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Predictive value of axillary nodal imaging by magnetic resonance imaging based on breast cancer subtype after neoadjuvant chemotherapy

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ABSTRACT

Background: Magnetic resonance imaging (MRI) is commonly used to determine residual breast disease after neoadjuvant chemotherapy (NCT) for cancer. Few studies have assessed its role in predicting nodal response, by cancer subtype.

Methods: A retrospective review was completed using our institutional cancer registry. Patients who started NCT from 2005 to 2010 with clinically node positive disease were evaluated. Those who underwent post-NCT breast MRI were selected. Radiologic response was determined by an independent review. Nodal involvement was confirmed pathologically after surgery.

Results: A total of 135 patients underwent post-NCT breast MRI. The positive and negative predictive values of MRI are 93% and 26%, respectively. A subset analysis by cancer phenotype demonstrates triple negative cancers have the highest sensitivity (68%) and luminal cancers have the highest positive predictive value (100%).

Conclusions: This study demonstrates that MRI post-NCT, even by cancer subtype, cannot reliably predict residual nodal disease because of high false–negative rates (low negative–predictive value).

Background

Neoadjuvant chemotherapy (NCT) has become a widely accepted initial treatment for certain breast cancer phenotypes. Advantages include the ability of NCT to downstage disease in the breast to facilitate more limited breast resection and to assess response to treatment, which provides prognostic information.[1] NCT has also been shown to impact axillary disease, leading to a pathologic complete response in the axilla in up to 40% of patients. Similar to breast tumor response to NCT, axillary nodal response may vary by tumor phenotype.[2]

Historically, surgical management of a patient with node positive breast cancer is complete axillary node dissection,

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regardless of response to NCT. This standard of a mandatory level 1 and level 2 axillary lymph node dissection (ALND) was explored by the ACOSOG Z1071 clinical trial.[3] Z1071 sought to assess the false negative rate of sentinel node biopsy in patients with N1 breast cancer after completing NCT. Because nodal disease can be eliminated by NCT in these specific subgroups, axillary evaluation with a sentinel lymph node biopsy (SLNB) was assessed. Prior studies reported unacceptable false negative rates in patients who have undergone NCT, hypothesized to be due to therapy-related lymphatic changes, which impair the dye and/or colloid migration to the SLN.[4] The results of ACOSOG Z1071 suggested that performance of an SLNB in selected situations after NCT, however, can be safe and effective. SLNB in cases where both blue dye and radiolabeled colloid is used, the initially positive lymph node is identified and removed at the time of surgery, and when at least three SLNs are examined, reveal an acceptable false negative rate of <10%.[3]

Taken together, assessment of the axilla radiographically prior to surgery but after NCT would be clinically helpful to increase the likelihood of success of SLNB as the definitive axillary surgery. The primary aim of this study is to assess the ability of post-NCT magnetic resonance imaging (MRI) to accurately predict axillary nodal status in clinically node positive (cN1) breast cancer patients who receive NCT. A secondary aim is to determine whether the accuracy of MRI varies by breast cancer tumor subtype.

Methods

Patient population

The University of Pittsburgh Medical Center (UPMC) Network Cancer Registry was used to conduct a retrospective review of all patients who began NCT from 2005 to 2010. Our proposal was initially approved as a quality improvement project. After all data were collected and analyzed, the project was submitted to the UPMC Review Board to enable dissemination of the results. Clinical and pathologic data were then collected from each patient who was cN1 without distant metastatic disease before systemic therapy. The nodal status on presentation was determined from the cancer registry. A total of 252 patients were identified. All patients had clinical stage 2 or 3 invasive breast cancer. Chemotherapy was given as per institutional standards of care. All HER2 positive patients received trastuzumab. Precise chemotherapy regimens were not recorded due to lack of predicted effect on primary end point. Retrieved data were subsequently stored once deidentified in REDCap, which is a secure web-based application. A chart review was then conducted to determine which patients had an MRI before their operation. Use of breast MRI after NCT was at the discretion of the surgeon. A total of 151 patients were identified. After excluding those with missing data ($n = 4$), unavailable images for review ($n = 5$), a diagnosis of lymphoma ($n = 1$), and HER2 equivocal status by fluorescence *in situ* hybridization ($n = 6$), a total of 135 studies were available for analysis.

Magnetic resonance imaging

All diagnostic imaging was completed at the Magee-Womens Hospital of UPMC Breast Center, a fully accredited breast imaging program. From 2005 to 2006, all MRIs were performed on a 0.5 T dedicated breast MRI unit (Aurora Inc, North Andover, MA), using a matrix 256 × 256 and a slice thickness of 2 mm which yielded a 1.4 mmol in-plane resolution. Three T1-weighted postcontrast series were obtained after intravenous injection of 0.1 mmol/kg body weight gadodiamide, with an average acquisition time of 4 min for each series. Images were interpreted on an accompanying workstation that performed subtraction processing. This subtraction was the method of fat suppression. No active fat suppression technique was used. From 2006 to 2010, MRIs were performed on a 1.5 T system (Excite, GE Medical systems Milwaukee, WI) using parallel axial imaging with a 7-channel phase array breast coil (Invivo Inc, Gainesville, FL), a matrix of 320 × 320 with a slice thickness of 3 mm, which yielded an in-plane resolution of 0.9 mm. T1-weighted images were obtained with fat suppression before and four times after administration of 0.1 mm/kg body weight gadodiamide and interpreted with the use of a computer-aided detection software (Cadstream, Milwaukee, WI). This allowed subtraction, maximum intensity projection images, and kinetic information. Each MRI was completed in preparation for surgery at or after the last chemotherapy dose.

MRI determination of nodal involvement

Axillary involvement after NCT via MRI was determined from an independent review by one of three dedicated Breast Radiology Fellows at Magee-Womens Hospital of UPMC. The cases were distributed evenly and randomly assigned. Standard anatomic landmarks were used to identify lymph nodes within level 1 and level 2 of the axilla. A positive MRI result was defined as a node measuring greater than 1 cm, a thickened cortex of >3 mm, loss of the fatty hilum, or an irregular contour as compared with the contralateral axilla.

Pathologic analysis

Processing of all of the lymph nodes was performed by the hospital's Department of Pathology. Lymph nodes that are grossly negative are submitted entirely for analysis and are placed into one cassette. If the nodal thickness is greater than 4 mm, it is further sectioned parallel to the long axis and submitted entirely. For grossly positive nodes, representative sections are processed for eventual analysis.

The degree of nodal disease for the study was based on the review of paraffin-embedded slides evaluated using either routine hematoxylin and eosin staining or immunohistochemical (IHC) staining, as indicated by cancer subtype. Microscopic or macroscopic disease was considered to be positive for nodal involvement. If no tumor cells or isolated tumor cells were reported, then the lymph node was deemed to be negative. American Society of Clinical Oncology (ASCO)-College of American Pathologists (CAP) guidelines were used for estrogen receptor (ER), progesterone receptor (PR), and HER2 positivity or negativity on an initial core biopsy. ER and PR