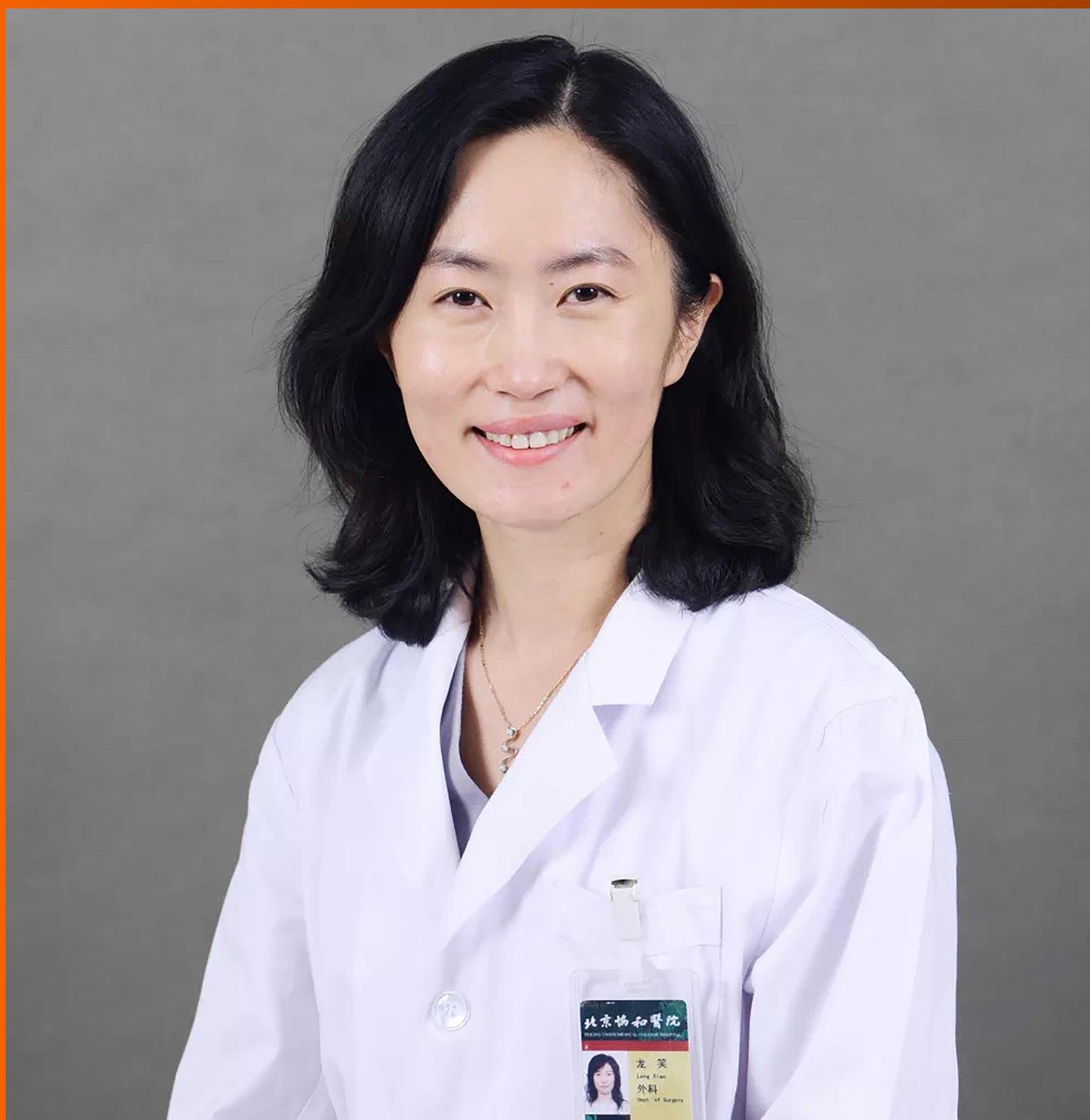


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## Biofat grafts as an orthobiologic tool in osteoarthritis: An update and classification proposal

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### Abstract

Among degenerative musculoskeletal disorders, osteoarthritis remains one of the main causes of pain and disability in the adult population. Current available alternatives to alleviate symptoms include conservative treatments such as physical therapy, anti-inflammatory drugs and an educational approach to lifestyle modification. The use of certain analgesics, such as opiates and corticosteroids offer short-term results but does not address the etiological source of pain and disability. In addition, prolonged use of such medications can cause additional complications. Therefore, the demand for regeneration of joint cartilage has led to an alternative approach called "orthobiologics". This alternative is based on cellular and molecular components capable of inducing and promoting tissue repair. Products derived from adipose tissue have been studied as an excellent source of orthobiologics in an attempt to promote joint cartilage repair. However,

