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A Closed-system Technology for Mechanical Isolation of High Quantities of Stromal Vascular Fraction from Fat for Immediate Clinical Use

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Background: Adipose tissue stromal vascular fraction (SVF) is increasingly used in the clinic. SVF separation from fat by enzymatic disruption is currently the gold standard for SVF isolation. However, enzymatic SVF isolation is time-consuming (~1.5 h), costly and significantly increases the regulatory burden of SVF isolation. Mechanical fat disruption is rapid, cheaper, and less regulatory challenging. However, its reported efficacy is insufficient for clinical use. The current study evaluated the efficacy of a novel rotating blades (RBs) mechanical SVF isolation system.

Methods: SVF cells were isolated from the same lipoaspirate sample (n = 30) by enzymatic isolation, massive shaking (wash), or engine-induced RBs mechanical isolation. SVF cells were counted, characterized by flow cytometry and by their ability to form adipose-derived stromal cells (ASCs).

Results: The RBs mechanical approach yielded 2×10^5 SVF nucleated cells/mL fat, inferior to enzymatic isolation (4.17×10^5) but superior to cells isolating from fat by the "wash" technique (0.67×10^5). Importantly, RBs SVF isolation yield was similar to reported yields achieved via clinical-grade enzymatic SVF isolation. RBs-isolated SVF cells were found to contain 22.7% $CD45^-CD31^-CD34^+$ stem cell progenitor cells (n = 5) yielding quantities of multipotent ASCs similar to enzymatic controls.

Conclusions: The RBs isolation technology provided for rapid (<15 min) isolation of high-quality SVF cells in quantities similar to those obtained by enzymatic digestion. Based on the RBs platform, a closed-system medical device for SVF extraction in a rapid, simple, safe, sterile, reproducible, and cost-effective manner was designed. *(Plast Reconstr Surg Glob Open 2023; 11:e5096; doi: 10.1097/GOX.0000000000005096; Published online 22 June 2023.)*

INTRODUCTION

Adipose-derived stromal/stem cells (ASCs) were first characterized by Zuk et al,[1] and like other adult mesenchymal stromal/stem cells (MSCs), ASCs have been shown to possess regenerative and immunosuppressive potentials.[2] ASCs are an attractive source of adult stromal/stem cells, as they can be isolated from fat harvested by routine liposuction, a procedure that has been in use for fat transfer and removal since the early 1970s,[3,4] which is considered safe, with relatively low complication rates.[5–7] Furthermore, fat for ASC isolation can be easily obtained by liposuction that can be performed in an operating room setting or even under local anesthesia alone and in an outpatient care setting.[8]

ASC preparation requires the isolation of nonfat cells from adipose tissue by enzymatic digestion, centrifugation to separate the fat from the nonfat fraction termed the stromal vascular fraction (SVF) and subsequent SVF culture. SVF consists of a heterogeneous mixture of cells, including various hematopoietic cell types, endothelial cells, and MSC progenitor cells.[9,10] Alternatively, instead of ASC preparation, freshly isolated SVF can be used immediately following liposuction within the surgical arena for regenerative and immunosuppressive purposes. The use of freshly isolated autologous SVF as an alternative to adult stromal/stem cells dramatically decreases the cost of treatment and regulatory burden since it eliminates the need for cell culturing.[11,12] Since the first reported use of SVF in 2007, in the aesthetic

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field,[13] its use has significantly expanded to a broad spectrum of clinical applications.[14] The leading clinical indications currently suggested and studied for the use of SVF are cell-assisted lipotransfer (CAL), in which SVF cells enhance fat survival following fat transplantation[15]; treatment of osteoarthritis,[16] in which cells are intra-articularly injected into injured joints; wound treatment[17,18]; and more.

The gold standard technique to obtain the SVF from an adipose tissue is enzymatic digestion of the tissue. In this process, the adipose tissue is washed, followed by enzymatic digestion, and the cells are separated from mature adipocytes, released oil, and enzyme solution by centrifugation. In general, enzymes such as collagenase, trypsin, or dispase are used to digest adipose tissue.[11] Enzymatic digestion effectively disrupts the functional extracellular matrix, leaving SVF as a heterogeneous mixture of cells.[10]

Despite its relative efficiency in SVF isolation from fat, enzymatic digestion of adipose tissue is time-consuming (~1.5–2 h) due to the long duration of the enzymatic dissociation of the fat tissue, and is relatively expensive due to the cost of GMP-grade enzymes and costly equipment requirement. In addition, it results in the contamination of isolated cells with the digesting enzyme. Moreover, clinical use of SVF produced by enzymatic digestion will require strict regulation, more than minimal manipulation, in both the European Union and United States further limiting the potential of SVF use [regulation (EC) no. 1394/2007].

This article describes a recently developed novel mechanical SVF isolation technology that circumvents the need for enzymatic digestion of fat tissue. This nonenzymatic isolation method replaces the enzymatic digestion with mechanical shear force to separate the cells or cell aggregates from adipose tissue. This technology involves the use of a swift, closed-system (liposuction is performed directly into the system), engine-driven device that extracts undamaged SVF cells from fat tissue.

