Autologous Fat Grafting:
Historical Review and Present Status

Many materials and techniques have been used to address soft tissue defects and deficits. The use of most of these substances and techniques has met with difficulties, including lack of persistence, foreign body reaction, unnatural texture, and increased potential for infectious disease transmission.

Fat, or adipose tissue, is an ideal substance that is readily available, natural feeling, and, in autologous use, will not cause adverse immunologic reactions. Essentially, the fat grafting procedure harvests fat from one part of the body where abundant supply exists and then implants it into another part of the body for cosmetic or reconstructive purposes.

Despite more than a century of fat grafting experience there is still no commonly accepted standard method used among physicians. Physicians have studied the details of the procedure, including tissue harvesting techniques, preparation and placement of the fat tissue. Ideal candidates for fat transfers, as well as long-term safety and efficacy. Despite all of these efforts they have not been able to resolve the unpredictability of fat survival leading to resorption of the transferred tissue.1,2

REFERENCES
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ADRCs, sometimes referred to as stromal vascular fraction cells, are a heterogeneous population of cells that include multipotent progenitors (referred to as adipose-derived stem cells), endothelial progenitor cells, leukocytes, mature endothelial cells, and vascular smooth muscle cells.

Early experience suggests that enriching a fat graft with ADRCs provides several benefits: it stimulates increased levels of growth factors which help form and maintain new blood vessels which in turn, provide necessary oxygen and nutrients for survival, thus allowing a graft to maintain volume. Moreover, compared to other adult sources of stem and regenerative cells, fat tissue is the richest source of these cells. For example, the cells that are used to generate cultured adult stem cells are 2,500-fold more abundant than bone marrow, the most studied source of these cells.8,9

ADRCs are capable of acting by at least three mechanisms: they naturally express a range of growth factors thereby enhancing formation of new blood vessels10 and stimulating repair and regeneration; they can differentiate to form replacement tissues and structures (for example, fat cells or new blood vessels);11 and they and other cell types within the ADRCs can modulate the inflammatory response, creating an environment that favors healing over scarring.12 The relative contribution of these three mechanisms in soft tissue grafting is not fully defined. Scientists are actively pursuing research designed to better understand the mechanisms.

Once the grafted fat is placed into its new location, its survival is initially dependent upon diffusion of nutrients from surrounding tissue and growth of new blood vessels into the transplanted fat fragments, leading to a permanent correction of treated site.6 Re-establishing a blood supply quickly is essential for successful graft survival. Grafting techniques that do not facilitate increased vascular development generally result in partial or complete loss of the graft tissue. This is why initial overcorrection or repeat fat injections is required to achieve satisfactory results.

Over the years physicians have used and refined many different methods for tissue collection and tissue injection, as well as explored other options in an effort to address these limitations, but they remain challenged by unpredictable resorption rates ranging from 50-90%.7 Recent studies suggest the use of adipose-derived stem and regenerative cell (ADRC) technology is a viable means to improve treatment of soft tissue defects.

Variables Influencing the Success of Autologous Fat Grafting4,5

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<tr>
<td>Aspirate or liposuction tissue</td>
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<td>Tissue volume</td>
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<td>Site of harvest</td>
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<td>Harvest instrumentation</td>
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<td>Mechanical force</td>
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<td>Separation of tissue (centrifugation or filtration)</td>
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<td>Delivery instrumentation</td>
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<td>Volume delivered</td>
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Successful Long-Term Method of Fat Grafting: Fat+Cells and Automation/Standardization

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In order to bring this powerful cell population into the operating theater, Cytori Therapeutics, Inc. developed a medical device, providing the physician with a cost- and time-effective means of controlling the variables of fat grafting.

The Celution® 800/CRS System is a CE marked medical technology that enables real-time, point-of-care access to adult ADRCs by automating the extraction, washing, and concentration of a patient’s own ADRCs within a closed system. These cells can then be delivered back into the same patient within a single surgical procedure. In addition, the system can wash and mix lipoaspirate with ADRCs to create a cell-enriched graft for immediate re-implantation into the same patient.

Overcoming Limitations through Automation & ADRCs - Cytori’s Novel Approach

Cytori researchers and clinicians investigated the use and addition of adipose-derived stem and regenerative cells (ADRCs) to the fat graft to assess improvement of graft survival. Study results from Cytori and collaborators demonstrate that ADRCs form the foundation for fat graft survival by releasing growth factors that help to form and maintain new blood vessels, thus restoring graft access to necessary oxygen and nutrients needed for survival.

Cytori developed the Celution® 800/CRS System, which automates and standardizes several aspects of fat grafting. Available to physicians in Europe and Asia, this platform technology allows the physician to wash the fat graft, extract the stem and regenerative cells residing within the tissue, and mix the fat with the cells to create a cell-enriched fat graft, which he or she can then re-deliver to the patient.
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Fat, or adipose tissue, is an ideal substance that is readily available, natural feeling, and, in autologous use, will not cause adverse immunologic reactions. In fact, the use and transferring of fat, also called fat grafting or lipofilling, is not a new concept; it reportedly dates back to 1893, when performed by a German physician to fill a soft tissue defect.1 Essentially, the fat grafting procedure harvests fat from one part of the body where abundant supply exists and then implants it into another part of the body for cosmetic or reconstructive purposes.

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