Comparison of Choline and Pharmacokinetic Parameters in Breast Cancer Measured by MR Spectroscopic Imaging and Dynamic Contrast Enhanced MRI

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Purpose:

Although an MRI scanner is a single stand-alone modality, different acquisition techniques may be applied to collect structural and functional information, including vascular or angiogenic properties measured by dynamic contrast enhanced MRI (DCE-MRI) and Choline (Cho) metabolism measured by proton MR spectroscopy imaging (MRSI). They may provide complementary information for a better characterization of the neoplasm. In this study, we investigated the correlation between Cho measured by MRSI and vascular parameters measured by DCE-MRI in breast cancer, to study whether the cell replication is associated with angiogenesis to support tumor growth. A co-registration program was developed to match the tissues contained within each MRSI voxel and DCE-MRI. The measured enhancement kinetics was analyzed with a 2-compartmental model to obtain K^{trans} and k_{ep}. The regional correlation between Choline level and DCE parameters from all Cho-positive voxels within each lesion was first investigated. Within each lesion the regional comparison was made. Then a mean characteristic Cho and mean DCE parameters were obtained from each lesion, and they were compared among all lesions. Furthermore, correlations in lesions with different morphology were evaluated.

Methods:

Fourteen patients (35-66 years old, median 48) with histological biopsy-proven breast cancer (longest dimension 2.4 – 11.6 cm, median 5.2 cm) were included. The study was performed using a 1.5T Philips Eclipse scanner. The imaging protocol consisted of Sagittal pre-contrast imaging, bilateral DCE imaging, and MRSI. DCE was performed using a 3D SPGR (RF-FAST) pulse sequence with TR= 8.1 ms, TE= 4.0 ms, flip angle= 20°, matrix size= 256x128, FOV= 38 cm, slice thickness= 4mm. The scan time was 42 sec per acquisition, 4 pre-contrast and 12-post contrast frames. After the dynamic scan was completed, subtraction images were generated on the scanner console. The 8x8 spectroscopic imaging grid was placed based on the sagittal view pre-contrast images and the axial view subtraction images, to cover most of hypointense lesion on sagittal view or enhanced lesions on axial view while minimizing inclusion of fat tissues. Dual water and fat suppression was applied. The point-resolved spectroscopic sequence (PRESS) sequence was used for spectroscopic imaging. The parameters were TR/TE = 1627/270 msec, matrix size = 8 × 8, FOV = 8 cm, and sagittal section thickness = 12mm, 4 averages. Each CSI voxel is 1.0 (superior-inferior) x 1.0 (anterior-posterior) x 1.2 (medial-lateral) cm^3, and that contained 96 DCE voxels. A corresponding DCE enhancement kinetics was calculated from these 96 voxels. If a Cho peak around 3.2 ppm was observed, the Cho signal-to-noise ratio (SNR) was measured. Three DCE parameters: % signal enhancement at 2-min (SE%-2min), as well as K^{trans} and k_{ep} analyzed using Toft's 2-comparments model, were obtained for comparison with Cho. The morphology of each lesion was categorized into mass, or the diffuse pattern. The maximum intensity projection (MIP) of subtraction images was generated, and from which the longest and perpendicular dimensions were measured to indicate lesion size.

Results:

The correlation between number of Cho-positive voxels in each case and the area of lesion (product of the longest and perpendicular dimension) are shown in Fig 1. It shows a highly significant linear correlation ($r = 0.99$, $p < 0.001$) among 10 cases presented as masses (i.e. larger lesion, more Cho-positive voxels); but not in the other 4 cases with the diffuse pattern. Fig.2 demonstrates a case with the mass type enhancement, presenting a pre-contrast hypointense, strongly enhanced lesion with well-defined boundary. There were 23 Cho-positive voxels, and among these there is a significant correlation between Cho SNR and SE%-2min (r= 0.55, p= 0.006) and K^{trans} (r= 0.50, p= 0.015). However, there is a large variation and the relationship is not linear. Cho SNR is not correlated with k_{ep} (r= 0.01, p= 0.66). Fig.3 demonstrates a case with the diffuse type enhancement pattern, where the enhanced tissues were intermixed with fat. There were only 3 Cho-positive voxels in this case. The mean Cho and DCE parameters were calculated from all Cho + voxels in each lesion, and compared among all 14 lesions. There was a significant correlation between Cho and SE%-2min (r= 0.75, p= 0.002), K^{trans} (r= 0.74, p= 0.003), and k_{ep} (r= 0.76, p= 0.002), with a relatively high correlation coefficient r. All together there were 125 Cho + voxels from 14 cases, and the linearity was low. The correlation coefficient r and the p values in 3 comparisons are summarized in Table 1.