METHODS

Approximately 200 mL of adipose tissue were collected from healthy donors (n = 30) and divided into three equal portions. The SVF was isolated by an enzymatic method, massive shaking (wash), or the engine-induced rotating blades (RBs) mechanical method. After isolation, obtained SVF was counted and characterized. The amount of SVF was normalized to 1 mL of intact fat.

Sample Collection

Subcutaneous abdominal adipose tissue samples were obtained from patients undergoing liposuction. Mean patient age was 42.3 ± 9.4 years, and mean body mass index was 27.3 ± 3.5 kg/m^2. All procedures were performed in accordance with the Declaration of Helsinki guidelines and approved by the ethics committee at the Tel Aviv Sourasky Medical Center (approval No. 0369-12-TLV). Written informed consent was obtained from all patients before surgery.

Takeaways

Question: Can a mechanical fat dissociation technology produce high-quality stromal vascular fraction (SVF) cells in sufficient quantities for efficient and rapid (15 min) intraoperation clinical use?

Findings: Our novel rotating blade–based technology isolated from fat high-quality SVF cells in quantities comparable to enzymatic-based clinical technologies/protocols.

Meaning: Our closed-system mechanical technology is a rapid, simple, safe, sterile, reproducible, and cost-effective SVF extraction technology that will likely broaden the use of SVF cells in clinical applications.

Adipose Tissue Harvesting

Power-assisted liposuction was performed by introducing a 3.0-mm diameter, blunt, hollow, 30-cm-long cannula (PAL-200E MicroAire power-assisted lipoplasty device, MicroAire Surgical Instruments LLC, Charlottesville, Va.) into the subcutaneous space through a small incision. Gentle suction was applied (<1 atm negative pressure). Standard Klein tumescent solution (1 mg adrenaline and 400 mg lidocaine per 1 L saline; the ratio of infiltration fluid to aspirate volume, 1:1–2:1) was applied for the superwet liposuction technique. No other fluids were needed. The fat was then decanted, and the fat fraction was aspirated into an empty sterile container.

SVF Cell Isolation

Enzymatic Digestion

Subcutaneous lipoaspirates were incubated with enzyme collagenase (0.075% type I collagenase, Sigma-Aldrich, St. Louis, Mo.) for 60 minutes at 37°C, with shaking. Fat was then separated by centrifugation (15 min, 400 g). The pellet was resuspended and passed through a 100-μm strainer. Nucleated cells were stained with a solution of 3% acetic acid and methylene blue (Stem-cell Technologies, Vancouver, BC, Canada) and counted manually, under a high-power light microscope.

RBs Mechanical Isolation of Cells from Fat

In a large container, lipoaspirate fat was mixed with saline, which was prewarmed to 37°C (350 mL volume). The fat/saline mixture was mechanically disrupted by an RB apparatus spun by an external engine; the procedure was performed at room temperature (RT) (Fig. 1). The mixture was centrifuged at 400 g for 15 minutes. Sedimented SVF cells were separated from floating adipocytes and passed through a 100-μm strainer. Nucleated cells were counted after staining samples with a solution of 3% acetic acid and methylene blue.

Isolation of Cells from Fat by Washing

Lipoaspirate fat was washed by adding prewarmed (37°C) saline and shaking samples for 15 seconds, followed by centrifugation at 400 g for 15 minutes. Sedimented SVF cells were separated from floating adipocytes and passed through a 100-μm strainer. Nucleated cells were counted

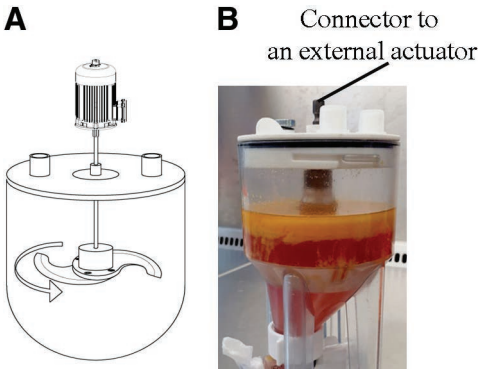

Fig. 1. The rotating blades (RBs) technology. A, A scheme of the RBs apparatus. Mechanical fat disruption was performed in a closed canister by actuator-driven RBs. B, A prototype of the mechanical fat disruption device.

after staining with a solution of 3% acetic acid and methylene blue.[19]

In all the experiments, we compared SVF cells isolated from the same lipoaspirate. After each isolation procedure, the recovery yield was calculated as the number of total SVF cells obtained divided by the initial volume of adipose tissue measured after the removal of infiltration liquid.

Cultured SVF

SVF cells were cultured in high-glucose Dulbecco's modified Eagle's medium (Gibco, Paisley, Scotland, United Kingdom), supplemented with 10% fetal bovine serum (Thermo Scientific HyClone, Tauranga, New Zealand), 60 µg/mL penicillin, 100 µg/mL streptomycin, 50 µg/mL kanamycin, 1 mM sodium pyruvate, 2 mM L-glutamine, and nonessential amino acids. After ~10 days, adherent cells named ASCs were observed in the culture plates, and nonadherent cells were removed.