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the lack of standardization regarding collection and processing protocols presents a challenge for the generalization of study results and determination of effectiveness. To the best of our knowledge, orthobiologics derived from fat have not yet been classified. Therefore, this manuscript proposes the HGS classification system which aims to describe certain parameters that are relevant to the quality of organic products regarding harvesting techniques (H), graft type (G), and number of centrifugations (S). The more parameters used would imply greater characterization and complexity of the evaluation of the biological product used. The HGS classification may provide a valuable contribution to the understanding of clinical procedures and research results, aiming to ultimately usher in a standardization of optimal practice.

**Key Words:** Orthobiologics; Adipose tissue; Mesenchymal stem cells; Regenerative medicine; Musculoskeletal disorders; Orthopedics

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**Core Tip:** Chronic musculoskeletal disorders remain one of the top causes of pain and disability in the adult population. The demand for musculoskeletal tissue regeneration has led to an alternative approach referred to as orthobiologics, which is based on cellular and molecular components capable of inducing and enhancing regenerative cascades in injured tissues. Adipose tissue-derived biological components are current orthobiologic tools being extensively studied and evaluated by regenerative medicine experts for their potential to treat musculoskeletal conditions. Since adipose tissue-derived orthobiologics have not yet been classified, to the best of our knowledge, this manuscript aims to propose the HGS classification system.

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## INTRODUCTION

Osteoarthritis (OA) is a common and very debilitating pathology, especially in elderly individuals<sup>[1]</sup>, but it can also affect younger individuals due to numerous factors<sup>[2]</sup>. Currently, with the aging of the population and with the increase in physical activities, skeletal muscle problems have also been increasing in equal proportion<sup>[3]</sup>.

OA is more prevalent in weight-bearing joints with the highest incidence in the knees; it may be idiopathic or secondary. The initial treatment consists of physical rest, modification of physical activity, weight loss, physiotherapy, orthosis, anti-inflammatories, analgesics<sup>[4]</sup> and, historically, injections of corticosteroids to relieve symptoms<sup>[5]</sup>. However, these treatments are palliative by managing only the symptoms. Currently, the use of hyaluronic acid (HA) can also contribute to decrease in pain and improvement of mobility due to its viscosupplementation potential. Additionally, high molecular weight HA is administered to further reduce oxidative stress and cell apoptosis<sup>[5,6]</sup>. HA is also thought to be a signaling molecule. These biological roles range from a purely structural function in the extracellular matrix to regulation through effects of cellular behavior *via* control of the tissue macro- and microenvironments, as well as through direct receptor mediated effects on gene expression.

In the field of orthopedics, when conservative treatment fails, the surgical procedure is usually indicated. In most cases arthroplasty may be recommended, however, it is known that these interventions have numerous complications and comorbidities that can lead to death in up to 5.6% of individuals operated<sup>[6]</sup>.

In view of the fact with the failure in conservative treatment and the aggressiveness of surgical intervention, the use of orthobiologics has become an outlet to avoid or postpone surgeries<sup>[7,8]</sup>, relying on the anti-inflammatory and reparative properties of

the patients' own cells for treatment of the injured tissues<sup>[9,10]</sup>.

Envisioning a new direction in cartilage regeneration, innovative therapies are being introduced, including platelet-rich plasma (PRP), bone marrow aspirate concentrate (BMAC) and adipose tissue with its different products<sup>[5,11]</sup>.

Mesenchymal cells can be found in many tissues<sup>[12]</sup>, but they are commonly extracted from bone marrow and adipose tissue. These cells are being studied extensively because they offer an alternative in the treatment of orthopedic pathologies since they have the ability to differentiate into other cell types<sup>[13]</sup>. They have great capacity for plasticity and self-renewal, in addition to exerting anti-inflammatory and immuno-modulatory roles<sup>[13]</sup>. However, the paracrine effects elicited by growth factors, cytokines, bioactive lipids as well as exosomes and microvesicles (which have been found to promote regeneration of damaged tissue) all play a fundamental role in orthobiological therapies<sup>[14,15]</sup>.

