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Oxidized regenerated cellulose in breast surgery: experimental model

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ABSTRACT

Background: Breast-conserving surgery (BCS) combined with postoperative radiotherapy has become the gold standard of locoregional treatment in patients with early-stage breast cancer. When large tumor resections are needed in small medium size breasts, oncoplastic procedures (OPP) have been introduced to improve the cosmetic result; but in several cases, OPP may be not sufficient to accomplish this purpose. Oxidized regenerated cellulose (ORC, Tabotamp fibrillar; Johnson & Johnson; Ethicon) has been reported to be useful in OPP to optimize the cosmetic results after OPP. However, no ultrastructural study is available on the use of ORC as a filler in BCS.

Materials and methods: A BCS cavity was simulated in both groin regions in 24 consecutive Wistar rats. The right groin underwent soft tissue displacement and ORC implantation, whereas the left groin was treated only by soft tissue displacement (control side). Rats were sacrificed at 10, 20, and 30 wk to evaluate volume retainment and microscopic features (vascularization, fibrosis, cell population, inflammation, liponecrosis, and capsule formation).

Results: The use of ORC was characterized by diffuse fibrosis and homogeneous neovascularization within the construct, with no capsule formation and no inflammation. Volume retainment was similar in the 20- and 30-wk specimens (mean 80.4%, standard deviation, 6.65 and mean 79.9%, standard deviation, 6.51).

Conclusions: Implanted ORC was well integrated within the soft tissue with diffuse fibrosis, angiogenesis, and absence of capsule formation. Preliminary results confirmed that this biomaterial could further contribute to optimize cosmetic results in the oncoplastic surgical spectrum of breast-conservation therapy.

1. Introduction

Breast-conserving surgery (BCS) combined with postoperative radiotherapy has become the gold standard of locoregional treatment for most patients with early-stage breast cancer, offering equivalent survival and improved body image and lifestyle scores as compared with mastectomy [1,2]. In the era of early diagnosis and effective neoadjuvant therapies, BCS can be offered to over two-thirds of breast cancer patients. The goals of BCS are to ensure a complete removal of the tumor with adequate surgical margins while preserving the natural shape and appearance of the breast. In some cases, achieving both goals may be quite challenging as the need to secure an oncologically safe

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resection is the first priority; BCS may lead to unsatisfying cosmetic results [3–7].

In the effort to overcome this difficulty and expand the use and efficacy of BCS, oncoplastic procedures (OPP) have been introduced in recent years gaining widespread attention both among surgeons and patients [8–10]. These procedures associate the best principles of surgical oncology with the best principles of reconstructive surgery to optimize oncologic safety and cosmetic outcomes.

OPP are characterized by more esthetic skin incisions, use of enlarged resection patterns, careful reshaping of the gland, eventually by repositioning of the nipple-areola complex (NAC) to the center of the breast mound, and symmetrization procedures on the contralateral breast to improve cosmesis.

In our Department, the adoption of OPP since 1998 has allowed to expand the use of BCS to over 80% of our breast cancer patients.

Over the last 7 y in performing OPP, we have started to use oxidized regenerated cellulose (ORC, Tabotamp fibrillar; Johnson & Johnson; Ethicon, New Brunswick, NJ) as a possible aid to reduce the risk of postoperative hematoma and infections. In the follow-up of these patients, the hemostatic and bactericidal value of this absorbable material was confirmed and an improvement of the cosmetic outcomes was also empirically observed. As a consequence, we have hypothesized a possible role for ORC as a reconstructive biomaterial that could facilitate the healing of the residual cavity and adopted its use in OPP also for cosmetic purposes, even developing and reporting encouraging surgical results of an innovative OPP that we called “quadrantectomy with oxidized regenerated cellulose(QORC) Technique” [11–13]. Although other authors have reported beneficial effects of ORC for several surgical procedures [14–20], the fate of ORC as a soft tissue filler has never been investigated before.

The purpose of this article was to report the results of our experimental study on Wistar rats in which a BCS cavity was simulated and a combination of soft tissue displacement and ORC implantation was performed to evaluate the macroscopic volume retainment and the microscopic histologic features involved in ORC soft-tissue implantation.

2. Materials and methods

On approval of the research protocol by the Ethical Committee of the Catholic University of Rome, we conducted the study on 24 consecutive Wistar rats.

All the Wistar rats were female, with an average weight of about 355 g (ranging from 280–410 g).

The three premises needed to simulate the surgical model for positioning ORC for filling purpose were:

- To define the size and the volume of the ORC complex to be implanted in the rat so that it would be consistent, with good approximation, with the average size of the implant used in clinical practice in relation to the weight and the average body build of a woman (60 kg/0.355 kg = 169): on the grounds of this analysis, the correct ORC volume for filling purpose to be tested in Wistar rats was found to be a cubic fragment of about 1 cm^3;
- To create a surgical cavity surrounded by flaps of well-vascularized adipose tissue with musculofascial tissue at its floor to simulate a BCS scenario: for this purpose, the groin was identified as an ideal site.
- Proliferation of cellular and structural components is triggered by factors secreted during the preceding inflammatory phase. It begins 3–4 d after injury and continues for 2–4 wk. During this time, there is fibroblast and endothelial cell proliferation, phenotypic alteration and migration as well as extracellular matrix deposition and granulation tissue formation [21,22]. The latter remodeling phase is achieved by specific matrix metalloproteins, which are tightly regulated, and neovascularization that occur in response to proangiogenic factors [23–26]. Late remodeling phase can last up to 7–12 mo from acute injury; therefore, to assess wound evolution and ORC tolerance and/or integration during late proliferation and even during remodeling phase, we periodically assessed ORC implant-surrounding tissue histologic evolution during a 30-wk period from surgical procedure.

To assess the efficacy of ORC as a filler, we defined the cases and controls as follows:

- Case: at the right groin, after creating the surgical cavity and shaping the vascularized adipose flaps, we implanted two 1-cm^3 fragments of ORC within the two vascularized adipose flaps, which were juxtaposed and shaped by means of nonabsorbable sutures, so to cover the ORC implant completely.
- Control: at the left groin, after creating the surgical cavity, and shaping the vascularized adipose flaps, which were then transposed one over the other, we did not implant ORC, letting the wound heal by primary intention.

2.1. *Surgical technique*

The animals underwent general anesthesia with ketamine (70 mg/kg) + Domitor (Orion Pharma; Pfizer Animal Health, Exton, PA) (0.5 mg/kg) administered by intramuscular injection. The inguinal and hypogastric regions were shaved. The rat was then placed on the surgical table in a supine position.

Under sterile conditions, we identified bilaterally the upper margin of the inguinal space, which is normally defined using as a reference at the base of the tail (medial margin) and the origin of the thigh (lateral margin), and joined these reference points by drawing a parabolic line with an upper convexity.

We then performed a skin incision along the drawn line, and we detached the cutaneous plane from the underlying adipose tissue, using a combination of blunt and pointed instruments, for a length of about 0.5 cm, carefully avoiding any surgical damage to the cutaneous flap.

We then identified the upper margin of the inguinal fat pad, on which we performed a full-thickness incision to the fascial plane, along its upper margin.

After having identified the superficial epigastric pedicle, we extensively dissected the inguinal fat pad from the muscular plain, taking the maximum care in preserving the integrity of the superficial epigastric pedicle responsible for the tropism of the inguinal fat pad itself. We identified a vascular arcade, springing from the superficial epigastric pedicle and supplying