Condensation of Tissue and Stem Cells for Fat Grafting

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KEYWORDS

• Fat grafting • Cell assisted lipotransfer • Adipose-derived stem/stromal cell • Tissue regeneration • Macrophages • Vascular endothelial cells

KEY POINTS

- Adequate centrifugation purifies and condenses aspirated adipose tissue and improves graft retention.
- We can condense tissue by removing unnecessary components of grafted tissue through decantation, filtrations or centrifugation.
- Condensation of adipose-derived stem/stromal cells (ASCs) is important to get better adipocyte regeneration after fat grafting and achieve tissue revitalizing effects.
- ASCs can be condensed by reducing adipocytes from the graft through mechanical processing or strong centrifugation.
- Supplementation of stromal vascular fraction or ASCs can also improve ASC/adipocyte ratio in the graft and is expected to obtain better outcomes for tissue volumization and revitalization.

INTRODUCTION

Adipose tissue has many types of cells other than adipocytes, which can be extracted as a cell pellet called stromal vascular fraction (SVF) through collagenase digestion of aspirated adipose tissue. SVF contains adipose-derived stem/stromal cells (ASCs), vascular endothelial cells, pericytes, adipose-resident macrophages, lymphocytes, and so on.[1] ASCs are regarded as a potent tool for cell base therapies because they have biological functions such as multidirection differentiation, growth factor secretion, and immunomodulation, and can be obtained readily in a large amount through liposuction.

Condensation of grafting adipose tissue is a key to achieve better volumizing effects (better volume retention) by fat grafting. It is particularly important when these is a limitation of injection volume (eg, breast) owing to the limited skin envelop, because an injection of excessive volume leads to severe ischemia and fat necrosis. Condensation of grafting fat can be achieved by means of removal of unnecessary components, such as water, oil, dead cells, and blood cells. Because aspirated fat tissue is relatively poor in stem cells (ASCs),[2] condensation of ASCs in the graft is another issue for seeking better volumizing effects.

Recently, regenerative effects of fat grafting are appreciated by many clinicians. Stem cell–depleted tissues such as irradiated tissue, chronically inflammatory tissue, and ischemic fibrous tissue are improved by fat grafting in quality, vascularity, and healing and expanding capacity.[3,4] It has been reported frequently that hypertrophic scarring and

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scar contracture are softer and that skin hyperpigmentation disappears after fat grafting.[5] Such regenerative/revitalizing effects of fat grafting are considered to be derived from ASCs in the tissue. Therefore, condensation of ASCs in the graft may be also crucial for such regenerating/revitalizing applications.

BASIC SCIENCE

Difference Between Aspirated Fat Tissue and Intact Adipose Tissue

Adipose tissue contains various types of cells including adipocytes and ASCs, as well as connective tissue (see the article by Mashiko and Yoshimura elsewhere in this issue for details). When surgeons aspirate fat, only fragile parts of adipose tissue are harvested through a suction cannula, whereas the honeycomb-like fibrous structures remain intact in the donor site.[6] The fibrous structure is predominantly composed of connective tissues and large vasculatures, which are considered to contain many ASCs. We have found that aspirated fat tissue contains only one-half the number of ASCs compared with intact fat tissue.[2] Stage-specific embryonic antigen-3–positive cells, which may be highly multipotent stem cells (muse cells),[7] locate around large vasculatures. These cells are also deficient in aspirated adipose tissue (unpublished data, Doi K et al, 2012). The relative deficiency of ASCs in aspirated fat tissue may be owing to (1) a substantial portion of ASCs being left in the donor tissue and (2) some ASCs being released into the fluid portion of liposuction aspirates, possibly owing to the act of an endogenous enzyme.[1,6] Thus, aspirated fat tissue is regarded as relatively ASC poor compared with intact fat tissue. This low ASC/adipocyte ratio may be a reason for long-term atrophy after fat grafting.[2]

Importance of Adipose-Derived Stem/Stromal Cells in the Grafted Tissue for Adipose Regeneration after Fat Grafting

ASCs have the potential to modulate or suppress immunoreaction,[8] differentiate into adipocytes,[9,10] vascular endothelial cells, or others and release angiogenic growth factors, such as hepatocyte growth factor and vascular endothelial growth factor, especially under hypoxic conditions.[11] ASCs were reported to contribute to angiogenesis during the adipose remodeling process after ischemia or fat grafting.[9–11] Our recent study using green fluorescent protein mice revealed that regenerated adipocytes after fat grafting are mostly originated from ASCs in the graft tissue, but not from other host-derived stem/progenitor cells, although new ASCs can be provided partly by bone marrow or other tissues.[12] It was suggested that only ASCs originally located adjacent to dying adipocytes can become adipocytes, although other ASCs can contribute in other ways, such as angiogenesis or release of growth factors.

RELEVANCE TO CLINICIANS

Graft Tissue Condensation

Liposuction aspirates contain some components unnecessary for adipose tissue engraftment/regeneration; water, oil (broken adipocytes), and blood cells (red blood cells and white blood cells). It is recommended to remove such components and reduce the graft volume without reducing the number of viable adipocytes and ASCs; this is called condensation of graft tissue. Tissue condensation is important, especially when there is a maximum limit in graft volume, such as with breast augmentation. There are 3 major methods for graft tissue condensation: decantation (gravity sedimentation), filtration with or without a vacuum, and centrifugation. Among the 3, centrifugation is most effective to remove the water content without losing ASCs, although some adipocytes can be broken by the mechanical force and the resulting condensed fat may become more viscous and need higher pressure to inject through a small cannula (**Fig. 1**).[13] Oil released from damaged adipocytes causes inflammation-like foreign materials, suggesting that removal of oil should be important for better healing after fat grafting.

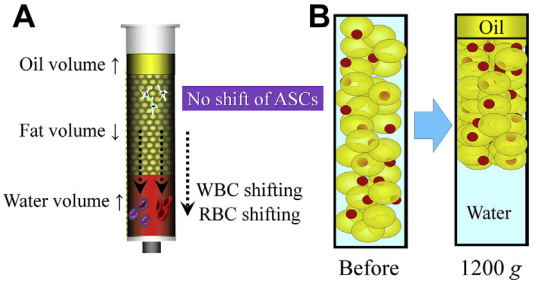

Fig. 1. Tissue and adipose-derived stem/stromal cell (ASC) condensation by centrifugation. (*A*) By centrifugation, fat volume becomes compact, water volume increases and oil will be clearly separated as a top layer. Many of red blood cells (RBCs) and white blood cells (WBCs) in the aspirated fat shift into the water portion after centrifugation, but most of ASCs remain in the fat portion. (*B*) By centrifugation at 1200×g for 3 minutes, fat volume decreases by 30%. Some adipocytes are broken and become oil as a top layer, but all ASCs remain intact and are concentrated in the condensed fat tissue.