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A Novel Method for Marking the Tumor Bed Margins in Partial Breast Reconstruction

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Abstract

Background: In New Zealand, Oncoplastic Surgery (OPS) is common, but partial breast reconstruction presents challenges for radiation targeting. Tissue rearrangement creates ambiguity when targeting the tumor bed with resultant overestimation of treatment volumes. Thus, adoptions of advanced methods of radiation have been hindered. This pilot study describes use of a novel 3-dimensional implant that provides scaffolding for tissue in growth during partial breast reconstruction and delineates the tumor bed more precisely to assist radiation planning and mammographic surveillance.

Methods: Following informed consent, 15 women were implanted with the 3-dimensional bio-absorbable implant. The device was sutured to the tumor bed during lumpectomy, and tissue flaps were mobilized and attached to the implant. Visualization of the marker and radiation treatment volumes were recorded and compared.

Results: The implant provided volume replacement and helped to maintain breast contour. Cosmetic outcomes were excellent; no device-related or radiation complications occurred. One patient had a post-operative hematoma that resolved after percutaneous drainage; there were no post-operative infections. Three year follow up shows no tumor recurrences, and no untoward effects. When compared to conventional radiation targeting, use of the implant showed a >50% reduction in treatment volume was possible in some cases. Three year mammograms show no significant artifact, normal tissue in-growth and minimal fibrosis.

Conclusion: This study describes a method of oncoplastic breast reconstruction using an implantable device that marks the site of tumor excision and provides for volume replacement with tissue in-growth. Patients tolerated it well, and radiation planning, positioning and treatment were facilitated.

Keywords: Breast reconstruction; New Zealand; BCT; PM; RT

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Introduction

New Zealand women are fortunate to have a robust screening mammography program offered by the private and public healthcare systems. This result in most women being diagnosed with early breast cancer and most women can undergo Breast Conservation Therapy (BCT) consisting of Partial Mastectomy (PM) with Radiotherapy (RT). For many patients, BCT has revolutionized surgical outcomes particularly since Oncoplastic Surgery (OPS) has been readily available in New Zealand since the 1990's.

However, oncoplastic reconstruction of the breast introduces several significant challenges. During these procedures, the surrounding glandular tissue is mobilized and rearranged to fill in volume deficits and improve the ultimate contour and shape of the breast to improve the post-surgical outcome. Most often, there is a remaining volume deficit and unfortunately cosmetic outcomes are commonly compromised. The literature notes this can be quite often with poor outcomes being reported as often as 30% of the time [1-3]. At times the excised tumor bed may end up at a location distant from the original excision site which can cause confusion or discrepancy in locating the appropriate region for Radiotherapy (RT) [4-7]. This disruption of the native glandular tissue of the breast can also result in fibrous scar tissue post-operatively that may obscure subtle changes on mammography as women are followed for the potential recurrence of cancer.

Figure 1: BioZorb®.

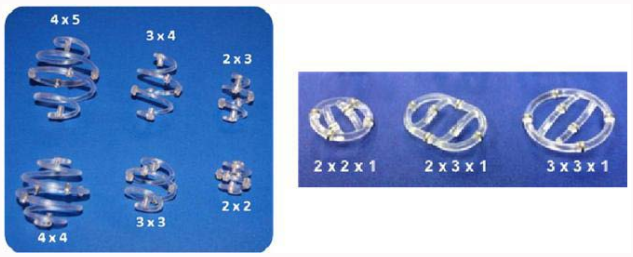

Figure 2: Various shapes and sizes available.

Some surgeons use small vascular clips in an attempt to mark the surgical tumor excision site. However, in actuality, these clips mark the boundaries of the entire lumpectomy cavity (tumor bed plus negative margins excised) as opposed to just the actual tumor bed that requires targeting for radiation accuracy. The clips have been known to migrate, and in most cases, radiation oncologists prefer to use the seroma cavity as a means for targeting post-operative radiotherapy [8].

Use of the seroma cavity has its own shortcomings, particularly in the case of oncoplastic reconstruction of the breast defect. First of all, surgeons often use tunneling and flap dissection leading from the skin incision to remote areas of the breast containing the tumor site. On post-operative CT imaging used for radiation planning this may create ambiguity and confusion for targeting. Seroma fluid can also extravasate into areas of the breast distant from any area of tumor where radiation would be unnecessary. In other circumstances, reconstructing the lumpectomy defect may actually obliterate the seroma cavity entirely leaving little to know evidence of where the radiation should be targeted in order to treat the tumor bed and surrounding margins.

