member, separate from the spring member, the flexible seal member surrounding the axis of rotation and preventing flow between the first seal face and the base.

84. A rotary seal according to claim 83, wherein the flexible seal member and the first seal face are disposed so that the force with which the spring member presses the first seal face against the second seal face is not substantially affected by pressure within the rotor.

85. A rotary seal according to one of claims 83 and 84, wherein the spring member and the flexible seal member are different portions of a single piece of material.

86. A rotary seal comprising:

a base;

first and second seal faces, which surround the axis of rotation and which spin in relation to each other;

means, surrounding the rotary seal's axis of rotation and mounted on the base, for applying a force pressing the first seal face against the second seal face and for

preventing flow between the first seal face and the base, wherein the means and the first seal face are disposed so that the force with which the spring member presses the first seal face against the second seal face is not substantially affected by pressure within the rotor.

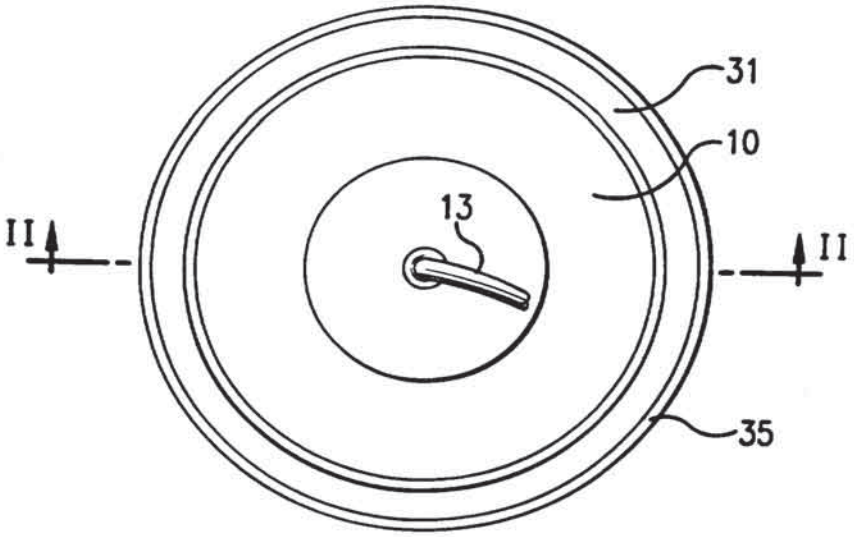


FIG. 1

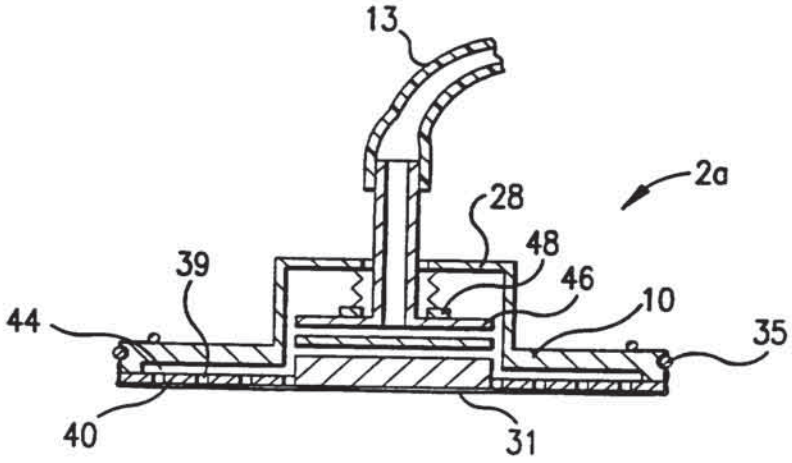


FIG. 2

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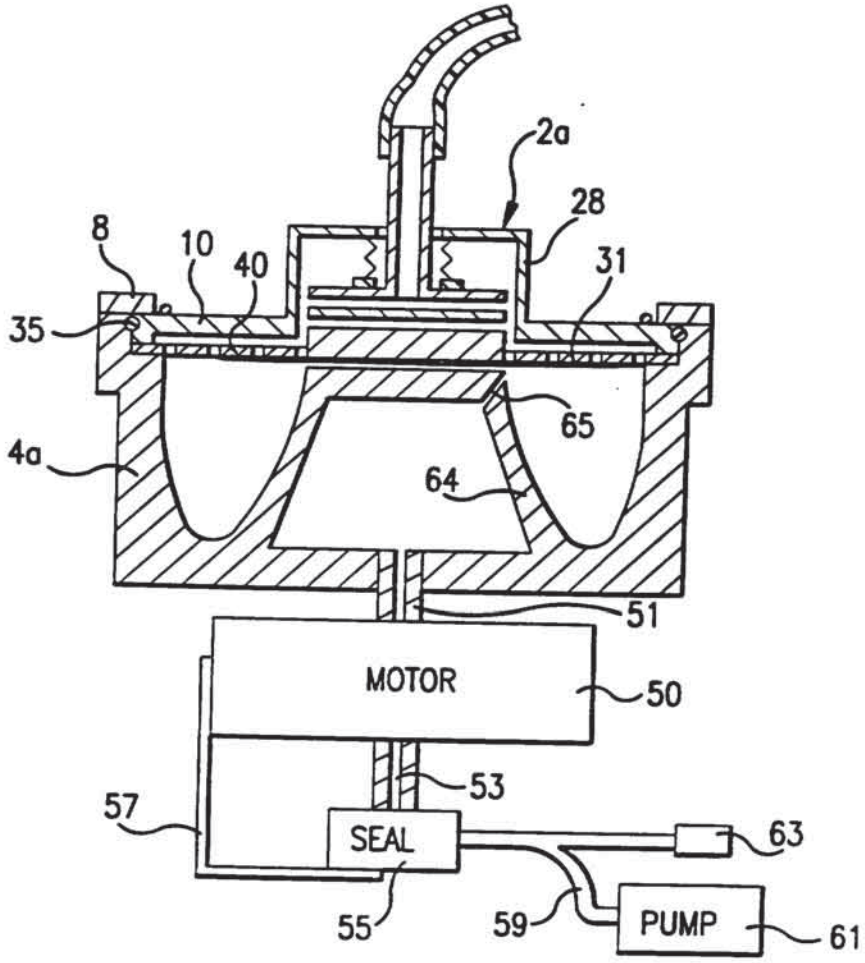


FIG.3

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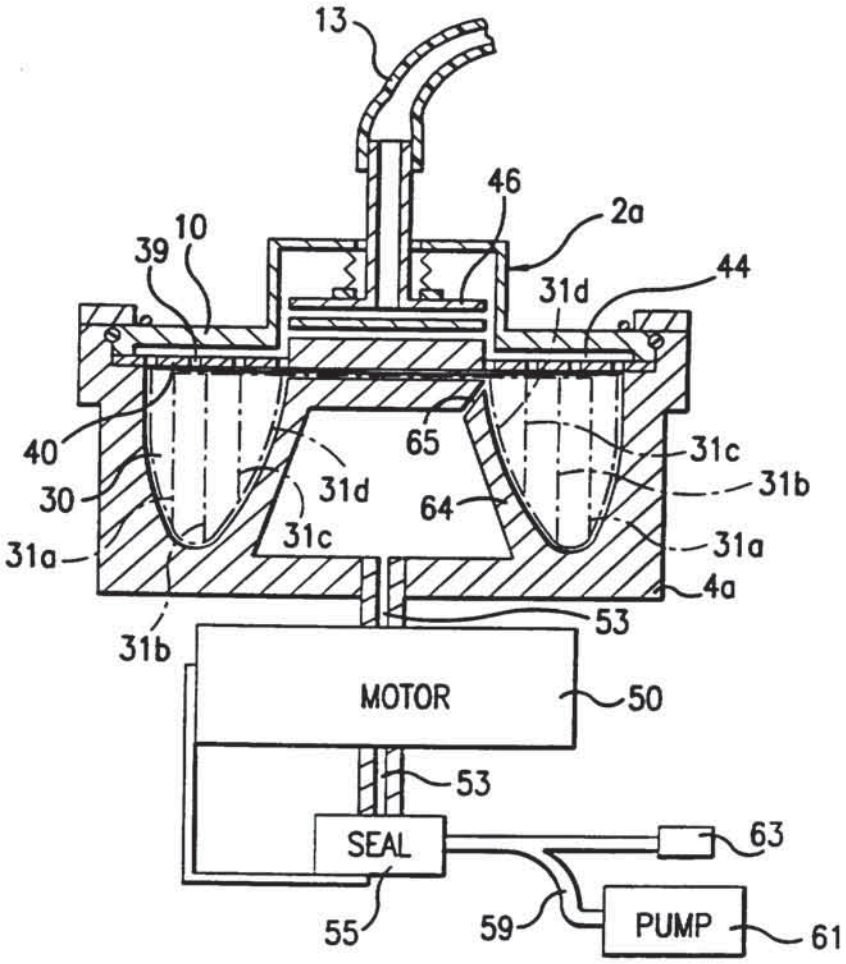


