Particle Separation Using Ultrasound Can Radically Reduce Embolic Load to Brain After Cardiac Surgery

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Background. **Microembolism during cardiopulmonary bypass has been suggested as being the predominant cause of neurocognitive disorders after cardiac surgery. Shed blood, normally retransfused into the patient during cardiopulmonary bypass, is a major source of lipid microemboli in the brain capillaries. A newly developed technique based on acoustic standing-wave separation of particles in fluid in microchannels, with the capacity to remove lipid particles in blood, is presented.**

Methods. **A separator consisting of eight parallel, high-fidelity microfabricated channels was actuated with an ultrasound field to create a standing wave. Three different concentrations of lipid particles (diameter, 0.3 μm) were added to blood samples with increasing hematocrits and introduced into the separator channels to separate lipid particles and erythrocytes.**

Results. **The mean separation rates for lipid particles were 81.9% ± 7.6% and for erythrocytes 79.8% ± 9.9%, and both were related to the hematocrit level of the incoming blood sample. The procedure was atraumatic and did not cause hemolysis.**

Conclusions. **Particle separation by means of an acoustic standing-wave technique can be used for atraumatic and effective removal of lipid particles from blood, with the possible clinical implication of reducing neurocognitive complications after cardiopulmonary bypass.**

(Ann Thorac Surg 2004;78:1572–8)

For the majority of patients undergoing cardiac surgery, the outcome in terms of cardiac function is excellent, and, for some, predicted long-term survival is increased. Despite improvements in surgical techniques during the recent decades, complications resulting from surgery persist. Of all the possible complications, cerebral complications are by far the most feared and costly. A meta-analysis showed an overall incidence of 1.7% of postoperative stroke [1]. Cognitive dysfunction after surgery, with symptoms dominated by deficits of memory retention and attention together with inability to learn new tasks, is more frequent, and figures ranging from 10% to 70% have been reported [2]. What is even more alarming is that many of these deficits are permanent. In a recent long-term follow-up, it was reported that 42% of patients suffered from cognitive dysfunction 5 years after surgery [3].

The origin of these cognitive deficits has been discussed for many years. Evidence is mounting that microemboli play a major role in this type of subtle brain damage [4–7]. Moody and coworkers [8, 9] reported massive embolization of lipid particles to the brain, amounting to millions of emboli in the capillaries of the brain. The source of the emboli was found to be the shed blood from the surgical field, into which lipids leak into the pericardial cavity from adipocytes in the mediastinum, subcutis, and bone marrow (Fig 1A) [10]. These emboli are often referred to as lipid microemboli, and the blood containing these lipid particles is normally retransfused into the patient if a heart-lung machine is used, leading to massive embolization of lipid particles, ranging in size from 5 to 50 μm.

As the currently available techniques for particle separation (filters and centrifuges) are inadequate to remove these lipid particles satisfactorily [11, 12], we set out to develop a new separation technique based on ultrasonic standing waves, realized in microfluidic channels. The separation of suspended particles using standing waves is itself not new, and has been described previously [13, 14]. Both these methods were, however, hampered by serious limitations, and cannot be used for this application.

The separation technique described here is based on silicon microstructure development, which enables the manufacture of high-fidelity, microchannel arrays in silicon wafers for online acoustic separation of microparticles in a parallel fashion for increased throughput.

Accepted for publication April 21, 2004.

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Drs Jönsson, Laurell, Nilsson, and Petersson disclose that they have a financial relationship with ErySave AB.

