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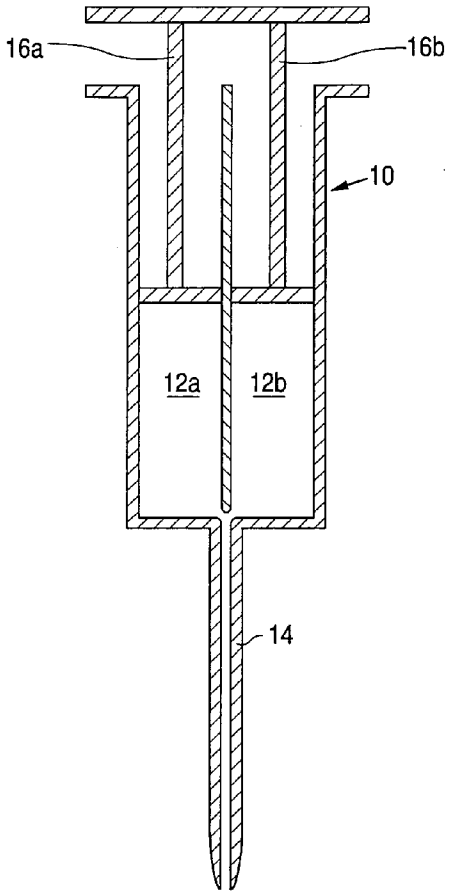
(54) Title: CO-MIXED HUMAN FAT AND GEL SUSPENSION IMPLANT MATERIAL



(57) Abstract: A fill material and method for treating human voids such as wrinkles. The fill material is a co-mixture of human fat from a patient and a gel suspension. After the fat and gel are mixed together, they are injected back into the patient from which the fat was harvested.

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CO-MIXED HUMAN FAT AND GEL SUSPENSION IMPLANT MATERIAL

[0001] This application claims the benefit of U.S. Provisional Application No. 60/859,877, filed November 16, 2006.

FIELD OF THE INVENTION

[0002] The present invention relates to implant materials, and in particular a unique fill material that combines human fat and a gel suspension.

BACKGROUND OF THE INVENTION

[0003] Injectable fill materials are well known, and are used to treat voids in the human body, such as facial wrinkles. One known fill material is autologous fat (fat harvested from the same patient that receives it). This autologous fat is known to be used in reconstructive, cosmetic, and correctional surgery. It is advantageous for the patient because it will not cause a negative reaction. It also has the advantage that it can become a soft permanent correction if it vascularizes and regenerates. There are some drawbacks, however, of using only viable fat as a filler. The viable fat must first be harvested from the patient. Since only a fraction of the harvested fat is suitable for re-injection, it can be problematic to harvest enough fat for the re-injection procedure. Also, processing the harvested fat while retaining cell viability can be difficult and result in producing insufficient amounts of viable fat suitable for re-injection. In addition, transplanting larger volumes of fat can lead to necrosis of some of the transplanted tissue, which over time, has been shown to cause a 40-60% reduction in the graft volume. Greater success can be achieved in transplanting smaller volumes of fat where diffusion can support cell survival.

[0004] Within the stromal vascular fraction of adipose tissue there are mesenchymal preadipocytes that are now thought to be adipose derived stem cells (ASCs). These multipotent ASCs have been shown to differentiate into adult adipocytes, back to preadipocytes, and into other cell types, including cartilage and bone. Many present studies have been focused on these individual ASCs for their regenerative and multipotent properties, as well as seeding them within an engineered porous scaffold, matrix and or construct. These matrices or scaffolds have been known to be made from synthetic protein-coated polytetrafluoroethylene, synthetic biodegradable PLGA, polyglycolic or hyaluronic acids and collagen. However, extensive additional time and effort must be spent isolating

the ASCs from the stromal vascular fraction with live and potent enzymes that catalyze the hydrolysis of the connective tissue. Typical enzymes to use for this hydrolysis are Collagenase Type I & Type II, and Trypsin. In addition, even though the ASCs undergo "washing" during the isolation process, there is a risk of introducing these harmful, potent enzymes within the transplanted tissue.