The choice of the extraction site may have a limiting character in the success of regenerative therapy. Among the donor sources, adipose tissue sources have a prominent place in the literature. Since 2001 Zuk *et al*<sup>[16,17]</sup> have shown that the stromal vascular fraction (SVF) contains stem cells capable of differentiating into cartilage, bone, muscle and fat. It has been shown that the immunophenotypes of BMAC and SVF cells are more than 90% identical<sup>[18]</sup>, however, one of the advantages of using fat is that it is easy to collect and it also offers more alternative extraction sites in the body. Additionally, if one compares 100 mL of BMAC with 100 g of adipose tissue, one may find 300 times more mesenchymal stem cells (MSCs) in adipose tissue<sup>[18,19]</sup>. Currently aiming at the paracrine understanding of mesenchymal cells, secretomes have been studied with analysis of pro-inflammatory cytokines such as interleukin 1B (IL-1B) which has a very important role in the pathogenesis of OA. IL-1B dramatically increases expression of matrix metalloproteinases that contribute to the degradation of articular cartilage; chondrocytes stimulated by IL-1B increase the secretion of nitric oxide and prostaglandins E2, which are major inflammatory mediators<sup>[20]</sup>. Mesenchymal cells display anti-inflammatory effects mainly by paracrine signaling action<sup>[21]</sup>.

In the present study, we will enumerate and describe the possible products of adipose tissue and their application in the treatment of OA as a regenerative therapy as well as the manipulation processes involved in the acquisition of mesenchymal cells.

Orthobiologics have been discussed in the literature with promising results, however, the lack of standardization regarding the methods of obtaining and processing the cells and associated components have led to uncertain conclusions in terms of efficacy and ability to generalize outcomes<sup>[22]</sup>. More specifically, the main components of orthobiologics, such as PRP, for example (platelet concentrations, growth factors, and cytokines), may vary based on the processing method, which might affect anabolic and anti-inflammatory properties and, consequently, lead to inconsistent outcomes<sup>[23]</sup>. Thus, the need for standardization and classification of orthobiologics is imperative for understanding procedures and dissemination of research outcomes. A classification system has been developed for PRP<sup>[22]</sup> and for BMAC<sup>[24]</sup>. However, no such classification exists for adipose tissue as an alternative orthobiologic tool. Thus, the purpose of this paper is to present a proposal for a classification system for adipose tissue-derived orthobiologics.

---

## MESENCHYMAL STEM CELLS

---

MSCs exhibit the potential ability to differentiate into mesodermal cell lineages (*e.g.*, cartilage, bone, fat, muscle, meniscus and tendon)<sup>[25]</sup>, which is fundamental for the regeneration process. Moreover, these cells elicit paracrine effects, and are therefore capable of altering their local microenvironment<sup>[26]</sup>.

Given the varying MSC markers that laboratories may use to characterize these cells, there is a lack in standard phenotypic criteria. This heterogeneity is also due to the fact that MSCs are able to express a range of cell-lineage-specific surface antigens that may differ depending on the culture preparation, duration, or plating density<sup>[27]</sup>. However, the Mesenchymal and Tissue Stem Cell Committee of the International Society for Cellular Therapy have proposed minimal criteria to characterize MSCs, which comprise the following attributes: Cells must be plastic-adherent when maintained in culture; Must be able to differentiate *in vitro* into chondroblasts, adipocytes and osteoblasts; and Must express CD105, CD73 and CD90 whilst lacking expression of CD45, CD11b, CD34 or CD14, CD79α or CD19 and HLA-DR surface

molecules<sup>[28]</sup>.

MSCs lack significant immunogenicity and can be easily isolated, which allows allogenic transplantation, but the MSC-exosomes do not appear to trigger immune-rejection and could be the optimal treatment in specific clinical scenarios in the future<sup>[29]</sup>.

Under allogenic circumstances, these cells should be considered immune evasive. However, the effects of MSCs in cellular-based therapies depend on the ability of these cells to home and engraft (long-term) into the target tissue<sup>[30]</sup>.