Published by Elsevier Inc

0003-4975/04/$30.00
doi:10.1016/j.athoracsur.2004.04.071

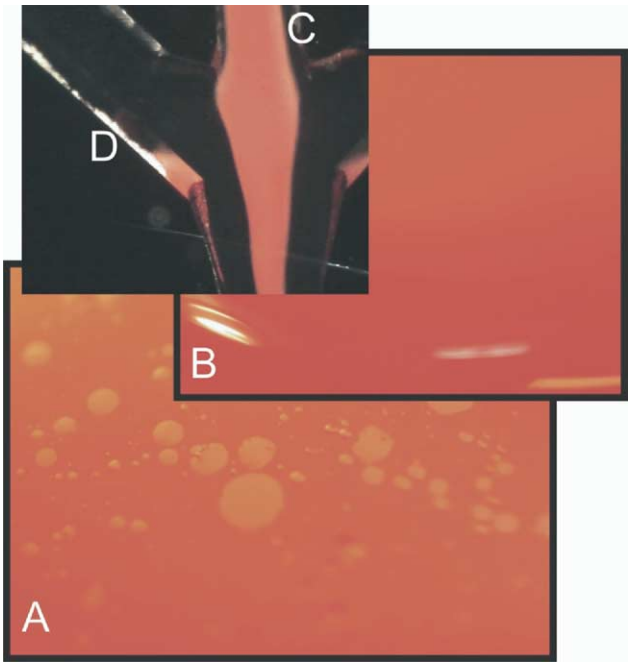

Fig 1. Shed human blood from the pericardial cavity with lipid particles visible on the surface (A). The same blood after being processed using particle separation with ultrasound standing-wave technique (B). A still from a video sequence during separation of a human blood sample showing erythrocytes in the center outlet (C) and lipid particles in the side outlets (D). The lipid particles can be seen as a white patch against the inferior wall of the side outlet. The direction of flow is from the bottom to the top of the image.

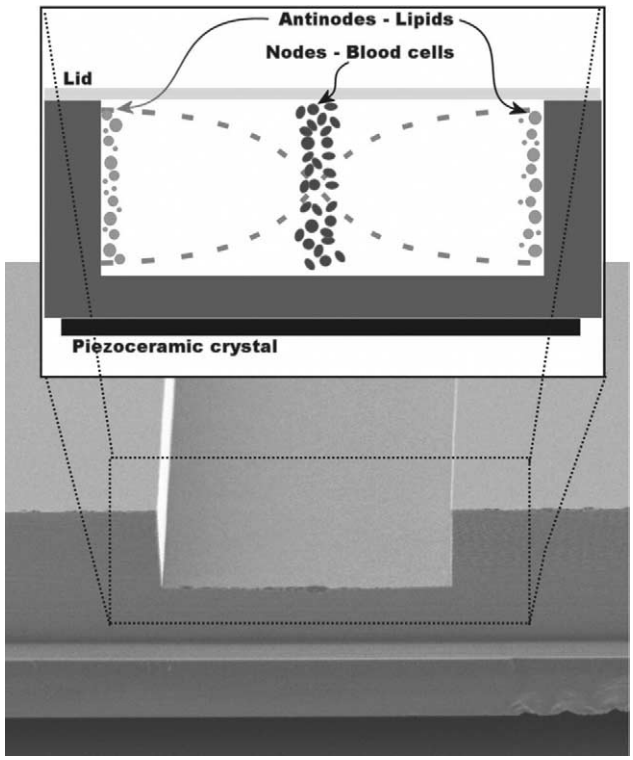

Fig 2. The principle of particle separation with ultrasound standing-wave technology. A scanning electron microscopy image shows the high-fidelity channels with vertical walls where separation is performed. Less-compressible particles with higher density (eg, erythrocytes) than the medium will move to the nodes, whereas more-compressible particles with a lower density (eg, lipid emboli) will gather at the antinodes.

The aim of this investigation was to test the efficiency of this separation method for erythrocytes and lipid particles and to demonstrate the feasibility of the technique for this specific purpose in cardiac surgery, possibly leading to a future role in reducing complications after cardiac surgery.

Material and Methods

Microchip Development

The microfluidic separation chip was manufactured by means of standard silicon processing techniques [15]. This microfabrication technique provides, in principle, perfectly vertical side walls of the microchannels as seen in the scanning electron micrograph (Fig 2). The fine accuracy of the side walls are a prerequisite for obtaining high-quality acoustic resonance in the microfluidic device. One benefit of this technique is that although the ultrasonic element is placed underneath the separation channel, the acoustic standing wave is obtained in the same plane as the silicon wafer, orthogonal to the direction of fluid flow (Fig 3). The high fidelity of the microfabrication process enables the manufacture of a separation device based on a parallel microchannel array. In this study, a separator with eight parallel channels was used (Fig 4).

