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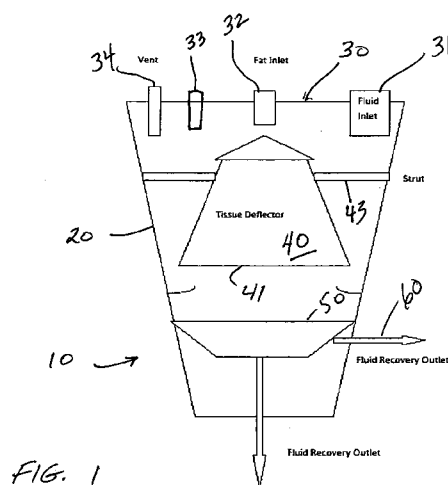
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(54) Title: DEVICE AND METHOD FOR DELIVERING MECHANICALLY RELEASED CELLS FROM LIPOSUCTION ASPIRATES



(57) Abstract: A lipoaspirate collection device to aid in the collection and processing of human tissue and fluid obtained during liposuction for use in point-of-care cell therapy. The collection device includes a collection body and a collection cap. The collection cap may have a fluid port, a lipoaspirate port, a vacuum port, and a relief valve. Within the central cavity of the collection device, a cone shaped may be positioned such that the apex of the cone is positioned underneath the lipoaspirate inlet through which the lipoaspirate fluid and tissue are introduced.

**Device and Method For Delivering Mechanically Released Cells from
Liposuction Aspirates**

This application claims priority to US provisional application 61/404,462, filed October 4, 2010, incorporated in its entirety herein by reference.

Field of the Invention

The invention herein relates generally to a device and method to obtain mechanically released adipose derived progenitor cells for use in point of care therapeutic applications.

Background of the Invention

Collection of adipose tissue through the application of liposuction methods is a common practice (Condé-Green, 2009). The procedure is easily performed in most cases, has a low morbidity rate, and results in the collection of large volumes of adipose tissue (Katz and Maiwald, 2005). Zuk, et al. (2001) was one of the first groups to demonstrate the presence of "stem" cells in adipose tissue collected via lipoaspiration. Their results have been confirmed in subsequent publications (e.g., Yoshimura, et al., 2006). Due to the presence of regenerative cells in the fat tissue, there has been growing interest in using tissue collected during liposuction for body contouring, facial/body enhancement and recontouring in patients suffering from soft tissue atrophy (Condé-Green, 2009). There also has been a growing interest in using the cells isolated from fat tissue for regenerative cell therapy in a variety of pathologies, including repair of orthopedic tissue injuries (Tapp, et al., 2009).

A number of publications demonstrate how lipoaspirates may be non-enzymatically processed to extract adipose-derived stem cells (ASCs) and progenitor cells from adipose tissue. It is apparent that viable cells can be obtained from mechanical dissociation of the fatty portion of lipoaspirate when collected following either centrifugation or washing of the fatty tissue, but non-enzymatic processing yields fewer cells per mL of lipoaspirate (Baptista, et al., 2009; Yoshimura, et al., 2006).

1 Collagenase digestion of the adipose tissue is the most common practice for
2 enzymatically digesting lipoaspirates. Enzymatic processing of adipose tissue may
3 yield a higher number of cells than current non-enzymatic processing methods;
4 however, enzymatic processing results in more difficult processing, slower return of
5 cells to the patient, higher cost to provide the cells, and more stringent FDA
6 regulation. Many processing methods, both non-enzymatic and enzymatic, also
7 ignore the fact that a significant amount of progenitor cells can be obtained from the
8 lipoaspirate fluid alone with minimal processing.

11 Summary of the Invention

12 The disclosed device and method provide a solution to the problems and
13 disadvantages described above by providing a device and method for facilitating the
14 collection and processing of adipose tissue and fluid obtained during liposuction.