These issues lead to known challenges for RT planning in the setting of breast conservation surgery, particularly since the uncertainty in targeting the tumor bed site is essential for the boost dose. Many studies have reported that these ambiguities can cause an overestimation of treatment volumes, resulting in unnecessary inadvertent radiation to surrounding normal tissues which in turn can result in compromised aesthetic outcomes [9,10].

Whereas for many years mastectomy was the only option for women, today the approach to surgery is customized for each patient depending upon many factors. As the field of OPS continues to gain popularity worldwide, the aesthetic appearance of the breasts before and after breast cancer surgery becomes an increasingly important consideration during surgical planning. However, just as important is the surgeon's ability to accurately and reliably mark the tumor bed for subsequent radiotherapy and follow-up imaging.

Table 1: Demographic information of pilot study patients.

Partial Mastectomy + Sentinel node biopsy	100% N=15 Patients
Nodal Status	94% Negative, 6% Positive
Tumor Size	0.2 cm - 3.7 cm
Tumor Grade	1-3
Complications	0 infections;1 post-op hematoma

In order to develop a better method of marking the tumor bed while performing partial breast reconstruction with OPS procedures, we evaluated the use of a 3-D marker that essentially behaves as a "mini" breast implant as it marks the tumor resection site. This new approach, using the mini implant, was studied in 15 patients undergoing BCT with oncoplastic reconstruction.

Materials and Methods

Following informed consent, fifteen patients were consecutively selected to have the 3-dimensional marker (BioZorb® Focal Therapeutics, Inc.) implanted at the time of Partial Mastectomy (PM) (Figure 1). The 3-dimensional marker is comprised of two materials (PLA and titanium) both of which have a long history of clinical use. The marker is available in a number of shapes and sizes in order to accommodate various configurations of surgical cavities that might be encountered (Figure 2).

All patients had pre-operative imaging studies including mammography, ultrasound and Magnetic Resonance Imaging (MRI) in order to determine extent of disease. Each patient had PM and sentinel lymph node biopsy, with one patient requiring a completion axillary dissection for a positive lymph node (Table 1).

In each case, an appropriate sized tissue marker was selected, and sutured in position at the surgical site of tumor excision (Figure 3A, 3B). Oncoplastic techniques including glandular tissue flaps were used to close the surgical cavities, and the surrounding margins of tissue were sutured directly to and through the 3-dimensional tissue marker. As standard procedure, monofilament bio-absorbable sutures were placed in at least 4 aspects of the surrounding breast tissue, and these sutures were then secured to the device in order to prevent the possibility of rotation and/or migration of the marker. Of note, the marker was useful in partial breast reconstruction using oncoplastic surgical techniques to bridge the area of the defect created by tumor excision and for additional volume replacement.

Final pathology findings were reviewed weekly by a multidisciplinary tumor board, and recommendations for adjuvant chemo and/or radiation therapy were formulated. All patients requiring adjuvant radiation therapy were referred for evaluation. Pre-treatment planning CT scans were generally performed 4 to 6 weeks following implantation, although timing varied considerably due to individual patient considerations (e.g. chemotherapy regimens). Multiple treatment plans were generated and compared, including standard tangent pairs, 3-D non-coplanar, split arc conformal VMAT, and a variant of split arc conformal VMAT. All treatment plans were in compliance with clinical guidelines as accepted per the NSABP B-39/RTOG 04-13 trial. Optimal treatment plans were selected and administered using various methods as deemed appropriate for each patient (whole breast or partial breast irradiation techniques).

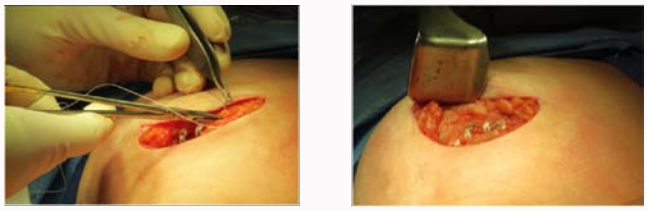

Figure 3A, 3B: The marker is sutured to the margins of the tumor bed; tissue flaps are mobilized and sutured to the device with at least 1cm of tissue overlying the device prior to layered closure.