The acoustic forces exerted on the particles are dependent on the density, compressibility, and size of the particles. The acoustic properties of lipid particles and erythrocytes are such that the acoustic force field acts in opposite directions on the two types of particles, thus

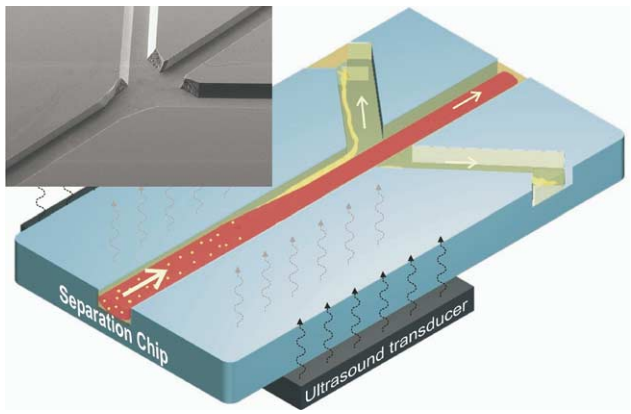

Fig 3. Schematic view of one 375-μm-wide separation channel and a scanning electron microscopic image of the trifurcation forming the center and side outlets in which the flow is be divided depending on the acoustic properties of the particles. The orthogonal placement of the ultrasonic transducer is also depicted.

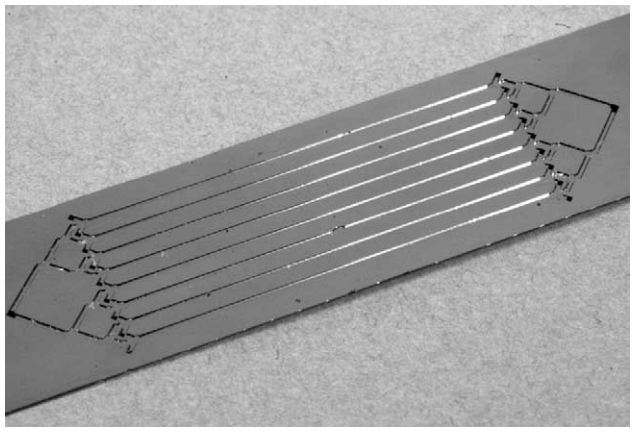

Fig 4. Photograph of a structure consisting of eight parallel channels, which was used in the study. The parallel channels are a prerequisite for increased throughput.

collecting the erythrocytes in the standing-wave pressure node and the lipid particles in the antinode [15, 16]. At the end of each separation channel, a trifurcation divides the flow of fluid and particles according to their spatial distribution in the channel (Fig 3) because the flow is completely laminar. Particles collected in the node of the standing wave (erythrocytes) are collected in the center outlet, and the lipid particles are collected in the side outlets of the microseparator.

Study Model

A lipid–blood phantom was constructed for the separation experiments. Bovine blood was anticoagulated with citrate and diluted with 0.9% saline solution to obtain predetermined hematocrit levels. Lipid particles mimicking lipid emboli were produced according to a standard protocol for sonicating tritium-labeled triolein with phospholipids [17] with minor modifications. A total amount of 800 mg of triolein (of which 1.875 mg was radioactive; 61 μCi/mg) and 8 mg of phospholipids were sonicated in 18 mL of phosphate-buffered saline. After sonication, 2 mL of 20% fatty-acid-free bovine serum albumin in phosphate-buffered saline was added. The resulting 4% triolein emulsion was diluted to obtain the various working solutions of triolein used in the experiments. This procedure yielded emulsified triglycerides with a mean diameter of 0.3 μm. Both blood and lipid emulsions were always used within 48 hours of preparation.

Eighteen different aliquots of blood and lipid with increasing concentrations of erythrocytes (hematocrits of 5%, 10%, 15%, 20%, 25%, and 30%) and lipid particles (0.5%, 1%, and 2%) were prepared. However, the aliquot with a hematocrit of 30% and 2% lipids would not mix owing to the high concentrations of particles, and had to be excluded from the study. For each of the 17 unique mixtures of blood and lipid particles, we made three independent measurements of hematocrit, hemolysis (measured as free hemoglobin in plasma), and lipid content (measured as beta radiation) in samples taken at the center and the side outlets, and before separation.

The flow was controlled with syringe pumps, and the flow rate was maintained at 0.5 mL/min for both center and side outlets by applying the syringe pumps after the structure. The ultrasonic transducer was operated with an 18.0 to 28.3 Voltage peak to peak sinusoidal signal at frequencies between 1.9739 and 2.0343 MHz.

