

Routine Breast MRI as a Screening Modality for Occult Contralateral Breast Cancer: Where Do We Draw the Line?

The use of magnetic resonance imaging (MRI) in the care of breast cancer patients has become increasingly more common because of its improved sensitivity over mammography in detecting occult malignancies in the breast. Yet, existing guidelines remain nonspecific in delineating which patients are ideal candidates for the study, and the clinical applications of breast MRI are seemingly sporadic from one center to the next. Practice guidelines published earlier this year by the National Comprehensive Cancer Network (NCCN) state that MRI “may be” useful in determining the extent of disease in the ipsilateral breast or for screening of the contralateral breast at the time of initial diagnosis, but acknowledge that there are no definitive data that demonstrate improved outcomes (1).

This large single institution study by Bernard et al. (2) adds significantly to the growing body of literature regarding the routine use of breast MRI to detect contralateral occult malignancies in patients with newly diagnosed breast cancer. The authors found contralateral cancers in 3.8% of patients, all of which were stage 0 or 1 at diagnosis and missed by mammography. These results parallel those of the ACRIN Trial 6667, where 3.1% of 969 women were found to have contralateral breast cancer detected solely by MRI (3). Together, these studies establish MRI as a more sensitive exam than mammography in detecting synchronous contralateral occult breast cancers. On the other hand, 17% and 12.5% of the studied patients, respectively, underwent biopsy of lesions that were deemed suspicious on MRI, and only 22% and 24.8% of those biopsies were subsequently found to be malignant on pathologic evaluation (2,3).

As earlier detection and treatment of these cancers has been associated with better outcomes, one might draw a conclusion that finding contralateral malignan-

cies in one in thirty patient justifies unnecessary biopsy in one out of every six patients. True to point, Bernard et al. concluded in their paper that “MRI should be considered in women newly diagnosed with breast cancer.” Are we really benefiting our patients overall by routinely ordering an MRI after diagnosis? Or, are we doing more harm than good? Where do we draw the line? For the same reasoning that we do not perform routine annual screening mammography on women at age 30, we should be cautious in performing routine MRI in every woman with breast cancer. Surely, we would find occult malignancies to warrant doing so, but at the cost of many unnecessary biopsies and a further inundation of mammography resources. As with the proverbial hammer and nail, should we perform an MRI in *every* woman who is diagnosed with breast cancer? Should we be hitting every nail on the head just because we hold a hammer and the nail has a head? Or, do we owe it to our patients to be more selective?

The cumulative incidence of contralateral breast cancer is estimated at 2–11%, placing these women at a two to six times higher risk than that of a woman in the general population developing her first cancer (4). It remains unclear, however, if these malignancies were present at the time of initial therapy and undetected by mammography, or if they developed at some point during surveillance. Yi et al. (5) reported that 5% of 542 patients with unilateral breast cancer who underwent contralateral prophylactic mastectomy were found to have an occult malignancy in the opposite breast. But what is the clinical significance of these cancers? Adjuvant chemotherapy has been shown to reduce the relative risk of contralateral cancer to 0.66, and hormonal therapy to 0.61 according to the Early Breast Cancer Trialists’ Collaborative Group (6). Whether this is reducing the risk of developing contralateral cancer at a later time or treating a cancer that was missed at initial diagnosis is unknown. Nonetheless, patients receiving adjuvant systemic therapies had fewer contralateral cancers. It

is assumed that earlier cancer detection will improve survival, but with vigilant routine screening of these patients during surveillance, metachronous lesions are still found early and still tend to be small and without evidence of nodal involvement (7). So, before we rush to opt for MRI in every woman with a diagnosis of resectable breast cancer, we need to be more clear on what is the clinical significance of the tumors that might have been missed if MRI was not done.

Finding an additional contralateral malignancy at the time of initial diagnosis may have the benefit of earlier treatment and possibly avoiding the need for second rounds of cancer treatments if found later. However, this must be balanced by the consequences of performing routine MRI. We often underestimate the angst felt by women who have been called back for an "abnormality" on their breast imaging. Increased anxiety and inflated levels of perceived risk may influence patients to choose bilateral mastectomy when it is not necessary. Second, breast MRI requires the use of gadolinium-based contrast agents, which have been shown to cause nephrogenic systemic fibrosis (NSF), a rare and debilitating disease that leads to fibrosis of the skin, joints, and eyes in patients with renal insufficiency (8). Significant delays in definitive surgical therapy also occur when further imaging is ordered after the initial MRI with subsequent biopsy of any suspicious lesions found. We must be careful, then, what we recommend to patients when 17% require additional unnecessary imaging studies and/or procedures to diagnose contralateral lesions in less than 4%. Lastly, according to statistics from the National Cancer Institute, 190,000 women will develop breast cancer this year in the United States, most of whom will be considered resectable (9). Do we really have enough trained breast imagers and resources to accommodate the number of MRIs that would be performed if all patients diagnosed with nonmetastatic breast cancer had an MRI as part of their diagnostic evaluation? These potential harms to the patient and strain on our health care system must be considered when we recommend routine consideration of MRI in patients with breast cancer, especially given that the clinical significance of finding contralateral cancers at the time of initial diagnosis is still unknown.

In light of the above arguments, Bernard et al. are to be commended for including in their main objectives an analysis of possible risk factors for contralateral cancers to attempt to identify a subgroup of

patients where MRI is most useful in decision making. After looking at various factors such as index tumor characteristics, age, menopausal status, family history, and breast density, it was determined that all of the contralateral cancers that were detected by MRI, but missed on mammography, were found in postmenopausal women. MRI did not detect any synchronous lesions in the contralateral breast of premenopausal women. In addition, when the authors analyzed the women in their study population that were age 70 and over, only one in 10 were recommended biopsy, and almost half of those were indeed malignant lesions (2). Perhaps performing MRI is most appropriate in postmenopausal women, and doing so in premenopausal women to look for contralateral lesions is not warranted. Furthermore, although not significant, the analysis showed a trend toward ER and HER2 positivity of the index tumor conferring an increased risk of contralateral cancers detected by MRI. Others have reported that an elevated Gail risk, an invasive lobular cancer histology, and multicentric disease are also predictive of finding contralateral cancer at the time of prophylactic mastectomy (5). Further study is needed in larger trials to confirm these findings and look for other subgroups of patients that may and may not benefit from MRI prior to operative therapy. As pointed out by the authors, the study population was predominantly Caucasian, and future studies should then include minority women as well.

One last point worth mentioning is that gene expression assays are being used with higher frequency in patients with early stage breast cancer to assess prognosis (10,11). In the study, patients with ER and HER2 positive index tumors were more likely to have occult contralateral cancers although not statistically significant. This raises the question, would molecular profiling of the index tumor be predictive of which patients are at high risk of contralateral cancers? It would be of interest to include the results of either or both of the available assays on the market to see if this might guide the use of MRI.

It is clear that there is some benefit to performing MRI in breast cancer patients, looking for contralateral cancers. But at what cost? The results of the analyses by Bernard et al. suggest that selective use is possible. We hope that further studies are undertaken to include minority patients, larger numbers overall, and to continue looking at predictive factors to help determine where MRI would be the most useful.

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