Standardized uptake values from PET/CT and PET/MRI in metastatic breast cancer: correlations and clinical implications

Authors

Presenting: Akshat Pujara (New York University School of Medicine)

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Purpose: The development of molecular MRI presents the opportunity to fuse PET and MR data without the ionizing radiation of CT. Before PET/MRI can be introduced into clinical practice, MR attenuation correction (MRAC) must be validated using CT attenuation correction (CTAC) as the gold standard. Thus, the aim of this study was to compare standardized uptake values (SUVs) from MRAC with those from CTAC specifically in the setting of metastatic breast cancer with regards to 1) breast cancer metastases, 2) normal structures, and 3) objective lesion conspicuity.

Materials and Methods: In this IRB-approved prospective study, 35 breast cancer patients (age 37 - 78 years, mean 58) underwent clinical 18-FDG PET/CT followed by PET/MRI between 8/2012 and 9/2013. One reader measured maximum and mean SUVs in breast cancer metastases (one per organ per patient) and ten normal structures from PET/CT and PET/MRI, which were compared using Spearman rank correlations. Metastasis/background SUV ratios and percent decrease of SUVs between exams were calculated.

Results: PET/MRI identified all patients with bone (n=16), liver (n=7), and non-axillary lymph node (n=8) metastases; PET/CT did not initially detect bone and liver metastases in one patient each. In thirty-one breast cancer metastases to these three organs, SUVmax and SUVmean from PET/MRI and PET/CT correlated strongly overall ($\rho = 0.84, 0.85$) and on an organ-specific basis ($\rho = 0.72 - 0.93$). Normal structures also demonstrated strong correlations between MRAC- and CTAC-derived SUVs ($\rho = 0.78$ SUVmax and SUVmean). SUV ratios of organ-specific metastases/corresponding normal tissue were significantly higher from PET/MRI in liver and non-axillary lymph nodes compared to PET/CT ($P < 0.02$), with no significant difference in bone. Percent decrease of SUVs between PET/CT and PET/MRI was significantly smaller in liver and non-axillary lymph node metastases compared to corresponding normal tissue ($P < 0.008$), with no significant difference between bone metastases and normal bone.

Conclusion: SUVs from PET/MRI correlate well with those from PET/CT in breast cancer metastases and normal structures. Higher metastasis/background SUV ratios from PET/MRI and smaller percent decrease of SUVs between PET/CT and PET/MRI led to increased conspicuity of liver and non-axillary lymph node metastases on PET/MRI.

Clinical Relevance: PET/MRI-derived standardized uptake values may be used for quantitation of 18-fluorodeoxyglucose activity. Accounting for differential pharmacokinetics of individual organs may allow PET-based imaging exams to be tailored to specific sites of breast cancer metastases.

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Diffusion-Weighted MRI Predicts Recurrence Risk in Invasive ER+/HER2- Breast Cancers

Authors

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Purpose: Oncotype DX (GenomicHealth, Inc) is an expensive multi-gene breast cancer tissue assay that helps guide adjuvant treatment by predicting 10-year relative recurrence risk. Breast MRI provides whole tumor characterization, and has shown promising correlation with prognostic factors. An imaging-based recurrence risk assessment that is non-invasive and not prone to sampling error may provide a cost-effective way to facilitate individualized therapies. We sought to evaluate the prognostic potential of MRI biomarkers by investigating associations with Oncotype DX scores.

Materials and Methods: After IRB approval, we retrospectively evaluated 106 consecutive women with ER-positive/HER2neu-negative, node-negative invasive breast cancer. Each underwent pre-surgical 3T breast MRI and Oncotype DX testing from 2010-2012. MRIs included dynamic contrast-enhanced (DCE) and diffusion-weighted imaging (DWI) (b=0, 800 s/mm^2) sequences. DCE features of lesion size, morphological type (mass; non-mass enhancement) and kinetics (initial peak enhancement; curve type); and DWI features of apparent diffusion coefficient (ADC) and contrast-to-noise ratio (CNR) were assessed. Oncotype DX scores were stratified into low (<18), moderate (1830), and high (>30) risk groups. Associations between MRI features and Oncotype DX were evaluated by Wilcoxon rank-sum and Fisher's exact tests.