The separation efficiency was measured as the ratio of particles collected from the center and the side outlets divided by particles collected in the side and center outlets combined, that is, the ratio of lipid particles in the side outlets to the center and side outlets, and the ratio of erythrocytes in the center outlet to the center and side outlets. This method for determining efficiency would yield 100% if all erythrocytes were recovered. Hematocrit determinations were performed with a standard hematocrit centrifuge. The lipid particle load was determined by measuring the radioactivity in whole blood, according to a standard scintillation counting protocol [18]. Hemolysis was determined using a HemoCue Low-HB device (Hemocue, Ängelholm, Sweden). The cutoff level for the device was 0.3 g/L. Levels below this value were set to 0.2 g/L for calculations.

Statistics

Group values are expressed as the mean ± standard deviation. For measurements of hemolysis (Table 1), data were grouped according to their predetermined hemat-

Table 1. Concentration of Red Blood Cells Expressed as Hematocrit, Before Separation and After Separation at Different Initial Concentrations, Together With the Hemolysis Before Separation and After Separation in Both Center and Side Outlets[a]

Predetermined Hematocrit	Measured Hematocrit in Phantom (%)		Hemolysis (g/L)		
	Before Separation	Center Outlet	Before Separation	Center Outlet	Side Outlets
5%	4.65 ± 0.40	7.89 ± 0.41	0.47 ± 0.21	0.41 ± 0.32	0.48 ± 0.29
10%	9.14 ± 0.03	15.14 ± 2.63	0.67 ± 0.40	0.56 ± 0.26	0.6 ± 0.38
15%	13.86 ± 0.34	21.62 ± 1.54	0.67 ± 0.45	0.58 ± 0.24	0.69 ± 0.39
20%	20.25 ± 4.95	25.09 ± 2.90	0.70 ± 0.40	0.64 ± 0.26	0.79 ± 0.42
25%	23.31 ± 2.68	30.64 ± 1.94	0.9 ± 0.0	1.41 ± 0.81	1.07 ± 0.26
30%	28.16 ± 0.58	38.06 ± 2.61	1.35 ± 0.21	1.05 ± 0.05	1.35 ± 0.23

[a] Values are grouped according to their predetermined hematocrit, ie, different lipid particle concentrations are in the same group. No significant difference was found between preseparation and postseparation hemolysis.

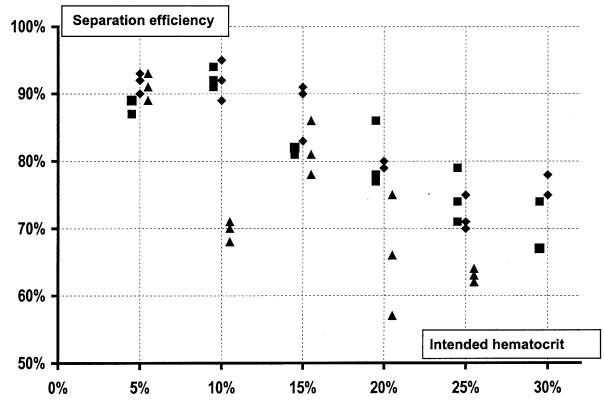

Fig 5. Separation efficiency of red blood cells measured as a function of hematocrit. Samples with 0.5% lipid particles (■), 1% lipid particles (◆), and 2% lipid particles (▲) were compared. Superimposed measurements are indicated by larger symbols.

ocrit (different lipid concentrations were grouped in the same hematocrit group). To test for differences between preseparation and postseparation hemolysis, a sign–rank test was used. Correlations were investigated with univariate analysis, and univariate regression analysis was performed to test dependency. A p value less than 0.05 was considered significant.

Results

Preseparation hematocrits for the different groups were all close to the intended hemoglobin concentrations for the experiments. In addition, hemoconcentration was seen, and hematocrits in blood from the center outlet ranged from 7.9% to 38.1% (Table 1). A low degree of hemolysis was seen in almost all preseparation samples. No change in the degree of hemolysis was seen as a result of the separation (Table 1).

The separation efficiency for erythrocytes, measured as the ratio of the center outlet to the side and center outlets, ranged between 94% and 57% with a mean of 79.8% ± 9.9% (Fig 5). The separation efficiency decreased with increasing hematocrit ($r = 0.70$, $p < 0.0001$).

The separation ratio of lipid particles measured as radioactivity ranged from 66% to 94% with a mean of 81.9% ± 7.6% (Fig 6). In contrast to erythrocytes, the separation ratio for lipids increased with increasing hematocrit in the incoming sample ($r = 0.33$, $p < 0.05$).