Cells from injured tissue release chemokines responsible for MSC recruitment. Once in the target tissue, MSCs are able to modulate wound-healing responses by reducing apoptosis and fibrosis, attenuating the inflammatory process. They also stimulate angiogenesis, cell proliferation and differentiation *via* paracrine and autocrine pathways<sup>[31]</sup>. These properties are attributed to the ability of MSCs to release key agents, such as vasculoendothelial growth factor, transforming growth factor beta, stromal-derived factor 1, and stem cell factor, among others. Also, they induce a downregulation of pro-inflammatory cytokines, including IL-1, IL-6, interferon- $\gamma$ , and tumor necrosis factor alpha (TNF- $\alpha$ )<sup>[32,33]</sup>.

MSCs also possess immunomodulatory properties as they are able to inhibit the activation of type 1 macrophages, natural killer cells, and both B and T lymphocytes<sup>[34]</sup>.

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## BIO FAT GRAFT

It is currently known that adipose tissue is one of the best sources of MSCs, which may also be referred to as MSCs or adipose-derived stem cells (ADSC)<sup>[35]</sup>. The benefit of using adipose tissue-derived products in OA, as previously mentioned, is its paracrine action with secretion and activation of hormones such as leptin, resistin and cytokines such as TNF alpha in mediating the chronic inflammatory process. Another advantage of using adipose tissue as a source of mesenchymal cells is the fact that there is no decrease in the number of these cells with age<sup>[36]</sup>.

In order to obtain all the benefits offered by ADSCs, there are some ways to prepare adipose tissue-derived products. The techniques involved in this procedure will be reviewed immediately in the following sections of this manuscript.

One noteworthy observation is that, unfortunately, there is a lack of standardization demonstrating which types of methods are most effective for obtaining and isolating mesenchymal cells from fat. The harvest result may sometimes be referred to as “Stem Cells-poor” aspirated fat.

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## OBTAINING FAT

In order to obtain adipose tissue, one may find convenient extraction sites described in the literature, such as the abdomen, thigh, hip, buttocks, and infra-patellar fat pad. The lower abdomen and hip regions have higher cell quality when compared to other locations; however, cell viability does not change with the donor site<sup>[19]</sup>.

There are four key steps that must be followed in order to obtain MSCs from adipose tissue, and the careful handling in order to optimize the harvesting procedure. Step 1: Donor area, how it is treated, technology utilized; step 2: Aspiration, closed or non-closed system; step 3: Processing, SVF isolation; and step 4: Injecting.

Sub cutaneous fat tissue for regenerative purposes may be obtained through the following procedures.

### **Step 1: Donor area preparation**

**Fragment resection**<sup>[37,38]</sup>: In this procedure, the removal of a block of fat from any donor area occurs; The advantage is the preservation of all the components including extracellular matrix and regenerative elements. With this fragment, the whole process of enzymatic digestion is prepared for separation of the mesenchymal cells and posterior cell culture. The major disadvantage is that enzymatic digestion affects the number of MSCs during manipulation. Elaborating, cell washing after collagenase administration may also imply the use of fetal bovine serum, which can dilute the concentration of MSC. Collagenase does not preserve the extracellular matrix where all the necessary elements or regenerative factors are found in the exact proportion and concentration. The incision made at the extraction site for acquisition of the necessary fat volume utilizes a closed system (air exposure), which can increase apoptosis.

**Suction-assisted lipectomy (SAL):** This technique is combined with tumescent infiltration with saline solution + anesthetic + adrenaline, in the subcutaneous area of the donor site in order to form a swelling and thus facilitate the liposuction process in addition to reducing bleeding<sup>[39]</sup>.

The advantage is that this is a closed system, with less incision at the donor site. The disadvantage is that the tumescent infiltration dilutes the proportion and concentration of the regenerative cells and particles, requiring the need for additional harvest process maneuvers. The mechanical disruption mechanism is also quite destructive towards the adipose tissue<sup>[29]</sup>.

**Liposuction with ultrasound<sup>[19,40]</sup>:** Adipose Tissue sonication process allows obtaining of only microclusters of cells and no breakdown of adipose tissue<sup>[41]</sup>. The major disadvantage is that this is not a closed system.

**Laser liposuction:** The use of the specific wavelength (1210-nm) laser to dissolve the bound cells (adipocytes, stem cells, extracellular matrix) to the connective tissue before aspiration facilitates suction and may promote cellular photostimulation, *via* a photochemical property of the infrared light 1210-nm. Centurión *et al*<sup>[29]</sup> demonstrate that the SAL technique can cause cell lysis; the use of certain lasers with affinity for water can cause tissue damage by increasing the permeability of the adipocyte cytoplasmic membrane<sup>[42]</sup>.

