How Does MR Imaging Help Care for My Breast Cancer Patient? Perspective of a Radiation Oncologist

Kaitlin M. Christopherson, MD\textsuperscript{a}, Benjamin D. Smith, MD\textsuperscript{b,}\textsuperscript{*}

KEYWORDS
- Partial breast radiotherapy • MR imaging • Breast cancer

KEY POINTS
- For patients with preinvasive breast cancer or early-stage breast cancer, MR imaging may help identify patients who are eligible for accelerated partial breast irradiation.
- In early-stage patients, MR imaging may provide benefit in accuracy and consistency of target volume delineation for radiation treatment planning, particularly in the preoperative setting.
- In select patients, MR imaging may identify extramammary disease that alters the overall treatment recommendation, target volumes, and/or doses of radiation therapy.
- MR imaging is capable of showing late sequela of radiation in patients with breast cancer and may have a role in examining late breast fibrosis in future studies.

INTRODUCTION

Radiation therapy (RT) can be used in almost every stage of breast cancer. In preinvasive and early-stage invasive breast cancer, radiation is used in the adjuvant setting after breast-conserving surgery. For advanced-stage patients, radiation may be indicated to treat regional nodal basins and the chest wall following mastectomy and axillary surgery. Even in stage IV disease, there is recently increased interest in aggressive local therapy, particularly in patients with limited metastases (oligometastatic cancer).

The general guiding principles of radiation include targeting malignancies while sparing normal adjacent tissue from high-dose radiation. To achieve the maximal balance between efficacy and morbidity, it is critically important to accurately define the radiation target. Current practice relies heavily on the utility of computed tomography (CT)-based radiation treatment planning. In the United States, CT-based simulation scans, or treatment planning scans, are the most commonly used planning method for radiation oncologists. On these images, the radiation oncologist defines the target, also referred to as the clinical treatment volume, and nearby organs at risk to avoid.

Given the range of possible radiation treatments in breast cancer, MR imaging has several possible applications for the radiation oncologist. Herein, the authors focus on the usefulness of MR imaging for the radiation oncologist in the setting of both early-stage disease and late-stage...
disease. For early-stage patients, MR imaging can aid in target delineation and radiation technique selection. For more advanced-stage patients, this article examines how MR imaging may help identify the extent of disease in addition to aid in target volume definition. Last, the authors comment on MR imaging in monitoring of late effects of radiation.

Early-stage patients

In early-stage and preinvasive cancers, radiation is used in conjunction with lumpectomy to minimize the risk of subsequent in-breast tumor recurrence and thus maximize the likelihood of breast conservation long-term survival. The most common radiation approach in early-stage disease is whole breast irradiation (WBI), in which tangential radiation beams are directed from the medial and lateral aspects of the affected breast for a series of daily treatments ranging from approximately 3 to 6 weeks (Fig. 1). A tumor bed boost, defined as additional radiation directed to the tissues immediately adjacent to the tumor bed, is frequently delivered following WBI to further lower local recurrence risks. Multiple randomized trials have demonstrated that lumpectomy followed by WBI confers survival equivalent to mastectomy, and as such, WBI is a commonly accepted standard of care.1–5 Accelerated partial breast irradiation (APBI) is a newer approach to delivery of radiation for breast cancer, in which only tissues immediately adjacent to the tumor bed are targeted and treated with radiation (Fig. 2). Currently, use of APBI is largely limited to women age ≥50 years with estrogen receptor–positive, node-negative tumors measuring 2 cm or less in size.6

Within the context of WBI and APBI, MR imaging has several important potential applications. First, by detecting the presence or absence of radiographically occult disease in the breast that is remote from the tumor bed, MR imaging can assist in determining which patients may be safely treated with APBI and which patients would be better served by WBI (or even mastectomy). Second, because of better soft tissue resolution than typically achieved with radiation planning CT scans, MR imaging may assist with delineation of the tumor bed to enhance treatment planning of APBI or the tumor bed boost. Third, recent investigations have focused on developing novel preoperative APBI treatment strategies, and in this setting, MR imaging can be invaluable in identifying the in vivo tumor and facilitating accurate targeting with radiation before surgery. Each of these important scenarios is discussed in detail in later discussion.