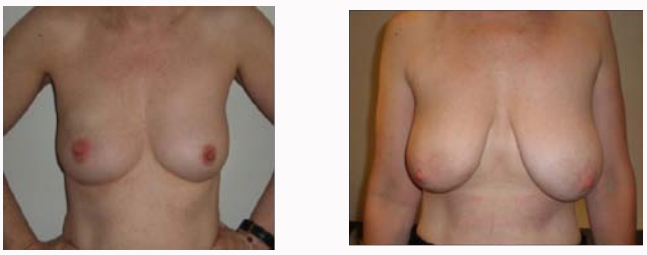

Figure 4A, 4B: Representative patient's 3-years after partial mastectomy, placement of marker during partial breast reconstruction, followed by radiation treatment.

Results

In this series of patients, the marker was easily incorporated into the surgeons' routine and did not prevent or exclude any necessary diagnostic or treatment efforts. There was no report of post-operative infection; however, one patient had a small hematoma that was drained percutaneously in the office under ultrasound guidance. No devices required removal and no other complications were noted. In two patients, the implant was palpable within the breast for greater than 12 months. Excellent cosmetic outcomes have been achieved in all patients with 4 years of follow-up and no reports of pain, discomfort, deformity of the breast or other adverse events. Two patients with typical outcomes in this group of 15 patients are shown in Figure 4.

The marker was easily identified and clearly delineated the margins of the tumor excision site on clinical imaging. Figure 5A shows a patient with a left medial lower quadrant tumor localized and ready for surgery. Figure 5B shows this patient's radiation planning CT scan with periareolar incision marked on the skin. The marker clearly identifies the region of the excised tumor bed for CT based treatment planning critically important in this case where tunneling was used to reach the tumor bed and is distant from the skin incision which is commonly used for boost targeting.

The most useful property of the 3-dimensional marker was in enabling more accurate targeting for radiation treatment planning and delivery. The marker assisted with conventional methods of radiation as well as facilitated the use of advanced methods such as accelerated radiotherapy-where the overall course of treatment was shortened from 6 weeks to 5 days. On average, the Planned Treatment Volumes (PTVs) were significantly reduced when using the marker as a target for planning. Figure 6A and 6B shows a case example where the marker identified the tumor excision site and enabled the patient to receive accelerated partial breast irradiation. The presence of the marker allowed the radiation therapy team to confidently exclude tissue changes associated with the surgery (e.g.

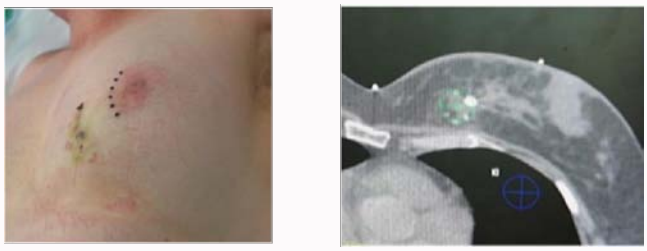

Figure 5: A) Patient with left medial quadrant tumor excised via periareolar incision. B) CT scan shows skin marker at areolar incision and marker (outlined in green) distant from incision site. Accurate marking of the tumor bed is critical for boost targeting and can be challenging with oncoplastic reconstruction of the partial mastectomy defect.

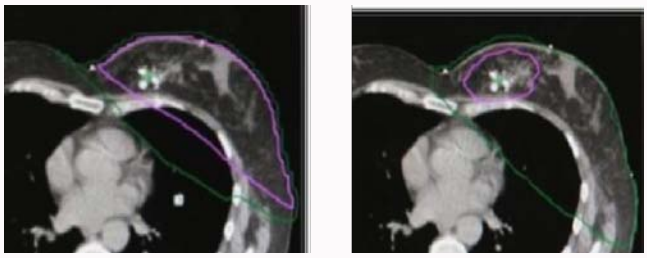

Figure 6: A) Standard whole breast volume outlined in pink. B) Pink outline shows smaller treatment volume obtainable using marker for planning.

Table 2: Comparative treatment volumes shown on CT above.

Whole Breast	Current Methods	BioZorb Marker
788cc	378cc	84cc

the surgical tunnel from the peri-areolar incision) from the target volume. When compared to conventional methods of determining the target volume, use of the marker resulted in treatment volumes that were reduced by >60%.

Figure 7 illustrates the ability to use the marker device to decrease ambiguity and thereby reduce the expansion volumes used in standard practice. Table 2 shows the quantitative differences between these radiation treatment planning techniques, and summarizes the resultant PTVs.

Discussion

Advances in breast conservation surgery have resulted in excellent survival rates, and many women have benefitted from the changes in surgical management of breast cancer. However, poor cosmetic outcomes after partial mastectomy are all too common and the options for correcting or improving these acquired breast deformities are limited [11-16]. Since the scientific community has confirmed and agreed that BCS is equivalent therapy for early stage breast cancer, other factors such as quality of life indicators become equally important, particularly in women with early stage breast cancer. These patients often find themselves free of disease but significantly disfigured leaving them disgruntled with their surgical outcomes.

