Interstitial Brachytherapy (IBT) as a Boost For Breast Cancer in Women With Augmentation Implants

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Number of figures: 3

Number of tables: 2

Running Title: Brachytherapy boost for breast cancer with augmentation implants

Conflicts of Interest: There are no actual or potential conflicts of interest.

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Purpose: To evaluate the efficacy and complication rates of radiotherapy via low dose rate brachytherapy with Ir-192 implants for breast cancer in women with augmentation implants.

Methods: From July 1976 to May 1991, 11 patients with prior breast augmentation were diagnosed with stage T1-2N0-3 breast cancer. All women underwent lumpectomy followed by axillary node dissection and brachytherapy boost of 20 Gy. This was followed by whole breast radiotherapy. Chemotherapy was given at the discretion of the medical oncologist and was given after radiotherapy. Primary endpoints were augmentation implant revision and complication rates. Secondary endpoints were time to locoregional recurrence, time to metastasis and overall survival.

Results: With mean follow up of 24 years, overall survival was 91%. No locoregional recurrences were reported. Overall metastases free survival was 82%. Median time to distant metastasis was 27 months. 4/11 (36%) of women suffered grade 3 implant contracture after radiation treatments. No patients suffered grade 4 contracture, infection, skin necrosis, or traumatic implant rupture. Revision rate was 27%. Median time to revision was 27 months.

Conclusions: None of our patients with augmentation implants and breast cancer treated by brachytherapy boost followed by whole breast radiotherapy had local relapse. In addition, there was a low rate of contracture. These findings are comparable to the conventional treatment of external beam radiotherapy and electron beam boost in patients with augmentation implants.

Keywords: Breast cancer, interstitial brachytherapy boost, breast augmentation, contracture rates

Introduction:

The treatment of early stage breast cancer includes mastectomy or breast conserving therapy with or without chemotherapy. Since the equivalence of these treatments were established (1-3), the rates of breast conserving therapy have increased. The European Organization for Research and Treatment of Cancer (EORTC) boost study revealed the benefits of a boost of 16 Gy in addition to 50 Gy whole breast irradiation (WBI) versus WBI to 50 Gy alone (4). The boost can be performed with external beam radiation therapy (EBRT) (5), or with IBT (6-9). However, breast conservation therapy in patients with breast augmentation remains controversial.

Breast conservation therapy is an attractive treatment option in patients with implants who have demonstrated concern about the appearance of their breasts (10,11). According to the American Society of Plastic Surgeons, in America approximately 347,524 females underwent cosmetic breast augmentation in 2007 (12). With approximately 9% of woman developing breast cancer in their lifetime, we can expect a substantial number of patients developing breast cancer in augmented breasts (10,11,13). The rate of acceptable cosmesis ranges from 33-100% with an average of 63% (11, 12, 14-17). The main source of poor cosmetic outcome is capsular contracture (17-19). Partial breast irradiation (PBI) may be an attractive option in these patients, but its use in patients with augmentation implants has been rarely reported in the literature. Kuske et al (20) reported on their experience using IBT as adjuvant therapy after lumpectomy and found excellent outcomes and cosmesis. The use of IBT is advantageous in these patients

as the breast tissue tends to be thin over the augmentation. However, the use of PBI alone after lumpectomy may be considered controversial, as follow up is short (21,22) and a recent meta-analysis revealed decreased locoregional control associated with PBI (23). However, 2 of the 3 studies cited in this report used inferior radiation techniques without radiographic localization of the lumpectomy site. In addition, these studies also had very loose inclusion criteria and therefore not surprisingly resulted in a high regional recurrence rate. The inclusion criteria for modern day partial breast trials are quite stringent as far as patient selection criteria is concerned, and are limited to patients with small size; non lobular; no LVI, negative lymph nodes and negative surgical margins (24).

Due to the controversy associated with using PBI alone, as well as the high contracture rate with WBI followed by electron beam boost, IBT was used as a boost with WBI in patients with breast augmentation. IBT is advantageous in this setting due to the increased dose falloff and thus decreased dose to the implant. In addition, IBT as boost has been advocated by several institutions (25-27). With the high numbers of patients who have undergone breast augmentation, it is important to report the outcomes and cosmetic effects of patients treated in such a fashion. We report our long term follow up of patients with augmentation implants treated with IBT as boost followed by WBI.

