Introduction
Numerous diseases of the connective and superficial tissues will at some point lead to a need for tissue recreation, to help patients have a normal social life and achieve acceptance of themselves and their condition.

Atrophy or dystrophy of the superficial tissues is a common clinical event in various congenital, genetic and acquired diseases. Radiodermatitis is often found in cancer patients undergoing radiotherapy. This condition can be successfully treated through the implantation of autologous adipose tissue, known as lipofilling. This constantly improving technique, first developed in 1997 by the American surgeon S. Coleman (1), is the result of more than a century of attempts to transplant adipose tissue (2,3). Adipose tissue is in fact an ideal filler, as it is totally biocompatible (as it is an autologous tissue), readily available, inexpensive, and enables good aesthetic results (4-6). These features make it preferable to other injec-
Lipofilling in skin affected by radiodermatitis: clinical and ultrasound aspects. Case report

In June 1996 the patient, then aged 41, underwent a right breast quadrantectomy with ipsilateral axillary lymphadenectomy due to an infiltrating ductal carcinoma. The surgery was followed by a cycle of radiotherapy and two cycles of adjuvant chemotherapy. In July, 5000 stem cells: 500 times more than the mesenchymal cells probably correspond to the preadipocytes, which have a high replication rate and produce a large amount of matrix proteins (8,9). 1 gram of fat tissue can produce about 5,000 stem cells: 500 times more than the mesenchymal cells present in 1 gram of bone marrow (10-12).

The main limitation of this technique is the variable duration of the results. There is currently great interest in identifying factors affecting the duration. The sampling technique, the way the aspirated tissue is handled before injection, and the implantation technique used all have an effect (4,13-15). This explains why some authors (16) in the international literature report almost complete resorption of adipose tissue in the months following surgery, while others note its almost total persistence. We generally find a certain degree of resorption (20-30%), so our injection technique is always hyper-corrective. Coleman recommends subsequent lipofilling sessions, to support the cumulative benefit of cell engraftment (17).

In recent years, the Department of Plastic, Reconstructive and Esthetic Surgery of the “Sapienza” University of Rome has tried to standardize the most suitable technique for volume correction following superficial tissue dystrophy as well as to establish a procedure to repair damaged tissue, especially skin affected by radiodermatitis. We report the case of a woman treated with two sessions of lipofilling 4 months apart for radiodermatitis subsequent to breast cancer treated by radiotherapy and breast implants.

Case report

In June 1996 the patient, then aged 41, underwent a right breast quadrantectomy with ipsilateral axillary lymphadenectomy due to an infiltrating ductal carcinoma. The surgery was followed by a cycle of radiotherapy and two cycles of adjuvant chemotherapy. In July 2000 local recurrence led the patient to undergo a right subcutaneous mastectomy with submuscular placement of a breast implant and adjuvant chemotherapy. Over the next two years, she underwent three operations for scar revision affecting the lower pole of the right breast, but the results were poor due to progressive tissue sclerosis caused by radiotherapy.

In December 2007 the patient, now aged 52, came to the Department of Plastic, Reconstructive and Esthetic Surgery of the Sapienza University of Rome with severe dystrophy and pain due to significant capsular contracture of the right breast implant, for which she had been making chronic use of painkillers. The skin of the periauricular region and lower quadrants of the right breast was discolored, dystrophic and hypomobile, with thickness and temperature much lower than the corresponding contralateral area.

Following her informed consent, the patient underwent an initial cycle of 8 months of treatment with a leukotriene inhibitor (18-20) (Zafirlukast, 20 mg per day) to reduce capsular contracture and pain. Following the success of this treatment, we then suggested the removal of the prosthesis and breast reconstruction with autologous tissue.

The patient later underwent two sessions (February and June 2009) of Coleman lipofilling of the right breast, with the dual aim of improving skin tissues and increasing its thickness in the areolar region and lower quadrants. Both sessions were conducted under local anaesthesia with sedation. In the first session, the abdomen was chosen as the donor area and in the second, the adipose tissue was harvested from the hips and peritrochanteric areas, to improve the patient’s body contours. The harvested tissue was transferred in 10 cc Luer-Lock syringes and centrifuged at 1000/2000 rpm for 3 minutes. The plasma and blood layers and the oil from damaged cells were removed with further purification. The purified fat was then implanted with Coleman’s cannulas, inserted through small incisions (1-2 mm) in the selected areas.

About 50 ml of purified fat was injected in the first session and about 70 ml in the second. The cannula entry points were sutured and a mildly compressive dressing applied to the lipofilled area for about one week. In the donor sites, the compressive dressing was left in place for two weeks. For three weeks thereafter the patient wore class II compression stockings during the day.

Focused ultrasound examinations were performed to assess the thickness between the epidermis and the outer limit of the peri-prosthetic capsule.

