Patterns of Enhancement on Breast MRI:
What Do They Mean and What to Do Next

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Dynamic contrast enhanced MR imaging of the breast is increasingly used in addition to the conventional breast imaging methods, mammography and ultrasound, to improve the detection and characterization of primary and recurrent breast cancer, and to evaluate response to therapy. The sensitivity of MRI for detection of breast cancer is very high, reported over 90% in most studies [1-2] and approaching 100% in invasive tumors. However, in ductal carcinoma in situ (DCIS) the sensitivity varies between 40% and 100% [3]. False negative exams can occur with DCIS and also with invasive ductal and lobular malignancies. The specificity of breast MRI was reported between 37% and 100%, in most studies varied from 50% to 70% [1]. The relatively low specificity of breast MRI is a disadvantage, and rigorous criteria for the interpretation of breast MRI findings have been proposed [4], as well as new imaging techniques based on molecular and cellular properties of tissues have been investigated [5-6].

How to interpret patterns of enhancement

Lack of enhancement: Highly predictive of benign finding, NPV for malignancy 96% [7]. Rarely non-enhancing tumors may include DCIS [3] and invasive carcinomas [7].

Benign morphologic criteria: Many benign breast lesions can enhance, non-proliferative lesions (mild hyperplasia, fibroadenomas), proliferative lesions without atypia (sclerosing adenosis, radial and complexing sclerosing lesions, moderate hyperplasia, intraductal papillomas), and atypical lobular and ductal hyperplasia.

Typical benign features for masses: smooth margins NPV 95%, dark internal septations NPV 98% [7]. If mass is lobulated and shows no or minimal enhancement, it is likely benign NPV 100% [7]. If mass is lobulated and shows moderate to marked enhancement NPV is 67%. Correlation between the enhancing portion of the lesion and T2-weighted signal is helpful [8] *(see T2W)*. In non-mass regional enhancement, the mild degree of enhancement is suggestive of benign etiology, NPV 92%.

Malignant morphologic criteria: Irregular or spiculated margins PPV 84%-91% [7], rim-enhancement PPV 40-86% [1], ductal distribution of enhancement, linear and/or branching PPV 24-85% [1], heterogeneous internal enhancement, and enhancing internal septations are features associated with malignancy. The moderate to marked degree of enhancement in non-mass regional enhancement has PPV 59% [7]. Regional enhancement with micronodular (stippled) pattern has been reported in both benign (fibrocystic disease) and malignant (DCIS) abnormalities [7].

Enhancement kinetics:

Type I: progressive enhancement curve – continuously increasing enhancement at each scan post contrast. It is usually associated with benign disease, 83% benign and 9% malignant [10], sensitivity and specificity to indicate a benign lesion is 52.2% and 71% [2].

Type II: plateau enhancement curve – initial increase and subsequent flattening of enhancement curve, has sensitivity 42.6%, and specificity 75% [2] as an indicator of malignancy.

Type III: washout enhancement curve – initial rise and subsequent decrease of enhancement. It is usually absent in patients with benign disease, specificity 90.4 % but has sensitivity of only 20.5% [2].

Both type II and III curves should be considered as suspicious for malignancy. The specificity of breast MRI is improved when both morphological and kinetic features are used in the interpretation [11]. Due to the overlap between different enhancement kinetics, it is not recommended to use the kinetics assessment alone.