FIG.4

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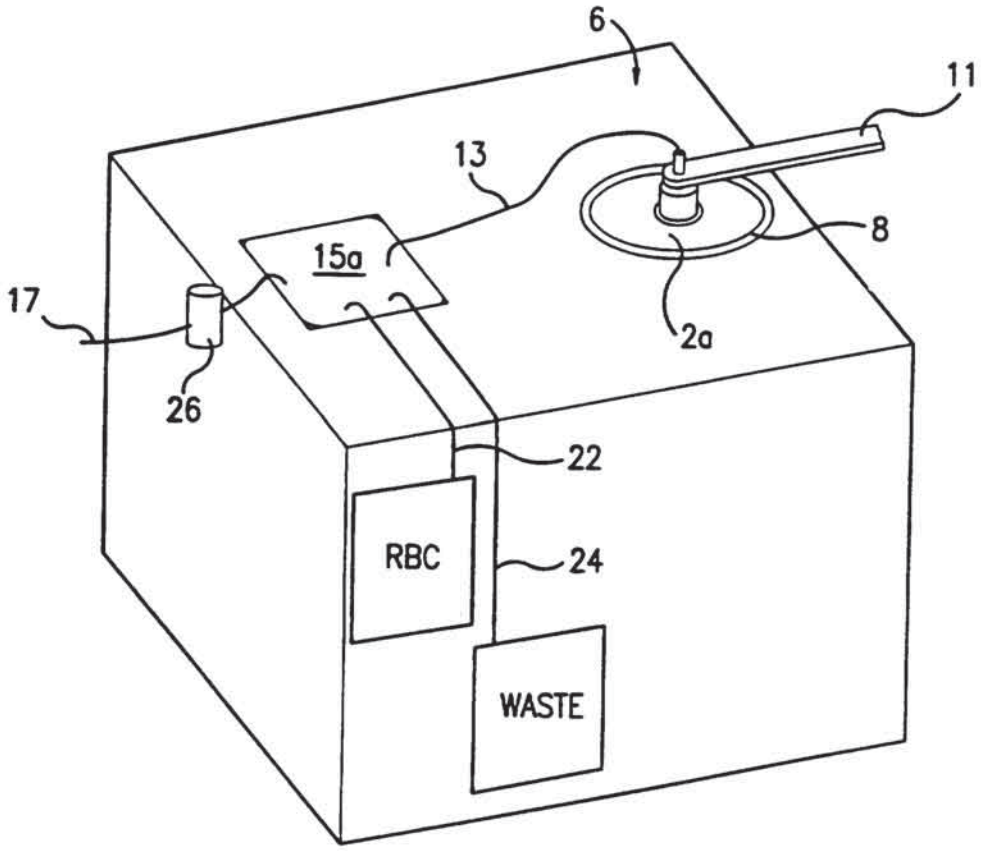


FIG.5

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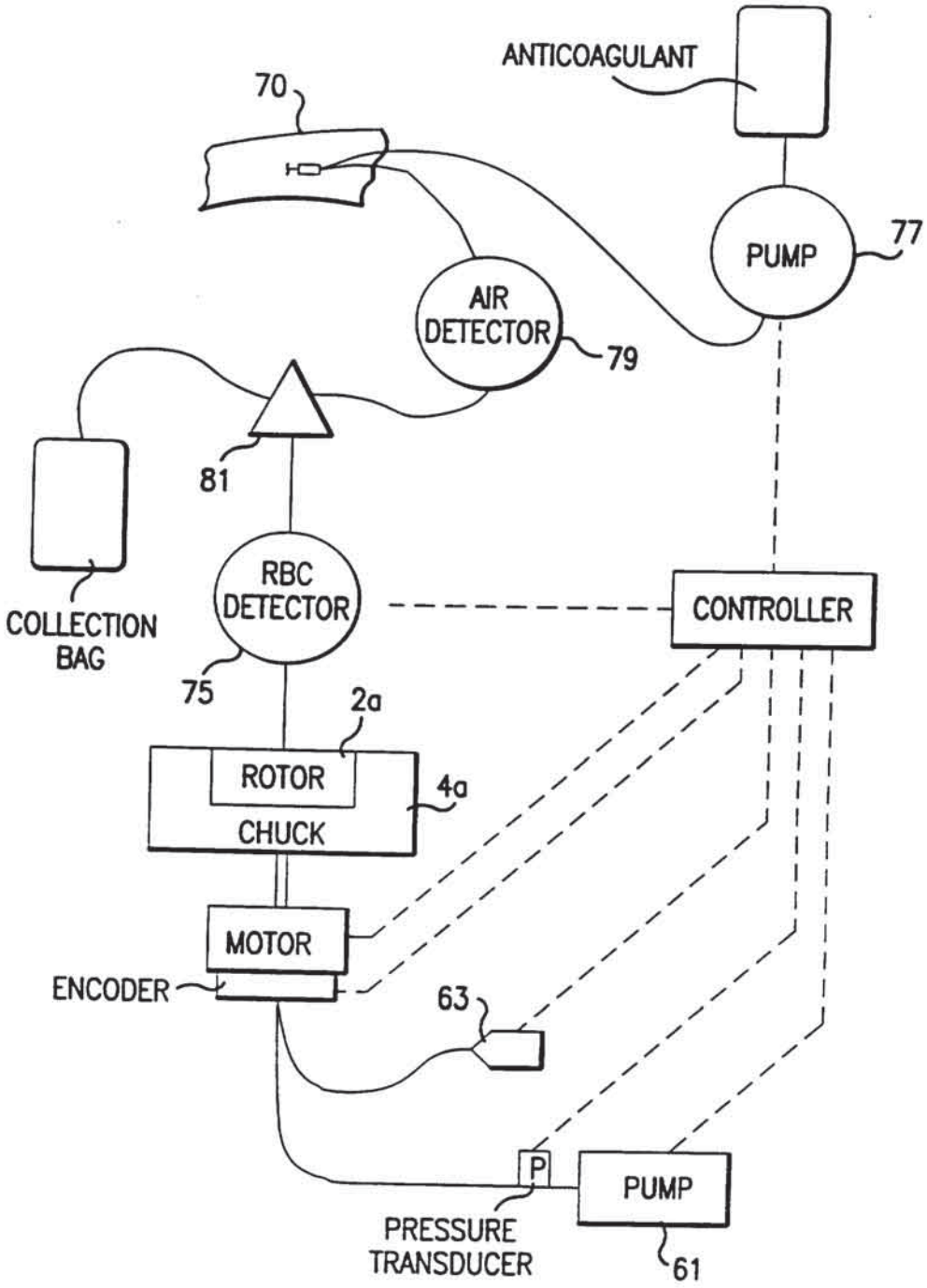

ANTICOAGULANT
70
PUMP
77
AIR DETECTOR
79
81
COLLECTION BAG
RBC DETECTOR
75
CONTROLLER
2a
ROTOR
4a
CHUCK
MOTOR
ENCODER
63
P
PUMP
PRESSURE TRANSDUCER
61

FIG.6

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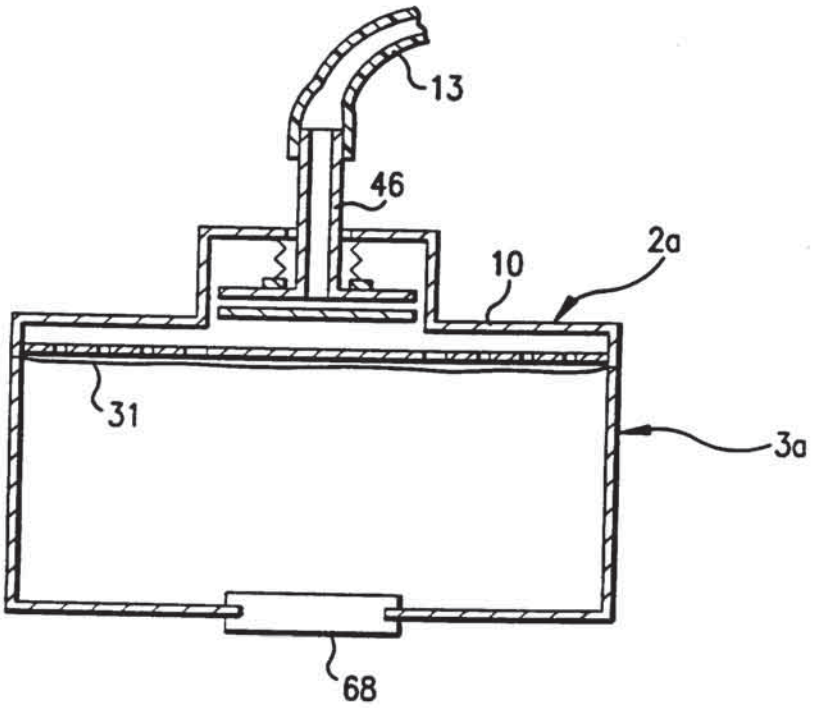