Flow Cytometry

The following mouse anti-human antibodies were used for flow cytometry staining: CD31, CD34 (PeproTec, London, UK), CD29, CD105, CD73 PE/Cy7 (BioLegend, San Diego, Calif.), and CD45 (BD Biosciences, San Jose, Calif.). All the IgG1kappa antibodies had their respective isotype controls. All antibodies were used at the dilution recommended by the manufacturer. Following staining, the harvested cells were incubated with a red blood cell (RBC) lysis solution (BD FACS Lysing Solution) and analyzed by flow cytometry (FACSCanto II, BD Biosciences). Flow-Jo software (Tree star, Ashland, Ore.) was used for data analysis.

SVF Surface Marker Analysis

SVF cells were harvested and simultaneously incubated with the antibody panels for 1 hour, in the dark, at RT. The six-color panel contained antibodies against CD31, CD34, CD29, CD73, and CD45. To exclude dead cells, the samples were stained with violet viability dye (ViViD, Molecular Probes, Invitrogen, Eugene, Ore.), as described in the manufacturer's protocol.

A gradual gating strategy isolated a distinct population containing only singlets and live cells, while discarding RBCs. Gating for $CD45^-$ cells was than performed. The CD45 cells were then gated to define the populations positive for CD31, CD34, CD73, and CD29.

ASCs Surface Marker Analysis

ASCs were harvested and incubated with the antibodies listed above. The seven-color panel contained antibodies against CD31, CD34, CD29, CD105, CD73, and CD45. Dead cells were excluded by ViViD staining. All antibodies were used at the dilution recommended by the manufacturer.

Differentiation

Adipogenic Differentiation

Confluent passage 1 ASCs were cultured in the adipogenic medium containing high-glucose Dulbecco's modified Eagle's medium (Gibco), supplemented with 10% fetal calf serum (Thermo Scientific HyClone, Tauranga, New Zealand), 10 µg/mL insulin, 1×10^{-6} M dexamethasone, 0.5 mM IBMX, and 50 µM indomethacin (all purchased from Sigma). The medium was replaced every 3–4 days. After 21 days, the cells were fixed in 4% formalin (20 min, RT) and stained with 0.5% Oil Red O (Sigma) for 10 minutes, at RT. Following staining, the cells were photographed (Olympus IX71 microscope, Olympus, Tokyo, Japan) with a DP73 camera and Oil Red O was extracted by 4% IGEPAL (Sigma) in isopropanol and its absorbance at 520 nm was measured using a TECAN Infinite M200 plate reader (TECAN, Männedorf, Switzerland).

Osteogenic Differentiation

Confluent passage 1 ASCs were cultured in StemPro Osteogenesis Differentiation medium (Gibco). The differentiation medium was replaced every 3–4 days. After 21 days, the cells were fixed in 4% formalin (20 min, RT) and stained with 2% Alizarin Red (Sigma), pH 4.2 (10 min, RT). Cells were photographed with an Olympus IX71 microscope equipped with a DP73 camera. Then, Alizarin Red was extracted by extraction solution (0.5 N HCl/5% sodium dodecyl sulfate) and absorbance at 415 nm was measured using a TECAN Infinite M200 plate reader (TECAN).

Statistical Analysis

Results are presented as mean ± SD. The statistical significance of the results was determined using a two-tailed Student t test. *P* values less than 0.05 were considered significant.

RESULTS

RBs Mechanical Isolation Achieved Human SVF Yields Comparable to Reported Enzymatic Clinical-grade Isolation

In all the experiments that were performed, we compared SVF cells isolated from the same lipoaspirate, by enzymatic digestion, RBs technology, or shaking and centrifugation ("wash").[19]

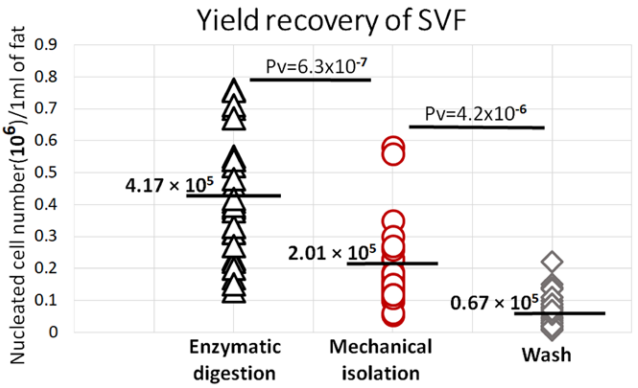

Fig. 2. Comparison of SVF yield achieved by different isolation methods. SVF was isolated from the same lipoaspirate, by enzymatic digestion ("enzymatic digestion"), our RBs mechanical isolation technology ("mechanical isolation"), by shaking and centrifugation ("Wash").

RBs mechanical isolation technology isolated an average $2.01\times10^5 \pm 1.2\times10^5$ SVF nucleated cells per 1 mL fat (n = 30). The yield was inferior to the yield obtained by enzymatic isolation [$4.17\times10^5 \pm 1.8\times10^5$ SVF nucleated cells per 1 mL fat (n = 30)], but was similar to the average yield obtained by clinical-grade enzymatic SVF isolation recently reported to be obtained using either the leading commercial enzyme-based Celution System (Cytori Therapeutics Inc.) (n = 70) or by manual isolation (n = 294)[20] and far superior to that achieved by the wash technique [$0.67\times10^5 \pm 0.51\times10^5$ SVF nucleated cells per 1 mL fat (n = 30)] (Fig. 2).