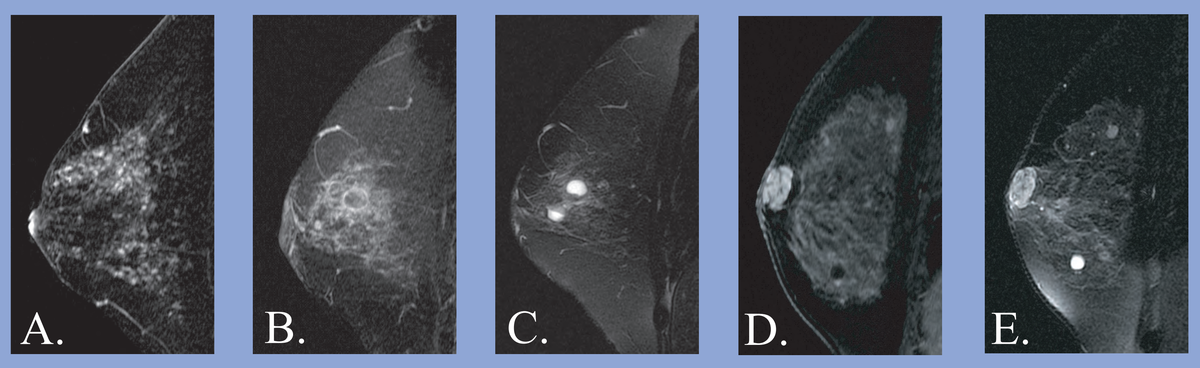


Figure 1. Benign features.
A. Regional micronodular (< 5mm stippled/puntate) enhancement in fibrocystic breast. B. Thin rim-enhancement around cyst in fibrocystic breast. Comparison to T2W image C. is important to recognize this as benign finding in this patient. D. Oval mass with smooth margins and enhancement with dark internal septations, typical for fibroadenoma. The assessment of lesion on T2W images E. is most helpful in younger patients. Myxoid fibroadenomas typical for young women demonstrate increased T2 signal. However, there are age-related sclerotic changes in fibroadenomas in older women, and greater prevalence of fibrotic low signal fibroadenomas in women over 50 reduces diagnostic value of T2 criterion [9].

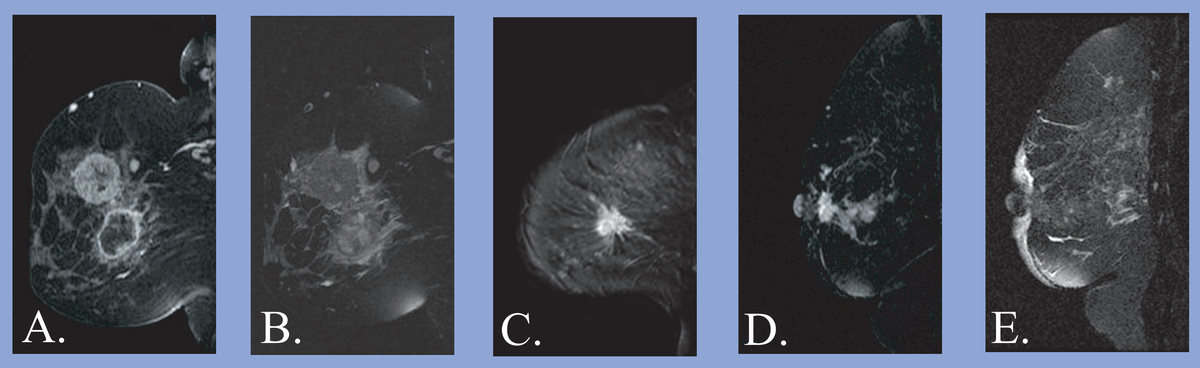
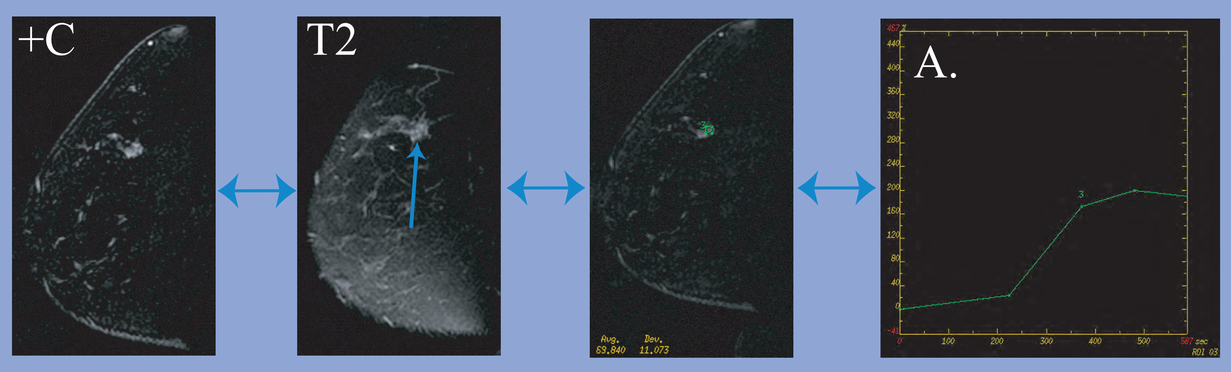


Figure 2. Malignant features.
A. Two masses - thin rim enhancement 4 o'clock left breast and heterogeneous enhancement with enhancing internal septations 2 o'clock - poorly differentiated ductal carcinoma with necrosis and signet ring cell features. B. T2W image of masses shows low signal characteristic of malignant lesions. C. Spiculated margins in infiltrating carcinoma with ductal and lobular features. D. Retroareolar mass with irregular margins and heterogeneous enhancement - infiltrating ductal carcinoma. Mass has low signal on T2W image E. typical for malignancy. Note focal skin thickening.



