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Accelerated partial breast irradiation

# Defining an optimal role for breast magnetic resonance imaging when evaluating patients otherwise eligible for accelerated partial breast irradiation

Kathleen C. Horst [a,*], Katherine E. Fero [a], Debra M. Ikeda [b], Bruce L. Daniel [b], Frederick M. Dirbas [c]

[a] Department of Radiation Oncology; [b] Department of Radiology; [c] Department of Surgery, Stanford University School of Medicine, Stanford Cancer Institute, United States

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ABSTRACT

*Background and purpose:* Pre-treatment breast magnetic resonance imaging (MRI) findings in a cohort of women prospectively evaluated for accelerated partial breast irradiation (APBI) are reviewed and characterized to determine the optimal use of MRI in these patients.

*Materials and methods:* Candidates initially deemed eligible for a prospective APBI trial based on physical examination, mammography, and ultrasound (US) were further evaluated with breast MRI before treatment. All abnormal MRI findings were biopsied.

*Results:* Between 2002 and 2011, 180 women who met inclusion criteria for APBI underwent breast MRI prior to treatment (median age = 59; range 38–86). 126 tumors (70%) were invasive carcinomas with or without associated DCIS, while 54 (30%) were pure DCIS. Breast MRI confirmed unifocal disease in 109 patients with 111 cancers (60.5% of MRI cohort). Multifocal disease was identified in 19 patients (10.5% of MRI cohort), while multicentric disease was present in 3 patients (1.6% of MRI cohort). Five patients (4%) had an MRI-detected contralateral cancer. False positive MRI findings were seen in 45 patients (25% of MRI cohort). Pre-menopausal patients and patients with tumors >2 cm were more likely to have MRI-detected multifocal/multicentric disease. While there was no statistically significant correlation between multifocal/multicentric disease and breast density, tumor histology, grade, ER status, or Her2/Neu expression, numbers in each category were small, suggesting a lack of statistical power to detect differences that may be clinically meaningful. One hundred and fifty-two of the 180 patients (84.4%) successfully completed lumpectomy and APBI, while 6.7% of the cohort underwent mastectomy.

*Conclusions:* Breast MRI identified additional disease in 12% of APBI candidates. Premenopausal women and patients with tumors >2 cm were more likely to have MRI-detected multifocal/multicentric disease.



The use of breast magnetic resonance imaging (MRI) in the evaluation and workup of women undergoing treatment for breast cancer has been controversial [1]. While some advocate that it can optimize surgical management, others contend that the poor specificity and high cost limit its overall usefulness [1]. Nonetheless, the American Cancer Society, the American College of Radiology, and the Society of Breast Imaging have identified a select group of high-risk patients for whom screening breast MRI is recommended. This group includes women who are BRCA 1/2 mutation carriers, those who have received chest irradiation at a young age, or those who have >20% lifetime risk of developing breast cancer based on a strong family history [2]. Furthermore, the European Society of Breast Cancer Specialists (EUSOMA) Working Group also recommends breast MRI for patients eligible for accelerated partial breast irradiation (APBI) [3–6]. In the United States, it has been acknowledged that breast MRI may be a valuable tool in selecting appropriate patients for APBI, yet, there are no specific guidelines for its use in this setting. APBI, which limits radiotherapy treatment to the lumpectomy cavity plus margin, is currently being investigated in multiple Phase III trials as a potential option in lieu of whole breast radiotherapy for women with early-stage breast cancer treated with breast conservation therapy [7,8]. Until the results of these trials are available, the American Society of Radiation Oncology has submitted a consensus statement for guiding patient selection for APBI treatment [9]. In addition to outlining which patients are suitable, cautionary, and unsuitable for APBI outside of a clinical trial, the authors conclude that there are insufficient data to justify the routine use of breast MRI in patients selected for APBI. This has been supported by Beal et al. who noted that for women in the "suitable" category (women >60 years of age with Stage I invasive ductal carcinoma), MRI

* Corresponding author. Address: Department of Radiation Oncology, Stanford University School of Medicine, Stanford Cancer Institute, 875 Blake Wilbur Dr, CC-G221A, Stanford, CA 94305-5847, United States.
*E-mail address:* kateh@stanford.edu (K.C. Horst).

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findings were falsely positive in 10 of the first 20 women they evaluated for APBI using high dose rate intraoperative radiotherapy (IORT), such that they did not obtain further MRI imaging in the remaining 30 women evaluated, noting no difference in outcome compared to those who did have a pre-treatment MRI [10]. Other groups, however, have identified abnormal MRI findings in 4–38% of patients evaluated for APBI [3,4,6,11–13].

In the current report, we review and characterize the pre-treatment breast MRI findings in a prospective cohort of women evaluated for APBI using either single-fraction IORT or fractionated post-operative external beam 3D-CRT to determine the impact of breast MRI on patient eligibility and to evaluate whether there is a subset of women for whom MRI is most appropriate.

## Methods and materials

Women $\geqslant$40 years of age with in-situ or invasive breast cancer were evaluated for an IRB-approved institutional trial investigating APBI using either single-fraction IORT delivered at the time of lumpectomy or re-excision lumpectomy, or fractionated post-operative 3D-CRT. Eligibility criteria were initially based on physical examination, mammography, and ultrasound (US) and included unifocal invasive carcinoma or ductal carcinoma in-situ (DCIS) measuring $\leqslant$2.5 cm in size. Exclusion criteria included invasive carcinoma associated with an extensive intraductal component (EIC), defined as when the component of intraductal carcinoma comprised of more than 25% of the primary tumor on pathologic review of the initial needle biopsy or surgical specimen and extended outside the invasive focus, invasive lobular carcinoma, tumor involving skin, tumor involving pectoralis fascia, defined according to preoperative imaging findings, or pathologic evidence of margins <2 mm and/or nodal disease.