[0005] Another known class of fill materials is synthetic gel fillers. The advantages of these types of gel fillers are ease of use and no need to harvest fat from the patient. However, such gel fillers are biodegradable, so that over time the void into which they are injected will reappear. To increase the duration of the fill, additives such as CaHA, PMMA or PLA beads have been added to the fills. These materials are not radiolucent and thus would interfere with medical imaging, and have had a history of other problems.

[0006] There is a need for an improved fill material that provides instant volume correction, actively promotes tissue in-growth for a near permanent fill, is radiolucent so it will not interfere with medical imaging, does not contain beads of material which could lead to calcifications, and can be supplied in large volumes to support surgeries where large volumes are required, such as breast and buttock rejuvenation procedures.

SUMMARY OF THE INVENTION

[0007] The aforementioned problems and needs are addressed by providing a fill material utilizing a mixture of both harvested human fat and a gel suspension, which can effectively be used to fill large volumes, provides better access of fat cells to surrounding tissue, and can be radiolucent to not interfere with diagnostic testing.

[0008] The fill material is for injection into a human patient, and includes human fat harvested from a patient, and a gel suspension co-mixed with the fat.

[0009] Other objects and features of the present invention will become apparent by a review of the specification, claims and appended figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] Fig. 1 is a cross sectional view of a double barrel mixing syringe for mixing and injecting the human fat and gel suspension material.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0011] The present invention is a unique fill material suitable for all tissue fill applications including large volume restoration or augmentation such as the buttock and breast. The unique fill material includes autologous human fat filler co-mixed with a gel suspension. The purpose of co-mixing the autologous human fat filler with a gel suspension is to provide a larger volume filler that allows angiogenesis and vasculogenesis of the adipose tissue while maintaining its volume. The autologous human fat co-mixed with a gel suspension is a biocompatible, radiolucent, longer lasting, multipotent filler.

[0012] The autologous human fat is obtained by manual or vacuum assisted aspiration of fat from a patient. To obtain the best result, the fat aspirant should be processed to eliminate a majority of blood and oil.

[0013] As used herein, the "gel" suspension is any appropriate material (implantable, biocompatible, biodegradable and sterile) that has a viscosity greater than that of water. Ideally, the gel suspension would also, but not necessarily, be substantially radiolucent, have long lasting volume enhancing properties, preserve volume (resulting mixed volume is no less than premixed volumes added together), or enhance volume (resulting mixed volume exceeds premixed volumes added together). For procedures such as breast augmentation, the gel suspension should be radiolucent and not contain any particles that might become points of calcification. For other applications, the gel suspension could contain materials for drawing water into the area for bulking, such as hyaluronic acid, or for adding bulk with or with out particles using a carrier to aide in injection.

[0014] The gel suspension can be organic or inorganic. There are a number of synthetic materials suitable for the gel suspension which have been reviewed and approved by the FDA. The FDA classifies these materials as implant, dermal, for aesthetic use. Any of these materials would fall under the gel suspension definition as used herein, given their viscosities are greater than that of water. These materials are generally biocompatible, sterile, and implantable in the dermis for the correction of moderate to severe facial wrinkles and folds and/or other soft tissue contour deficiencies.

[0015] One of the more popular synthetic material suitable as the gel suspension is stabilized, hyaluronic acid (HA) generated by streptococcal bacteria and formulated to a specified concentration, suspended in a physiological buffer with a specified pH level. HA

is an acid that is produced naturally by the body. One specific example of a HA based gel suspension is Restylane® Injectable Gel, distributed by A-Med, Inc.

[0016] Another popular synthetic material is injectable microparticles of poly-L-lactic acid, a biocompatible, biodegradable, synthetic polymer from the apha-hydroxy-acid family. This poly-L-lactic acid comes in the form of a sterile lyophilized cake which is then reconstituted prior to use by the addition of sterile water for injection, USP (SWFI) to form a sterile non-pyrogenic gel suspension. One specific example of poly-L-lactic acid based gels is SCULPTRA™, manufactured by Aventis Pharmaceuticals Inc.