16 The lipoaspirate extraction system of this invention mechanically stresses adipose
17 tissue that will be infiltrated and removed. Mechanical stress might induce the
18 migration of useful cell types into the area, thereby enhancing their concentration and
19 improving the yield of useful cell types, such as progenitor cells. Use of a vacuum to
20 suction the area of tissue to be probed will serve to limit the degree of trauma being
21 introduced to the patient that can occur in liposuction procedures. The system also
22 limits the probing of the adipose tissue to defined locations and geometries. Ports
23 may also be designed to further control the depth of penetration during each probe
24 event. More gentle collection conditions should provide for a higher number of viable
25 cells collected compared to standard liposuction practice.

27 In one respect, this invention is a device to facilitate the collection and processing of
28 mechanically released adipose derived progenitor and/or stem cells from fluid
29 obtained during liposuction, comprising: a collection body having an upper collection
30 body cap wherein the collection body cap has a fluid port for introducing fluids, a
31 lipoaspirate port through which lipoaspirate is introduced, a vacuum port, wherein the
32 collection body has a central cavity in which is positioned a cone shaped deflector
33 such that the apex of the cone is positioned pointed toward the upper collection body
34 cap and such that the apex is positioned underneath the lipoaspirate inlet.

35 The cone may include a series of holes positioned near the apex of the cone to
36 prevent an air lock, wherein the holes may optionally be covered by a disc to deflect

1 tissue away from the holes. In one embodiment, the collection body has a
2 substantially cylindrical shape. The device may include a debris capturing trough,
3 constructed with various micro-texturing patterns to facilitate the retention of debris
4 and circumferentially disposed along the inner wall of the collection body beneath the
5 circular base of the deflector; the trough optionally including a lip to help capture any
6 sinking debris and the collection body further including a pit beneath the debris
7 capturing trough to collect any additional sinking debris. The device may further
8 include at least one fluid recovery outlet to remove fluid from the collection body, and
9 optionally an additional filter placed adjacent to the fluid recovery outlet to prevent
10 any additional debris from leaving the collection body. The device may include
11 needleless entry technology, so that it can be maintained in a sterile manner, but is
12 readily accessible for connecting to a tube for removing the fluid. The device may be
13 arranged such that the fluid recovery outlet is laterally positioned above the pit, so
14 that only fluid exits through the fluid recovery outlet. The device can be formed from
15 stainless steel and plastic materials.

16
17 In another broad respect, the invention is a lipoaspirate extraction system
18 constructed from a variety of materials, including stainless steel and plastic, used to
19 extract lipoaspirate materials from a patient in a surgical field comprising: an adipose
20 disruption component, an infiltration component, and, an extraction component. The
21 system may include a means to mechanically disrupt adipose tissue using any
22 number of mechanisms, including, but not limited to, a vacuum, ultrasound,
23 massage, fluid jets, or mechanical rollers, wherein the mechanical means can be cycled
24 on and off as appropriate. The adipose disruption component may include two
25 devices; one to provide mechanical stress and a second, discrete device that is used
26 to apply a vacuum to maintain the position of the adipose disruption component. The
27 infiltration component may include at least one infiltration port through which a
28 cannula or alternative device may be introduced to deliver infiltration fluids between
29 the dermis and muscle, said fluids comprising, but are not limited to, physiologically
30 compatible fluids like Lactated Ringer's, saline, Phosphate Buffered Saline, all of
31 which can be obtained as sterile and non-pyrogenic fluids, and said fluids may
32 additionally contain other agents, including, but not limited to, epinephrine and
33 lidocaine. The extraction component may include vacuum capabilities to maintain
34 the position of the extraction component, through which a specially designed
35 extraction probe or alternative device may be introduced to extract lipoaspirate
36 material.

1 In another broad respect the invention is a method of using a device to extract and
2 collect mechanically released adipose derived progenitor cells wherein: lipoaspirate
3 material will enter a collection device through an entry port, said collection device will
4 be pre-filled with a fluid to facilitate separation between the fluid, fat tissue, and
5 debris, and, sinking debris will flow down the outer surface of the deflector and settle
6 into a trough or pit where the lipoaspirate fluid can then be removed through fluid
7 recovery ports. The lipoaspirate extraction system may be used either
8 simultaneously or sequentially with a lipoaspirate collection mechanism and, the
9 lipoaspirate extraction system can be used to promote the mechanical release of
10 cells from the tissue matrix in-vivo, at the collection site, before, and/or during the
11 actual extraction and collection of adipose tissue and fluids.