Comparable Stem Cell Progenitor Cell Yields in SVF Isolated Using the Enzymatic or the RBs Mechanical Technique

To better define the cell composition of SVF, the surface marker expression profile of cells isolated by the different techniques was determined using a six-color flow cytometry panel (Fig 3A). MSCs arise solely from the $CD45^-$ population, which represents the nonhematopoietic cells. Analysis of the SVF isolated by the different techniques revealed a higher proportion of $CD45^-$ cells in enzymatically and RBs mechanically isolated cells (41% and 30.4%, respectively) compared to the wash isolation technique, which yielded only 15% of $CD45^-$ cells (Fig. 3B).

A similar proportion of $CD45^-CD31^-CD34^+$ stem cell progenitors[10] was observed in enzymatically and RBs mechanically isolated cells (24.5% and 22.7%, respectively), whereas the wash isolation technique yielded a significantly lower proportion (only 9%) (Fig. 3C). In parallel, a significant percentage (28% ± 10%) of $CD45^-CD31^+CD34^+$ endothelial cells was observed in enzymatically isolated cell samples, whereas they were practically non-existent (3% ± 0.8%) in both RBs mechanically isolated cells and cells isolated by a wash (data not shown). A high proportion of $CD73^+CD29^+$ mesenchymal cells (98% ± 5%) was identified within the $CD45^-CD31^-CD34^+$ cell subpopulation, regardless of the isolation method used (data not shown).

SVF Cells Isolated by RBs Mechanical or Enzymatic Techniques Display Similar Yields of ASCs

Only 1%–10% of SVF cells are reported to be stem cell progenitors that can propagate under culture conditions.[10] Thus, comparing the quantity of stromal/stem cells obtained following 10 days of SVF culture expansion can provide a reasonable estimate of the percentage of stromal/stem cell progenitors within each SVF preparation. After 10 days in culture, a significantly higher number of cells was obtained from samples that had been enzymatically ($15.01\times10^3 \pm 3.93\times10^3$) or RBs mechanically ($13.06\times10^3 \pm 3.80\times10^3$) isolated as compared to those isolated by washing only ($8.12\times10^3 \pm 2.87\times10^3$) (Fig. 4A). All 10-day-old cultures demonstrated the expected surface marker expression patterns ($CD45^+$, $CD34^+$, $CD31^+$ <2% and $CD73^+$, $CD105^+$, $CD29^+$ >90%), verifying the ability of SVF cells to form ASCs in culture (Fig. 4B). Taken together, enzymatically and RBs mechanically isolated SVF samples contained a comparable percentage of stromal/stem cell progenitor cells. In contrast, SVF cells isolated by washing harbored fewer stromal/stem cell progenitors than both RBs mechanically and enzymatically isolated SVF.

SVF Cells Isolated by RBs Mechanical or Enzymatic Techniques Demonstrate Comparable Adipogenic and Osteogenic Differentiation Potentials

One of the main characteristics of ASCs is their multipotent nature, which enables them to differentiate into fat, bone, and cartilage.[10] Therefore, the multipotent potential of SVF cells isolated by enzymatic, RBs mechanical, and washing techniques was evaluated. Cultured cells that were isolated by either RBs mechanical or enzymatic methods demonstrated similar fat and bone differentiation potential (Fig. 5). Interestingly, cells isolated by washing displayed reduced fat differentiation potential compared to RBs mechanically and enzymatically isolated cells.

DISCUSSION

Use of SVF for the treatment of a diversity of clinical indications is an attractive cell therapy alternative due to the growing clinical evidence that supports its efficacy, the relative ease of obtaining adipose tissue for SVF isolation, the low cost of SVF treatment compared to cell therapy utilizing cultured stromal/stem cells, and the high stromal/stem cell abundance in adipose tissue compared to other available adult tissues. Enzymatic fat disruption is currently considered the gold standard for clinical production of SVF from adipose tissue; however, despite its efficiency, it has many disadvantages that limit its intraoperative use. Limitations include its relatively long duration (1.5–2 h), the regulatory burden of enzyme use, and the cost of the process that requires the use of costly GMP enzymes and complex equipment. To overcome these disadvantages, this work presented a novel nonenzymatic SVF cell isolation approach that uses RBs to mechanically disrupt fat. The quality of SVF cells isolated using the RBs mechanical method was similar to that of SVF cells isolated by enzymatic digestion. Although the quantity of SVF isolated using the RBs mechanical method was inferior to

