

Evidence Discussion (ONC 11)

Initial staging

Evaluation of disease in the breast/axilla with breast MRI:

The American Society of Breast Surgeons Consensus (ASBrS) statement, and the American Board of Internal Medicine (ABIM) Choosing Wisely Guidelines, recommend against the use of routine MRI in the preoperative workup of patients with breast cancer. (ASBrS: *Consensus Guideline on Diagnostic and Screening Magnetic Resonance Imaging of the Breast*, 2017) Two randomized controlled trials found that preoperative MRI did not lead to a reduction in positive margin rates. (Peters et al., 2011; Turnbull et al., 2010) Meta-analyses have shown that the use of preoperative MRI is not associated with any improvement in local recurrence at eight years, nor distant recurrence-free survival. (Houssami et al., 2014). According to another meta-analysis, MRI to detect additional ipsilateral and/or contralateral breast lesions is of low value. (Plana et al., 2012). The high false positive rate leads to significant patient anxiety, unnecessary biopsies, and a higher mastectomy rate regardless of the findings of the biopsies. (Cozzi et al., 2023). Preoperative MRI is noted to be associated with a significant increase in the time to definitive surgery and therefore delaying care. (Chagpar et al., 2022). In patients with inconclusive conventional imaging, MRI may be a useful adjunct. (Lee, Smith, Levine, Troiano, & Tocino, 1999)

National Comprehensive Cancer Network (NCCN) guidelines note that there is considerable controversy in the use of MRI based on breast density (NCCN, 2024). They note that MRI advocates argue that it has a high sensitivity to find occult disease in “dense breasts where mammographically occult disease is more likely to elude preoperative detection”; however, MRI detractors note the high percentage of false-positive findings, resulting in further workup, overestimation of extent of disease and increased frequency of mastectomy.

Breast MRI has been shown to find occult primary cancers in roughly two thirds of patients who present with positive axillary lymph nodes, allowing for definitive surgical management. (de Bresser, de Vos, van der Ent, & Hulsewé, 2010). While there is no question that breast MRI can detect occult breast cancers; however, it is also clear that there is no benefit gained in using MRI to do so in all patients. For those who already have biopsy-proven multifocal or multicentric disease, one could argue that MRI may be helpful in elucidating whether disease exists in the intervening breast tissue thereby aiding in tumor size estimation and the decision to opt for mastectomy vs. lumpectomy.

While atypical lesions and lobular carcinoma in situ are associated with an increased risk of developing breast cancer, the data remain uncertain regarding the role of MRI in these populations (Port, Park, Borgen, Morris, & Montgomery, 2007). Breast MRI has also been shown to more accurately predict tumor size in patients with invasive lobular carcinoma than conventional imaging (Hovis et al., 2021). While data are limited on the use of breast MRI in the setting of Paget’s disease of the breast, one study found that for patients with a histologic diagnosis of Paget’s disease and a negative mammogram, MRI was able to detect occult cancer in 4/8 (50%) patients. (Morrogh et al., 2008)

Lymphatic mapping with lymphoscintigraphy and/or SPECT/CT:

Sentinel node biopsy is important in the staging of patients with breast cancer. However, lymphoscintigraphy has limited utility in this setting.(Chagpar et al., 2005) In patients with recurrent disease who have had previous axillary surgery, lymphoscintigraphy with SPECT/CT may be helpful in delineating alternate drainage pathways.(Borrelli et al., 2017) In patients who have had a positive axillary node prior to neoadjuvant chemotherapy, some authors have also found the technique to be helpful in identifying the previously positive clipped node, which may not be subsequently identified as a sentinel node.(Christin, Kuten, Even-Sapir, Klausner, & Menes, 2019).

Systemic staging with CT Chest, Abdomen, Pelvis, and bone scan vs. PET/CT:

The NCCN guidelines state to “consider additional imaging studies only in the presence of signs and symptoms of metastatic disease and for patients who are clinically high risk”.(NCCN, 2024). This is in keeping with ASCO’s Choosing wisely guideline which recommends against performing PET, CT, and radionuclide bone scans in the staging of early breast cancer at low risk for metastasis,(ASCO, 2021) and the ACR Appropriateness Criteria which similarly states that systemic staging is “usually not appropriate” for all newly diagnosed clinical Stage I-IIA (early stage) breast cancer patients, and clinical Stage IIB-III (late stage) patients with ER+/HER2- breast cancer.(American College of Radiology (ACR) *Appropriateness Criteria Imaging of Invasive Breast Cancer*, 2023. Over a third of patients with inflammatory breast cancer will have distant metastatic disease at presentation,(Kleer, van Golen, & Merajver, 2000) and NCCN does recommend staging studies in these patients.(NCCN, 2024).