12
13 In another broad respect, the invention is a method of using a device to extract and
14 collect mechanically released adipose derived progenitor cells, comprising:
15 Introducing lipoaspirate material will into a collection device through an entry port,
16 said collection device being pre-filled with a fluid to facilitate separation between the
17 fluid, fat tissue, and debris, wherein the collection device has a central cavity in which
18 is positioned a cone shaped deflector such that the apex of the cone is positioned
19 pointed toward the upper collection body cap and such that the apex is positioned
20 underneath the lipoaspirate inlet, and allowing debris to flow down the outer surface
21 of the deflector and settle into a trough where the lipoaspirate fluid can then be
22 removed through fluid recovery ports.

23 24 **Brief Description of the Drawings**

25
26 FIG. 1 shows a lipoaspirate device 10 of this invention.
27

28 29 **Detailed Description of the Invention**

30 **Lipoaspirate Collection Device**

31
32 The lipoaspirate collection device is designed to aid in the collection and processing
33 of human tissue and fluid obtained during liposuction for use in point-of-care cell
34 therapy. The collection device decants fluid from lipoaspirate materials, eliminating
35 floating and sinking debris for quick and easy evacuation of fluid and cells from the

1 container. The collection device may also be used to rinse the lipoaspirate material
2 to extract more progenitor cells.

3
4 In one embodiment, as shown in FIG. 1, the collection device 10 includes a collection
5 body 20 and a collection cap 30. The collection cap 30 may have a fluid port 31 for
6 introducing fluids, a lipoaspirate port 32 through which lipoaspirate is introduced, a
7 vacuum port 33, and a relief valve port 34. Each port in the collection cap 20 may
8 include a tight fitting cap for sealing each port. These tight fitting caps may be
9 connected to the collection cap 20 in a manner that keeps the tight fitting caps in
10 close proximity to their respective ports.

11
12 The collection body may take a substantially cylindrical shape. Within the central
13 cavity of the collection device, a cone shaped deflector 40 may be positioned such
14 that the apex of the cone is positioned underneath the lipoaspirate inlet through
15 which the lipoaspirate fluid and tissue are introduced. The circular base 41 of the
16 deflector is large enough to nearly reach the inner wall of the collection device. A
17 series of small holes may be positioned near the apex of the cone to prevent an air
18 lock. The holes may be covered by a disc to deflect tissue away from the holes.
19 This disc will be attached to the outer surface of the deflector at its apex. The
20 deflector itself may be attached to the inner wall of the collection device via the
21 placement of a plurality of struts 43 designed to maintain the position and orientation
22 of the deflector within the cavity. A debris capturing trough 50 may be
23 circumferentially disposed along the inner wall of the collection body, just underneath
24 the circular base of the deflector. The trough may include a lip to help capture any
25 sinking debris. The deflector and trough may also be constructed with various micro-
26 texturing patterns to facilitate the retention of debris. The collection body also
27 includes at least one fluid recovery outlet 60 to remove fluid from the collection body.
28 An additional filter may be placed adjacent to the fluid recovery outlet to prevent any
29 additional debris from leaving the collection body. The fluid recovery outlet may
30 incorporate needleless entry technology, so that it can be maintained in a sterile
31 manner, but is readily accessible for connecting to a tube for removing the fluid. The
32 collection device may also include a wide base to maintain the collection device in an
33 upright position.

34
35 In an alternative embodiment, the collection device may include a pit at the bottom of
36 the collection body to collect any sinking debris. The fluid recovery outlet is laterally
37 positioned above the pit so that only fluid exits through the fluid recovery outlet.

