

## Case Report

# Treatment Volume Reduction using the Biozorb® Device in Ipsilateral Breast Recurrence Treated with Second Conservation Therapy

Mark G. Trombetta<sup>1,3\*</sup>, Shaakir Hasan<sup>1</sup>, Mary Beth Malay<sup>2,3</sup>, and Thomas B. Julian<sup>2,3</sup>

<sup>1</sup>Department of Oncology, Allegheny General Hospital, USA

<sup>2</sup>Department of Surgery, Allegheny General Hospital, USA

<sup>3</sup>Drexel University College of Medicine, Pittsburgh Campus, USA

## \*Corresponding author

Mark Trombetta, F.A.C.R., Allegheny General Hospital, 320 East North Avenue, Pittsburgh, Pa 15212, USA, Email: Mark.Trombetta@ahn.org

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## Keywords

- Retreatment
- Breast cancer
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## Abstract

Ipsilateral breast tumor recurrence [IBTR] following conservation therapy for early breast cancer occurs in women in small, but significant numbers. The standard of care for such recurrences has developed as salvage mastectomy in most of the literature, despite a lack of evidence-based methodology. Repeat surgical conservation with retreatment radiotherapy is an emerging standard of care and is being developed with significant evidence-based trials supporting such. In this emerging evidence, the volume of retreated breast tissue has been found to directly correlate with retreatment cosmesis as graded by the Harvard cosmesis scoring system proposed in 1979 and still in use today. We present the case of a patient who developed an IBTR with confounding imaging characteristics in proximity to the original malignancy which required wider re-excision and which may have required a significant volume of breast retreatment without some method of limiting radiotherapeutic retreatment volume.

## ABBREVIATIONS

3D-CRT: 3-Dimensional Conformal Radiotherapy; DCIS: Ductal Carcinoma In-Situ; IBTR: Ipsilateral Breast Tumor Recurrence; BCT: Breast Conservation Therapy; BZ: BioZorb®; WBRT: Whole Breast Radiotherapy

## INTRODUCTION

More than 1.7 million women were diagnosed with breast cancer worldwide in 2012 [1-5], most of whom will undergo breast conservation therapy [6] which became a standard of care following the reporting of data in landmark trials from Italy and the United States [7,8]. After completion of adjuvant therapy there are still approximately 2- 20% [range 2- 36%] of patients who, after a minimum 10 year follow-up develop IBTR [7]. Even when enhanced with hormonal manipulation, the recurrence rates drop to 2-20% in lower risk and hormonally sensitive patients [6,7].

For IBTR, the international standard of care for local recurrence following breast conservation therapy has been salvage mastectomy, which is physically well tolerated by most women and has demonstrated salvage local control rates of greater than 90 % [9,10]. We have previously argued that the "standard" was accepted despite the absence of convincing evidence [1].

Multiplenumbers of studies have shown that mastectomy is devastating to many women [11-13] and in response to this early work reporting suboptimal outcomes; the RTOG has recently completed a retreatment protocol using hyperfractionated external beam radiotherapy [14].

## MATERIALS AND METHODS

A 65 year old white female was diagnosed with ductal carcinoma in-situ [DCIS] of the breast in 2011 shortly after breast reduction surgery. She was treated by lumpectomy and whole breast radiotherapy at that time [WBRT] where she received 5040 cGy at 180 cGy perfraction with a mixed 6/15 MV photon beam followed by an electron boost of 1400 cGy at 200 cGy per fraction to the Gross Target Volume [GTV] plus a 1.5 cm margin. Following radiotherapy, she received tamoxifen 20 mg daily for a total of five years. She developed onlygrade II erythema following radiotherapy and was closely followed for six years until she developed suspicious microcalcifications with 2.0 cm of the original treatment site,. By definition, this is within the limit for in-field IBTR. It should be mentioned that her cosmesis deteriorated to Harvard score II originally [4]. She underwent a core biopsy of the lesion which demonstrated recurrent DCIS that was estrogen and progesterone receptor positive. The 2 neu was not over expressed [her 2 neu assay is now standard at our institution for DCIS, but was not in 2011].

A preoperative MRI demonstrated a [2.7 x 1.6 cm] lesion in the area of biopsy; however a [5.7 cm x 3.0 x 2.3 cm] non-specific region of hyperintensity was seen immediately adjacent to the original lesion. The patient was sent for a radiation oncology opinion for consideration of retreatment. The patient was also referred in consultation to plastic and reconstructive surgery where she discussed the option of salvage mastectomy and immediate reconstruction with flap rotation versus tissue expanders and silicone implant placement. Following this, a multidisciplinary discussion was held in the weekly System Breast Conference. In view of the slightly more apparent cosmetic defect already identified, she considered both approaches, but finally chose repeat lumpectomy, with the understanding that, if the non-specific hyperintensity contained recurrence as well after a bracketed resection, she would have a very large volume of tissue for re-irradiation. At the time of re-excision, careful intraoperative sectioning allowed precise placement of the BioZorb® device [Focal Therapeutics, Aliso Viejo, California, USA] [Figure 1] which was sutured in place by the breast surgical oncologist following direct identification of the tumor bed and excluding a large volume of pathologically benign, but radiographically concerning tissue. The patient then underwent targeted 3D-CRT which delivered a total dose of 3850 cGy at 385 cGy per fraction twice daily to a planning target volume [PTV] of 1.5 cm from the surface of the device [1.0 cm at the chest wall interface] and separated by a minimum of 6 hours between fractions. Respiratory motion was observed at free breathing during simulation and the chest wall motion did not vary by more than 0.5 cm (Figure 1-3).