FIG.7

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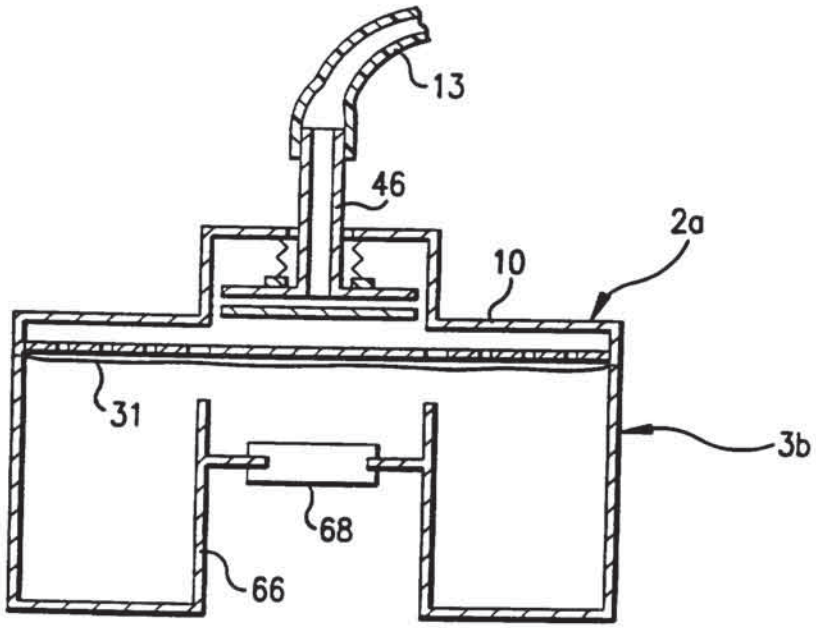


FIG.8A

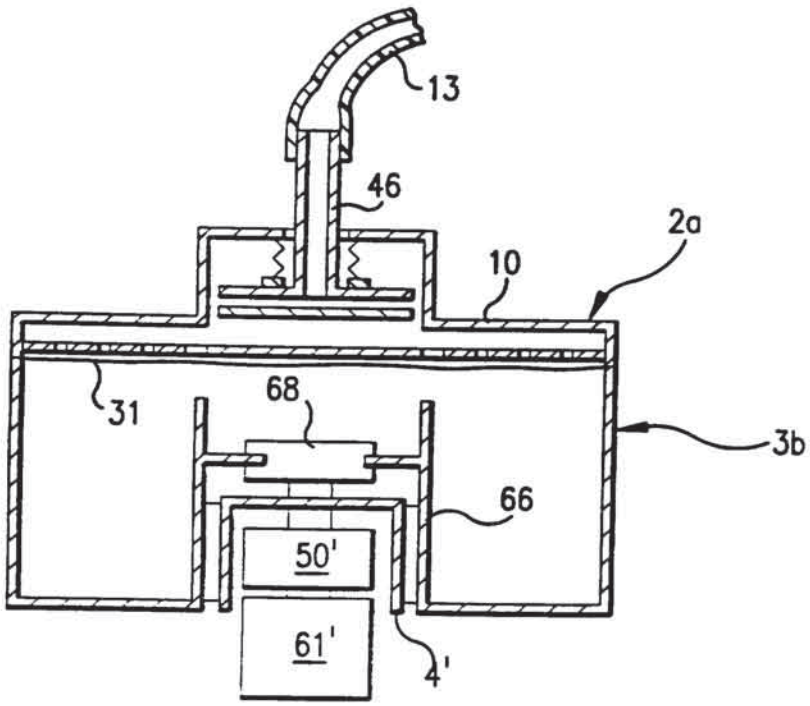


FIG.8B

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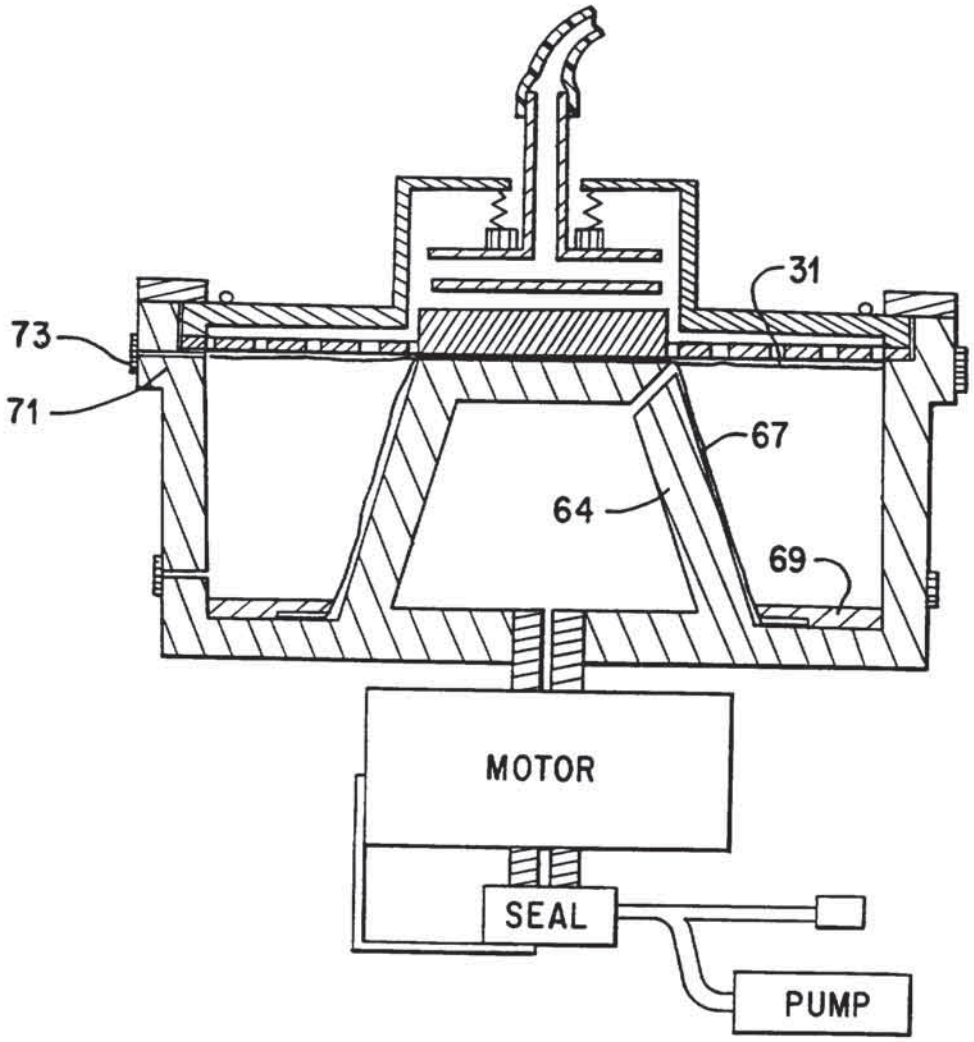


FIG. 9

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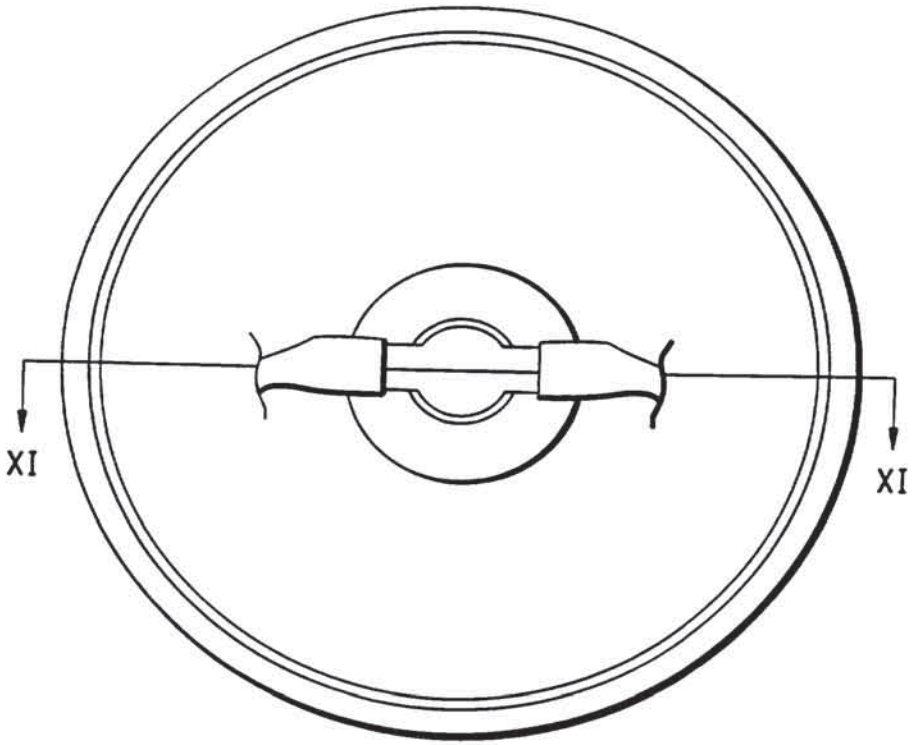


