

Breast Vascular Maps with Gadobenate Dimeglumine (Gd-BOPTA): Association between Invasive Cancer and Ipsilateral Increased Vascularity

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Since the first use of Gd-DTPA, clinical breast MR studies have been performed using this or similar agents characterized by vascular/interstitial biodistribution, with a T1 relaxivity ranging 4.3–4.8 mM⁻¹s⁻¹, resulting in a comparable enhancement. Gd-BOPTA (MultiHance, Bracco Imaging SpA, Italy) is also a two-compartment agent (12–14), but it shows a partial hepatobiliary biodistribution and a two-fold higher T1 relaxivity (9.7 mM⁻¹s⁻¹) compared to Gd-DTPA due to a capacity for weak and transient interaction with serum albumin, a property shown to be advantageous for MRI of brain lesions and MR angiography (MRA). The aims of this study were to compare three Gd-BOPTA with a standard dose of Gd-DTPA for MR evaluation of breast vessels and to evaluate the accuracy of one-side increased vascularity as an indicator of ipsilateral breast cancer on Gd-BOPTA-enhanced MR images.

METHODS AND MATERIALS

The present study was a retrospective evaluation of MR exams and pathology files of patients, as part of a phase II study to compare three different doses of Gd-BOPTA with a single dose of Gd-DTPA for contrast-enhanced MRI of the breast (29). Ninety-five women (age 54.3±12.0 years) with known or suspected breast cancer received in random fashion either Gd-BOPTA at 0.05 (n=24), 0.1 (n=24), or 0.2 (n=24) mmol/kg or Gd-DTPA at 0.1 (n=23) mmol/kg (2 ml/sec; saline flush, 20 ml). 1.5-T MRI of the breast was performed in prone position with double breast coil using a 3D T1-w. FLASH sequence (TR ≤13 msec, flip angle 20–30°, in-plane resolution ≤2 mm², no-gap ≤ 3-mm partitions). One plain and five contrast-enhanced images were acquired beginning at 0, 2, 4, 6 and 8 minutes post-contrast; only plain and first dynamic phase at 2 minutes was used for the current study. Coronal and axial MIPs were obtained from the subtracted (contrast-enhanced minus pre-contrast) images for a blinded random assessment. A score ranging 0–3 (poor–extensive) was assigned to each pair of MIPs on the basis of the number, length and conspicuity of the vessels. A second evaluation of the 72 patients whose MR examination was performed with Gd-BOPTA was performed: when one-side vascular MIP was considered increased in comparison with the other, the patient was considered to have “one-side increased vascularity”.

Of the 72 patients studied with Gd-BOPTA, 69 had pathologic examination of the breast lesion after surgical excision (n=63) or core biopsy (n=6). When a malignant lesion was found at pathological examination in the breast with one-side increased vascularity at MIP maps, asymmetry was considered a true positive associated finding.

RESULTS

Considering the four patients groups as a whole, 68 patients (and 70 breasts, due to two bilateral cancers) were found afflicted with cancer. The maximum diameter of the main malignant lesions was 24.0±18.7 mm. The scores assigned to MIPs obtained with Gd-BOPTA at 0.05, 0.1 and 0.2 mmol/kg were 1.90±1.07, 1.94±0.95 and 2.00±0.75, respectively. The corresponding score with Gd-DTPA at 0.1 mmol/kg was 1.24±0.84. Global variability analysis revealed significant differences ($P = 0.018$, Kruskal-Wallis). Significantly higher scores for each of the Gd-BOPTA dose groups compared to the Gd-DTPA dose group were found ($P = 0.002–0.044$ (Mann-Whitney U test)).

Two of the 69 patients with pathologic control studied with Gd-BOPTA, and for whom breast lesion pathology was available, had bilateral cancers with symmetric breast vascular maps. The remaining 67 lesions comprised 50 invasive cancers (invasive ductal carcinoma, n=43; invasive lobular, n=4; invasive ductal/lobular, n=3) and 17 benign lesions. Asymmetry of breast vascularity due to the presence of one-side increased vascularity was observed in 47 of the 67 patients. In 44 (94%) of these 47 patients the increased vascularity was associated with histologically-proven ipsilateral breast cancer. The three false positives were a 7-mm papillomatosis of (0.1 mmol/kg dose), and a 8-mm papilloma of and a 15-mm hyperplasia (0.2 mmol/kg dose). Considering 6 false negatives, sensitivity, specificity, PPV and NPV of one-side increased vascularity as associated with ipsilateral breast cancer was 88% (44/50), 82% (14/17), 94% (44/47), and 70% (14/20), respectively, giving an overall accuracy of 87% (58/67).

DISCUSSION

MRA of the breast is intrinsically integrated into the standard breast examination when a contrast-enhanced dynamic 3D imaging technique is used. Our experience reveals that Gd-BOPTA at doses as low as 0.05 mmol/kg bodyweight enables high quality vascular maps of the breast to be obtained and that the angiographic effect at this and higher doses is significantly greater than that obtained with a standard 0.1 mmol/kg dose of Gd-DTPA, in agreement with previous MRA studies conducted with Gd-BOPTA in other vascular territories. Our findings also suggest that vascular map asymmetry may be a finding frequently associated with ipsilateral invasive breast cancer: sensitivity and specificity values of 88% and 82%, respectively, suggest that vascular asymmetry could be considered a corollary MR sign of invasive breast cancer.

The presence of breast ipsilateral vascular prevalence associated with cancer may be due to reduced flow resistance in the tumor vessels, to higher metabolism of the tumor, to angiogenic stimulation of the whole breast or to a combination of these possibilities. In our opinion the first two possibilities may play a role in determining whole breast increased vascularity when the cancer is relatively large in comparison with the dimension of the breast. Conversely, angiogenic stimulation by the tumor to the whole breast is more likely when the cancer is small.

In conclusion, the present study suggests that Gd-BOPTA may have preferential properties over Gd-DTPA for MR evaluation of breast vascularity and that one-side increased breast vascularity is frequently associated with ipsilateral invasive breast cancer. However, further work is clearly warranted to assess the additional value of vascular map asymmetry as a sign of breast malignancy compared with the established dynamic and morphologic criteria. Additional work should focus not only on patients with invasive cancer, but also on patients with in-situ cancers and in a larger population of women with benign lesions or without lesions at all.

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