Results: The 106 invasive tumors (median size=19mm, range 7-130mm) included ductal (n=91), lobular (13), and mixed (2) histologies. Tumor maximum ADC values were significantly lower in high (n=5, 1.17x10^-3 mm^2/s) versus low (n=50, 1.72x10^-3 mm^2/s, p=0.02) and moderate risk groups (n=51, 1.87x10^-3 mm^2/s, p=0.01), and mean ADC values showed a similar trend (p=0.09). CNR was also higher in high risk (3.27) versus low (2.32, p=0.02) and moderate risk groups (2.42, p=0.01). There were no differences in DWI parameters between low and moderate risk groups (p>0.05). There were no significant associations between DCE features and Oncotype DX scores (p>0.05).

Conclusion: DWI may provide complementary and predictive information regarding tumor recurrence risk for patients diagnosed with invasive breast cancer and warrants further investigation.

Clinical Relevance: Our study suggests that DWI characteristics correlate with Oncotype DX Recurrence Scores and may be helpful in identifying aggressive tumors with high recurrence risk in need of a more tailored treatment.

Accuracy of Abbreviated MRI for Breast Cancer Screening

Authors

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Purpose: To study the utility of an abbreviated breast MRI protocol for breast cancer detection in a screening population.

Materials and Methods: A retrospective IRB approved study was performed on 260 consecutive high risk screening MRIs in 260 women at an academic center from 01/01/2012-06/30/2012. Four breast radiologists with 8-28 years' experience participated in the study. The abbreviated breast MRI protocol (AP) consisted of axial pre-contrast, single post-contrast, and subtraction sequences. For phase one of the study, comparison studies were not available. Maximum intensity projection (MIP) images were coded as positive, indeterminate, or negative and the AP evaluated for suspicious lesions and need for recall for complete MRI. T2-weighted images were then reviewed and final recommendations noted. Radiologists' interpretation time was recorded. Phase two of the study provided comparison imaging and callback results were re-analyzed. Recall rates were compared to the initial prospective interpretation, which included the complete MRI with dynamic imaging and kinetic analysis.

Results: Acquisition time for the AP was 3 minutes, AP with T2 8 minutes, and full MRI protocol 17 minutes. 155/260 (59.6%) patients had heterogeneously dense or dense breasts. Our cohort of 260 patients with average age of 52 years (26-78yrs) had 7 cancers (4 invasive, 3 in situ). 5/ 7 cancers were identified in heterogeneously dense or dense breasts. MIPs were positive in 3/7 (43%), indeterminate in 3/7 (43%), and negative in 1/7 (14%) cancers. 5/7 cancers were identified by all readers, 1/7 cancers by 3 of 4 readers, and 1/7 cancers by 2 of 4 readers. The initial mean callback rate without comparison imaging was 25.2% (20.7-28.8%); however, with comparisons, this decreased to 13.6% (10.8%-18.4%; sensitivity 63-82%, specificity 91-94%, PPV 51-70%, and NPV 92-99%; kappa=0.56 (CI 0.55-0.58)). T2 images changed management in only 3.0% (1.2-6.5%) of cases. Average read time for the AP with T2 was 2.5 minutes (1.6-4.0mins).

Conclusion: Our study shows that the abbreviated MR protocol can reliably detect breast cancer, with improved specificity compared to whole breast screening ultrasound. Further studies need to be performed to determine how this can be incorporated into a supplemental screening program.

Clinical Relevance: Legislation requiring patient notification of breast tissue density and the increased risk of cancer causes an increase in supplemental screening. Whole breast screening ultrasound has varied reported sensitivity and suboptimal specificity. Our study suggests an abbreviated breast MRI protocol may be a viable alternative for supplemental screening.

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Clinical Impact and Quantification of Prone to Supine Position in Breast MRI

Authors

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Purpose: Standard diagnostic breast MRI utilizes prone positioning, however breast surgery is performed supine. Breast MRI may be performed prior to breast conserving therapy (BCT) to identify the extent of disease and assist with surgical planning. To date studies on diagnostic MRI for newly diagnosed breast cancer have not shown an improvement in re-excision rates. We sought to evaluate the impact of prone to supine positioning on tumor deformation and displacement, and potentially aid in planning BCT and improving the re-excision rates.