FIG.10

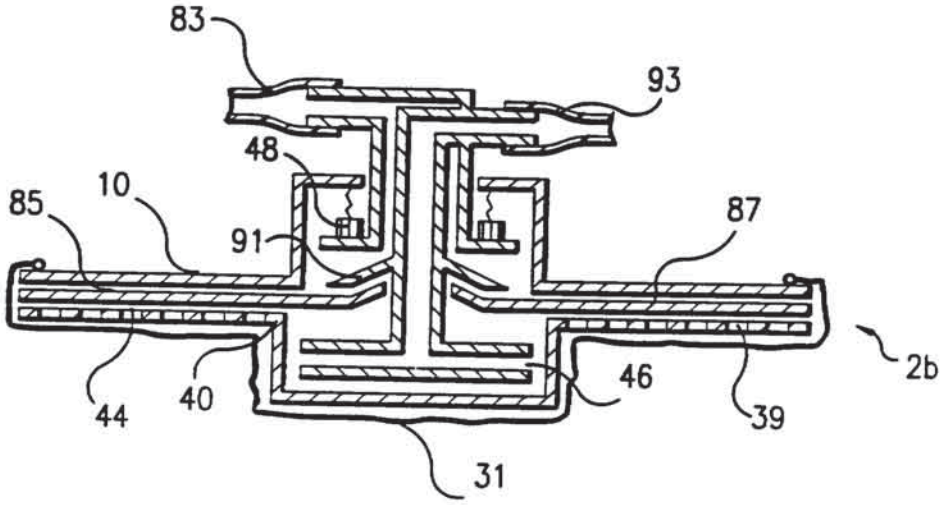


FIG.11

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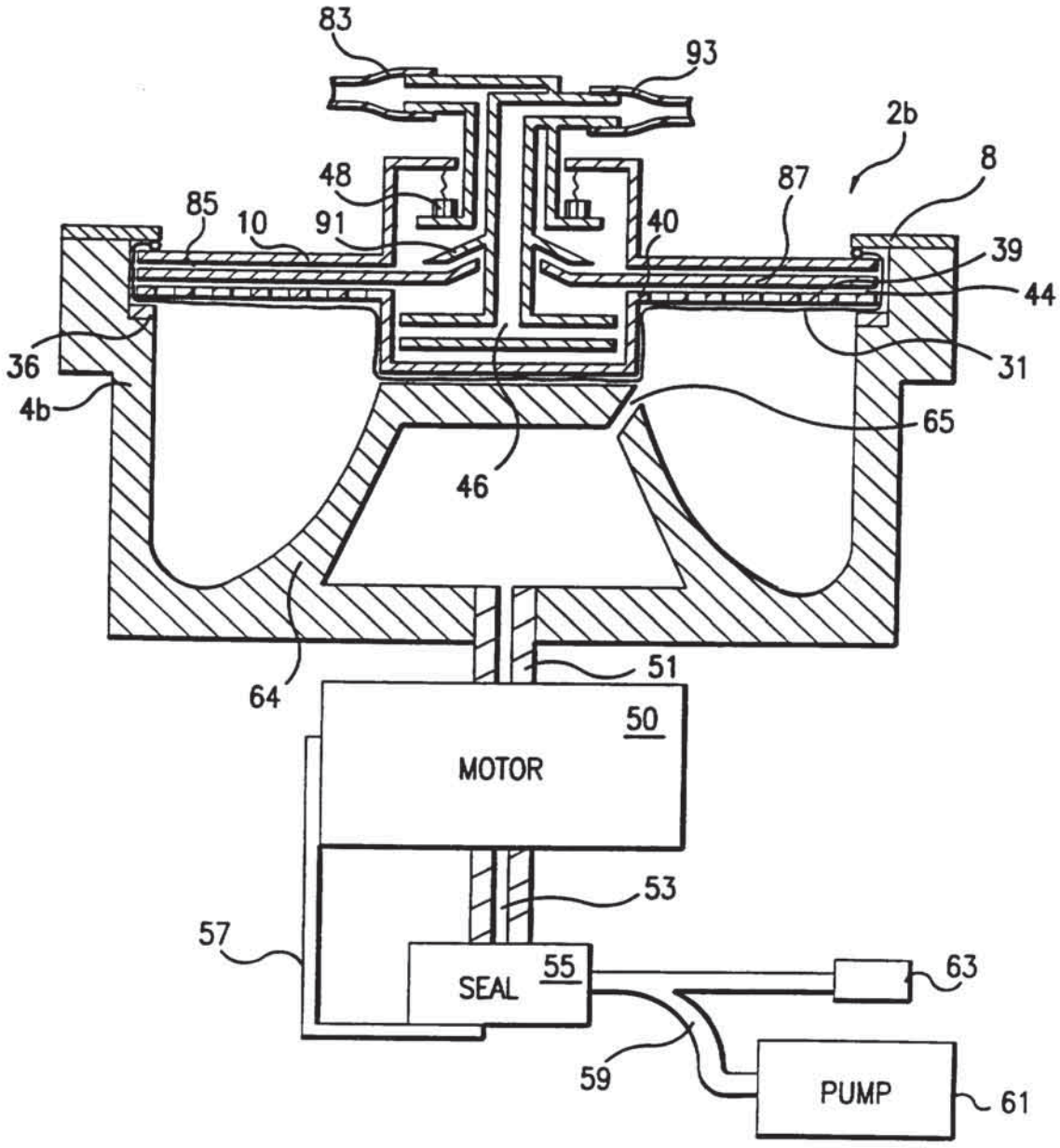

83
93
2b
8
48
87
85
10
91
40
39
44
36
31
4b
65
46
64
51
50
MOTOR
53
57
SEAL
55
63
59
PUMP
61

FIG. 12

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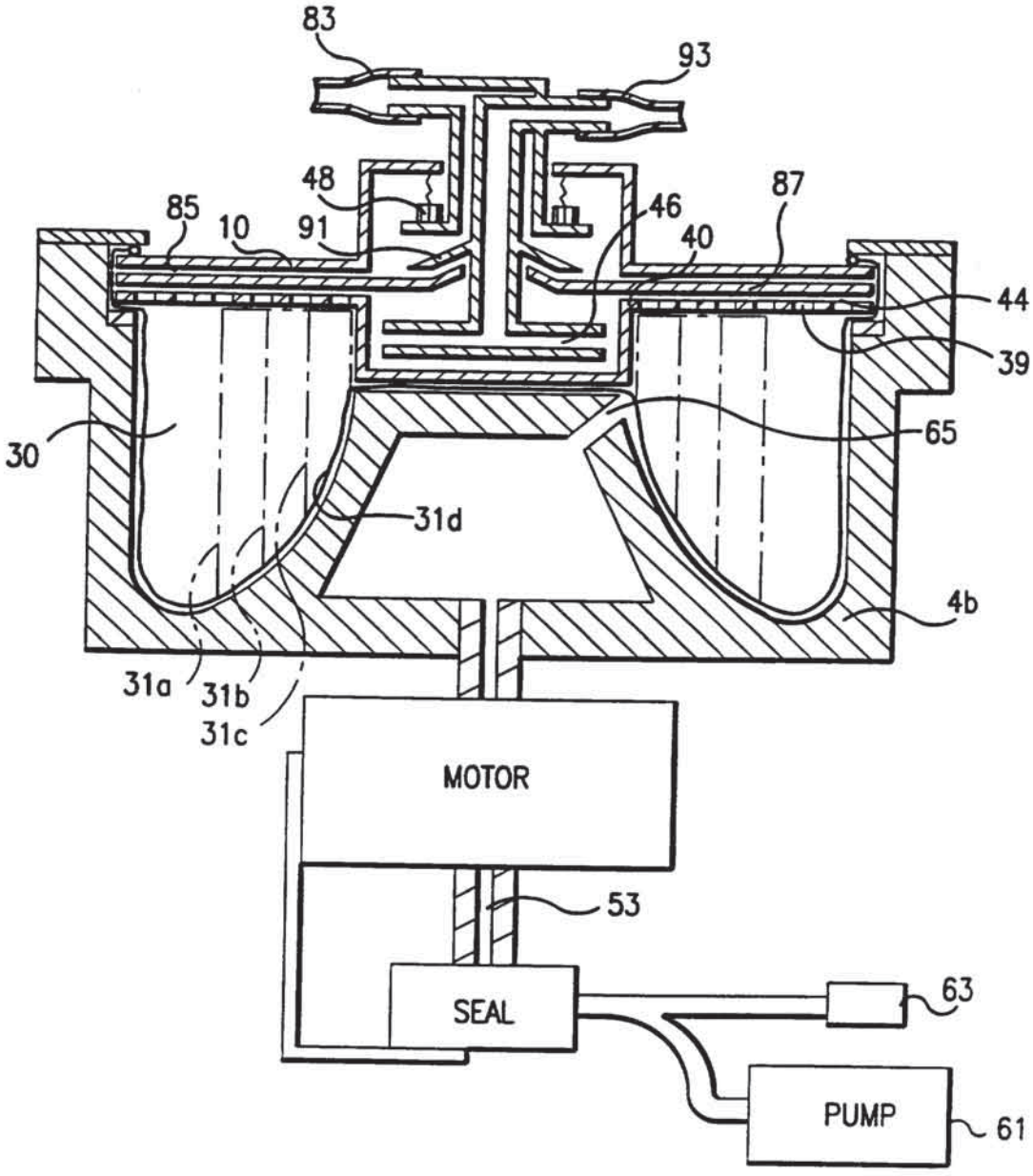