NCCN guidelines recommend CT scan for the work up for distant metastatic disease; PET may be useful if conventional imaging is suspicious or inconclusive. (NCCN, 2024)

Restaging

Evaluation of disease in the breast/axilla with breast MRI:

Breast MRI has been shown to predict extent of pathological tumor response in the breast and lymph nodes after neoadjuvant systemic therapy better than conventional imaging, although may over- or under-estimate residual tumor size.(Yeh et al., 2005)

While some authors have found the use of MRI to be helpful in terms of estimating size of ipsilateral breast tumor recurrences and finding multifocal or multicentric disease,(Walstra et al., 2020) others have found that the addition of MRI in this context did not significantly change management and increased time to definitive therapy.(Sutherland et al., 2022) However, as previously noted, MRI may be a useful adjunct in situations where conventional imaging is inconclusive. (Lee, Smith, Levine, Troiano, & Tocino, 1999)

Systemic staging with CT Chest, Abdomen, Pelvis, and bone scan vs. PET/CT:

As patients with symptoms for distant metastatic disease would have had systemic staging prior to neoadjuvant chemotherapy and/or surgery, there is no indication to repeat these until treatment is completed. However, for patients with metastatic disease, NCCN guidelines recommend CT chest, abdomen and pelvis with contrast every 2-4 cycles of chemotherapy or every 2-6 months of endocrine therapy and bone scan is recommended every 4-6 cycles of chemotherapy or every 2-6 months of endocrine therapy. Restaging using these modalities is also advised if there is concern for progression of disease. In particular, they note that PET/CT is not routinely indicated for restaging “because of the absence of a reproducible, validated, and widely accepted set of standards for disease activity assessment”.(NCCN, 2024)

Surveillance

Evaluation of disease in the breast/axilla with breast MRI:

NCCN guidelines suggest that “the utility of MRI in follow-up screening of most patients with prior breast cancer is undefined”, but recommend annual MRI in patients with a personal history of breast cancer who were either younger than age 50 or who have dense breasts.(NCCN, 2024)

However, as breast cancer patients may have residual breast tissue in the ipsilateral or contralateral breast for which certain genetic mutations may increase the risk of subsequent cancers, breast MRI would also be indicated in such patients. (NCCN, 2024)

Patients with a clinical lifetime risk estimated to be $\geq 20\%$ lifetime risk prior to their diagnosis of breast cancer and/or who had a history of ADH or lobular neoplasia would have been candidates for breast cancer screening with breast MRI regardless (see BR 5.1) and therefore, would equally be eligible for this screening modality after breast cancer treatment, as long as they had not had bilateral mastectomies.

Patients who have had bilateral mastectomies have little residual tissue, and therefore, surveillance with breast imaging would be of little value. A recent meta-analysis found that the rate of occult cancer in patients with mastectomy and the rate at which MRI detected cancer in patients after mastectomy was well below the current BIRADS benchmark for women with genetic predispositions to cancer.(Smith, Sepehr, Karakatsanis, Strand, & Valachis, 2022)

Systemic surveillance with CT Chest, Abdomen, Pelvis, and bone scan vs. PET/CT:

The NCCN guidelines state “In the absence of clinical signs and symptoms suggestive of recurrent disease, there is no indication for laboratory or imaging studies for metastases screening”.(NCCN, 2024) This is in keeping with ASCO’s Choosing Wisely guideline which similarly recommends against surveillance testing with biomarkers or imaging for asymptomatic breast cancer patients who have been treated with curative intent.(ASCO, 2021) Several studies have shown no benefit from routine imaging which can result in unnecessary radiation exposure and biopsies, and lead to misdiagnosis and

treatment related complications.(Jochelson M, 2013) A recent study also found that more intensive screening for metastasis did not result in improved survival.(Cheun et al., 2021)

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