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In support of the Choosing Wisely campaign: Perceived higher risk leads to unnecessary imaging in accelerated partial breast irradiation?

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Abstract

Accelerated partial breast irradiation (APBI) is an increasingly utilized modality for early stage breast cancer as part of breast conservation therapy (BCT). There remains concern regarding local recurrence, requiring more frequent post-radiation surveillance imaging. The purpose of this study is to determine clinical significance of frequent surveillance in this perceived higher risk population. Patients treated at a community academic medical center from 2005 to 2013 with partial breast radiation were retrospectively identified. All patients were treated with lumpectomy followed by balloon based APBI. Diagnostic, clinical, radiographic, and outcomes data were collected. One hundred and sixty-nine patients were identified. Median age at time of diagnosis was 63. Stage was 0, I, and II in 27%, 64%, and 9%, respectively. Most patients had pure invasive ductal cancer. Ninety-two percent and 99% of patients had imaging performed by 6 and 12 months (± 3 months) respectively. Median interval between end of radiation and first image, and subsequent 3 images were 6, 6, 9, and 12 months, respectively. Median follow-up was 49 months for all patients (range 7–106). Six patients experienced local recurrence: 4 invasive, all clinically detected, and none within the first 2 years. One patient had mammographically detected recurrent ductal carcinoma in situ. No mammographic images within the first year lead to diagnosis of recurrent cancer. APBI via balloon base brachytherapy offered women excellent locoregional control rates. Frequent mammographic surveillance did not result in increased detection of early recurrent disease. The result of our study are in line with the Choosing Wisely campaign recommendations to perform no more than annual follow-up for women who have completed radiation as part of BCT, with first imaging done at 6–12 months. We recommend mammographic surveillance be performed no more frequently than annually, with first image after BCT to be done 12 months from completion of radiation.

BACKGROUND

Increasing use of screening mammography in the 1980s resulted in diagnosis of breast cancer at earlier stages of the disease process, but led to increase in diagnosis of pre-invasive disease as well. Similarly, radiation therapy techniques have evolved to better target and treat sites of disease with decreasing toxicity and improved long-term control. Combined with the increasing utilization of long-term hormonal blockade, there has been an ever increasing population of long-term survivors after breast conservation therapy (BCT). As a result, mammography has become the cornerstone of surveillance given the small but persistent risk of locoregional disease in the treated breast as well as second primary disease in the ipsilateral or contralateral breast. While there has been clear benefit of improved survival with utilization of surveillance mammography after BCT, there is no accepted consensus on the frequency of necessary imaging. Typically, this has been done every 6–12 months after completion of BCT at many institutions.

Several studies have shown the lack of clinical significance in every 6 month ipsilateral mammographic surveillance.¹⁻⁴ Given the need to redefine the value offered in the diagnosis, treatment, and long-term surveillance of breast cancer, the Choosing Wisely guidelines released by the American Society of Radiation Oncology (ASTRO) in 2013 recommends no more than annual follow-up for women who have completed radiation as part of BCT, with first imaging to be performed at 6–12 months.⁵ The most recent National Comprehensive Cancer Network breast cancer guidelines (Version 2.2016) recommends annual mammography, as does the American Society of Clinical Oncology breast cancer survivorship care guidelines.^{6, 7} However, more frequent imaging continues to be variably utilized based on institutional practices, particularly in subgroups felt to be at higher risk of local recurrence or second primary. While whole breast radiotherapy has been a routine and integral component of BCT, there remains concern regarding risks of recurrence in patients treated with accelerated partial breast irradiation (APBI). This perceived risk often leads to increased imaging surveillance. The purpose of this study is to review clinical utility of frequent surveillance imaging after BCT in a cohort of patients treated with balloon based APBI at one academic institution.

METHODS/MATERIALS

Records of patients treated with balloon based APBI for in situ and invasive breast cancer (IBC) from 2005 to 2013 were reviewed after institutional review board approval was obtained. All patients had pretreatment mammogram, as well a minimum of 2 post-BCT surveillance mammograms. All patients were treated with BCT, which included lumpectomy with the aim of negative margins, followed by APBI with balloon based therapy. APBI delivery was 34 Gy in 10 fractions given twice daily mostly with MammoSite (Hologic, Bedford, MA), but included a few Contura (Hologic). Adjuvant chemotherapy and hormonal blockade was delivered at the discretion of the medical oncologist. Patients with radiographic surveillance or post-treatment follow-up at outside institutions were excluded.