83
93
48
85
10
91
46
87
40
44
39
65
30
31d
4b
31a
31b
31c
MOTOR
53
SEAL
63
PUMP
61

FIG. 13

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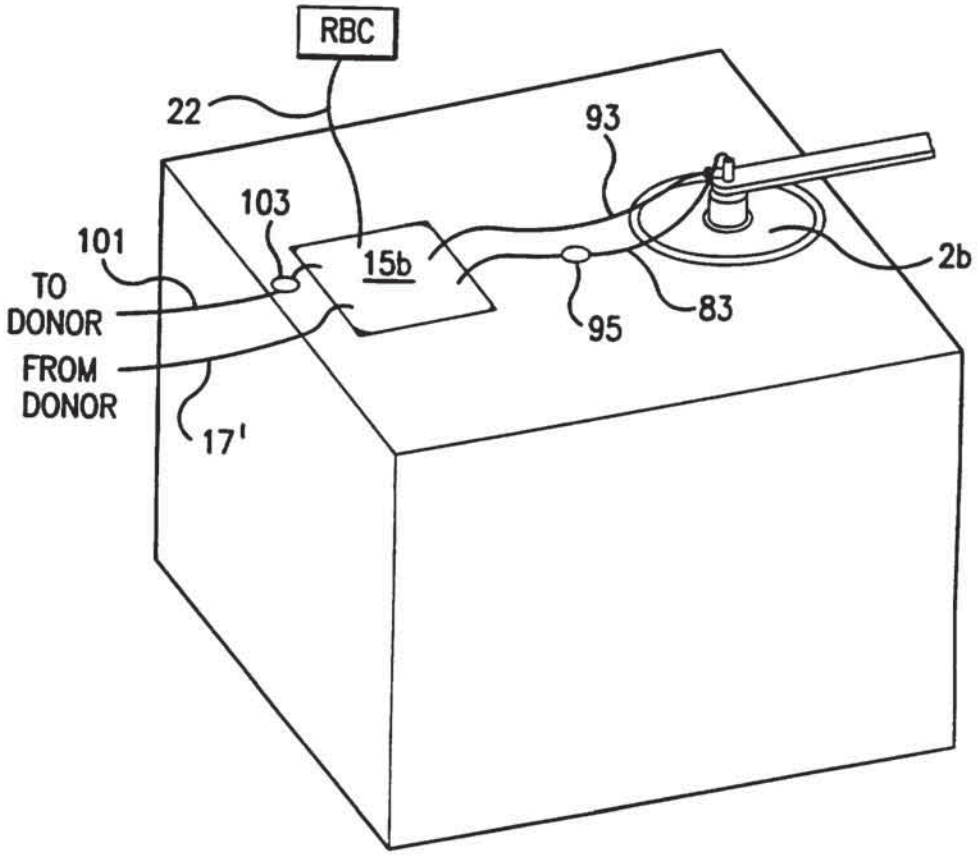


FIG. 14

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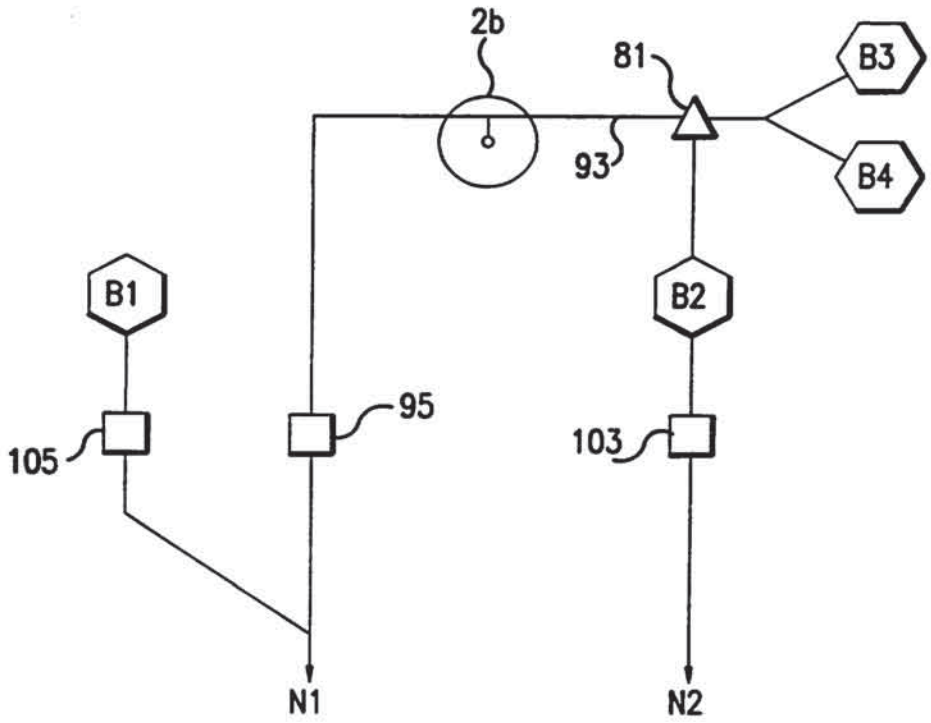


FIG.15

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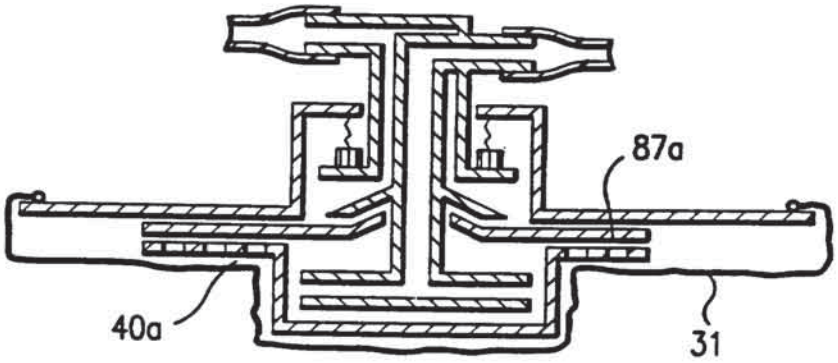


FIG. 16

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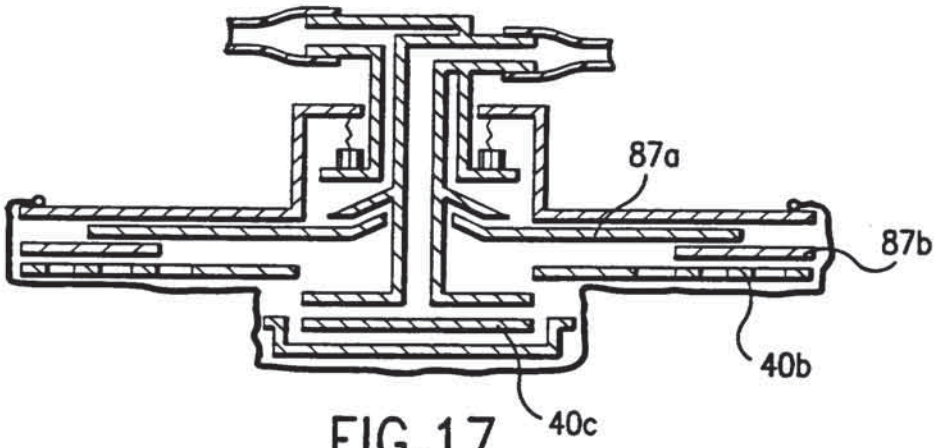