Periodic ultrasound examination revealed changes in the thickness of the subcutaneous tissue, while increased perfusion in the lipofilled areas was observed with power Doppler (Fig. 1). Analysis of the data reported in Table 1 shows that the implanted tissue was never completely absorbed. Two months after the first session, the overall increase in the thickness of the treated area was 228.57% (Fig. 2 a-b). Immediately prior to the second session (Fig. 2 c), the thickness had dropped to 114.29% of the baseline, demonstrating implanted tissue resorption of 50%. Two months after the second session, there was a 160% increase in the overall thickness compared to the baseline. This confirms the cumulative effect of multiple lipofilling sessions (8,17). The greatest resorption was in the lower outer quadrant of the right breast (right LOQ), the main area affected by chronic radiodermatitis.

Clinically, the tissues showed a steady improvement, with the color and temperature ever closer to that of the surrounding healthy skin. On palpation the skin also appeared significantly thicker and more mobile in comparison with the initial examination. The skin of the right submammary sulcus, which was initially fibrous and strongly adherent to the underlying tissues, was now easy to pinch. The discomfort originally reported by the patient had diminished to the extent that she felt no need for the final scheduled session.

A follow-up examination 21 months after the second session showed enduring trophism, and the increased softness of the treated tissue could be perceived from the improved profile of the lower breast (Fig. 2d).
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**Fig. 1** - Ultrasound images: lower outer quadrant (LOQ) of the right breast a) prior to treatment and b) 3 months after first lipofilling session. The ultrasound examinations were performed by the same operator, using ATL Ultrasound HDI-5000.

**Fig. 2** - a) Pre-treatment: clear depression of the lower pole of the right breast, that is discolored and retracted at the scar of the previous quadrantectomy, axillary dissection and radiotherapy. b) Two weeks after the first lipofilling session: clear overall improvement in the lower pole. c) Four months after the first session, ready for the second session. There is still evident thickening of the superficial tissues of the LOQ and the right mammary sulcus and an improved breast shape. d) Follow-up 21 months after the second session: almost complete maintenance of the result.

**Table 1** - Variations in subcutaneous thickness on ultrasound examination.

<table>
<thead>
<tr>
<th></th>
<th>APD R UOQ</th>
<th>APD R LOQ</th>
<th>Right under-areola region</th>
<th>Right sub-mammary sulcus</th>
</tr>
</thead>
<tbody>
<tr>
<td>US baseline</td>
<td>0.30 cm</td>
<td>0.12 cm</td>
<td>0.18 cm</td>
<td>0.10 cm</td>
</tr>
<tr>
<td>US 2 months after 1st lipofilling</td>
<td>0.64 cm</td>
<td>0.50 cm</td>
<td>0.39 cm</td>
<td>0.57 cm</td>
</tr>
<tr>
<td>US 4 months after 1st lipofilling/prior to 2nd lipofilling</td>
<td>0.42 cm</td>
<td>0.17 cm</td>
<td>0.41 cm</td>
<td>0.50 cm</td>
</tr>
<tr>
<td>US 2 months after 2nd lipofilling</td>
<td>0.50 cm</td>
<td>0.33 cm</td>
<td>0.48 cm</td>
<td>0.51 cm</td>
</tr>
</tbody>
</table>

*US = ultrasound; APD = anteroposterior distance between the outer edge of the periprosthetic capsule and the skin surface; UOQ = upper outer quadrant; LOQ = lower outer quadrant. All ultrasound examinations were performed by the same operator using ATL Ultrasound HDI-5000.*
Discussion

Radiotherapy is essential to "sterilize" any residual neoplastic foci after surgery as well as in cases of metastatic disease. The dose used is generally about 50 Gy if the disease is subclinical, and 60 Gy or more in the presence of a macroscopic residual in the operative site (21). However, side effects include radiodermatitis of healthy tissues. This normally affects the keratinocytes and is associated with erythema, scaling and edema, gradually progressing to fibrosis of the subcutaneous tissue and, in severe cases, to radionecrosis, in which the massive dose of ionizing radiation causes cell death and destruction. Melanocytes are also affected, resulting in skin discoloration (8).

The pathogenetic hypotheses advanced to explain this pathological progression focus on the role of the vascular component of the irradiated tissue: the vessels become hyper-permeable, leading to changes in local blood flow. Ultrastructural analysis by Rigotti et al. revealed clear signs of ischemia in relation to a microangiopathy, with a reduction in capillaries and visible duplication of the basal membrane. There was ectasia of the vessel lumen and endothelial cell activation, as demonstrated by the abundant cytoplasm and the presence of microfilamentous vesicles. A space between the endothelial cells and pericytes was always visible and the adipocyte lysosome was damaged. Deposits of collagen and cellular debris consisting of fragments of membrane and external lamina were seen in the connective tissue, suggesting adipocyte rupture (8).

References

16. Ezeke RA. Transplantation of purified autologous fat: a 3-year

Conclusions

Ultrasound examination of the treated tissues during follow-up enabled us to document a real, persistent increase in subcutaneous thickness and improved vascular blood flow, confirming the validity of the transplantation of autologous adipose tissue in the treatment of skin with radiodermatitis.