Methods:

Eligible patients included woman with prior breast augmentation diagnosed with T1/2 N0-3 breast cancer. Patients with metastatic disease, non- infiltrating ductal carcinoma histology, or history of non-skin cancer were excluded from this analysis. All

patients were treated with breast conserving therapy. All women underwent lumpectomy followed by axillary node dissection. After completion of the lumpectomy, hollow steel needles were placed to encompass the lumpectomy cavity with a 1-2 cm margin. Peri-operative placement was chosen as it was felt that the localization of the target was more precise than delayed interstitial implant due to direct visualization of the excision cavity. In addition, cosmetic outcomes have been found to be similar with either approach (6). In patients with subpectoral implants, the brachytherapy implant was performed by placing the needles in 2 planes, the superficial plane with 15 cm needles and deep planes, which required 20 cm needles. The needles were placed in an interdigitated fashion, approximately 1-1.5 cm apart to encompass the lumpectomy cavity. In patients with subglandular implants, the brachytherapy implant was performed by placing needles in 1-2 planes, depending on the volume of breast tissue between the skin and breast implant. Hollow plastic catheters were then threaded through the steel needles, which were then removed from the breast. The lumpectomy cavity was then treated to 20Gy with IR-192 ribbons at 0.5 Gy/hour. These procedures were then followed by WBI to 50.4 Gy at 1.8 Gy per fraction. Standard tangential fields were used. For patients with lymph node positive disease, supraclavicular fields were used at the discretion of the radiation oncologists. Chemotherapy was given at the discretion of the medical oncologist, depending on the stage of disease. Chemotherapy was given after the completion of whole breast radiotherapy, and consisted of cyclophosphomide, methotrexate and 5 fluoro-uracil. Patients were followed up every 3 months for 2 years, then every 4-6 months for the next 3 years and then yearly thereafter. Primary endpoints were

complication free survival and augmentation implant revision rate. Secondary endpoints included time to locoregional recurrence, time to metastasis and overall survival. Complications included grade 3-4 breast implant contracture, infection, skin necrosis and traumatic implant rupture. Contracture was evaluated using the Baker classification system seen on table 1 (28). Endpoints were calculated using the Kaplan Meier method. Locoregional recurrence was evaluated by clinical exam, mammograms and ultrasound. Distant metastases were evaluated by CT scans, bone scans and other imaging modalities and labs neccessary. Multivariate analyses was calculated using the proportional hazards Cox modeling with statistical inferences on the actuarial curves made using log rank tests.

Results:

From July 1976 to May 1991, 11 patients with breast augmentation with T1-2N0-3 breast cancer were treated with lumpectomy and axillary nodal dissection followed by PBI boost and WBI. Mean age was 61 years. Patient characteristics are summarized in Table 2. With mean follow up of 24 years, overall survival was 91% (Fig 1). No locoregional recurrences were reported. On last follow up, ten out of eleven patients were alive. 4/11 (36%) women had positive axillary nodal involvement upon diagnosis. On last follow up, three of the four patients with nodal metastases are alive. Overall metastases free survival was 82%. Median time to distant metastasis was 27 months. 4/11 (36%) of women suffered grade 3 implant contracture after radiation treatments. No patients suffered grade 4 contracture, infection, skin necrosis, or traumatic implant rupture. Complication free survival was 64% (Fig 2). Revision rate was 27% (Fig 3).

Median time to revision was 27 months. Neither the use of chemotherapy or type of breast augmentation implant significantly predicted for complication free survival. Neither age, T-stage, nodal status, nor ER status significantly predicted for either local control, distant metastases, overall survival, or revision-free survival on both univariate and multivariate analyses. The 15-year actuarial revision-free survival for T1 and T2 tumors were 67% and 80%, respectively (p=0.73). The 15-year actuarial revision-free survival for those less than 40 and those greater than 40 years old were 80% and 67%, respectively (p=0.55).

Discussion:

Breast conservative therapy for patients with breast augmentation remains controversial. WBI followed by a boost in patients with augmentation implants is associated with increased rates of breast implant contracture. Contracture is likely due to the deposition of collagenous scar tissue around the breast implant. This results in breast tenderness, pain and decreased cosmetic satisfaction. In efforts to decrease the total dose to the implant, we adopted the approach of using peri-operative IBT as boost followed by WBI in these patients with augmentation implants. Our goal with IBT as a boost was to use the increased dose falloff and thus decrease the total dose to the implant. 36% of our patients suffered grade 3 breast implant contracture, and none developed grade 4 contracture. These results are favorable to those described in the literature (15,18,19). Cordeiro et al (19) revealed a 68% rate of capsular contractures in patients treated with postmastectomy radiation. Mark et al (15) reported a capsular contracture rate of 57% in patients treated with segmental mastectomy followed by radiation. Handel et al reported a

capsular contracture rate of 65% in similarly treated patients (18). They argue that due to the high incidence of capsular contracture, breast conservation therapy with WBI may not be the optimal treatment of primary breast cancer in augmented women.