Basic demographic, pathologic, pre- and post-treatment imaging, treatment, locoregional control, and survival data were captured. Dates and type of imaging performed were

captured. Imaging consisted primarily of mammogram, but a few patients had magnetic resonance imaging (MRI). The time frame for imaging was calculated using the date ± 3 months. Biopsies as a result of radiographic imaging were recorded. Local recurrence was defined as disease identified in any quadrant of the irradiated breast. Time to local recurrence was defined as time from completion of radiation to date of pathologic diagnosis of recurrent disease. Statistical analysis was performed using R software (Version 3.2.3).

RESULTS

Records of 169 patients were reviewed. Median age at diagnosis was 63: 15% 50, 28% 51–59, and 57% >60 years of age, respectively; 96% of patients were Caucasian. Stage was 0: 46 (27%), 1:108 (64%) and 2:15 (9%). Pathologic and diagnostic characteristics for the cohort can be found in Table 1. Median time from surgical excision to completion of radiation (RT) was 1 month (range <1–4).

Primary mode of imaging was mammogram, but some patients were imaged with MRI. Median time from end of RT to first image was 7 months (range <1–29 months). Imaging was performed in 92% of patients at 6 months. One hundred and sixty-five, 328, and 560 images were performed in the first 6, 12, and 24 months after completion of radiation, respectively. Average number of images per patient within the first 6, 12, 18, and 24 months from completion of radiation was 1.2, 1.6, 2.5, and 3.2, respectively (Table 2). Median number of images per patient was 7 (range 2–15) for all patients. Median interval between end of radiation and first image, and subsequent 3 images were 6, 6, 9, and 12 months, respectively.

No patients were found to have abnormal imaging at 6 months. Three patients (1.7%) were found to have abnormal mammograms by 12 months. This resulted in benign biopsy in two patients, and MRI for further evaluation in one patient. Overall, 25 patients required any biopsy: 18 due to abnormal mammograms, 6 due to clinical concern, and 1 at the time of mastectomy.

Median follow-up was 49 months for all patients (range 7–106). Six patients experienced recurrence during this period: one ductal carcinoma in situ (DCIS) diagnosed via surveillance mammography at 27 months, and four ipsilateral IBC diagnosed clinically at 42, 73, 73, and 76 months. Additionally, one patient had DCIS diagnosed on prophylactic mastectomy 2 years from completion of RT. Patients with IBC recurrence had surveillance imaging in the 6–12 months prior to diagnosis. One patient presented with metastatic disease at 19 months. Additionally, three patients were diagnosed with contralateral breast cancer. Five patients had expired: 3 due to second non-breast cancer, 1 due to metastatic breast cancer, and 1 due to other comorbidities.

DISCUSSION

The increasing utilization of imaging both in the diagnosis of breast cancer as well as post-BCT surveillance has significantly changed the landscape of breast cancer, resulting in earlier detection of disease which has translated into long-term survivorship. Improved outcomes have been demonstrated with early detection of local recurrence as well as second

primary breast cancer with the use of post-BCT surveillance imaging.^{1, 8} However, with rising healthcare costs, all parties involved are striving to identify the best allocation of resources while maximizing patient satisfaction and outcomes. Given the large number of breast cancer cases diagnosed annually, as well as increasing survival of this patient population, the frequency of surveillance imaging is a particularly relevant question. The second list of five recommendations as part of the Choosing Wisely campaign put forth by ASTRO recommends against more than annual surveillance of patients after BCT.⁵ However, there is great variability in acceptance and implementation of guideline recommendations, and more hesitation in subpopulations that are felt to be at higher risk of recurrence, such as those treated with APBI. Our study does not support the use of more than annual imaging surveillance in this cohort. Various studies in patients treated with BCT using conventional radiation have supported similar findings. In a study of 1432 patients treated with BCT, 2 and 9 recurrences were identified with mammography at less than 1 and 2 years, respectively. Mammographic yield during the first 2 years was not greater than that in the general population.⁹ Our group has previously reported the mammographic yield for the first 2 years following BCT in comparison to the general population, with no difference found between compliant and noncompliant patient populations at 6 months from completion of BCT. These findings were cited as data supporting the Choosing Wisely recommendations by ASTRO.