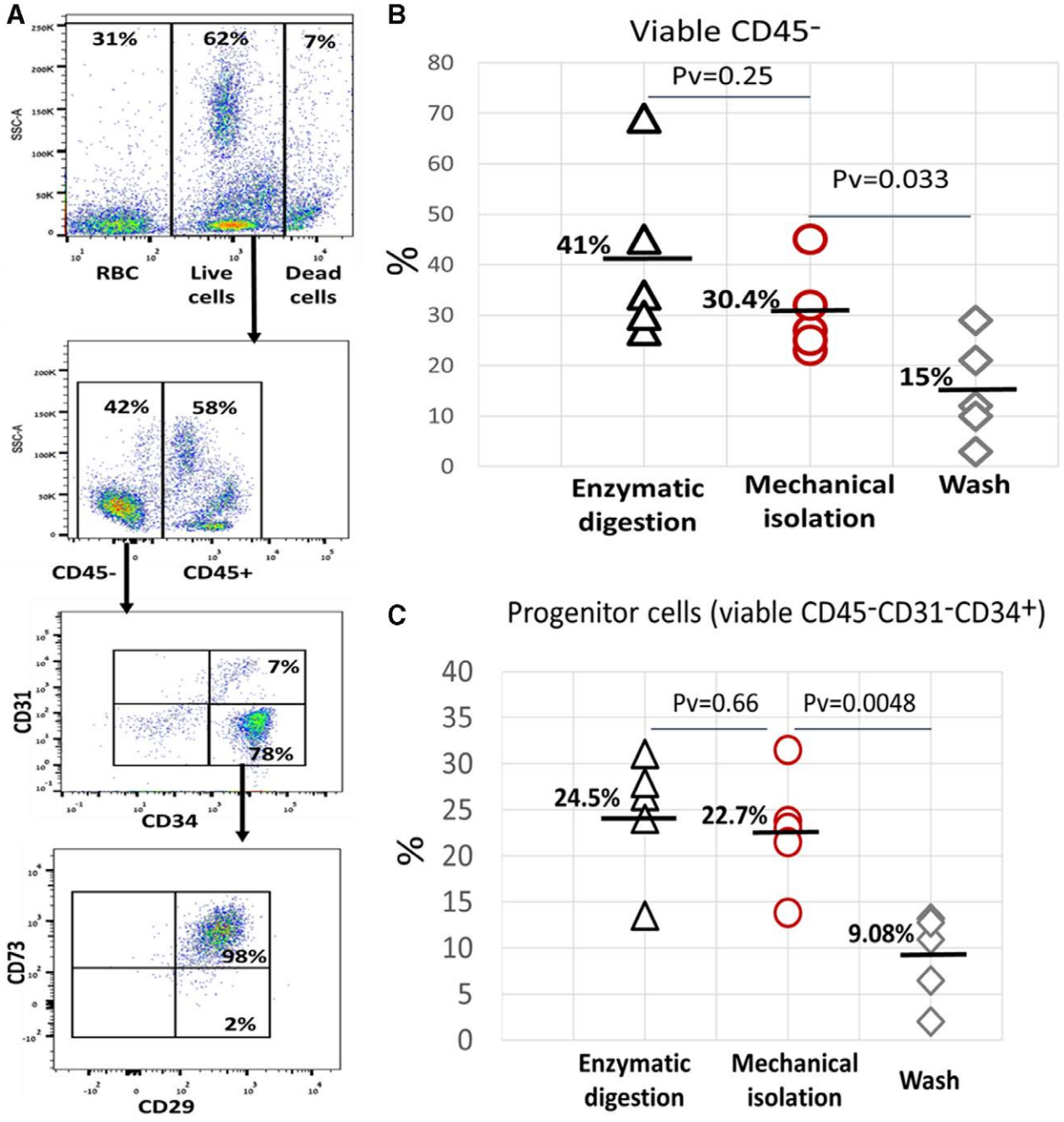

Fig. 3. Cell surface marker expression among SVF cells isolated from fat by enzymatic digestion, RBs mechanical disruption, or washing. SVF cells were isolated from the same lipoaspirate by enzymatic digestion ("enzymatic digestion"), our RBs mechanical isolation technology ("mechanical isolation") and by shaking and centrifugation ("Wash"). SVF cells were stained with a six-color flow cytometry panel, treated with a fixating RBC lysis buffer and analyzed by flow cytometry. A, The gradual gating strategy shown included only viable cells, determined by low ViViD staining, but discarded RBCs. B, Comparison of the nonhematopoietic cells subpopulation ($CD45^-$) or (C) $CD45^-CD31^-CD34^+$ subpopulations within SVF isolated by the different methods. n = 5. SSC-a, side scatter area.

the yield obtained by enzymatic isolation, it was similar to the average yield obtained by clinical-grade enzymatic SVF isolation recently reported to be obtained using either the leading commercial enzyme-based Celution System (Cytori Therapeutics Inc.) (n = 70) or by manual isolation (n = 294),[20] making the RBs technique highly relevant to clinical use. Importantly, however, SVF isolation using this nonenzymatic method was achieved in under 15 minutes, a drastically shorter interval than enzymatic isolation. Taken together, these results demonstrate the feasibility of the proposed nonenzymatic isolation approach as a fast, low-cost alternative to clinical enzymatic protocols.

