Clinical Use of Adipose-Derived Stem Cells for Breast Volume Enhancement

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Implantation of artificial prostheses is a standard method of breast augmentation, but complications derived from the foreign body, such as capsular contracture, malposition, implant rupture, and infection, occur at a relatively high rate (10 to 20 percent) and frequently result in removal or replacement of implants.

In addition, hospitals in Japan reject women who have breast implants from undergoing mammography as part of annual social health examinations because of a potential risk for implant rupture by external pressure. On the other hand, the use of autologous fat tissue for the breast has not gained acceptance due to lack of consensus on its safety, as well as concern that the development of micro-calculations could complicate mammogram evaluation.

Advantages

Although autologous and a low rate of graft survival due to partial retraction is known that remains to be resolved, autologous fat transplantation offers many advantages, such as the lack of scars and complications associated with foreign materials. It was recently re-evaluated as an alternative to breast implants for augmentation or reconstruction [3], possibly reflecting issues technical advances in autologous fat transfer and the radiological detection of breast cancer [1].

Tissue-specific progenitor cells in adipose tissue can differentiate into various cell lineages. These progenitors, known as “adipose-derived stem/progenitor cells” (ASCs), are expected to become valuable tools in a wide range of cell-based therapies. ASCs have been used in clinical trials of treatments for bone defects (autologous fresh ASCs), retinal glial fibroblast-derived ASCs, and cultured ASCs in fibrotic grafts, graft-versus-host disease (nonautologous ASCs), and adenogenital spermatic (catalyzed cultured ASCs combined with autologous fat tissue).

ASCs are believed to act as progenitors of adipocytes and vascular cells, mediate adhesion of other tissues to the extracellular matrix, specifically around vessels, and are a main contributing population to adipose tissue turnover and remodeling, such as during repair (adipose tissue is considered to take over even after a period of 2 to 10 years) [5].

In order to address the problems of liposuction, we designed a new strategy, called cell-assisted lipotransfer (CAL), based on the finding that aspirated fat tissue contains fewer vessels and ASCs than does intact fat tissue and also on our hypothesis that the relative deficiency of tissue-specific progenitors in aspirated fat tissue might contribute to the slow survival rate and progressive atrophy of transplanted fat tissue, as was partially confirmed in animal studies [4]. In the CAL strategy, the progenitor deficit was compensated by augmentation with autologous fraction (SFV) isolated from a separate volume of aspirated fat tissue.

Our experience with the cell-assisted lipotransfer technique showed generally satisfactory clinical results without any major complications.

Speculated roles of ASCs in CAL are:
1. To differentiate into adipocytes and contribute to adipose regeneration;
2. To differentiate into vascular endothelial cells or muscle cells and may promote angiogenesis;
3. To release angiogenic growth factors such as hepatocyte growth factor (HGF); and
4. To survive as original ASCs (i.e., adipose tissue progenitors).

Cellular and molecular events that occur in the grafted adipose tissue during the early period (ischemia and subsequent reperfusion phase) after transplantation have not been well studied. However, adipose tissue and vascular remodeling occurs after experimental ischemic reperfusion injury and, during the repair process, ASCs were a main proliferating cell population and promoted adipose tissue regeneration by releasing HGF [1].

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In a clinical trial of CAL (more than 200 cases since 2003), the SVF comprising 10 to 40 percent ASCs was freshly obtained from half of an aspirated fat sample via collagenase digestion and reconceived with the remaining half of the aspirated fat sample, concentrating relatively progenitor-poor aspirated fat tissue into progenitor-rich grafts.

Our experience with the CAL technique showed that atrophy of transplanted progenitor-enriched fat grafts was minimal, and clinical results were generally satisfactory without any major complications, suggesting that ASC supplementation is effective and safe [6].

Pre- and postoperative evaluations included mammography, magnetic resonance imaging (MRI), ultrasonography, and three-dimensional treatment that enabled volumetric evaluations of the breast with the patient in a standing posture.