A sample of shed blood collected from a patient undergoing cardiac surgery was processed in a separate experiment. From visual examination by macrophotography, we estimated complete removal of all macroscopic lipid microemboli in this model (Fig 1).

Comment

We describe here a novel ultrasound technique with the ability to separate and remove lipid particles from blood. Microembolism has been suggested by many investigators to be the main contributor to the pathogenesis of neurocognitive complications after cardiac surgery [5, 6, 19, 20]. Moody and coworkers [8, 9] showed that there was an increased number of lipid microemboli in brain capillaries after experimental cardiopulmonary bypass, and referred to them as small capillary arteriolar dilatations (SCADS). Brooker and coworkers [10] found that these originated from the pericardial shed blood that is routinely retransfused to the perfusion circuit by means of cardiotomy suction.

During cardiopulmonary bypass the hematocrit is intentionally reduced, as induced hypothermia increases the viscosity of the blood, but it is also done to avoid unnecessary transfusions. A crystalloid priming solution is therefore added to achieve a hematocrit of approximately 20% to 25%. In shed blood, the hematocrit is even lower as it gets mixed with saline solution or other slush fluids used during surgery. The efficiency of the ultrasound separator regarding the removal of lipid particles ranged between 66% and 94% with a mean of 81% at the hematocrit levels investigated. This is much better than that which can be achieved with other methods, such as cell wash by means of centrifugation or filters, currently used in clinical practice.

Saline cell washing, followed by centrifugation (cell-saving device technology), reduced the number of emboli by approximately 50% [12]. However, the method has several drawbacks. The process is intermittent with a need to collect a minimal batch volume (typically 400 to 500 mL) before washing can be initiated, and the devices are large, occupying space in an already crowded environment. Hemolysis is always a side effect, probably as a result of the extreme gravitational force (500 to 2,000 g) exerted on the erythrocytes when the centrifuge reaches the maximum speed.

With filters, an even lower reduction in the number of emboli was achieved. Kincaid and coworkers [12] reported that approximately 30% to 40% was removed, and

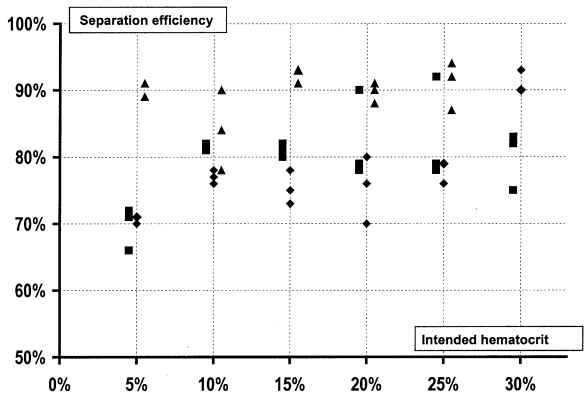

Fig 6. Separation efficiency of lipid particles cells as a function of hematocrit measured by radioactivity. Samples with 0.5% lipid particles (■), 1% lipid particles (◆), and 2% lipid particles (▲) were compared. Superimposed measurements are indicated by larger symbols.

a recent study also showed a 30% reduction [11]. Filters will eventually become saturated, resulting in rapid reduction of filtering capacity [11]. Also, it is generally believed that filters only disperse larger emboli into smaller ones. The typical arterial line filter in use has a pore size of 40 μm, and will still allow lipid particles large enough to wedge in small brain capillaries to pass through.

It might be argued that our test model with very small lipid particles (0.3 μm in diameter) was not optimal, as clinically relevant microemboli must be of a considerably larger size. However, the force exerted by the ultrasound on particles scales with the volume of the particle. A 10-μm particle has a volume 37,000 times larger (the cube of 10/0.3) than that of a 0.3-μm particle. Consequently, the force exerted will be 37,000 times greater. It is therefore reasonable to assume that the separation ratio will increase as the particles become larger. To demonstrate that this method also allows for the removal of larger lipid particles, we tested shed blood from the pericardial cavity of a patient and found by visual inspection that all the lipid droplets had been removed (Fig 1).

