Breast cancer: Proton MR-spectroscopy evaluation with a point-resolved spin-echo sequence (press) and histopatological correlation

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Authors: A. Pecchi, B. Canossi, R. Battista, P. Torricelli; Modena/IT
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Purpose

In vivo, Proton Magnetic Resonance Spectroscopy ($^1$H-MRS) is a non-invasive technique that can provide tumor metabolic informations, in particular about choline-metabolism. According to the literature, it shows a 100% sensibility and 88% specificity when used in combination with Magnetic Resonance Imaging (MRI) for the detection and the characterization of breast lesions.

The study with $^1$H-MRS is based upon the observation of high levels of choline compounds, such as phosphocholine, glycerophosphocholine and taurine (phospholipid components of cellular membranes), that are present in malignant breast tissue at the frequency of 3.14-3.34 ppm on the spectrum at 1.5T. Moreover a single peak of choline is referred to “Total choline-containing compounds” (tCho). The reason is that the multiple resonances cannot be spectrally resolved with the software actually in use (1.5T-3.0T).

During tumor progression, there’s a metabolic imbalance between phosphatidilcholine biosynthesis and its catabolism. As a consequence, the normal metabolic pathways of cellular membranes are changed, involving the presence, in particular of this compound, in tumor cell, that can explain the peak of tCho at this range of frequency.

Moreover there is a correlation between choline compounds metabolism (a marker of cellular replication) and the hypervascularized breast lesions. Consequently, the measure of choline concentration is in relationship with all parameters which define the typical enhancement of tumor lesion.

The results obtained may often be influenced by breast cancer heterogeneous nature. So, some invasive lesions present a much lower tCho level than others with the same nature, or a negative peak, like benign lesions. According to the literature, the different choline distribution patterns and its concentration ranges reflect the intrinsic heterogeneity of breast lesions.

The purpose of this study is to compare the different histopathological patterns of breast cancer with presence or absence of choline peak at MR-Spectroscopy.

Methods and Materials

45 confirmed breast cancer, detected at MRI, were studied with single-voxel $^1$H-MR Spectroscopy using the Point-Resolved Spectroscopic Sequence (PRESS). The MRI study was performed using a 1.5T scanner (Achieva, Philips Medical Systems, NL) with surface breast coil. The PRESS sequence parameters were: TR: 2000-msec, TE:
288-msec, FA: 90°, NEX: 128 and automatic shimming for the spectral water and fat suppression. Using the images obtained after contrast media injection, on the three orthogonal planes a single voxel of 1cm$^3$ was positioned on the lesion characterized by a suspected enhancement. The acquisition time of the sequence was about 10 minutes. The MR spectrum was analyzed by a medical physician. So, the informations obtained were postprocessed with the application of Fourier transformation, Gaussian signal filters, frequency, phase and baseline corrections. In this way it was possible to optimize the spectrum profile. When the signal-to-noise ratio (SNR) of the Cho at 3.14-3.34 ppm was >2 the peak was considered significant according to the literature.

The presence/absence of choline was correlated with histological tumors type, grading, diameter, proliferative index and status of hormonal and HER-2 receptors.

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**Results**

23/45 breast cancer were Cho-positive and 22/45 Cho-negative at spectroscopic sequence.

The PRESS sequence showed a 51% sensitivity.

Invasive ductal cancer (IDC) was the most common histotype in both groups, but ductal cancer Cho-negative at histopathological analysis showed extensive in-situ component.
<table>
<thead>
<tr>
<th>HISTOPATOLOGY</th>
<th>Cho-positive</th>
<th>Cho-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ductal cancer</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Lobular cancer</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Mucinous cancer</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Colloido - cancer</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ductal/lobular non invasive cancer</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

The Cho-positive lesions showed a middle diameter of 2.3 cm, the Cho-negative lesions of 1.9 cm.

Like 74% of lesions without Cho were G3, this 68% of lesions with Cho.

Like the proliferative index was 30% in lesions Cho-positive and 14% in Cho-negative, this hormonal receptor was positives in 48% of lesions Cho-positive and in 70% of Cho-negative.