There are several take home points from our findings. First, our locoregional control rates are in line with both large registry reported data as well as institutional series.¹⁰ This is despite having a fairly young demographic that falls into the cautionary and unsuitable appropriateness criteria for APBI.¹¹ This becomes a more salient point in an even older population that may benefit less from frequent surveillance. Even with longer follow-up, it is unlikely to expect that our results would be different than that reported in the literature. This provides support to our recommendations for the first surveillance mammogram at 12 months after completion of BCT. Second, we support that surveillance requires both clinical examination as well as mammographic evaluation, given that the majority of recurrences in our study were clinically diagnosed. In a study by Ashkanani et al., 52% and 48% of local recurrences were diagnosed clinically and mammographically, respectively, at a median follow-up of 3.5 years.³ While mammographic techniques have improved over the last 10 years since their report, we accept that with longer-term follow-up, we may have been able to detect more recurrences mammographically. Third, it is well known that mammographic abnormalities are more prominent in the first 2 years after BCT, and hence can be mistaken for recurrent disease.^{12, 13} These include edema, fibrosis, seroma, and calcifications as the breast tissue changes due to the acute effects of surgery and radiation therapy. During this period, it can be difficult to differentiate true recurrences from surgical and radiation induced change to the site of treatment. Of the 15 biopsies performed due to mammographic abnormalities in our study, 10 were performed in the first 2 years, resulting in one diagnosis of IBC. Ashkanani et al. found similar findings, where five benign biopsies were performed based on the 6 or 18 month mammographic results.³ Such early radiographic changes can lead to more interventions such as biopsies, and contribute to patient anxiety and increased healthcare costs, again supporting no more than annual surveillance imaging.^{14, 15} Fourth, we did not identify contralateral breast disease within the first 2 years of follow-up. This

would argue against the importance of timing of the mammogram in concordance with the last annual bilateral mammogram rather than 1 year after completion of radiation therapy as part of BCT. This finding was recently confirmed in a retrospective cohort of 342 patients treated with BCT, where one patient (0.3%) was found to have positive biopsy confirmed disease based on 6 month imaging.¹⁶ Finally, various factors compound the frequency of surveillance imaging, such as patient wishes, payer practices, institutional culture, and practitioner concern regarding litigation.¹⁷ As we move into an era of increasing cost scrutiny, it will be important for resource allocation to mirror patient outcomes.

CONCLUSION

Patients treated with balloon based APBI as part of BCT for early stage breast cancer have excellent locoregional control rates, despite the perceived risk otherwise. Mammographic surveillance at a frequency more than annually did not result in improved disease detection despite the increase in the number of biopsies associated with imaging within the first 2 years. Given the low absolute risk of disease recurrence in this population, we recommend no greater than annual mammographic surveillance in patients treated with balloon based APBI as part of BCT.

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Table 1.

Demographics

Histology	
In situ	46 (27%)
Invasive	84 (50%)
In situ + Invasive	39 (23%)
AJCC T stage	
0	46 (27%)
1	111 (66%)
2	12 (7%)
Lymph node evaluation	128 (76%)
Chemotherapy	27 (16%)
Hormonal blockade	132 (78%)
ER	139 (82%)
PR	122 (72%)
HER2	10 (6%)

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Table 2.

Imaging by type at selected timepoint after completion of radiation

	6 months (± 3 months)	12 months (± 3 months)	18 months (± 3 months)	24 months (± 3 months)
Mam alone	147	147	106	102
Mam + U/S	9	8	9	8
Mam + MRI	1	–	–	1
MRI alone	6	10	3	3

Mam, mammogram; MRI, magnetic resonance imaging.

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