Existing methods have a limited efficiency in removing emboli, which may explain why studies of the clinical outcome of emboli removal have shown negative or conflicting results [4, 7]. The present method can cleanse blood of at least 80% of particles. In fact, a separation efficiency greater than 90% was achieved at least once for every sample, and it is reasonable to believe that further improvements and fine tuning of the technique will result in a separation ratio of at least 90% for small particles (diameter less than 1 μm), and probably even higher for larger particles. This will enable us to perform better studies to assess the impact of microemboli removal on the patient's neurocognitive outcome.

The separation rate for erythrocytes ranged between 57% and 95% with a mean of 80%. The test point with low separation ratio could be attributed to artifacts, such as trapping of air bubbles in separation channels, which were not detected by the operator. When these outliers were excluded and relevant hematocrit for the clinical situation chosen ($\leq$20%), the mean recovery rate was 85%. Some erythrocytes were lost to the side outlets, but this can be improved by adjusting the flow velocities in the center and side outlets.

No process-related hemolysis was observed. Ultrasound can, however, be used to achieve hemolysis by inducing shear forces by cavitation [21]. These forces depend on both frequency and intensity, and normally lower frequencies will yield larger forces [22]. On the other hand, low-intensity ultrasound, which is used, for instance, in diagnostic procedures, produces no significant cavitation, and has been proven safe throughout the years [23]. The application of an acoustic standing wave displaces some particles, eg, erythrocytes, to the nodes, and they are thus positioned at a location where no cavitation is present. However, cavitation is present at the antinodes (where lipids are collected), but with the frequency and intensity used in this model, the cavitation forces are weak at the antinodes. For comparison, it can be mentioned that cell-saving device technology displaces erythrocytes to the periphery, where the gravitational force is the highest, which could explain the hemolysis seen after centrifugation [24, 25]. The acoustic separation technique shows no evidence of exposing blood cells to strong shear forces. We found no hemolysis in this study, and the technique seems to be atraumatic to cells, which further adds to the clinical benefit.

Ultrasonic standing-wave techniques, for the purpose of particle separation, have been described earlier [13, 14]. However, these techniques were neither developed for nor tested with blood. Gröschl [13] manufactured a device with a standing wave between two transducers centimeters apart. This device resulted in substantial turbulence, with low efficiency, and only low concentrations of particles could be processed. The technique described in this paper uses the benefits of laminar flow in microfluidic channels. An estimate of the laminar flow index, the Reynolds number, for the flow velocity and channel dimensions used and blood as the fluid yields a value of less than 20 (a Reynolds number of less than 2,000 is considered to indicate laminar flow). Thus, the extremely laminar flow in the channels is another contributing factor to the high separation ratio. Hawkes and Coakley [14], on the other hand, tested single-line separation with low throughput and low precision. The novelty of our technique is the micromechanic fabrication, yielding an extremely high precision, together with a two-dimensional, distribution of channels. The fabrication of a microchannel array (Fig 3) makes it possible to realize parallel channels actuated by a single transducer. Parallel channels are a prerequisite for the scalability and the increased throughput needed to meet clinical demands. The presented device with eight parallel channels can handle 60 mL/h, and at least a 20-fold increase in throughput will be necessary to meet clinical demands. This can be achieved by increasing the number of parallel channels. In addition, the planar technology of channels can also be used to realize serial processes, with improved separation efficiency. For example, two-stage separation could increase the separation efficiency further. If the recovery rate for erythrocytes is 90% in the first step, a second step would yield another 90% recovery of the 10% remaining, resulting in 99% overall recovery.

It was not the aim of this study to investigate the separation efficiency for leukocytes or thrombocytes. However, their physical properties in terms of density and compressibility resemble those of erythrocytes, and, therefore, they will most likely follow erythrocytes to the center outlet. This separation platform can be used in several other fields of particle separation. The physical properties that determine the force exerted on the particles are the density, compressibility, and size. Other biologic particles, such as bacteria, macromolecules, lipoproteins, and viruses, have physical properties that could make separation possible with acoustic technique. We propose the acronym PARSUS (particle separation using ultrasound) be used for this generic separation technique.

In conclusion, a novel technique, using an ultrasound standing wave in a microdomain for the separation of lipid particles in shed blood, is presented. The microembolic load on brain capillaries during cardiac surgery can be abolished or reduced. Whether this, in turn, will lead to an overall improvement in the neurocognitive outcome of individual patients must be assessed in further studies. The generic platform has inherent properties of scalability and design flexibility enabling the implementation of the technique in other types of particle separation.