[0017] A suitable organic gel suspension is human-based collagen. Specific examples of human-based collagen materials are CosmoDerm™ 1 and 2, and CosmoPlast™, manufactured by Allergan. These materials are composed of highly purified human-based collagen that is dispersed in phosphate-buffered physiological saline containing 0.3% lidocaine.

[0018] Other gel suspension materials suitable for soft tissue augmentation include, but are not limited to, bovine based collagen fillers (Zyderm® and Zyplast®), fibrin glue, alginate and RGD and YGSIR-modified alginate gels. RGD and YGRID are cell-binding sequences of laminin and fibronectic, respectively. These binding sequences are used to help the cells bind to an engineered construct.

[0019] It should be noted that while synthetic gel suspensions are preferred, non-synthetic gel materials that are implantable, biocompatible, biodegradable, sterile, and have a viscosity greater than water can also be mixed with the autologous fat filler to result in the co-mixed fill material suitable for tissue fill applications. Examples of such non-synthetic materials can include monomers and/or polymers from materials such as acids, proteins and carbohydrates.

[0020] Once the human fat and gel suspension are prepared, they are mixed together, preferably at a 1:1 ratio. However, the ratio may change to provide the best results. One suitable mixing technique is the use of a double barrel mixing syringe 10, which includes a pair of chambers 12a/12b in fluid communication with a mixing nozzle 14 that efficiently mixes and injects the fat and gel materials from the two chambers as plungers 16a/16b are pressed downward in chambers 12a/12b, as shown in Fig 1. Preferably, but not necessarily, the mixing nozzle 14 terminates in a surgical needle tip that can be inserted into the patient.

The use of syringe 10 is advantageous because the syringe 10 will mix the fat and gel in the desired proportions, while injecting the mixture into the target site, all in a single action. Alternately, the human fat and gel suspension can be mixed together in a container before being added to a syringe or other delivery device. Other well known mixing techniques could be used as well, such as mixing paddles or a "add and shake" technique.

[0021] One advantage of using a fill material of autologous fat and gel suspension is that gel suspension acts as a biocompatible, bio-absorbable, intracellular matrix taking up volume while the adipose tissue has time to undergo angiogenesis, vasculogenesis, and the more immediate inosculation. As the gel suspension is slowly being absorbed by the body, the adipose tissue, since it is relative thinned out, will vascularize, re-grow, and fill the volume being left behind by the gel suspension as it is being absorbed; ultimately providing a full correction of the treated area. This feature also provides the added benefit of using this co-mixture for larger fill procedures like breast augmentations. In larger fill procedures, it is sometimes very difficult to harvest the necessary volume of adipose tissue. Thus, using the fat and gel co-mixture helps solve this problem.

[0022] Another advantage of using co-mixed autologous fat and gel suspension is that it allows the autologous fat within the suspension to be thinly injected. The thin cross section of the autologous fat allows each fat cell greater access to the vasculature surrounding it and therefore greater ability to vascularize and regenerate. It also allows for the fat to grow through the gel suspension creating its own 3D matrix. In contrast, an injection of only autologous fat would have a cross section of 100% harvested fat. The fat cells in the center of this cross section would have minimal, if any, access to the vasculature of the tissue surrounding it, thereby being susceptible to cell necrosis.

[0023] Yet one more advantage of using co-mixed autologous fat and gel suspension is that many suitable gel suspensions are radiolucent. This allows the gel suspension to be invisible to x-rays, which greatly benefits future diagnostic testing such as mammograms. Further, the co-mixture of autologous fat and gel suspension is easier and more time efficient to use, and is more cost effective, compared to co-mixing adipose derived stem cells with a tissue engineered construct. There is no need to spend the extra time and effort to isolate the stem cells from the adipose tissue. In addition, there is no risk of introducing the harmful, potent enzymes that are used to break down the connective tissue and isolate the stem cells, products that are still not approved for use by the FDA.