1 **Lipoaspirate Extraction System**

2
3 In another embodiment, a lipoaspirate extraction system is used to extract
4 lipoaspirate materials from a patient in a surgical field. The lipoaspirate device may
5 be constructed from a variety of materials, including stainless steel and plastic.
6 Stainless steel construction allows the extraction system to be repeatedly autoclaved
7 without alteration of the physical integrity of the device. On the other hand, the
8 extraction system can be made out of plastic, rendering it disposable. The
9 lipoaspirate extraction system comprises an adipose disruption component, an
10 infiltration component, and an extraction component. The lipoaspirate extraction
11 system may be constructed such that the adipose disruption component, infiltration
12 component, and extraction components are all incorporated into one device or
13 separate devices.

14
15 The adipose disruption component mechanically disrupts adipose tissue using any
16 number of mechanisms, including, but not limited to, a vacuum, ultrasound, fluid jets,
17 or mechanical rollers. For example, the lipoaspirate extraction system may be a
18 vacuum based system. The vacuum housing may take a circular, elliptical, or
19 alternative shape depending on the site on which the liposuction is to be performed.
20 The variation and degree of suction can be controlled by standard means known in
21 the art. Alternatively, if mechanical stress is applied through means such as
22 massage or ultrasonic energy, it is contemplated that the vacuum can be cycled on
23 and off as appropriate. In this regard, it may be appropriate to have two devices in
24 use, one to provide mechanical stress and a second, discrete device that is used to
25 apply a vacuum to maintain the position of the adipose disruption component. It also
26 might be appropriate to design a single device that performs both functions.

27
28 The infiltration component includes at least one infiltration port through which a
29 cannula or alternative device may be introduced to deliver infiltration fluids between
30 the dermis and muscle. Candidate fluids include, but are not limited to,
31 physiologically compatible fluids like Lactated Ringer's, saline, or Phosphate Buffered
32 Saline, all of which can be obtained as sterile and non-pyrogenic fluids. The
33 infiltration fluid may or may not contain other agents, including, but are not limited to,
34 epinephrine and lidocaine. Each infiltration port may include a septum, which can be
35 separately sterilized and aseptically affixed to each port. Assembly of such ports and
36 fixtures also could occur prior to sterilization of the device. The ports may be
37 designed in such a way that it is possible to insert a cannula or other probe from the

1 outside of the device into the device's lumen without breaking the vacuum. The
2 infiltration component may also include vacuum capabilities to maintain the position
3 of the infiltration component. Depending on the stability of the device relative to
4 maintaining a seal and therefore the vacuum, it may be possible to close the vacuum
5 port by turning a valve. Alternatively, the vacuum may be applied continuously during
6 the procedure by maintaining connection to an appropriate source of vacuum.

7
8 The extraction component may include vacuum capabilities to maintain the position
9 of the extraction component. The extraction component includes at least one
10 extraction port through which a specially designed extraction probe or alternative
11 device may be introduced to extract lipoaspirate material. Each extraction port may
12 include a septum, which can be separately sterilized and aseptically affixed to each
13 port. Assembly of such ports and fixtures also could occur prior to sterilization of the
14 device. The ports may be designed in such a way that it is possible to insert a
15 cannula or other probe from the outside of the device into the device's lumen without
16 breaking the vacuum. The extraction probe may include a flange along the probe
17 body to limit insertion of the cannula through the extraction ports. The extraction
18 probe may also be specially designed to limit extracted lipoaspirate material primarily
19 to interstitial fluid.

20
21 The lipoaspirate extraction system and collection device may be used together or
22 separately. Extracted lipoaspirate fluid may then be manually processed to
23 concentrate ASCs and progenitor cells. These cells may then be delivered to the
24 patient for use in regenerative cells therapies.

25
26 One method of using the collection device is in conjunction with standard liposuction
27 techniques, which are used to remove lipoaspirate materials from the surgical field.
28 The lipoaspirate material will enter the collection container through the lipoaspirate
29 port. The collection device will be pre-filled with a fluid to facilitate separation
30 between the fluid, fat tissue, and debris. Sinking debris will flow down the outer
31 surface of the deflector and settle in the trough. Lipoaspirate fluid can then be
32 removed through the fluid recovery ports.