FIG.17

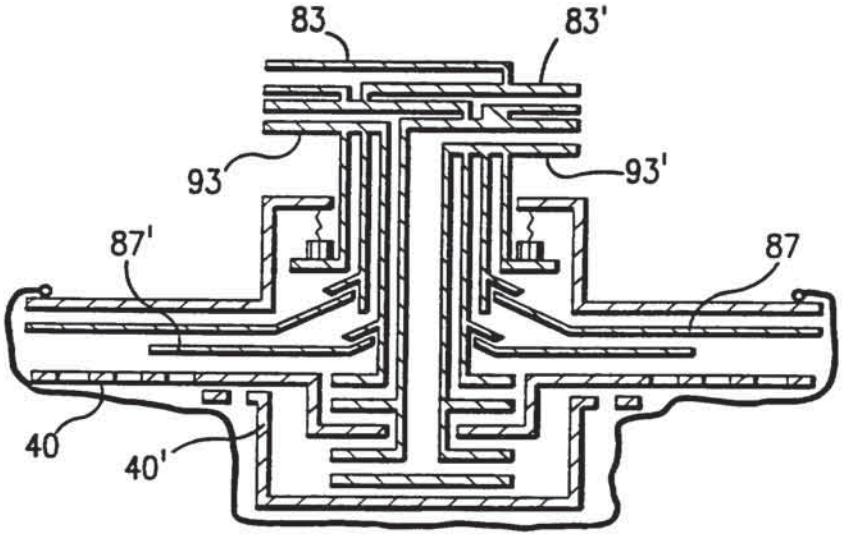


FIG.18

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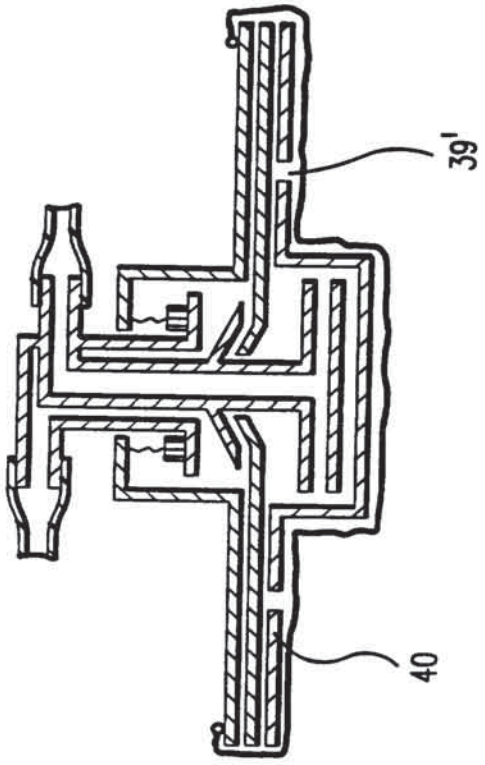


FIG. 19A

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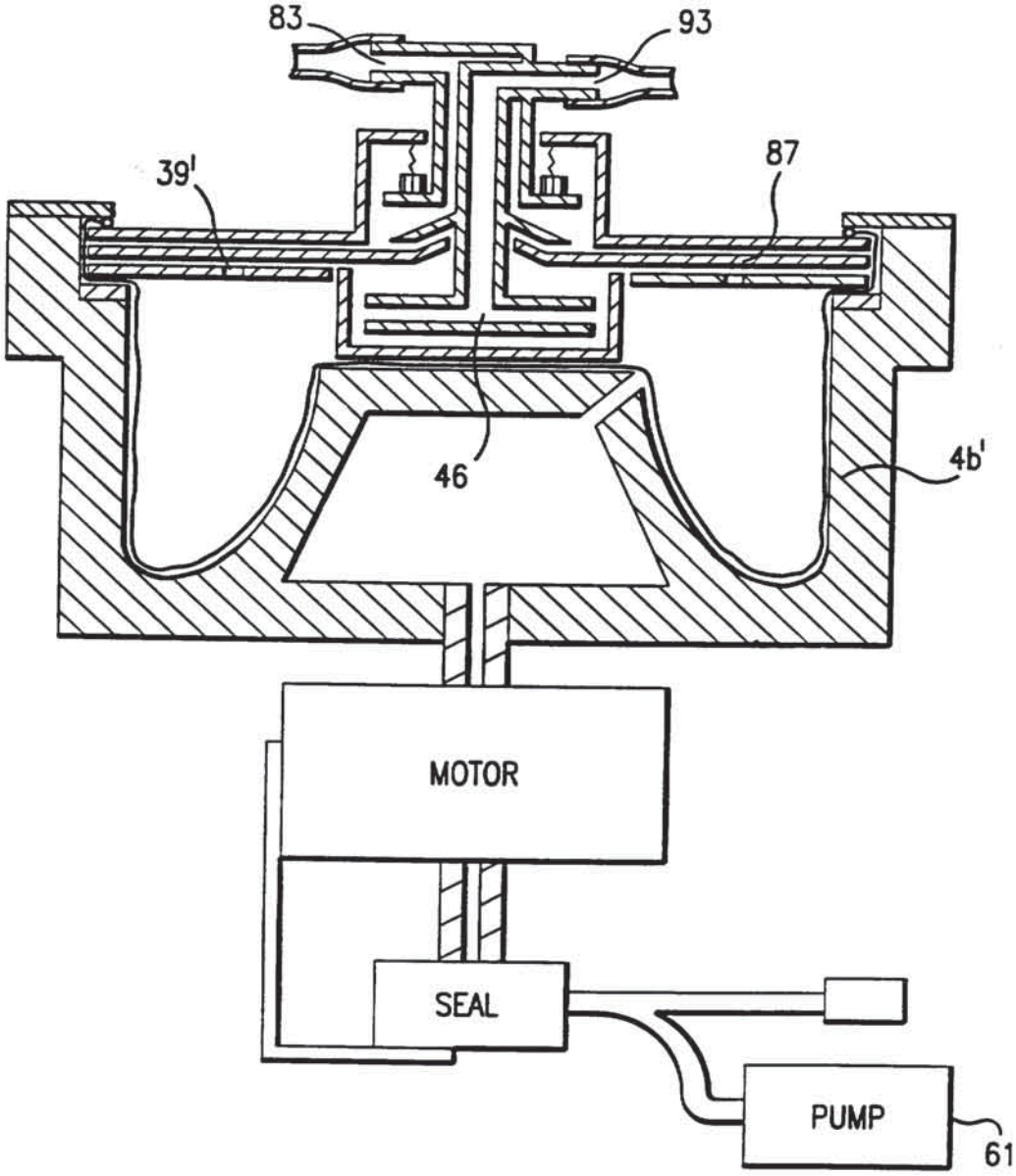