[0024] It is to be understood that the present invention is not limited to the embodiment(s) described above and illustrated herein, but encompasses any and all variations falling within the scope of the appended claims.

What is claimed is:

1. A fill material for injection into a human patient, comprising:
human fat harvested from a patient; and
a gel suspension co-mixed with the fat.

2. The fill material of claim 1, wherein the gel suspension is hyaluronic acid.

3. The fill material of claim 1, wherein the gel suspension is poly-L-lactic acid.

4. The fill material of claim 1, wherein the gel suspension is human-based collagen.

5. The fill material of claim 1, wherein the gel suspension is bovine-based collagen.

6. The fill material of claim 1, wherein the gel suspension is fibrin glue.

7. The fill material of claim 1, wherein the gel suspension is an alginate gel.

8. The fill material of claim 1, wherein the gel suspension is a monomer.

9. The fill material of claim 1, wherein the gel suspension is a polymer.

10. The fill material of claim 1, wherein the human fat and the gel suspension are co-mixed at a ratio of one to one.

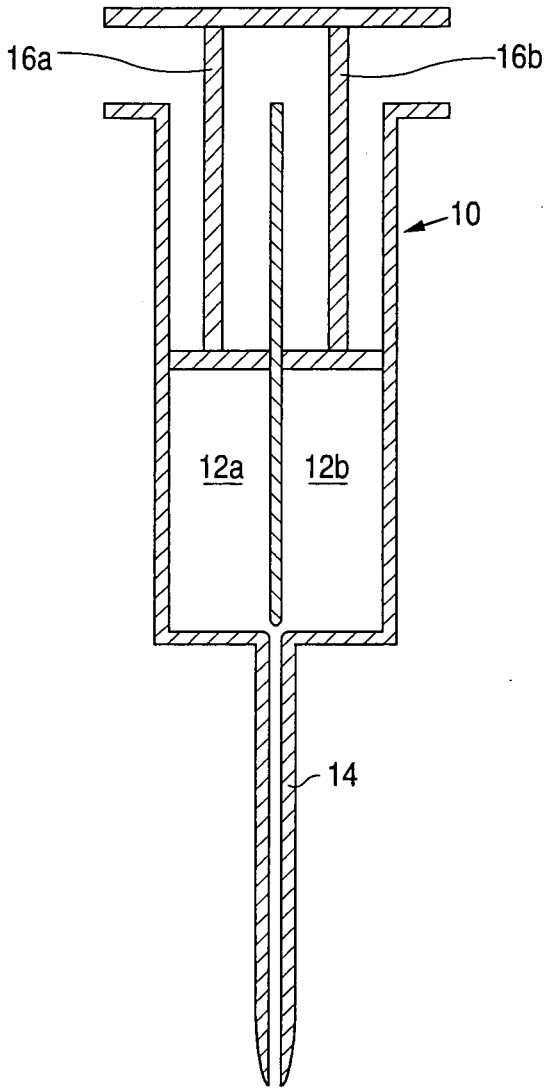

FIG. 1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 07/24094

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61F 2/02 (2008.01)
USPC - 623/23.72
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)
USPC:623/23.72

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC:424/486; 424/423 (text search-see terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST(USPT,PGPB,EPAB,JPAB); DialogPRO(Engineering); Google Scholar
Search Terms Used: autologous,fat,human,gel,hyaluronic,restylane,lactic,sculptra,cosmoderm, cosmoplast,zyderm, zyplast,fibrin,alginate,monomer,polymer,implant,injectable,fill,augmentation, adipocyte,transplant,suspension,adipose

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 2006/0093644 A1 (QUELLE et al.) 04 May 2006 (04.05.2006) para [0005],[0008],[0016], [0017],[0019],[0020], and [0038].	1-5 and 9-10 ---- 6-8
Y	US 2005/0208095 A1 (HUNTER et al.) 22 September 2005 (22.09.2005) para [0424],[0980], [0990],[1426],[2292],[2294], and [2300].	6-8

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"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
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"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

Date of the actual completion of the international search	Date of mailing of the international search report
06 March 2008 (06.03.2008)	08 APR 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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