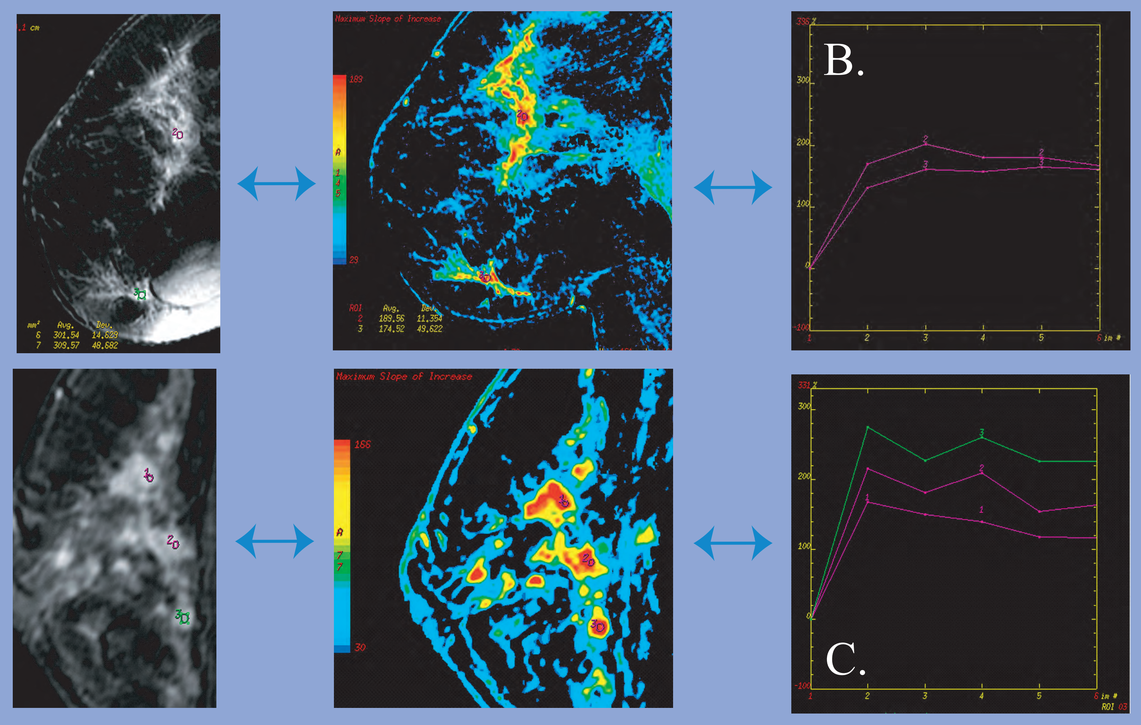


Figure 3. Enhancement curves.
A. Type I curve in a lesion stable over 2 years. This patient had contralateral breast cancer. Note that 8 mm mass shows minimal lobulations and T2 bright signal (arrow).
B. Type II curve in invasive lobular carcinoma, multifocal and bilateral. Note non-mass-like regional enhancement. Foci with maximum slope of signal increase post contrast (red) were selected for ROI.
C. Type III curve in infiltrating lobular carcinoma, multifocal. Clumped non-mass-like enhancement was found in all four quadrants. Note that ROIs were selected in rapid peak enhancement areas.