Patients who met initial eligibility criteria and were interested in APBI using single fraction IORT were scheduled for pre-operative contrast-enhanced breast MRI to exclude mammographically or clinically occult disease elsewhere in the affected breast. Patients who already had surgical excision with tumor-free margins $\geqslant$2 mm and a negative sentinel lymph node biopsy were eligible for post-operative APBI using 3D-CRT and underwent breast MRI prior to radiotherapy. For patients who had already had surgery, the pre-treatment MRI was obtained within 6 weeks of surgery. Tumor size was evaluated initially by mammography and/or US in those patients who underwent MRI before surgery and by imaging plus final pathology in those who underwent MRI after surgery.

Patients were eligible for single fraction IORT if the patient presented to the clinic pre-operatively, the imaging suggested that the surgical resection could be performed in a single procedure with a high probability of obtaining negative margins, and the surgeon intraoperatively assessed that nodes were tumor-free by touch preparation or frozen section and that the procedure could be accomplished without adverse complications (i.e., appropriate distance from the nipple-areolar complex to avoid nipple-areolar necrosis). Patients were eligible for post-operative fractionated 3D-CRT if there was uncertainty as to whether negative margins could be achieved in a single procedure, the patient presented to the clinic after having surgery elsewhere, or the patient preferred to have final pathologic information before proceeding with radiotherapy. Written informed consent was obtained from all patients prior to treatment by both the surgical and radiation oncology teams.

Since 2002, breast MRI was performed in the prone position using a 1.5-Tesla magnetic resonance scanner (Echospeed; GE Medical Systems, Milwaukee, WI) with a dedicated phased array breast coil (MRI Devices, Waukesha, WI). The intravenous injection consisted of 0.1 mmol/kg gadolinium DTPA using a power injector. Acquired sequences included axial T1 spin echo, sagittal pre-contrast 3-dimensional (3-D) SSMT, sagittal fat suppressed T2 fast spin echo, sagittal dynamic 3-D spiral imaging during infusion of gadolinium contrast agent, sagittal eccentric high resolution, 3D SSMT, and sagittal dynamic 3-D spiral imaging during wash-out of contrast material. Spiral k-space sampling was used. The raw data were then post processed on the GE Advantage Windows workstation [14,15]. Curves were classified as suspicious or benign according to the kinetic uptake and washout [14]. The MRI was timed in relation to the menstrual cycle in cases where it was feasible with respect to the patient's availability, regularity of her cycle, and when it did not significantly delay the workup and treatment of the cancer. Menstrual cycle information was recorded on a breast history form that was available for evaluation by the diagnostic radiologist at the time of interpretation.

MRI findings were reviewed by dedicated breast diagnostic radiologists who are fellowship trained in breast imaging and breast MRI. Characteristics reported on pre-treatment breast MRI included size and morphology of the mass or cavity, the location, the description of mass margins, and the dynamic enhancement patterns according to the ACR BI-RADS MRI Reporting System [16]. Patients with suspicious or indeterminate MRI findings concerning additional disease beyond the index lesion underwent second-look focused US. If the finding was identified by US, a biopsy was performed under US guidance. If, however, the finding was not seen by US, an MRI-guided biopsy was performed. Final pathology from these biopsies was correlated with the abnormal MRI findings. Multifocal disease was defined as biopsy-proven additional tumor noted within 3–4 cm of the primary or clearly within the same quadrant of the breast. Multicentric disease was defined as biopsy-proven additional tumor noted >4 cm from the primary or clearly within another quadrant of the breast.

Pathologic characteristics of both the index lesion and the additional biopsies were recorded, including histology, estrogen receptor (ER) status, progesterone receptor (PR) status, Her2/Neu expression, and presence or absence of lymphovascular invasion (LVI). Mammographic breast density was recorded as being predominantly fatty, scattered fibroglandular tissue, heterogeneously dense, or dense.

Statistical analysis was performed using SPSS 18.0. Chi-squared test was used to determine the association between categorical patient and tumor characteristics and the presence of multifocal/multicentric disease. Fishers' exact test was used when sample sizes were small. Analysis was also performed to determine the association between patient and tumor characteristics and the incidence of false positive MRI findings. A $p$ value $\leqslant$0.05 was considered statistically significant.

## Results

Between 2002 and 2011, 260 women met initial eligibility criteria and were evaluated for APBI using either single-fraction IORT delivered at the time of lumpectomy or re-excision lumpectomy, or post-operative fractionated 3D-CRT. Of these, 180 patients proceeded on protocol and underwent pre-treatment MRI. The remaining 80 patients were excluded prior to obtaining MRI for the following reasons: the patient declined participation in the protocol, patient was found to be a BRCA mutation carrier, patient had received neoadjuvant chemotherapy, patient had implants in place, insurance declined treatment at the institution, patient chose mastectomy, patient chose to receive surgery and/or radiotherapy closer to home, review of outside pathology revealed invasive lobular histology or EIC.

Clinical and pathologic characteristics of the 180 patients who underwent pre-treatment MRI and their index lesions are detailed