Intraoperative SVF administration (ioSVF) procedures optimally include a liposuction, SVF isolation from the

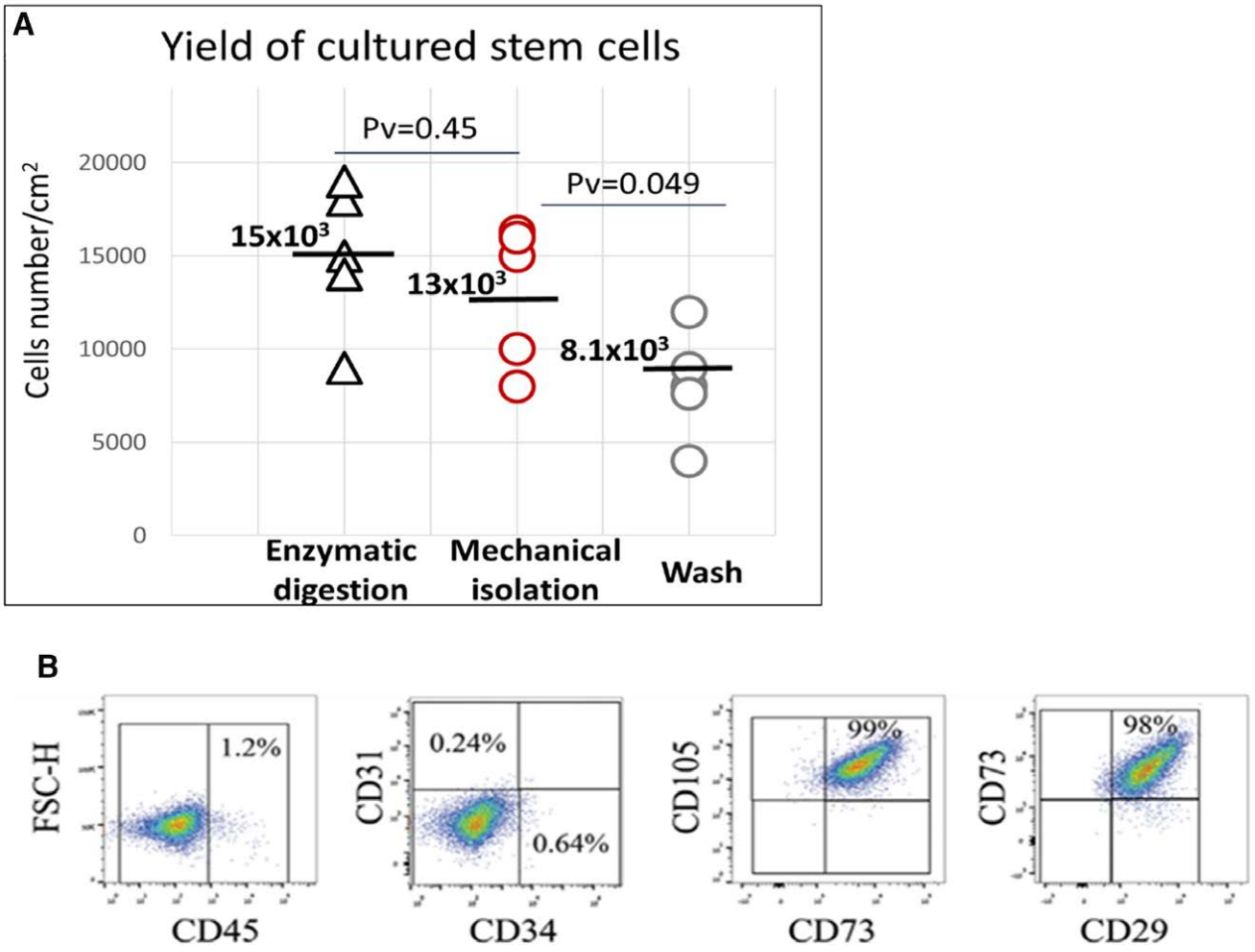

Fig. 4. Yields of ASCs from samples isolated using different techniques. A, SVF cells were isolated from the same lipoaspirate, by enzymatic digestion ("enzymatic digestion"), our RBs mechanical isolation technology ("mechanical isolation"), or shaking and centrifugation ("wash"), and equal quantities of viable isolated SVF cells were seeded, cultured for 10 days, and then harvested and counted. n = 5. B, ACSs were stained with a seven-color flow cytometry panel, treated with a fixating buffer, and analyzed by flow cytometry.

collected fat and immediate autologous SVF administration. Intraoperative SVF can be performed either in a clinic or in an operating room. In addition to the mere benefits of SVF administration, the main benefit of ioSVF is the ability to perform two separate procedures at a single appointment, possibly saving costly operating room time. To enable ioSVF, SVF isolation must be rapid, simple, and preferably performed in a sterile manner, without the need for a clean room or a biologic hood, to ensure regulatory standards. The presented novel nonenzymatic RBs SVF isolation method is rapid (<15 min) and efficient, providing for SVF yields and quality comparable to the gold standard enzymatic SVF isolation method. Based on this method, a closed system was designed and patented[21] to enable ioSVF in a rapid, simple, sterile, and cost-effective manner, in both clinic and operating room settings (Fig. 6).