With the use of a laser with a wavelength of 1210 nm in the adipose tissue, a selective photostimulation effect has been described. This technique may guarantee up to 98% viability of adipocytes, remaining unchanged. Additionally, since it relies on photobiomodulatory effects, it is also proven to generate an increase in mitochondrial activity<sup>[29,42]</sup>.

In all of the techniques there is minimal patient discomfort and low morbidity in the extraction site<sup>[43]</sup>. Oedayrajsingh-Varma *et al*<sup>[19]</sup> demonstrated that the use of ultrasound requires a greater amount of time for the growth of cells in culture when compared to fat fragmentation and SAL.

### **Step 2: Aspiration: closed or non-closed system**

Closed system uses a syringe connected to the cannula, avoiding air exposure.

Non-closed system: Using a syringe connected to the cannula but exposes the material to air during processing maneuvers. An aspiration machine may also be utilized however air exposure is increased during the collection process and, therefore, the apoptotic response of cells.

### **Step 3: Processing adipose tissue and SVF isolation**

Minimal-grade manipulation (MGM) or high-grade manipulation (HGM) (C).

**MGM:** This refers to techniques that performed during the same surgical session and inside the same operating room, but only if the tissue is harvested, treated, and re-implanted.

Among the techniques listed as MGM, one can find 3 ways to treat Fat: (1) Mechanical disruption: Decantation, filtration, centrifugation, emulsification, and other techniques described as Coleman's technique. These include direct ultrasonic cavitation, cell assisted lipotransfer, Nanofat (Tonnard), SAL; (2) Exogenous enzymatic digestion: Exogenous collagenase is used, increasing the cost, the manipulation and the risk of side effects if any enzymatic residue is present in the final product. Devices like Cytori Celution and Unistation may be utilized, as examples; and (3) Endogenous Enzymatic collagenase activation - One STEP™ technique: This involves infrared 1210-nm laser activation of the endogenous quiescent collagenase, present in the subcutaneous tissue. Activation is made in a single step. This process denatures the connective tissue, liberating the MSCs and preserved adipocytes, with mitochondrial stimulation *via* cytochrome C oxidase. After adipose tissue aspiration, a simple centrifugation is performed in order to isolate the SVF, in a closed system with minimal manipulation.

**HGM:** This includes characterization, expansion, cultivation and all the other complementary laboratory techniques. In some countries HGM is strictly prohibited.

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## METHODS OF ISOLATION OF MESENCHYMAL CELLS

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### ***SVF isolation by enzymatic digestion***

The use of fat digestion through collagenase is the most widely used method when the objective is to culture and expand mesenchymal cell<sup>[44]</sup> Collagenase separates fat into 2 distinct layers: The floating fraction of mature adipocytes, and the cellular components in the lower aqueous portion<sup>[45]</sup>, which are separated by centrifugation, gravity or *via* the use of filters. However, the presence of collagenase in injectable products for the treatment of orthopedic conditions is not allowed by the Food and Drug Administration, so it is well-suited for cell culture and expansion studies only. There are also additional methods involving the administration of lecithin to obtain SVF.

### ***SVF isolation without enzymes***

Due to the regulatory issue related to the isolation of mesenchymal cells with collagenase, other methods were considered in order to try to achieve this isolation with an acceptable level of effectiveness.

Most of these techniques involve a mechanical breakdown of the adipose tissue to obtain SVF through microfragmentations, however the cell yield is much lower when compared to the enzymatic method because adipocytes establish strong bonds with collagen that are not easily released with mechanical force<sup>[46]</sup>.

Authors have described the method of filtering and emulsifying fat through small filters called “nano-filters”<sup>[47]</sup>, which is why the term “nano-fat” is used. This method consists of the passage of fat through some filters, which causes emulsification of this product. Since some researchers have previously identified the presence of mesenchymal cell markers, these alternative biological products are currently being widely used in aesthetic medicine with promising results<sup>[48]</sup>.

Perhaps the combination of techniques with centrifugation and filtration can produce a higher concentration of mesenchymal cells, eliminating the use of enzymes. This reduces the cost, processing time and remains in compliance with the regulatory bodies for therapeutic use. Currently, there are some kits on the market that assist in cell separation, using filtration with or without saline wash, whilst other kits employ centrifugation steps. However, there is still a lack of standardization and a better comprehension of the product obtained from these different devices.