Patient Selection for Accelerated Partial Breast Irradiation

For early-stage patients who may be candidates for APBI, breast MR imaging may be of value to the radiation oncologist by identifying the presence of malignant foci remote from the tumor bed, which, if present, would disqualify the patient from being eligible for APBI.7–10 For example, Tendulkar and colleagues9 reviewed 260 patients with early breast cancer treated at the Cleveland Clinic and correlated findings on mammography, MR imaging, and surgical pathology. The objective was to determine if MR imaging was more sensitive than mammography in patient selection for APBI. They focused on patients who would have been eligible for National Surgical Adjuvant Breast and Bowel Project B-39 (a prospective trial evaluating APBI) based on clinical-pathologic grounds. MR imaging detected synchronous, mammographically occult, primaries in 5.8% of patients, most commonly in the ipsilateral breast. They noted that invasive lobular carcinoma (ILC), in contrast to invasive ductal carcinoma, was significantly associated with additional ipsilateral disease (18% of these patients).

A similar study from the University of Chicago prospectively evaluated the benefit of MR imaging for more than 500 patients being screened for APBI and concluded that preoperative breast MR imaging rendered 12.9% of patients ineligible for APBI. Risk factors for eligibility included tumor size ≥2 cm, age less than 50, ILC, and Her-2/neu amplification. A combination of these factors was used to generate a risk score that predicted the likelihood that MR imaging would render a patient ineligible for APBI.9

In total, these and other studies indicate that preoperative MR imaging could alter recommendations for partial breast irradiation in up to 13% of patients. Most commonly, MR images reveal more extensive ipsilateral disease or multifocality, but can also detect contralateral breast lesions as well.10–14 Known multifocal or multicentric disease would be a contraindication for APBI. It is important to take into account certain clinical and pathologic factors, such as young age, tumor size, and invasive lobular histology, which may lead to a higher yield of additional findings on breast MR imaging. For a young patient with ILC, or a patient with a 2-cm or greater tumor, who is motivated for APBI, it may be reasonable to consider breast MR imaging to rule out possible multifocal or multicentric ipsilateral disease.14,15
For patients with an indication for postoperative radiation, treatment planning usually begins with a CT simulation scan 3 to 6 weeks after surgery. At the time of simulation, the radiation oncologist contours the tumor bed based on soft tissue change seen on CT and radiopaque clips left by the surgeon to mark the tumor bed. This contour is critically important, because it will be used to delineate the treatment volume for either APBI or, in the setting of WBI, the external beam tumor bed boost. Accurate delineation of the tumor bed is critical to achieve optimal radiotherapy outcomes. Failure to delineate the entirety of the tumor bed could lead to higher risk of local failure, because volumes at risk for recurrence that are not delineated could harbor residual disease that would not be adequately treated. Conversely, inclusion of non–tumor bed tissue within the tumor bed contour results in a larger volume of radiated tissue, which may yield increased late risks of soft tissue fibrosis and/or suboptimal cosmetic outcome. In consideration of the importance of accurate tumor bed delineation, various groups have investigated the utility of MR image fusion with CT-based radiation treatment planning to improve accuracy of tumor bed delineation. MR imaging obtained in the treatment position may be fused in the radiation planning software to aid in
contouring of the tumor bed. MR image fusions for radiation therapy target volume delineation have proven useful in other disease sites, such as the central nervous system, head and neck, sarcoma, genitourinary, and gynecologic cancers, so it is reasonable to posit that a similar approach could be useful for breast cancer.

A study from Jolicoeur and colleagues\textsuperscript{16} evaluated the value of postoperative MR image fusion to CT-based planning for brachytherapy planning in the supine treatment position. They evaluated the accuracy of contours between practitioners. Consistency in target volume definition is typically measured as interobserver variability, with more accuracy correlating to low variability. The use of MR fusion led to a reduction in the volume of tumor bed contoured by 30\% to 40\% with little interobserver variability.\textsuperscript{16} Although this study is promising and potentially clinically meaningful, other similar studies have reported discordant findings regarding the usefulness of MR image fusion with CT-based treatment planning scans.\textsuperscript{16–20} In light of the conflicting evidence, at this time the authors’ group does not routinely obtain MR imaging to assist in tumor bed delineation, although it may be considered in rare cases whereby tumor bed delineation is critically important and CT-based imaging is difficult to interpret.