Various attempts have been made in recent years to overcome the disadvantages of enzymatic adipose tissue dissociation and to replace it with a more rapid fat dissociation approach.[22] Fat emulsification,[23] the most prevalent mechanical method for fat disruption to date, brakes fat by employing mechanical strain on harvested fat by different technics (eg, Lipogems, TULIP NANOFAT SET, Lipocube), resulting in a liquid fat form, generally termed microfat or nanofat, reflecting the reduced fat particle size. Despite claims that fat emulsification results in SVF enrichment, there are conflicting reports regarding SVF cell survival and viability following fat emulsification.[24,25] In addition, fat emulsification methods do not generate reproducible results since the mechanical fat disruption is highly dependent on the force exerted by the surgeon. Interestingly, fat emulsification using the lipocube technique is performed by passing fat through a mesh with a knife-like sharp interphase. However, despite partial similarity, our technology that utilizes actuator-driven RBs is different in the direction of the mechanical force inflicted (rotating), in the nature of blades and most importantly by the fact that it always inflicts the same mechanical force and for the same duration of time since it uses an independent actuator. Thus, our novel fat disruption RBs mechanical device (Fig. 6) integrates a surgeon-independent actuator, resulting in controlled, homogenous mechanical

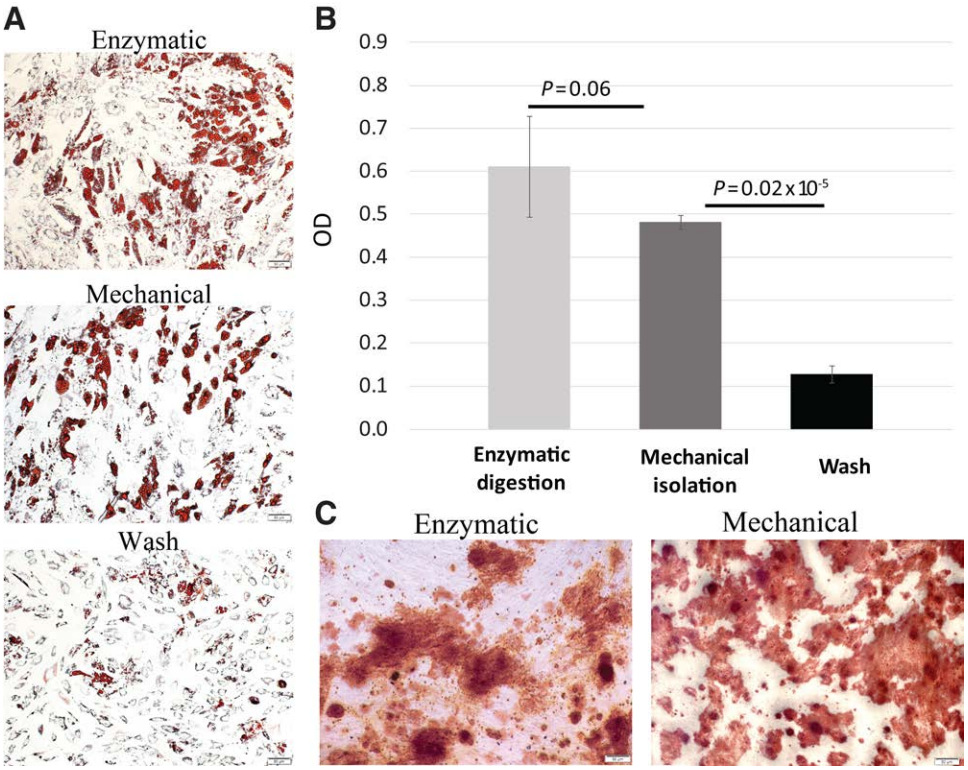

Fig. 5. RBs mechanically and enzymatically isolated SVF cells display similar fat and bone differentiation potentials. A, Adipose-derived stromal/stem cells isolated using enzymatic digestion, RBs mechanical isolation, or wash techniques were incubated in a fat differentiation medium or with control medium for 3 weeks. The cells were then stained for fat with Oil Red O and photographed. B, Oil Red O was extracted and quantified. n = 4. C, Adipose-derived stromal/stem cells isolated using enzymatic digestion or RBs mechanical isolation techniques were incubated with a bone differentiation medium or with control medium for 3 weeks. The cells were then stained for bone with Alizarin red and photographed.

fat disruption and emulsification, ensuring highly reproducible clinical results and intact emulsified fat. In addition, following SVF isolation using our approach, large quantities (>100 mL) of undamaged emulsified fat are available for microfat transfer.

An alternative approach employs mechanical dissociation of fat tissue, by different means, followed by SVF separation from fat by centrifugation. Despite the ability of some of these methods to isolate SVF cells, thus far, reported SVF cell yields have been very low in comparison to enzymatic digestion and cell quantities are inadequate for most suggested clinical applications.[19,26–28] Tiryaki et al recently claimed to have achieved high yields of SVF cells by mechanical means; however, their findings are somewhat questionable since the SVF quantities isolated by enzymatic isolation in their report were 3.38×10^6/1 mL fat, which is far beyond the average cell quantities obtained via enzymatic methods (~2–6×10^5/1 mL fat).[20] In addition, the authors fail to indicate whether the reported isolated SVF quantity was per 1 mL fat following fat mechanical breakage or per 1 mL of the original fat.[29]

In light of the large volume of human samples examined in the study (n = 30) and the repeated ability of the novel RBs technology to extract high quantities of high-quality SVF cells similar to the ones obtained by the gold standard enzymatic SVF isolation, we believe that the technology should be further developed to allow its use in the clinical setting. To achieve this, a clinical-grade device is in development. Since the SVF cells obtained using the RBs device are similar to the ones obtained by enzymatic extraction, their successful and efficient use is anticipated in various indications in which the clinical efficacy of enzymatically extracted SVF was previously demonstrated such as CAL[30] and for the treatment of osteoarthritis.[16,31] Furthermore, the fact that it enables rapid extraction of SVF cells (~15 min) in a closed sterile device provides the RBs technology significant advantages over enzymatic SVF extraction methods for ioSVF use.