## RESULTS AND DISCUSSION

The patient tolerated the retreatment well without toxicity in the acute setting. She was evaluated at 2 and 4 weekspost radiotherapy and has now begun her new follow-up. She is scheduled for observation and imaging follow-up only without systemic therapy in view of her previous completed five year anti-estrogen therapy.

### Discussion

Treatment options for IBTR include mastectomy, local excision and resection, systemic therapy [usually reserved for those patients who also present with distant disease], and repeat conservation.

We and others have written extensively on retreatment breast conservation [15-17], and the GEC-ESTRO group released the results of the largest multi-center trial of retreatment to date [18]. One clear principle emerges from these studies: that the most important metric in the management of retreatment radiotherapy patients [even more so than in de-novo patients] is the need for treatment volume limitations to prevent acute and long-term morbidity. The BioZorb® device acted as a fiducial when placed directly in the area at risk in the lumpectomy specimen after careful marginal assessment intraoperatively using frozen sectioning. The radiotherapy was delivered following conformation of the final pathology and when sufficient incisional healing had taken place [4 weeks post-operative]. The difference in the overall volume between the BioZorb® GTV volume and



Figure 1 Axial view.

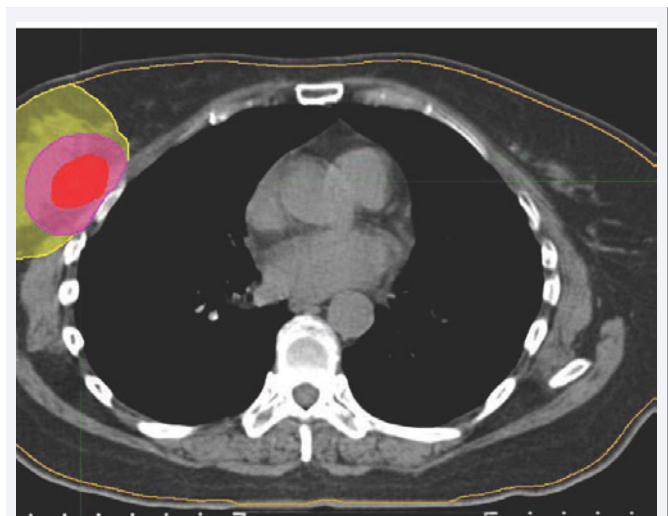


Figure 2 Coronal view.



Figure 3 Sagittal view.

Abbreviations: Red contour is GTV (Gross Target Volume); Pink is CTV (Clinical Target Volume); Yellow is PTV\_EVAL (Planning Target Volume for Evaluation) for the BioZorb® device. Whitish larger density is the traditional GTV.

the traditional GTV volume including the pathologically proven negative specimen was 16.5 cc versus 81.6 cc respectively [Table 1].

This large volumetric difference is not unexpected considering the formula for volume of a sphere;

$$[4/3] \pi r^3$$

Patients with a significant surgical defect or limited remaining breast tissue should generally not be considered for repeat conservation from a cosmetic standpoint. Even in this situation, a face-to-face discussion should be held with the patient who would be willing to accept a sub-optimal cosmetic outcome as a consequence of a 2<sup>nd</sup> conservative treatment. We have noted that nearly all patients prefer even a physically changed natural breast as opposed to mastectomy in our experience [1]. However mastectomy, the accepted standard of care, must be discussed as an option with all patients.

We recommend consideration of repeat conservation in patients with favorable recurrent tumor characteristics only according to the criteria noted in Table 2.

The substantive reduction of target volume allowed by use of the BioZorb<sup>®</sup> device reduced the risk of adverse event by an unknown quantification, however; we know that volume is the greatest driver of adverse event in radiotherapy. As such, this device provided an excellent three-dimensional target for guided target reduction. It has been extensively reported that surgical clips placed to identify the tumor cavity are unreliable due to common migration. The BioZorb<sup>®</sup> device has not had such issues as it is fastened in multiple points consistent with its three-dimensional nature. Additionally, the device provides a small lattice work structure that actually improved her cosmesis when compared to the pre-operative state. Whether that sustains is as yet, unknown. However, the patient is extremely happy with the symmetry she now enjoys. The patient is now 3 months out from the procedure and has avoided so far, the known acute

and long term complications such as fat necrosis, infection, and mastalgia. Her Harvard Cosmesis is scored at 1 [the best cosmetic effect], which is an improvement from the pre-surgical state. This appears as an anomaly to us.

## CONCLUSION

The BioZorb<sup>®</sup> device can provide an excellent fiducial guidance in volume reduction for repeat breast conservation and potentially other indications. Further clinical study is warranted to fully explore the opportunities with this device.

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**Table 1:** Volume differences between BioZorb<sup>®</sup> Gross Target Volume (GTV) and Traditional GTV.

	Volume (cc)	Volume Reduction
Traditional GTV Cavity	81.6	65.1 cc (79%)
GTV Biozorb <sup>®</sup>	16.5	
Traditional PTV_eval Cavity	324.3	246.5 cc (76%)
PTV_eval Biozorb <sup>®</sup>	77.8	

**Table 2:**

1. Overall and relative breast size (projected adequate post-operative breast tissue)
2. Single tumor with maximum tumor size of 3.0 cm
3. Negative final margins of resection and no additional suspicious lesions on imaging
4. No clinically apparent lymphadenopathy
5. Generally no evidence of metastatic disease. (Excludes patients whom suspected long term survival is possible)
6. Patient preference (desirous of breast preservation)
7. Are well informed about the risks versus benefits of the procedure and the alternatives

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