**Defining the Preoperative Accelerated Partial Breast Irradiation Target**

As previously mentioned, RT is most commonly delivered postoperatively after breast surgery.

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Fig. 2. Representative example of partial breast CT-based radiation plan. The red volume represents the tumor bed contour, and the aqua volume represents a volumetric expansion of 2.0 cm around the tumor bed to create a clinical treatment volume. Skin rendering is also shown. (Courtesy of Elizabeth Bloom, MD, Houston, TX.)
There are inherent difficulties associated with this method because of seroma and/or hematoma formation that may enlarge the radiated volume, and variability of clip placement around the tumor bed cavity. In other disease sites, such as soft tissue sarcomas, esophageal, and rectal cancers, radiotherapy is used preoperatively. Preoperative radiation has certain advantages, principally the potential to facilitate smaller treatment volumes and lower doses of radiation. Disadvantages include risks of impaired wound healing postoperatively. Recent emerging literature has sought to define the role of preoperative radiotherapy for patients with breast cancer in an effort to mitigate some of the inherent difficulties related to postoperative treatment planning. These studies focus on contouring accuracy to ensure tumor coverage, without excess normal tissue exposure to RT, with ultimate goals of reducing late toxicities.

A study by den Hartogh and colleagues examined preoperative tumor delineation on both CT and MR imaging for patients undergoing breast-conserving surgery. The study sought to quantify the consistency of preoperative tumor delineation among 4 observers. When delineating gross tumor, there was high interobserver agreement for both CT and MR images. Contours obtained from MR images resulted in larger contours (compared with CT based), because MR images were able to show details of more irregularly shaped and spiculated tumors. Despite this fact, when comparing both CT and MR preoperative tumor volumes with postoperative tumor bed volumes in other studies, both sets of preoperative tumor volumes were considerably smaller. These findings suggest that preoperative MR-guided APBI may allow for more accurate and precise treatment volumes.

Preoperative partial breast radiation is not used off-protocol at present, but there is ongoing investigation in this arena. Modern protocols for preoperative partial breast radiotherapy commonly use MR images to aid in target delineation and thus treatment planning. As radiation oncologists, the authors look forward to emerging data regarding the efficacy and safety of this treatment approach.

**ADVANCED-STAGE PATIENTS**

In more advanced breast cancer cases, radiation may be necessary after mastectomy, axillary surgery, and chemotherapy to decrease the risk for local-regional recurrence and improve disease-specific survival. For patients with node-positive and locally advanced cancers, it is important to accurately determine the extent of disease at initial presentation as well as the final pathologic stage, when determining radiation treatment volumes and doses. Of the routine breast imaging modalities, MR imaging is the only modality that routinely encompasses extramammary sites in the examination. For radiation oncologists, extramammary findings that could alter treatment recommendations include those representing locally advanced disease, such as internal mammary (IM) or mediastinal adenopathy, skin involvement, and sternal involvement. For widely metastatic disease, radiation may play no role. MR findings may upstage a patient, emphasizing the need for accurate and detailed preoperative imaging, whereby MR imaging may provide information that would not be available from mammography or ultrasound in primary breast cancer staging.

**Identification of Locally Advanced Disease: Extensive Lymphatic Spread/Sternal Involvement**

Bones of the chest wall, lungs, liver, and additional nodal stations can be seen on some breast MR images depending on the institution’s set scan range. Up to one-third of breast MR images show extramammary findings. Most extramammary findings are benign, but 10% to 20% are malignant, with a higher likelihood of malignancy in patients undergoing MR imaging for staging of a known invasive cancer. Knowing that the most common sites of metastases in breast cancer are lymph nodes and bone, careful attention to draining nodal basins, ribs, sternum, and spine on breast MR imaging may reveal additional disease. Additional findings in these locations may contribute to staging and prognosis. Enlarged IM nodes can readily be seen on breast MR imaging as enhancing nodal masses (Fig. 3). IM involvement obviously alters the stage of the breast cancer, and invariably, patients with IM involvement will require trimodality treatment. Because the IM nodes are rarely dissected at surgery, this nodal