FIG.19B

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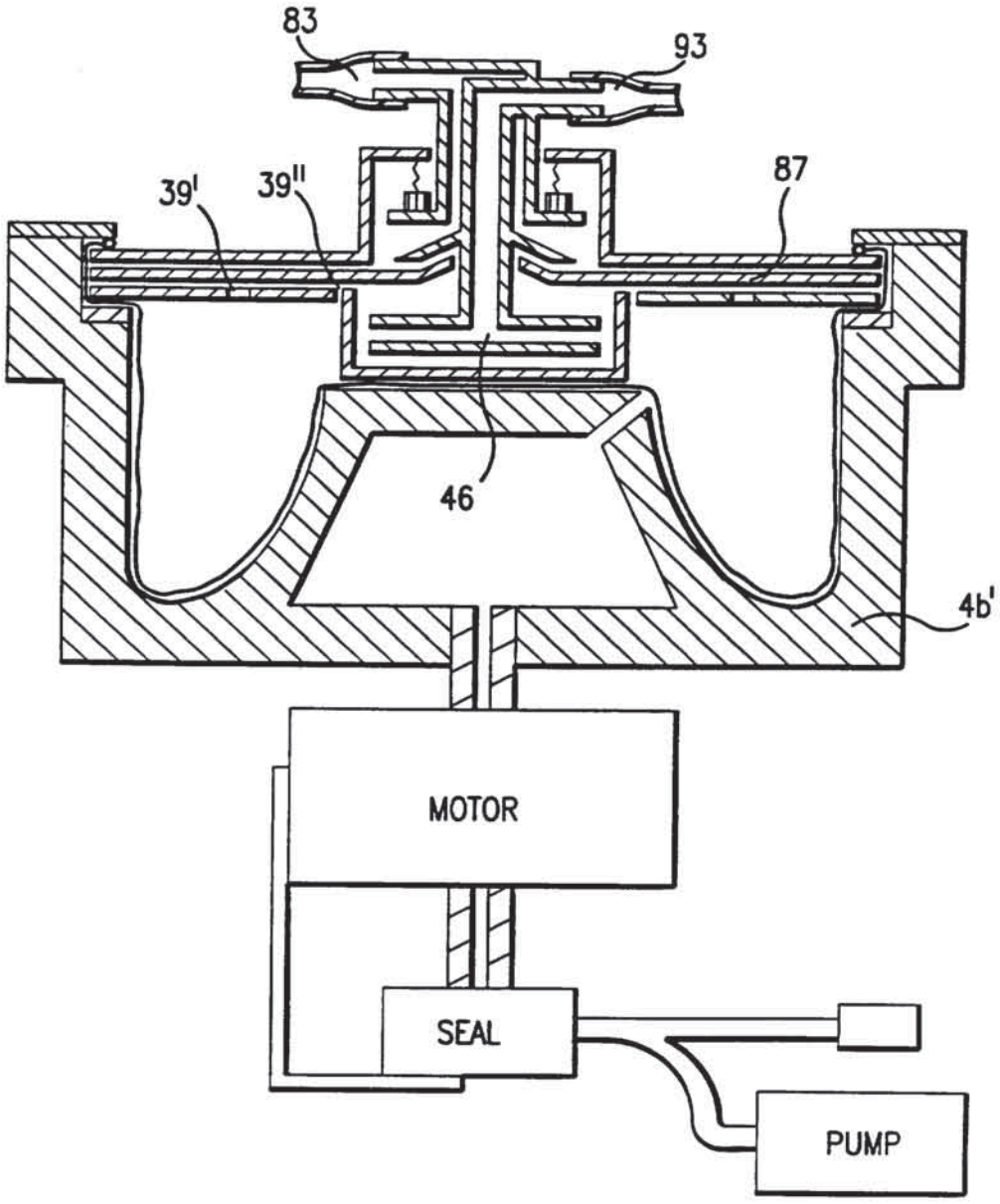


FIG.19C

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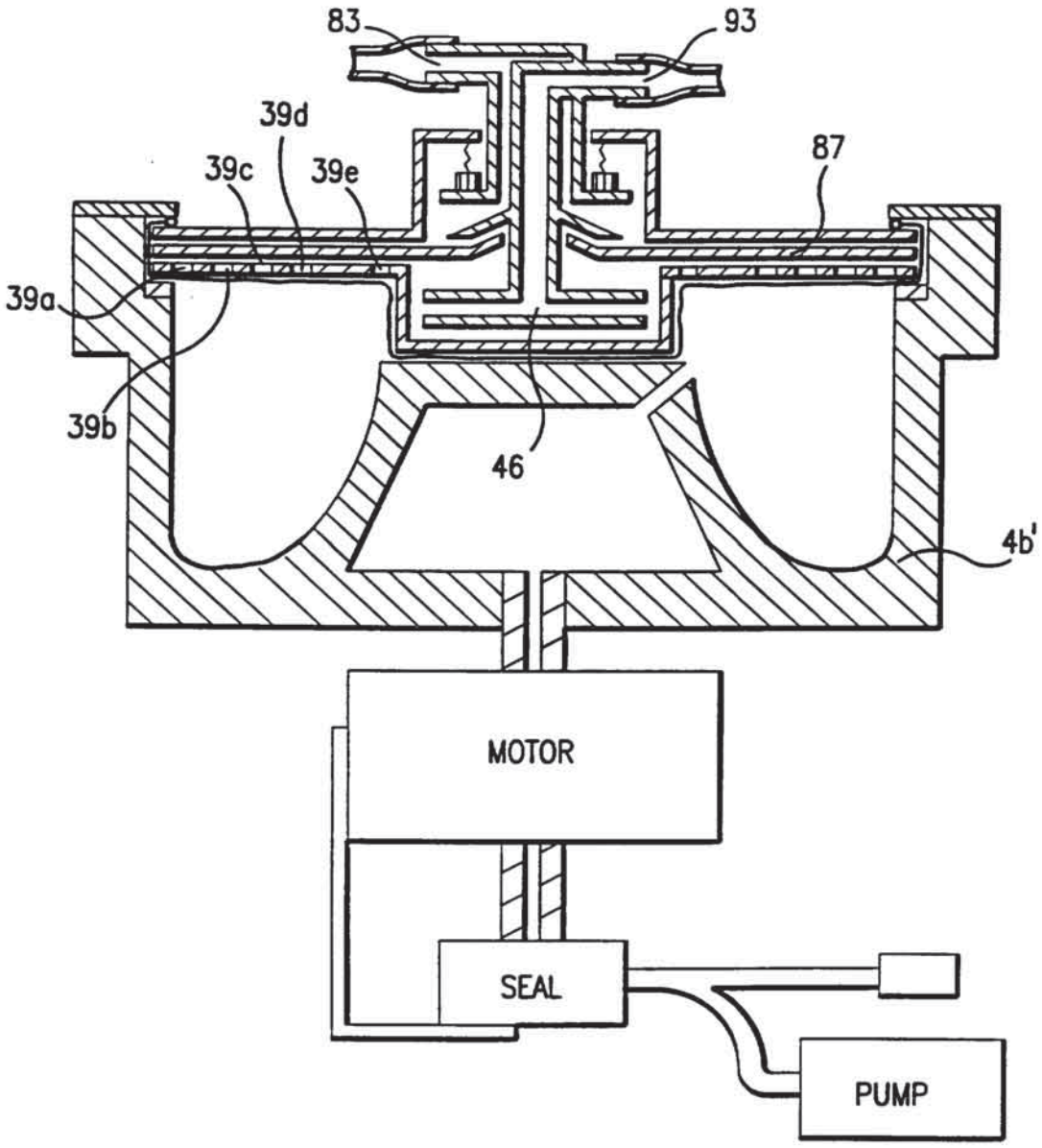


FIG.19D

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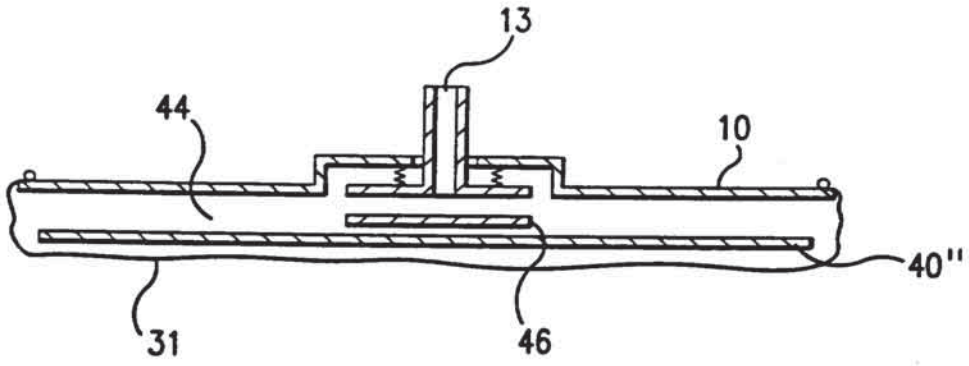