33
34 In an alternative method, the lipoaspirate extraction system may be used in
35 conjunction with any lipoaspirate collection mechanism known in the art. The
36 lipoaspirate extraction system can be used either simultaneously or sequentially with
37 a lipoaspirate collection mechanism. The lipoaspirate extraction system can be used

1 to promote the mechanical release of cells from the tissue matrix in-vivo, at the
2 collection site, before, and/or during the actual extraction and collection of adipose
3 tissue and fluids. The system mechanically stresses an area of adipose tissue to
4 induce the migration of useful cell types into the area, thereby enhancing their
5 concentration and improving the yield of useful cell types, such as progenitor cells.
6 Thus, it may be beneficial to apply the mechanical stress before and/or during the
7 infiltration of fluid and then to continue to apply the stress after the infiltration has
8 been completed. It is contemplated that there could be a delay in the initiation of a
9 subsequent step in order to maximize the yield of cells at the conclusion of the
10 process. For example, it might be appropriate to mechanically stress the collection
11 site one or more days in advance of the target date for collection. It further is
12 contemplated that there might be periods of "incubation" during which the tissue is
13 not mechanically stressed and allowed to "rest" before applying more stress. An
14 extraction probe may be delivered through specific ports to remove primarily
15 interstitial fluid from the adipose tissue. Lipoaspirate materials are extracted into a
16 collection device.

17 Although illustrative embodiments have been shown and described, a wide range of
18 modifications, changes, and substitutions are contemplated in the foregoing
19 disclosure and in some instances, some features of the embodiments may be
20 employed without a corresponding use of other features. Accordingly, it is
21 appropriate that the appended claims be construed broadly and in a manner
22 consistent with the scope of the embodiments disclosed herein.

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- 7

Claims**What is claimed is:**

1. A device to facilitate the collection and processing of mechanically released adipose derived progenitor and/or stem cells from fluid obtained during liposuction, comprising:
 - a collection body having an upper collection body cap wherein the collection body cap has a fluid port for introducing fluids, a lipoaspirate port through which lipoaspirate is introduced, a vacuum port,
 - wherein the collection body has a central cavity in which is positioned a cone shaped deflector such that the apex of the cone is positioned pointed toward the upper collection body cap and such that the apex is positioned underneath the lipoaspirate inlet.
2. The device of claim 1, wherein the cone includes a series of holes positioned near the apex of the cone to prevent an air lock, wherein the holes may optionally be covered by a disc to deflect tissue away from the holes.
3. The device of claim 1 wherein the collection body has a substantially cylindrical shape.
4. The device of claim 2, further comprising:
 - a debris capturing trough or pit, constructed with various micro-texturing patterns to facilitate the retention of debris and circumferentially disposed along the inner wall of the collection body beneath the circular base of the deflector; the trough optionally including a lip to help capture any sinking debris and the collection body further including a pit beneath the debris capturing trough to collect any additional sinking debris.
5. The device of claim 2, further comprising:

1 at least one fluid recovery outlet to remove fluid from the collection body, and
2 optionally an additional filter placed adjacent to the fluid recovery outlet to
3 prevent any additional debris from leaving the collection body.
4

5 6. The device of claim 4 comprising:

6 needleless entry technology, so that it can be maintained in a sterile manner,
7 but is readily accessible for connecting to a tube for removing the fluid.
8

9 7. The device of claim 4 wherein the fluid recovery outlet is laterally positioned
10 above the pit of claim 3, so that only fluid exits through the fluid recovery outlet.

11 8. A method of using a device to extract and collect mechanically released
12 adipose derived progenitor cells, comprising:

13 Introducing lipoaspirate material will into a collection device through an entry
14 port, said collection device being pre-filled with a fluid to facilitate separation
15 between the fluid, fat tissue, and debris, wherein the collection device has a
16 central cavity in which is positioned a cone shaped deflector such that the
17 apex of the cone is positioned pointed toward the upper collection body cap
18 and such that the apex is positioned underneath the lipoaspirate inlet, and
19

20 allowing debris to flow down the outer surface of the deflector and settle into a
21 trough where the lipoaspirate fluid can then be removed through fluid
22 recovery ports.
23
24