### ***Automated devices for isolation of SVF***

Automated devices are already available on the market for the separation of mesenchymal cells from liposuction. The first system described was in the USA, “Cytoris Celution”<sup>[49]</sup>. Lastly there is a non-enzymatic method for the acquisition of SVF referred to as ultrasonic cavitation.

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## PROPOSAL OF A NEW CLASSIFICATION SYSTEM FOR ADIPOSE TISSUE-DERIVED PRODUCTS: THE HGS CLASSIFICATION

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The lack of standardization of adipose tissue-derived products for regenerative medicine has emerged, thus the need to classify the processing methods in regards to quality and procedural details has been established<sup>[23]</sup>. Classification of such factors would allow for procedural standardization and interpretation of both clinical results and research findings. The HGS classification system comprises the three main techniques involving liposuction for harvesting, which is represented by the letter H; Graft, which is represented by the letter G (SVF isolation method); and the letter S which refers to spin, indicating the inclusion or exclusion of centrifugation.

The HGS classification is focused on whether the cellular and molecular content present in the product is evaluated and described, increasing the complexity of description/characterization. For each letter there is a sub grouping, as follows.

For letter H (Harvesting -liposuction): (1) SAL; (2) Ultrasound assisted; and (3) Laser assisted.

Letter G (represents the method for isolation of the SVF- Graft) there is (1) Decantation (washing); (2) Microfragmented (Nanofat); (3) SVF non-enzymatic; (4) SVF enzymatic; and (5) Automated devices.

In this description (H), we have yet another subgroup which is also presented in the form of numbers for cell characterization, described as follows: (1) Product is to be collected and injected with no additional analysis; (2) The cellular content would be assessed by a cell counter, which would enable quantification of mono- and

polymorphonuclear cells, giving the number of total nucleated cells; (3) Dosage of molecular content, such as interleukins and/or growth factors is made by multiplex platform or ELISA technique; (4) Indirect quantification of MSC number measured through colony forming unit (CFU) in culture; (5) Phenotyping of MSC and HSC for characterization through flow cytometry – it is wise to use a full panel for the CD (cluster of differentiation) surface markers, especially of the MSC since there many markers for positive and negative evaluation; and (6) For the complete characterization of MSC, the *in vitro* differentiation into the mesodermal trilineage is necessary, which means the induction of chondrocytes, adipocytes and osteocytes.

For letter S (Spin- inclusion or exclusion of centrifugation steps): (1) Yes; and (2) No.

The representation of the HGS classification is shown in [Table 1](#).

The purpose of classification is to be descriptive for collection, graft type, characterization and centrifugation. This should be considered in order to standardize the publications and facilitate the understanding of the type of fat products, especially in terms of quality.

The idea of this classification is that for each type of fat products used the increase in the number indicates higher complexity of the evaluation of the biological product obtained. For example, when a study or procedure with adipose tissue reports that the adipose tissue was collected *via* SAL, with decantation and injected after centrifugation, it would be classified as H1, G1-1, S1, according to the HGS classification. On the other hand, if it is collected with the aid of ultrasound, microfragmentation without centrifugation and cell count is performed, then it would be classified as C2 H2-2 S2. This is applied successively, always in correspondence with the subgroups of the letter H (3 subgroups), the two subgroups of the letter G being the first related to the separation technique, and the second subgroup related to the characterization of adipose tissue, and finally the two subgroups of the letter S. It is worth remembering that for letter G in the second subgroup, when we characterize the sample it is possible to have more than one number. For example, the product went through cell count and CFU, so in this case we would use the numbers 2 and 4 in the second subgroup. An example is presented below.

Liposuction procedure using laser (H-3); enzymatic digestion technique for separation of mesenchymal cells (G-4) with cell count (2), dosage of cytokines (3), CFU (4) and MSC phenotyping (5); and lastly, centrifugation (S). Result: H3, G4 (2-5), S1.