Materials and Methods: As part of our Phase I clinical trial on investigating intraoperative MRI for BCT margin assessment in the Advanced Multi-modality Image-Guided Operating (AMIGO) suite, 7 patients with breast cancer were evaluated with prone diagnostic and supine pre-procedural dynamic contrast enhanced MRI (DCE-MRI). First post-contrast prone and supine images were rigidly registered based on thoracic cavities using the Mutual Information criterion, and 3D tumor models were created using SegmentCAD module in 3D Slicer. The 3D models were further registered using Iterative Closest Point (ICP) registration. Sixty-five geometric, structural and heterogeneity metrics were computed using HeterogenityCAD module. Some of the measures included volume, surface area, compactness, maximum 3D diameter, sphericity etc. Distance of the tumor center from nipple, chest wall and skin were also computed.

Results: 3D models of the 7 tumors in supine and prone position were superimposed after ICP registration. Mean percent changes (calculated as prone minus supine tumor metrics) were computed: volume = -20.3±46.61; surface area: -3.4±27.96; max 3D diameter: 11.2±26.01; sphericity = -8.3±11.0, compactness = -15.3±26.15; spherical disproportion = 11.5±47.29; Hausdorff distance (mm) = 5.6±2.3, tumor displacement in right-anterior-superior coordinates = (0.2±43, 29.5±22.5, 4.39±34.87 mm). Change in distances from: chest wall = 21.0±10.2 mm; nipple = 13.8±12.7 mm; and skin = -0.1±3.3 mm.

Conclusion: Substantial tumor deformity occurs between prone and supine positioning. Tumors are larger in volume and surface area, and closer to the nipple and chest wall on supine compared to prone images. Further studies are necessary to validate the utility of supine MRI to plan BCT and potentially reduce re-excision rate.

Clinical Statement: Standard diagnostic breast MRI is performed with prone positioning, however breast surgery is done supine. We evaluated the impact of prone to supine positioning on breast tumor deformation and displacement. Supine diagnostic MRI may assist in achieving more accurate tumor delineation and in surgical planning for breast conserving therapy.

Caption: Prone (blue) and supine (green) tumor imaging

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Association of menstrual cycle timing with BIRADS, background parenchymal enhancement, and PPV in screening Breast MRI

Authors

Presenting: Yolanda Bryce (Memorial Sloan Kettering Cancer Center)

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Purpose: To assess whether there is an association between outcome of screening MRI in premenopausal women and the stage of the menstrual cycle in which the study is performed.

Materials and Methods: All premenopausal women who underwent a screening MRI in 2011 who clearly stated their menstrual cycle day where included in the study and among other factors indication, BIRADS, background parenchymal enhancement (BPE), presence or absence of prior study, and positive predictive value of any subsequent biopsy (PPV3) were assessed. In total, 759 patients were included in the study. Chi-square test and Fisher's exact test were used to calculate level of significance.

Results: Results are presented in Table 1. There was no statistically significant association between week of menstrual cycle and BPE (p=0.628), final BIRADS assessment (0.463), or PPV3 (p=0.174).

Conclusion: Outcome of screening MRI in premenopausal women does not vary significantly as a function of the week of the menstrual cycle.

Clinical Relevance: Timing screening breast MRI for the second week of the menstrual cycle may not make a difference in outcome and may not be necessary.

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Mammographically and sonographically occult lesions and background parenchymal enhancement: MRI-DCE kinetic analysis

Authors

Presenting: Nathaniel Margolis (NYU School of Medicine)

Nathaniel Margolis (NYU School of Medicine), Alana Lewin (NYU School of Medicine), Linda Moy (NY), Amy Melsaether (NYU)

Purpose: Dynamic contrast enhanced (DCE) breast MRI is highly sensitive, however its high false positive rate leads to many unnecessary biopsies. To better differentiate between normal tissue and malignant and benign lesions, we compared MRI-DCE kinetic features of background parenchymal enhancement (BPE) with mammographically and sonographically occult malignant and benign lesions.

Materials and Methods: Retrospective kinetic analysis of malignant and benign lesions and BPE controls in patients who underwent MR guided biopsy was performed using computer-automated detection software. BPE controls were randomly selected areas of enhancement in the contralateral breast. Twenty-one consecutive malignant lesions from 2007-2009 and 64 consecutive benign lesions from 2009 were included. Region of interest analysis was performed; the most enhancing portion was selected for kinetic curve analysis to calculate peak enhancement (PE), time to peak enhancement (TTP), and signal enhancement ratio (SER).