FIG.19E

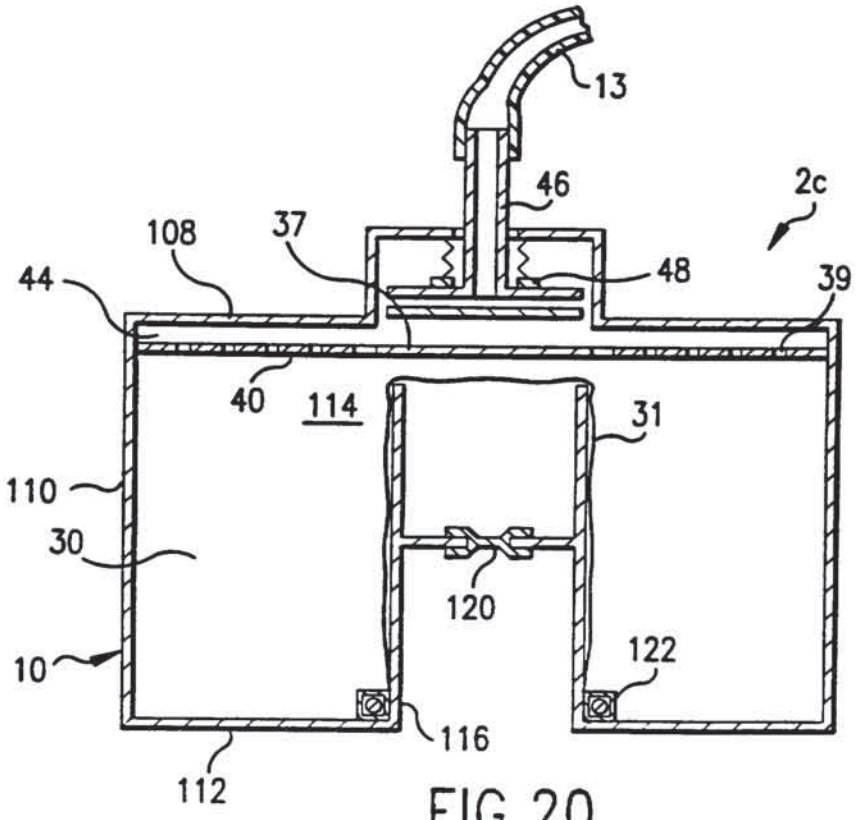


FIG.20

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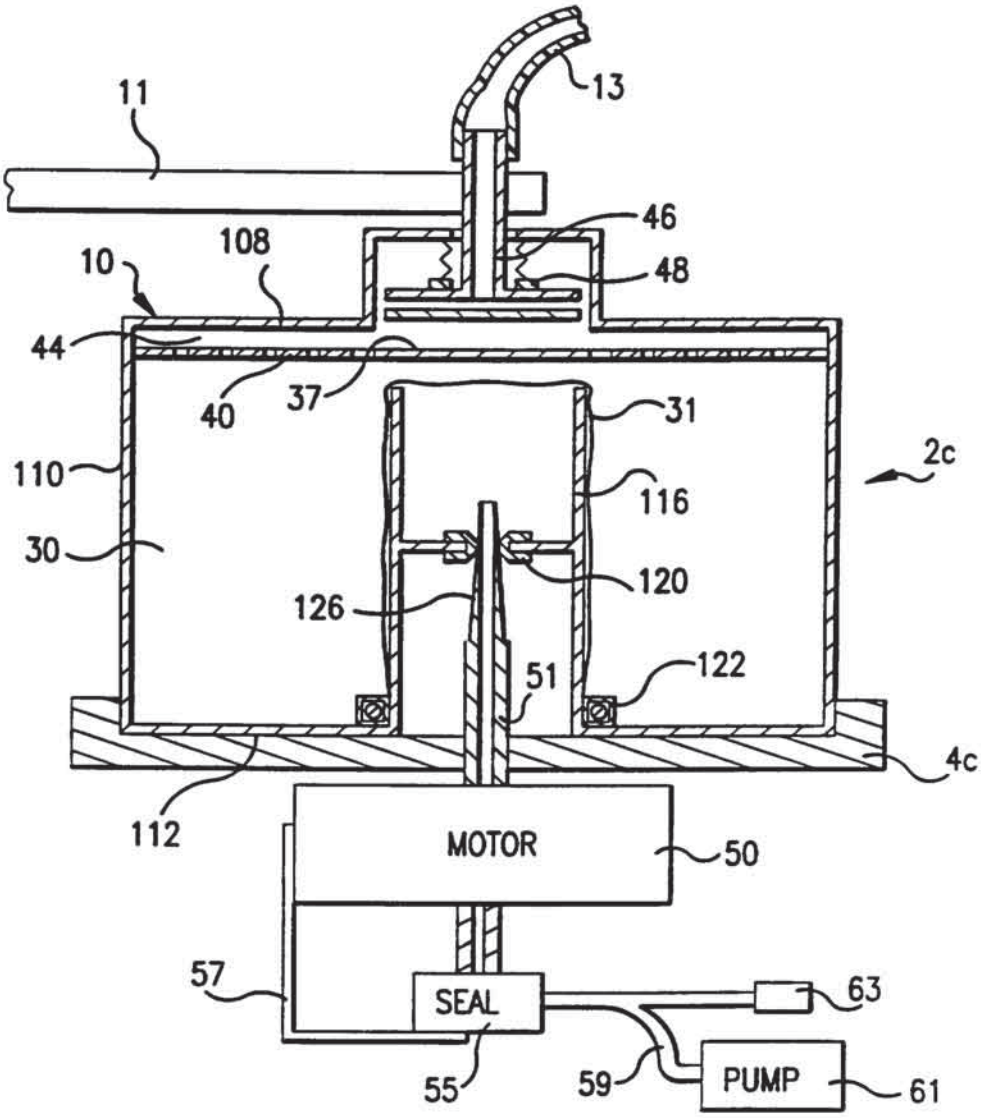


FIG.21

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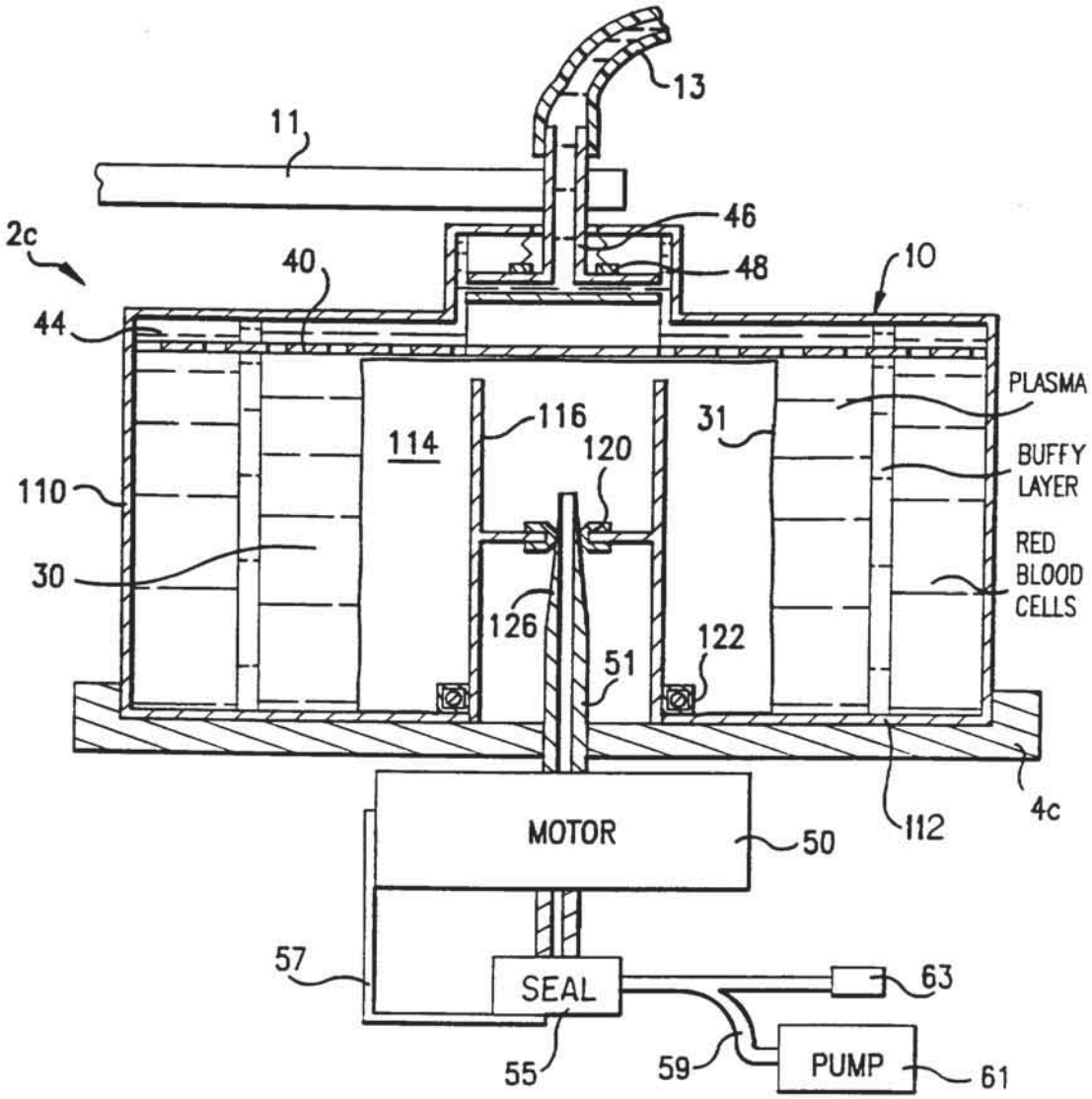


FIG.22

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