<table>
<thead>
<tr>
<th>Cholina</th>
<th>MIDDLE DIAMETER</th>
<th>GRADING III</th>
<th>PROLIFERATIVE INDEX (%)</th>
<th>E/P - HER-2 RECEPTOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2.3 cm</td>
<td>68%</td>
<td>30%</td>
<td>48%</td>
</tr>
<tr>
<td>No</td>
<td>1.9 cm</td>
<td>74%</td>
<td>14%</td>
<td>70%</td>
</tr>
</tbody>
</table>

Images for this section:
Fig. 1: Fig 1 (A-C) The MRI shows extensive and irregular area of enhancement in the left breast (A: white arrow). The intensity-time curve shows high percentage of maximum enhancement, with fast wash-in and wash-out (B). The MR-spectroscopy analysis of the lesion shows the colina peak at 3.2 ppm (C: black arrow). The signal/noise ratio (SNR) is 16.81. The histological evaluation of the specimen shows ductal invasive breast cancer with grading III, high proliferative index, negative E and HER-2 receptors.
**Fig. 2:** Fig 2 (A - E) The MRI shows nodular area of enhancement with lobular shape in the left breast (A-C: white arrow). The intensity-time curve shows high percentage of maximum enhancement, with fast wash-in followed by plateau - wash-out (D). The MR-spectroscopy analysis of the lesion shows the absence of colina peak at 3.2 ppm (E: black arrow). The signal/noise ratio (SNR) is 1.5. Histopatology shows invasive ductal cancer with extensive in situ component, positive E/P receptors.
**Fig. 3:** Fig 3(A-D) The MRI shows area of enhancement with irregular border and shape in the left breast, near to the scar of past quadrantectomy (A-B: white arrow). The intensity-time curve shows moderate enhancement, with fast wash-in followed by plateau (C). The MR-spectroscopy analysis of the lesion shows the absence of colina peak at 3.2ppm (D: black arrow). The signal/noise ratio (SNR) is 0.67. The histological evaluation of surgical specimen shows invasive ductal cancer, positive ormonal and c-ERB2 receptors, with extensive comedo - in situ ductal cancer.
Fig. 4: Fig 4 (A-D) The MRI shows nodular area of enhancement with irregular border in the right breast (A-B: white arrow). The intensity-time curve shows high percentage of maximum enhancement, with fast wash-in followed by plateau (C). The MR-spectroscopy analysis of the lesion shows the colina peak at 3.2ppm (D: black arrow). The signal/noise ratio (SNR) is 5.93. The histological evaluation of surgical specimen shows mucinosus invasive breast cancer with high proliferative index and negative E/P HER-2 receptors.
Fig. 5: Fig 5(A-G) The MRI shows extensive tumoral area with irregular border and shape in the left breast (A-D: white arrow). The intensity-time curve shows high enhancement, with fast wash-in followed by plateau-wash-out (E). The MR-spectroscopy analysis of the lesion shows the presence of colina peak at 3.2ppm (F-G: arrow). The histological evaluation of surgical specimen shows invasive ductal cancer, grading III, negative ormonal and c-ERB2 receptors.
Conclusion

According to the literature in our experience the use of $^1$H-MRS showed very high specificity and positive predictive value, so confirming that the spectroscopic sequence can detect the choline presence only in malignant lesions.

There is a limitation as regard to the results for the influence of heterogeneous feature of breast cancer. About histological typing, most of invasive tumors demonstrate the same aspect on the spectrum with elevation of tCho.

Differently, for in situ ductal carcinoma (DCIS) the results are contrasting. In literature there aren't studies that can show a correlation between the in situ histotype and the intrallesional accumulation of choline-containing compounds but it's reported that DCIS and IDC with an extensive in situ component are likely to be negative for choline at MR spectroscopy. In agreement with literature in our study the cho-negative ductal cancer had an extensive in-situ component.

The only one certainty is the existence of a relation between low tumor aggressiveness and the absence of choline peak on the spectrum.

In this study, in fact the correlation between Cho-positive and Cho-negative breast cancers shows that the proliferative index together with the hormonal receptor status presents a different distribution. In particular Cho-positive cancers have high proliferative index and are often negative for hormonal-HER-2 receptors, so having a worse prognosis than Cho-negative cancers.

Based on technical evolutions breast $^1$H-MRS is achieving a role that could be effectively use fine in routine clinical practice. Our study results suggest that the differences in choline detection and histopathological breast cancer features may be useful for the biological characterization of breast lesions and the radiologist dedicated to breast imaging can profitably use this procedure for obtaining tumor tissue metabolism informations.

References


**Personal Information**

A. Pecchi*, B. Canossi*, R. Battista*, P. Torricelli*,

* Department of Radiology, University of Modena and Reggio Emilia, Modena, Italy