References

1. Naylor AR, Mehta Z, Rothwell PM, Bell PR. Carotid artery disease and stroke during coronary artery bypass: a critical review of the literature. Eur J Vasc Endovasc Surg 2002;23:283–94.
2. Mahanna EP, Blumenthal JA, White WD, et al. Defining neuropsychological dysfunction after coronary artery bypass grafting. Ann Thorac Surg 1996;61:1342–7.
3. Newman MF, Kirchner JL, Phillips-Bute BRH, et al. Longitudinal assessment of neurocognitive function after coronary-artery bypass surgery. N Engl J Med 2001;344:395–402.
4. Pugsley W, Klinger L, Paschalis C, Treasure T, Harrison M, Newman S. The impact of microemboli during cardiopulmonary bypass on neuropsychological functioning. Stroke 1994;25:1393–9.
5. Stump DA, Rogers AT, Hammon JW, Newman SP. Cerebral emboli and cognitive outcome after cardiac surgery. J Cardiothorac Vasc Anesth 1996;10:113–8.
6. Taggart DP, Westaby S. Neurological and cognitive disorders after coronary artery bypass grafting. Curr Opin Cardiol 2001;16:271–6.
7. Whitaker DC, Newman SP, Stygall J, Hope-Wynne C, Harrison MJ, Walesby RK. The effect of leucocyte-depleting arterial line filters on cerebral microemboli and neuropsychological outcome following coronary artery bypass surgery. Eur J Cardiothorac Surg 2004;25:267–74.
8. Moody DM, Bell MA, Challa VR, Johnston WE, Prough DS. Brain microemboli during cardiac surgery or aortography. Ann Neurol 1990;28:477–86.
9. Moody DM, Brown WR, Challa VR, Stump DA, Reboussin DM, Legault C. Brain microemboli associated with cardiopulmonary bypass: a histologic and magnetic resonance imaging study. Ann Thorac Surg 1995;59:1304–7.
10. Brooker RF, Brown WR, Moody DM, et al. Cardiotomy suction: a major source of brain lipid emboli during cardiopulmonary bypass. Ann Thorac Surg 1998;65:1651–5.
11. de Vries AJ, Gu YJ, Douglas YL, Post WJ, Lip H, van Oeveren W. Clinical evaluation of a new fat removal filter during cardiac surgery. Eur J Cardiothorac Surg 2004;25:261–6.
12. Kincaid EH, Jones TJ, Stump DA, et al. Processing scavenged blood with a cell saver reduces cerebral lipid microembolization. Ann Thorac Surg 2000;70:1296–300.
13. Gröschl M. Ultrasonic separation of suspended particles—part II: design and operation of separation devices. Acust Acta Acust 1998;84:632–42.
14. Hawkes JJ, Coakley WT. Force field particle filter, combining ultrasound standing waves and laminar flow. Sens Actuators B 2001;75:213–22.
15. Nilsson A, Petersson F, Jönsson H, Laurell T. Acoustic control of suspended particles in micro fluidic chips. Lab Chip 2004;4:131–5.
16. Gröschl M. Ultrasonic separation of suspended particles—part I: fundamentals. Acust Acta Acust 1998;85:432–7.
17. Holm C, Österlind T. Lipase and phospholipase protocols. In: Dolittle MH, Reue K, eds. Methods in molecular biology. Totowa, NJ: Humana Press, 1999;109:109–21.
18. Evangelista S, Cochet P, Bromet N, Criscuoli M, Maggi CA. A distribution study with (14)C-otilonium bromide in the rat: evidence for selective tropism for large intestine after oral administration. Drug Metab Dispos 2000;28:643–7.
19. Murkin JM. Etiology and incidence of brain dysfunction after cardiac surgery. J Cardiothorac Vasc Anesth 1999;13(Suppl 1):12–17.
20. Stump DA, Kon NA, Rogers AT, Hammon JW. Emboli, and neuropsychological outcome following cardiopulmonary bypass. Echocardiography 1996;13:555–8.
21. Miller MW, Battaglia LF. The relevance of cell size on ultrasound-induced hemolysis in mouse and human blood in vitro. Ultrasound Med Biol 2003;29:1479–85.
22. Leighton TG. Cavitation in standing-wave fields. In: Leighton TG, ed. The acoustic bubble. San Diego, CA: Academic Press, 1997:495–504.
23. Barnett SB, Ter Haar GR, Ziskin MC, Nyborg WL, Maeda K, Bang J. Current status of research on biophysical effects of ultrasound. Ultrasound Med Biol 1994;20:205–18.
24. Elawad AA, Ohlin AK, Berntorp E, Nilsson IM, Fredin H. Intraoperative autotransfusion in primary hip arthroplasty. A randomized comparison with homologous blood. Acta Orthop Scand 1991;62:557–62.
25. Klodell CT, Richardson JD, Bergamini TM, Spain DA. Does cell-saver blood administration and free hemoglobin load cause renal dysfunction? Am Surg 2001;67:44–7.