CONCLUSIONS

The current work introduced a novel RBs mechanical fat disruption technique based on operator-independent actuator RBs. The method enabled rapid (<15 min), reproducible isolation of high quantities of high-quality adipose stromal/stem cells, similar to the yields achieved with clinical-grade enzymatic SVF isolation.[20] Based on this isolation method, a closed-system medical device was designed

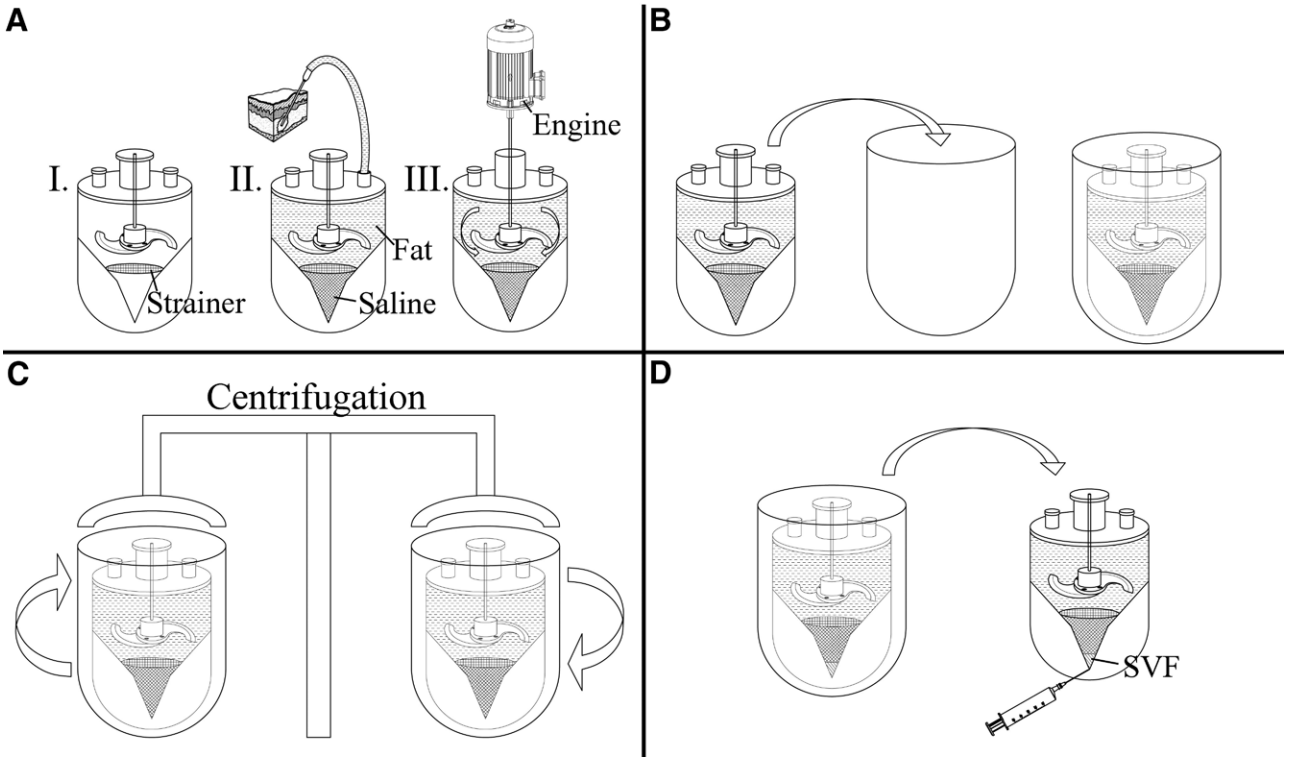

Fig. 6. Schemes of the RBs mechanical SVF isolation clinical system. A, The device (I) is directly connected to the liposuction cannula and fat is vacuumed directly into device (II). Fat is then mechanically dissociated by an RB activated by an external engine (III). The device is disconnected from the external engine, positioned in the centrifuge bucket (B), and then centrifuged to isolate SVF from fat by sedimentation (C). D, SVF cells are collected by a syringe from the device and clinically applied. The device is sterile and is intended for one-time use. The engine is a separate unit and is made for multiple uses.

and patented to enable ioSVF in a rapid, simple, sterile, and cost-effective manner in both clinical and operating room settings. This nonenzymatic method serves as a viable alternative to the current gold standard SVF enzymatic isolation method, reducing valuable surgery time, costs, and regulatory burden.

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DISCLOSURES

Drs Solodeev, Gur, and Shani are inventors on a patent describing the technology described in the article. The other authors have no financial interest to declare.

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