Correcting these defects in the post-operative period is very challenging and options are limited often requiring additional surgical intervention such as mastectomy with complex breast reconstructions using fat grafting, myocutaneous tissue transfer, etc. Multiple surgeries may be required, and the hazards of operating on irradiated tissue bring with it the risk for additional complications

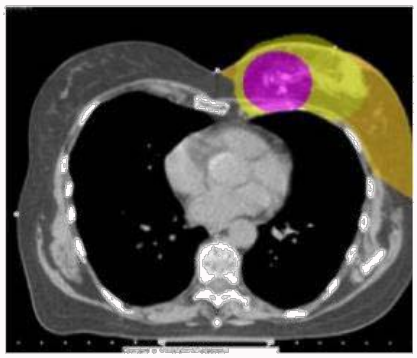

Figure 7: Comparison of radiation planning techniques and resultant treatment volumes.
Pink: volume using marker as a guide
Yellow: volume using seroma (most common method)
Orange: standard whole breast volume

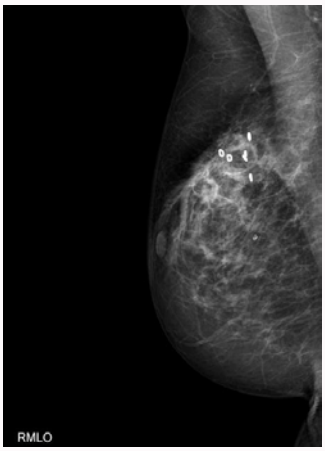

Figure 8: 3-year post-op mammo showing marker in tumor bed and minimal fibrosis.

and potential failures of routine methods for breast reconstruction. Thus, an implantable device that could be placed at the time of partial mastectomy for local breast reconstruction to help maintain breast contour presents itself as a potentially valuable asset in regards to improving patient outcomes. In addition, if this same device were able to concomitantly serve as a distinctive marking tool for the purpose of identifying the original tumor bed for targeting radiation and post-operative surveillance the benefits to patient care would most certainly be innovative and worthwhile (Figure 8).

The recent ASTRO guidelines supporting the use of accelerated methods of radiation therapy are an exciting look at the future of shortened courses of radiotherapy for early breast cancer patients [17]. However, good aesthetic results in these patients are dependent upon limiting the volume of normal surrounding tissues exposed to radiation. Thus, use of a consistent method for marking the excised tumor bed as demonstrated in this pilot study will be an important aspect of being able to accurately target and plan appropriate treatment volumes in order to expand the use of these radiation techniques.

Our experience with use of this marker containing a fixed array of clips that is sutured into the area of tumor excision shows this to be a novel method for eliminating the ambiguity inherent in cases where oncoplastic techniques are used for partial breast reconstruction with tissue rearrangement. As seen in this initial group of patients, limiting radiation exposure of surrounding tissues by decreasing target volumes of the boost dose and or planned treatment volume will help to improve outcomes by limiting fibrous scarring. The improvement in aesthetic outcomes after breast conservation therapy was evident in these 15 patients (Figure 4A, 4B).

Conclusion

Accurately identifying and delineating the tumor resection site of partial mastectomy is a difficult task and is subject to considerable variability among clinicians in generating treatment plans for adjuvant radiation therapy. In this pilot series of patients, we assessed the utility of a novel 3-dimensional, bio-absorbable tissue marker that served as a "volumetric" implant within the tumor resection site. Placed at the time of surgery and secured to the margins of the tumor resection cavity, the 3-D marker allowed the radiation planning clinician to confidently exclude regions of tissue that would otherwise be included in the planning treatment volume.

We have confirmed the utility of this device in clinical imaging, including radiation treatment planning and delivery. The presence of the implanted marker enabled the use of accelerated techniques for delivery of radiotherapy by facilitating volume reduction in the treatment plan. The reduced number of dose fractions offers advantages to the patient in terms of fewer daily visits and faster completion of treatment (e.g. 5 to 7 days *vs.* 5 weeks). In addition, this offers significant potential advantages to the healthcare system in terms of the total cost of delivering radiation therapy for breast cancer patients with potential savings of up to 50% of treatment costs (e.g. $7.5k *vs.* $15k $NZ).

As a result of this pilot study, an expanded clinical trial for the use of this device as a new method of partial breast reconstruction has been underway in the public healthcare system in Auckland, New Zealand.

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