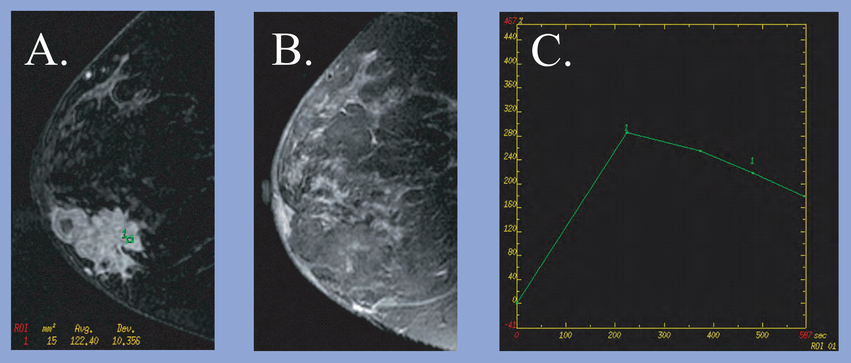
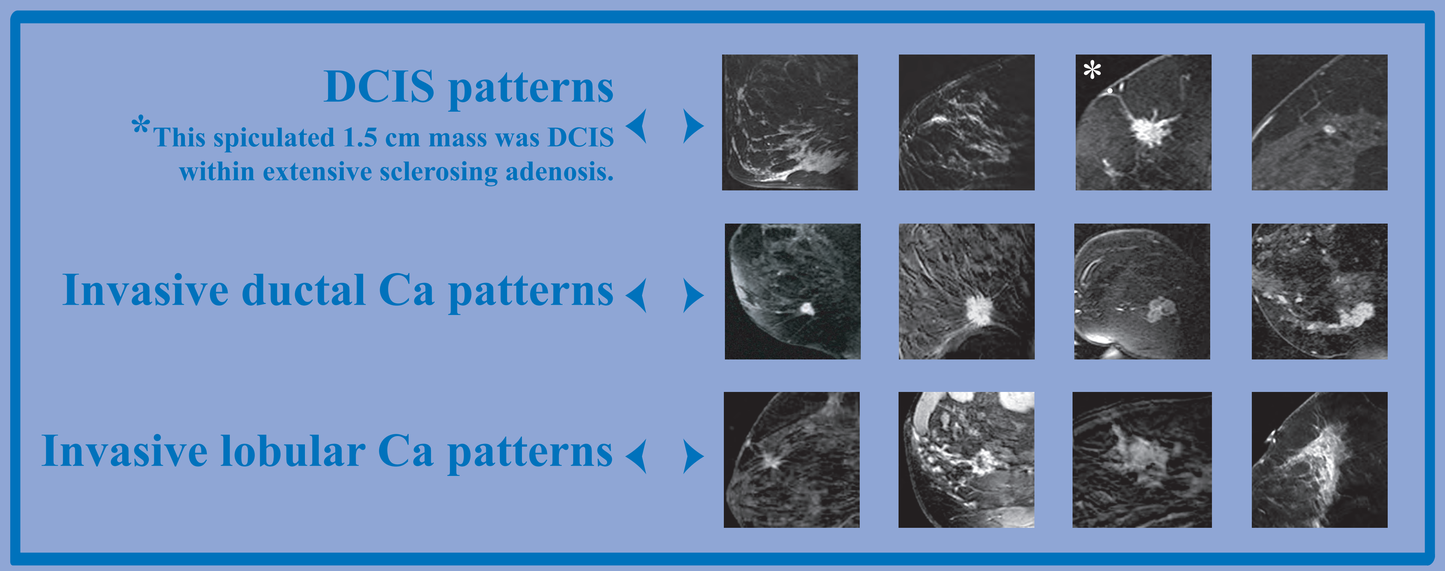


Figure 4. 28-year-old woman, 3 months post partum, with palpable mass - infiltrating ductal carcinoma, moderate to poorly differentiated. A. Contrast enhanced image shows irregular mass with irregular and spiculated margins typical for invasive carcinoma. B. T2W image shows low signal within the enhancing portions of mass. C. Enhancement curve is type III, with rapid peak enhancement and washout delayed-phase.



How to image

Dedicated breast surface coils: Some coils are equipped with the compression plate, advantage of compression - minimization of patient motion, decrease in the thickness of the breast and shorter imaging time. Too excessive compression can compromise enhancement of breast tumor leading to false negative result.

Contrast enhancement: Most tumors can be visualized only after intravenous contrast administration, usual dose 0.1 mmol/kg injected as a bolus often followed with 10-20 cc saline flush (hand or power injector). High-resolution T1-weighted images without or with fat saturation, thin slice thickness and no gap are performed for optimal sensitivity, best obtained with 3D gradient echo sequences in less than 2 minutes: allows for acquisition of several post-contrast sequences and both lesion morphology and enhancement kinetics can be analyzed. Morphological features are best evaluated with high spatial resolution imaging, thus imaging with higher matrix and smaller field of view is recommended [14]. Architectural feature analysis can be performed at any point during the first 4 minutes and 30 seconds following contrast injection [15].