Fig. 3. MR imaging showing pathologic left-sided IM (arrow) adenopathy.
chain must be treated with relatively high doses of radiation to yield long-term local-regional control. Breast MR imaging can be useful to the radiation oncologist to follow response to chemotherapy of a positive IM node and may influence volume of IM nodal basin covered with radiation and the final radiation dose delivered. An isolated sternal lesion may be noted on staging MR imaging (Fig. 4), and subsequently targeted with postoperative radiation in select patients with oligometastatic disease.

Identification of Locally Advanced Disease: Skin Thickening/Inflammatory Breast Cancer

In primary tumor staging, skin involvement leads to a stage T4 diagnosis and requires more local-regional treatment. Skin involvement is typically regarded as a physical examination finding, but MR images can also identify skin involvement on initial staging of a patient with breast cancer and can serve to clarify equivocal findings on examination. Inflammatory breast cancer (IBC) is the most aggressive form of breast cancer, characterized by physical examination findings of skin redness and edema. Although clinical features are necessary to confirm IBC diagnosis, MR imaging can support a clinician’s examination findings. The National Comprehensive Cancer Network guidelines recommend optional MR imaging in the staging of patients with IBC. MR imaging can elucidate inflammatory changes in the breasts by showing skin changes in conjunction with edema and detects skin edema more often than mammography. MR imaging can be particularly helpful in the setting of patients with clinical features of IBC in the absence of a readily defined breast mass on conventional mammography and ultrasound. Patients with inflammatory presentation are also more likely to have regional nodal or distant spread, so MR imaging can be useful to outline the full extent of disease before initiation of any therapy. In the evaluation of IBC, an MR imaging examination can clearly show an asymmetrically large breast, with thickened skin edema and sometimes diffuse involvement of the affected breast (Fig. 5).

RADIATION SIDE EFFECTS

Radiation can lead to long-term tissue changes and the potential for side effects. For patients with breast cancer, late effects can include breast and lung fibrosis, which result in clinically symptomatic side effects in the minority of patients. As mentioned previously, standard whole breast or post-mastectomy radiation involves using tangential fields to treat the whole breast or chest wall and invariably requires radiation beams to pass through the lung immediately posterior to the chest wall (typically on the order of 2 cm depth of lung). Treating this small strip of lung rarely leads to symptomatic clinical complaints for patients, but more commonly does result in radiographic lung changes. In subsequent breast MR images after breast cancer treatment radiation, fibrosis in this area can be visualized as a subpleural linear band of enhancement.

There is also interest in quantifying radiation-induced breast fibrosis, especially as it related to quality of life and cosmetic outcomes. A study from Hammer and colleagues found the volume

![Fig. 4. Sagittal MR imaging showing enhancing lesion in the sternum (arrow). This finding was noted for a patient undergoing initial evaluation for what was thought to be stage II breast cancer.](image1)

![Fig. 5. MR image showing skin thickening, edema, and multiple foci of enhancement (arrows) in a patient diagnosed with right-sided IBC.](image2)
of breast tissue receiving $\geq 55$ Gy correlated with rates of grade 2 fibrosis. If MR imaging can be optimized to more accurately identify the tumor bed and minimize boost volumes compared with CT, this could prove useful in potentially reducing late fibrosis. There have been few published studies on the value of MR imaging in assessing the degree of post-RT fibrosis. MR elastography is a tool used to measure stiffness in soft tissues and may prove useful in the future in quantifying post-RT breast fibrosis.

SUMMARY

MR imaging can assist the radiation oncologist in patients with both early and advanced disease breast cancer. Radiation oncologists thus need to evaluate MR breast images, when obtained, to ensure that these imaging findings are taken into consideration when developing a radiation therapy management plan. Future research may establish a definitive role for MR imaging in facilitating preoperative partial breast radiation therapy and in quantitatively measuring the extent of postradiation soft tissue toxicity.

REFERENCES