Table 1: Correlation analysis with Cho SNR

	SE%2-min	K^{trans}	k_{ep}
23 voxels (Fig.2 pt.)	r= .55 p= .006	r= .50 p= .015	r= .01 p= .66
14 lesions (14 pts.)	r= .75 p= .002	r= .74 p= .003	r= .76 p= .002
125 voxels (all 14 pts.)	r= .43 p< .001	r= .40 p< .001	r= .19 p= .034

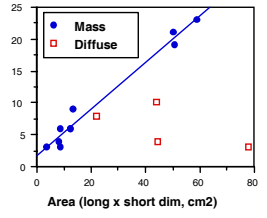
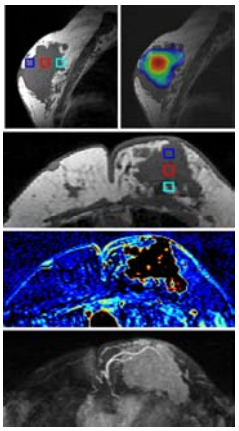


Fig.1 Correlation between the number of Cho + voxels with lesion size, r = 0.99, p < 0.001.



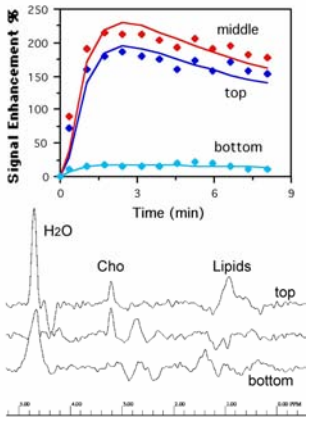
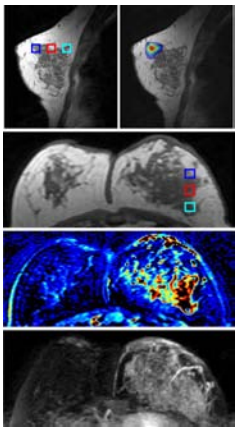


Fig.2 The DCE-MRI enhancement kinetics and MR spectra measured from 3 voxels in one mass lesion. There were 23 Cho + voxels. The blue & red voxels show high enhancements, and a high Cho peak.



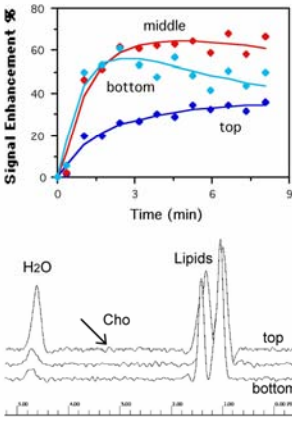


Fig. 3 The DCE-MRI enhancement kinetics and spectra measured from 3 voxels in one diffuse lesion. There were 3 Cho + voxels. Only the top blue voxel shows a barely detectable Cho peak.

Discussion:

In this study the metabolic information (Cho measured by MRSI) was correlated with angiogenesis (vascular parameters measured by DCE-MRI) in breast cancer. All parameters showed a wide variation within each lesion, and there were no consistent correlations between regional Cho and DCE parameters within the lesion of each individual patient. This finding might be attributed to the heterogeneous nature of breast cancer. The characteristic Cho and DCE-MRI parameters were obtained for each lesion by averaging over all Cho-positive voxels. In these 14 patients there was a significant linear correlation between Cho with DCE parameters, with r = 0.74 - 0.76. The results suggested that overall there is a correlation between Choline metabolism and angiogenesis activity, but not regionally within each tumor. Since Choline is associated with cell replication and angiogenesis is required to support tumor growth, this may explain the physiological mechanism for the correlation.

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