Trade-off between spatial and temporal resolution: By increasing the spatial resolution (512 imaging matrix), at the expense of temporal resolution, the assessment of subtle morphologic details of breast lesions improves significantly and leads to the increase in diagnostic accuracy. There is loss of some kinetic information regarding enhancement rates (wash in rate within the first 2 minutes), but it was shown that the enhancement rate is a relatively weak diagnostic criterion with broad overlap between benign and malignant lesions. However, the kinetic information regarding time enhancement course pattern is preserved with acquisition times of up to 2 minutes [14].

Interpretation pitfalls:

Post contrast scan time > 2 mins - the washout may no longer be appreciated when the first post contrast images are obtained too late after peak enhancement while documenting the descending part of the signal time curve.

Kinetics ROI too large or in suboptimal location - optimal ROI should be adjusted to the size of lesion 2-10 mm and should be placed in the region of strongest enhancement on the first post-contrast scan, best appreciated on the maximum slope of enhancement color maps (Figure 5.).

Ambiguity of imaging findings - i.e. post-surgical changes, physiologic breast changes

When to image

- During first half of the menstrual cycle (days 3 -14) [12] to minimize false positive results due to the enhancement of normal breast parenchyma.
- 28 days or later after surgery [13] to assess for residual disease. MRI may not be able to exclude small foci of residual tumor, but it may be helpful in identifying gross residual disease or unsuspected multifocal-multicentric tumor. Findings suggestive of residual tumor: thick > 5mm, irregular or nodular enhancing rim around the resection cavity. Postoperative site can enhance up to 6 months without XRT and up to 18-24 months after XRT [1].

Whom to image – indications

Screening

- high risk of breast cancer (BRCA1/2 mutation carriers)
- strong family history of breast cancer, especially when conventional breast imaging limited due to conditions that may impair interpretation, such as silicone and non-silicone augmentation or radiographically dense breasts
- contralateral screening in a patient newly diagnosed with breast cancer
- search for occult primary in women with axillary metastases
- previous biopsy-proved atypia or lobular carcinoma in situ

Problem solving/therapy planning or follow up

- problematic mammogram, one view abnormality, other modalities in-conclusive
- determination of local extent of malignancy, chest wall involvement, preoperative staging
- postoperative assessment - postlumpectomy for residual disease, especially when positive margins
- treatment response in neoadjuvant chemotherapy
- invasive lobular carcinoma histology, evaluation of extent, multifocality, and multicentricity
- infiltrating ductal carcinoma histology , determination of the extent of disease, particularly in breast conservation candidates
- recurrence of breast cancer – suspicion of recurrence when clinical and/or mammographic findings are inconclusive and postoperative tissue reconstruction with tissue transfer flaps
- differentiation between scar and tumor

T2 - weighted signal:

T2 hyperintensity within the viable (enhancing) portion of the lesion is highly suggestive of benign histology [8]. However, T2 signal intensity is not reliable predictor of benignity in irregular or spiculated masses. Colloid carcinoma can present as smooth T2 bright and non-enhancing mass [7]. On T2-weighted images, breast cancers are more likely (87%) iso- or hypointense with respect to breast parenchyma (Figures 4-5) [9]. Dark internal septations on T2-weighted images are typical for benign fibroadenomas (Figure 1.). Rarely, adenoid cystic carcinoma may show internal dark septations that do not enhance [7]. T2-weighted signal intensity of breast lesion is used as a secondary criterion to confirm the diagnosis of benignity established by the primary morphologic features not to rule out breast cancer.