INVITED COMMENTARY

Removal of lipid particles has become of interest after the alarming results of Moody and colleagues [1] on lipid embolization in brain arterioles after cardiac surgery. It resulted in various attempts to reduce lipids in retransfusion blood, which would be beneficial after cardiac surgery, but also after orthopedic surgery. Despite the known side effects of retransfusion from the wound area, autologous blood transfusion is increasingly used to reduce the use of allogenic blood. A major problem in justifying the efforts, time, and costs to clear retransfusion blood from lipid particles is to obtain evidence of clinically relevant brain damage and evidence for the dominant role of lipid particles.

First of all, brain damage has been reported with very different significance. A number of studies could not show any deterioration in cognitive functions, whereas biochemical markers of brain damage, such as S100β and enolase, showed in some studies small and transient appearance. Clearly, the specificity of such tests is not sufficient or sensitive enough to demonstrate brain damage. Perhaps new markers, such as carnosinase, may appear relevant for monitoring brain damage.

The second problem is that lipid particles are only one of the suspects of brain damage. Gaseous emboli, macromolecules, inflammatory agents, and leukocyte-platelet aggregates may be involved in occlusion of the small vasculature as well. In their discussion the authors indicated that, eg, macromolecules may also be removed by the current technique of particulate separa-

0003-4975/04/$30.00
doi:10.1016/j.athoracsur.2004.05.043

tion, but other potential sources of embolization possibly remain in retransfusion blood. The combination with other techniques to remove platelets, leukocytes, and products that affect hemostasis or inflammation may be a future option.

Third, the reuse of shed blood is a matter of dispute. It depends on the operation time, preference of surgeons, and need for immediate volume during the procedure. To obtain the technique widely used, it must be simple, fast, and cost effective.

Nevertheless, the PARSUS technique presented here offers new possibilities to improve the quality of retransfusion with high efficacy for removing potential dangerous lipid particles. Hopefully these qualifications will be supported by adequate monitoring instruments. It would be exciting to see the efficacy of a larger scale PARSUS device in clinical practice.

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Reference

1. Moody DM, Brown WR, Challa VR, Stump DA, Reboussin DM, Legault C. Brain microemboli associated with cardiopul-monary bypass: a histologic and magnetic resonance imaging study. Ann Thorac Surg 1995;59:1304–7.

Online Discussion Forum

Each month, we select an article from *The Annals of Thoracic Surgery* for discussion within the Surgeon's Forum of the CTSNet Discussion Forum Section. The articles chosen rotate among the six dilemma topics covered under the Surgeon's Forum, which include: General Thoracic Surgery, Adult Cardiac Surgery, Pediatric Cardiac Surgery, Cardiac Transplantation, Lung Transplantation, and Aortic and Vascular Surgery.

Once the article selected for discussion is published in the online version of *The Annals,* we will post a notice on the CTSNet home page **(http://www.ctsnet.org)** with a **FREE LINK** to the full-text article. Readers wishing to comment can post their own commentary in the discussion forum for that article, which will be informally moderated by *The Annals* Internet Editor. We encourage all surgeons to participate in this interesting exchange and to avail themselves of the other valuable features of the CTSNet Discussion Forum and Web site.

For November, the article chosen for discussion under the Adult Cardiac Surgery Dilemma Section of the Discussion Forum is:

Surgical Reconstruction of the Left Main Coronary Artery: Fresh Autologous Pericardium or Saphenous Vein Patch
Ehud Raanani, MD, Alexander Kogan, MD, Yaron Shapira, MD, Alex Sagie, MD, Ran Kornowsky, MD, and Bernardo A. Vidne, MD

Tom R. Karl, MD
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