## DISCUSSION

Aiming to improve the quality of life in patients with musculoskeletal disorders, regenerative medicine has been occupying a space with novel research for the improvement of pain and tissue repair<sup>[50]</sup>. Mesenchymal cells obtained from adipose tissue exert important roles and have recently been gaining prominence in numerous publications. In 2006, Nguyen *et al*<sup>[51]</sup> revealed improvements in quality of life questionnaires from patients with knee OA (KOA) who were treated with SVF combined with PRP. In a randomized double blind clinical trial, Hong *et al*<sup>[52]</sup> showed the efficacy of SVF (with collagenase) compared to hyaluronic acid in patients with KOA. In 2017, Yokota *et al*<sup>[53]</sup> revealed that the scores used to analyze the improvement parameters were significantly higher 1 mo after the infiltration of SVF in the knees of osteoarthritic patients. In the literature, we also found a review including 17 articles evaluating SVF for OA, with the majority of fat products coming from the abdominal region and being processed with the use of collagenase. Most of the results were satisfactory but the articles compiled in this review do not have a level of evidence capable of validating the efficacy of the treatments.

Based on some current articles, the use of mesenchymal fat cells appears to be extremely safe with encouraging results when functional outcomes and pain alleviation are taken into consideration, suggesting that this biological approach may play a promising role as a suitable treatment for OA.

It is known that mesenchymal cells elicit a broad range of effects favoring intra-articular modulation and delaying degeneration through their paracrine action as well as offering the possibility of tissue repair due to the presence of stem cells in the vascular stroma. Although most studies demonstrate superior results with mesenchymal cell culture, Jurgens and Col obtained excellent results with the use of SVF in a single procedure<sup>[54-56]</sup>, however further studies comparing the two modalities must be performed in order to propose a definitive answer to this question.

As is the case with the majority of biological products, we verified a wide variety of preparation techniques, collection sites, non-standardized therapeutic protocols and

Table 1 HGS classification system

HGS classification system	
<b>H</b> Harvesting (Liposuction)	(1) Suction-assisted lipectomy; (2) Ultrasound assisted; and (3) Laser
<b>G</b> Graft: (1) Decantation (washed); (2) Microfragmented (Nano); (3) SVF non enzymatic; (4) SVF enzymatic; and (5) Automated devices	(1) Collection and injection; (2) Cell count; (3) Dosage of cytokines (GF and/or IL); (4) CFU; (5) MSC phenotyping; and (6) Differentiation evaluation
<b>S</b> Spin	(1) Yes; and (2) No

SVF: Stromal vascular fraction; MSC: Mesenchymal stem cell; CFU: Colony forming unit.

concomitant treatments, which compromise the comparison between studies<sup>[54]</sup>. Due to the numerous forms of presentation and approach, there is a lack of standardization in order to render the results more effective. To affirm which technique is better for MSC harvesting, it is necessary to analyze and compare MSC both in quantity and quality (% of CD markers). Another important factor is the presence/preservation of extra cellular matrix, paracrine factors, exosomes, and cytokines in the final product. Therefore, the use of expanded cells for the scope of science may bring greater security because it allows greater control of the product with cell count and the possibility of better characterization of the sample<sup>[57,58]</sup>.

New technologies appear to enhance harvesting, like the laser technology, but current devices with specific wavelengths and absorption/affinity for water may not be adequate due to possible lipolytic reactions by increasing the temperature (photo-thermal effect). Only a novel infrared laser 1210-nm wavelength (One STEP™ technique) offers an absorption/affinity for fat *via* photochemical properties<sup>[42]</sup>.

The quality of the lipoaspirate is not affected when using different cannula size or negative pressure in the SAL procedures<sup>[59]</sup>. What may affect the quality and quantity of the aspirated material is the mechanical disruption mechanism of the technique.

## CONCLUSION

Given all the information, physically debilitating conditions such as OA are still highly challenging pathologies for professionals seeking a definitive treatment. The search for ideal biologic products has become an increasingly common practice but this goal has not been reached just yet, despite the growing number of clinical trials envisioning an effective treatment protocol. In scientific terms, however, it is safe to infer that the levels of evidence for the use of SVF in the treatment of OA are still under early development but certainly promise great results in the near future.

Although studies using adipose tissue for the treatment of various musculoskeletal disorders have shown promising clinical results, inconsistent preparation methods with deficient reporting has led to questionable outcomes with respect to generalization and reproducibility. In order to optimize the efficacy and safety of fat products, and to allow validation and standardization of such products, studies should report stepwise descriptions of the preparation protocol and additional information to further classify the product used. The HGS classification focuses on describing parameters that are relevant for the quality of biological products, such as the collection technique, cell count and molecular content dose. The HGS classification would contribute to a greater understanding of the type of harvest, clinical procedures and research outcomes and, over time, lead to a standardization of best practice. Together, we believe that the HGS classification proposal is an easily recalled and useful method for the classification of fat products.

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