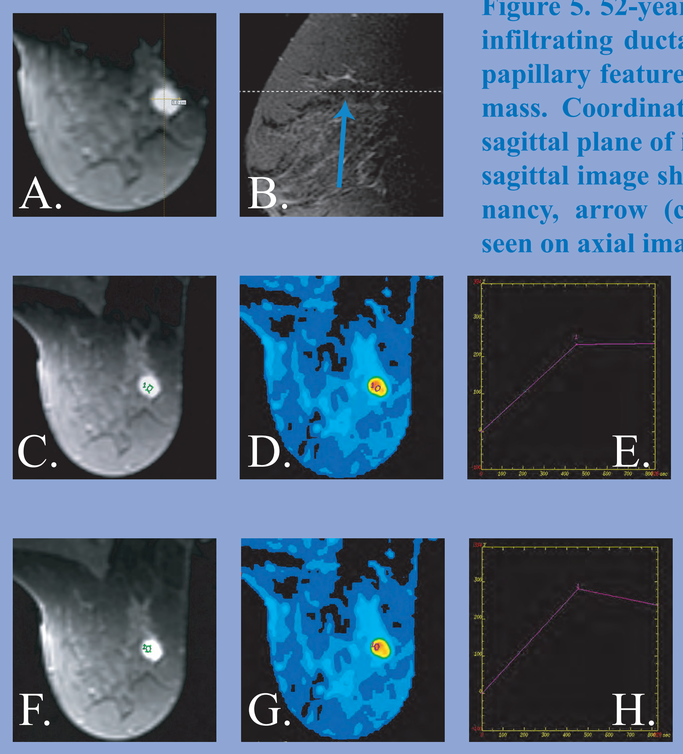


Figure 5. 52-year-old woman with 10 mm infiltrating ductal carcinoma with micropapillary features. A. Intensely enhancing mass. Coordinate on axial image marks sagittal plane of image (B). B. T2W fat-sat sagittal image shows dark signal of malignancy, arrow (coordinate through mass seen on axial image A).

C. ROI was selected in center of mass. D. Maximum slope of enhancement map shows that peak enhancement was off-center, not covered by ROI. E. Enhancement curve shows type II pattern.

F-G. ROI placed in area of peak enhancement.

H. Enhancement curve shows now type III washout pattern.

Using multiplanar coordinates allows for precise localization of masses and correlation between post contrast images and T2-weighted images. This becomes important when small masses are being analyzed. For the assessment of enhancement kinetics, it is important to select ROI in the portion of the tumor with maximum peak enhancement. When ROI is randomly placed in the mass, the enhancement curve may be variable and yield lower specificity.

Future developments:

The novel imaging methods that have the potential to improve specificity for the identification of breast malignancy are focusing on the multiparametric MRI, proton magnetic resonance spectroscopic imaging (MRSI), and 23Na sodium MRI. When used in combination, these techniques provide a comprehensive data set with potential to diagnose breast disease with higher accuracy than any single measure alone. A combination of MRI, MRSI, and 23Na sodium MR parameters may be examined in a single MR study [5-6].

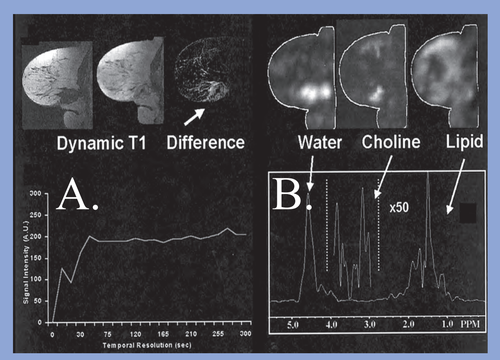


Figure 6. 63-year-old woman with invasive ductal carcinoma. A. Enhancement curve from mass shows type II (plateau) pattern. B. Representative spectrum and magnified (50x) region demonstrates detectable Choline signal (SNR = 6.6) in the mass at 3.2 ppm. *Jacobs et al. JMRI 2005;21:23-28.*

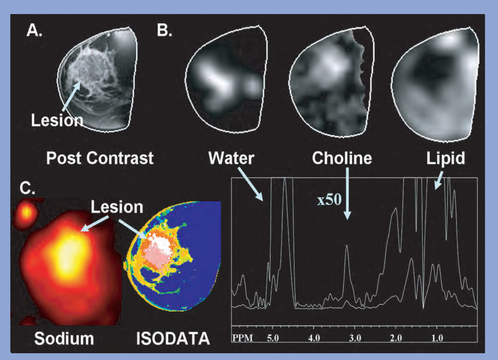


Figure 7. 43-year-old woman with invasive lobular carcinoma. Mutliparametric ISODATA cluster analysis map shows overlap of sodium and proton spectroscopy data corresponding to enhancing mass. Cancer shows increased level of Choline and about 50% elevation of tissue sodium concentration.

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