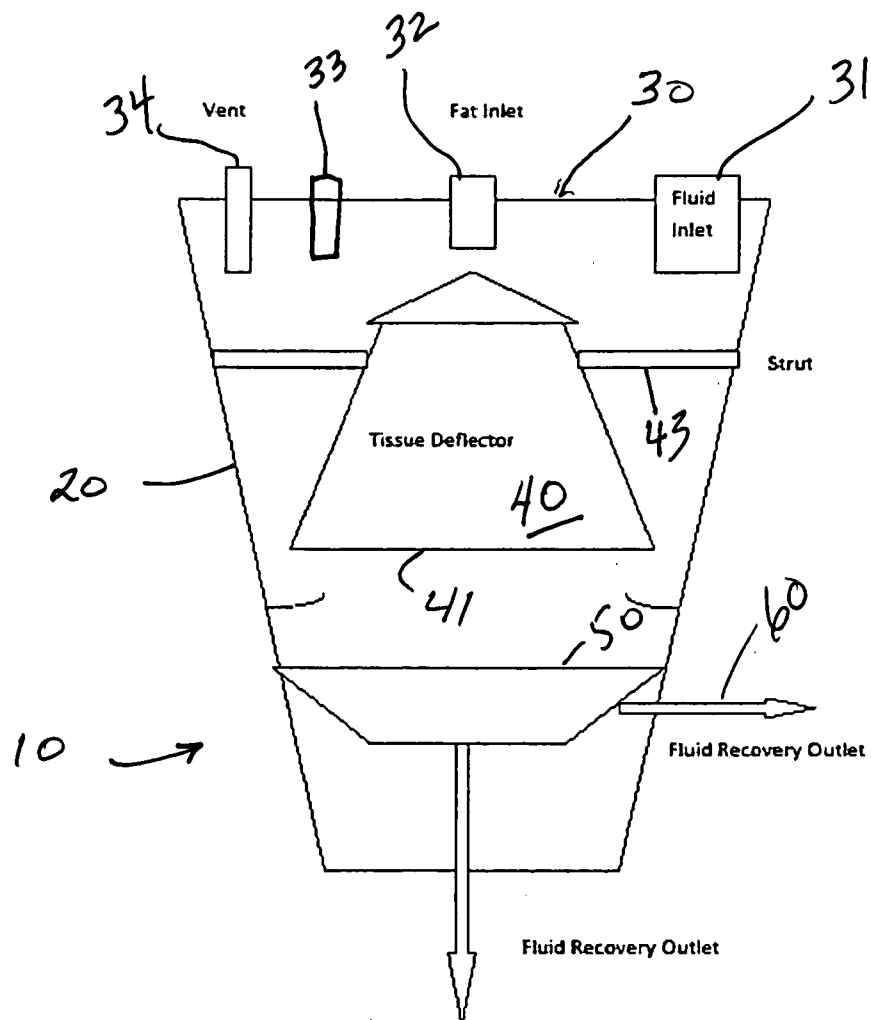


FIG. 1

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2011/001706

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C12N 5/02 (2011.01)

USPC - 435/378

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - C12N 5/02 (2011.01)

USPC - 210/781, 782; 435/283.1, 378, 379, 381; 494/ All subclasses; 604/319, 333

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)

PatBase, Google Patents, Google

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 7,429,488 B2 (FRASER et al) 30 September 2008 (30.09.2008) entire document	1, 3, 8
Y	US 5,156,586 A (FITCH, JR. et al) 20 October 1992 (20.10.1992) entire document	1, 3, 8
Y	US 2007/0264704 A1 (VAN TOEVER) 15 November 2007 (15.11.2007) entire document	8
A	US 5,256,376 A (CALLAN et al) 26 October 1993 (26.10.1993) entire document	1-8
A	US 5,478,744 A (SANFORD et al) 26 December 1995 (26.12.1995) entire document	1-8
A	US 2008/0243028 A1 (HOWARD et al) 02 October 2008 (02.10.2008) entire document	1-8

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Date of the actual completion of the international search

30 December 2011

Date of mailing of the international search report

13 JAN 2012

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