Mammography showed microcalcifications seen 24 months only in a few cases, and MRI analysis showed that the fatty layers around the mammary gland became substantially thicker at 12 months. Costumiform (SVF) was detected by MRI or echography in several cases after 12 months. For breast augmentation, progenitor-enriched fat tissue with a mean volume of 260ml was transplanted, and 100–200ml augmentation was achieved at 12 months. The 10-month measurements showed that the transplanted adipose tissue was gradually absorbed during the first two post-operative months but that the breast volume showed change minimally thereafter. The surviving fat volume varied among patients and the graft take ranged from approximately 40% to 80%.

The roles for the variations in enhancement volume remain to be fully understood, and multiple factors are likely to affect the clinical outcomes. Patient factors include skin redundancy of the breast. Technical factors include device, liposuction techniques, period and temperature of fat preservation, and injection techniques. For liposuction of breasts, we think that devices such as a long (6.6mm) 18-gauge needle and a screw-in tip are very useful and may affect clinical results. Although a large-volume (200–400ml) augmentation cannot be achieved by this method, patients obtained well-shaped and augmented breasts with natural contours without having concerns about future possible complications derived from implants.

Other applications

CAL was applied not only to breast augmentation but also to a variety of other tissue augmentation or reconstruction: breast augmentation after mammoplasty, replacement of breast implants, and harvesting of fat from breast. Personal breast reconstruction, and autologous breast augmentation. It is noted that clinical outcomes of CAL-assisted breast augmentation immediately after implant removal were much better than what we expected; this may be related to redundancy of the breast skin, which was formerly expanded by breast implants.

Similarly, because the breast skin of women with a history of pregnancy and breast-feeding has expanded due to enlargement of the mammary glands, their breasts can more easily accept a larger injection volume than that of women with no history of pregnancy. It is clear that breast surgeons who have expanded the application of CAL are not good candidates for large-volume lipotransfer technique.

Our experience with breast augmentation with CAL is encouraging so far, especially in quality of the breast skin.
Africa with cleft lips and palates.

Says Miller:

"To be successful, the foundation
had to be led by South African med-
cal and non-medical volunteers
and sustained by South African
private operators. Prof. Madovre
shows OMH's mission to provide
free medical care to all children
and adults suffering with facial
defects and has the experience
and position to lead the foundation
and make this a reality."

Professor Madovre says: "If there
are kids out there that require
our help, we want to – and must – help
them. This world must be improved
for all."

In addition to leading missions
cross South Africa, Swaziland and
Madagascar, Prof. Madovre has
started and spearheaded Africa's
first World Care Program based
at Indoni Albert Luthuli Central
Hospital in Durban. This program
provides free craniofacial surgery
to patients in and around Africa
throughout the year while also
providing educational opportuni-
ties to Southern African medical
professionals interested in this type
of surgery.

We wish to target countries where
there is little or no care for cleft
patients. One of these countries
has been the island of Madagascar.
This country has a population of
just below 20 million with no cleft
services. We have performed two
operations thus far, in November
2007 and May 2008, and operated
on 132 and 211 patients respec-
tively.

It is not unusual to see adults with
cleft lips. In May 2008, 46 adult
patients were operated on. There
is still a huge backlog of patients
and another mission is planned for
November 2008.

Professor And Madovre is the
Head of the Plastic and Recon-
structive Surgery at Indoni Albert
Luthuli Central Hospital and also
the Medical Director of Operation
Smile Southern Africa (OSSA). He
has been an integral part of the
organization since the South Afri-
can branch was officially registered
in 2006. www.operationsmile.org

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breast tissue. Further controlled
studies with longer follow-up are
required to substantiate more defini-
tively the efficacy and safety of this
procedure. Adipocytes are very
fragile and easily die in an operat-
ing room, before injection. Through
research seeking more facts about
what the adipose tissue is and how
it repairs from systemic injury,
we could handle and manipulate
adipose tissue more gently and
strengthen and improve auto-
transplantation in the future.

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