An alternative to WBI in these patients is PBI. Recent reports in the literature reveal promising results with the use of PBI (21,22). The recent emergence of PBI is important as it is an attractive option for patients with breast augmentation due to decreased exposure of the breast implant to irradiation. As a result, the rates of breast implant contracture may be expected to decrease with decreased exposure of the breast implant. However, the use of PBI is reserved for a select group of patients. Typically, these include patients with early stage breast cancers, and proper amount of breast tissue between the BT implant and skin. Recently, the American Society of Radiation Oncology reported a consensus statement regarding the appropriate candidates for PBI. These patients include those older than 50 years of age, have ductal histology, clear margins, and no larger than 3 cm in size. (24). Kuske et al (20) reported on their experience using IBT as PBI in patients with breast augmentation. They reported 95% excellent cosmetic outcome and no patients observed any implant contracture. No patients experienced in breast failure or nodal recurrence. Though very promising, that study had different patient populations as our own study. In our study we had included patients with involved lymph nodes, which was considered a contraindication for treating such patients with PBI alone although this may be in question (29). Until further studies

confirm the safety of PBI in patients with involved lymph nodes , we recommend WBI in those patients.

The boost can be administered in many different fashions. However, the boost dose may significantly contribute to breast fibrosis (31) and therefore impact cosmesis in these patients. Therefore, the type of boost delivered to patients becomes increasingly important when considering its effects on cosmesis. These include EBRT, mammosite catheters (Cytyc, Bedford, Mass) (5), IBT and multicatheter balloons such as the Contura (Senorx Inc. Irvine CA) and SAVI (strut assisted volume implant)(Cianna Medical Inc., Alisa Viejo CA) applicators (32,33). As mentioned above, EBRT as boost may be disadvantageous secondary to dose from the exit beam and breathing motions. Placement of the balloon based or STRUT based catheters may be technically impractical secondary to small amount of tissue between the skin and breast implant. IBT is advantageous as multiple catheters can be placed according to the breast tissue volumes. It also increases the amount of dwell times and positions for dose optimization. It may also relay radiobiologic advantages as continuous low dose radiation may decrease repair and increase cell kill (34). In addition, immediate brachytherapy may counteract tumor cell multiplication secondary to reoxygenation and recruitment from Go-phase at debulking of gross disease (34). Furthermore, IBT has been reported in some cases to have better local control than electron boost (25-27). In our cohort of patients, none suffered any infield recurrences. This is similar to the low rates of recurrence in other reports (7,25-27). Wazer et al (25) reported a 5 year local relapse of 3.9% in patients treated with WBI followed by IBT as boost. Krishnan et al (7) reported an 11 year local recurrence of

7.7%. In addition, Wazer et al (36) found that cosmesis was not adversely affected by interstitial implant used as a boost. Whether or not the boost given by IBT or multicatheter balloons is superior to electron beams as a boost remains controversial .

The chemotherapy used during the period of this study, CMF, is largely no longer used. Methotrexate has been associated with decreased cosmetic outcomes. Abner et al (35) revealed in their study decreased cosmetic outcomes when patients were treated with CMF based chemotherapy. Wazer et al (36) also found that the use of CMF based chemotherapy resulted in increased complication rates. Despite these findings, our patient population still had relatively good cosmetic outcomes compared to other studies. Unfortunately, our study had too few patients to see a difference in cosmetic outcomes with the use of CMF. Furthermore, the use of CMF has been abandoned in our institutions, replaced with doxyrubicin based therapies.

Our study has several drawbacks such as the inherent selection bias associated with any retrospective analysis and the small number of patients included in this study. Therefore, an accurate survival and pattern failure analysis in such a small, heterogeneous group of patients could not be expected. In addition, patients were treated with low dose rate brachytherapy with Ir-192, which increases radiation exposure to staff and physicians. Most institutions would treat patients using HDR techniques secondary to ease and convenience of such a method. However, the single largest disadvantage is that IBT is a procedure that many radiation oncologists do not have the knowledge or experience to perform. For these reasons, many institutions have moved away from using interstitial brachytherapy as the method of PBI. However, with the introduction of the multicatheter

balloons such as the SAVI may help to circumvent that issue, as long as there is sufficient breast tissue between the skin and breast implant.

In conclusion, the use of IBT as a boost with WBI is a feasible option in patients with augmentation implants. Locoregional recurrences did not occur in our cohort. Rates of breast contracture and revisions needed seem to be favorable compared to those reported in the literature with WBI followed by external beam or electron beam boost. This may be due to increased dose falloff associated with IBT. Other multicatheter balloon devices such as the SAVI or Contura may be an alternative to the placement of interstitial BT catheters. Further studies should be performed to explore this subject, as the number of patients who seek breast augmentation are increasing.

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Figure 1. Overall survival.

Figure 2. Complication free survival.

Figure 3. Revision free survival.