Results: There was significantly greater PE (268% vs 204%, p=0.002) and shorter TTP (281 s vs 370 s, p=0.01) in malignant lesions versus their BPE controls. Greater PE was also seen in malignant nonmass enhancement versus BPE controls (290% vs 189%, p=0.007) and a trend toward shorter TTP (255 s vs 323 s, p=0.07). Malignant masses demonstrated significantly shorter TTP versus BPE controls (305 s vs 413 s, p=0.04) and a trend toward greater peak enhancement (248% vs 218%, p=0.22). While there was a significantly shorter TTP for benign lesions versus BPE controls (262s vs 297s, p=0.001), there was no difference in PE (270% vs 267%, p=0.73). There was no significant difference between benign and malignant lesions in terms of TTP, PE, or SER. There was a strong positive correlation between BPE peak enhancement and benign lesion peak enhancement (r= 0.55). There was no correlation between BPE peak enhancement and malignant lesion peak enhancement (r= -0.07)

Conclusion: For lesions only seen on MRI, similarity of PE between the lesion and BPE suggests benignity. Lesion PE greater than that of BPE suggests malignancy. Mammographically and sonographically occult benign and malignant lesions, however, cannot be reliably separated based on kinetics without comparison to BPE. Further study is warranted to assess whether this metric could be used to reduce unnecessary biopsies.

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Are patients with high breast MRI background parenchymal enhancement at greater risk for breast cancers with poor prognostic markers?

Authors

Presenting: Eralda Mema (Columbia University Medical Center)

Eralda Mema (Columbia University Medical Center), Ellie Kwak (Columbia University Medical Center), Victoria Mango (Columbia University Medical Center), Lauren Friedlander (Columbia University Medical Center), Elise Desperito (Columbia University Medical Center), Rend Alkhalili (Columbia University Medical Center), Ralph Wynn (Columbia University Medical Center), Richard Ha (Columbia University Medical Center)

Purpose: To investigate an association between breast cancer prognostic markers and breast MRI background parenchymal enhancement (BPE), a possible risk factor for breast cancer.

Materials and Methods: A HIPAA compliant retrospective study from 1/2010 to 2/2014 identified 328 breast cancer patients who had pre-operative assessment of prognostic markers including age, menopausal status, lymph node status, tumor size, Ki-67 index, ER/PR/HER2 status, nuclear grade and histologic subtype. These patients underwent breast MRI and 3 breast fellowship trained radiologists by consensus classified contralateral breast BPE. The level of BPE was assessed using a combination of unenhanced and post contrast-enhanced sagittal T1-weighted images and was recorded on a 4-point scale in accordance with BI-RADS categories. Student's t test and Chi square test were used for analysis using the collapsed BPE categories (1/2 = low vs. 3/4 = high).

Results: Patients with high BPE were significantly younger [mean age 49.6 years, 95% CI (47.4-51.7)] compared to patients with low BPE [57.0 years, 95% CI (55.5-58.6), ($p < 0.0001$)]. More pre-menopausal patients demonstrated high BPE (52.7%, 59/112) compared to post-menopausal patients (21.8%, 47/216), ($p<0.001$). High BPE was associated with larger tumors [mean size, 2.64 cm, 95% CI (2.32 to 2.98)] compared to low BPE [2.42 cm, 95%CI (2.19-2.65)] but was not significant ($p=0.2630$). No significant association with high BPE was present in the following patients: Patients with axillary lymph metastasis compared to no lymph node metastasis (25% vs. 32.6%, $p=0.2733$); patients with high nuclear grade tumors compared to intermediate/low grade tumors (21.5% vs. 23.8%, $p=0.8403$); patients with high (>=15%) Ki-67 index tumors compared with low (< 15%) Ki-67 index tumors (37.5% vs. 37.2%, $p=0.9687$); patients with HER2+ tumors compared to ERorPR+/HER- tumors, (29.3% vs. 32.5% $p=0.7217$); patients with triple negative tumors compared to ERorPR+/HER- tumors, (30.0% vs. 32.5% $p=0.8379$); patients with invasive ductal carcinoma compared to invasive lobular carcinoma (31.5% vs. 31.6%, $p=1.0$).

Conclusion: High BPE is associated with younger premenopausal women with breast cancer. High BPE is not associated with other poor prognostic markers including positive lymph node status and tumors with large size, high Ki-67 index, HER2+/triple negative status and high nuclear grade.

Clinical Relevance: Similar to mammographic density, breast MRI BPE has been shown to be a possible risk factor for breast cancer. Whether women with high BPE are at greater risk for breast cancers with poor prognostic markers is important to understand in order to develop risk prevention strategies.

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