RadioGraphics

Proton (^{1}H) MR Spectroscopy of the Breast[1]

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TEACHING POINTS
See last page

Proton (hydrogen 1) [^{1}H]) magnetic resonance (MR) spectroscopy provides biochemical information about the tissue under investigation. Its diagnostic value in cancer is typically based on the detection of elevated levels of choline compounds, choline being a marker of active tumor. The two main potential clinical applications of ^{1}H MR spectroscopy are *(a)* as an adjunct to breast MR imaging to improve specificity in differentiating benign from malignant lesions, and *(b)* for monitoring or even predicting response to treatment in patients undergoing neoadjuvant chemotherapy. Preliminary data are promising, with study results suggesting that ^{1}H MR spectroscopy may decrease the number of benign biopsies recommended on the basis of MR imaging findings and may help predict response as early as 24 hours after the first dose of neoadjuvant chemotherapy. Although several limitations currently exist that make the technique premature for clinical use, further evaluation with larger, preferably multicenter trials is certainly warranted.

Abbreviations: DCIS = ductal carcinoma in situ, PPV = positive predictive value, SNR = signal-to-noise ratio

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Introduction

Proton (hydrogen 1) [^{1}H]) magnetic resonance (MR) spectroscopy is not a new technology, having been used to provide biochemical information about biologic tissues for over 30 years. ^{1}H MR spectroscopy has been approved by the U.S. Food and Drug Administration and is widely used for evaluation of the brain and prostate gland. Overall, however, its evolution has been slow in the clinical setting and even slower in breast studies. Although quantification of metabolite levels is routinely performed in ^{1}H MR spectroscopy of the brain, it is more difficult to perform in breast evaluation because of the heterogeneous distribution of the glandular and adipose tissues (1). With respect to the breast, ^{1}H MR spectroscopy is still an investigational technique with a promising future in the clinical setting.

Teaching Point

The diagnostic value of ^{1}H MR spectroscopy in cancer is typically based on the detection of elevated levels of choline compounds, choline being a marker of active tumor (2). These compounds have methyl protons that resonate at a chemical shift of 3.2 ppm (3). The composite resonance at 3.2 ppm includes contributions from choline, phosphocholine, glycerophosphocholine, myoinositol, and taurine (4).

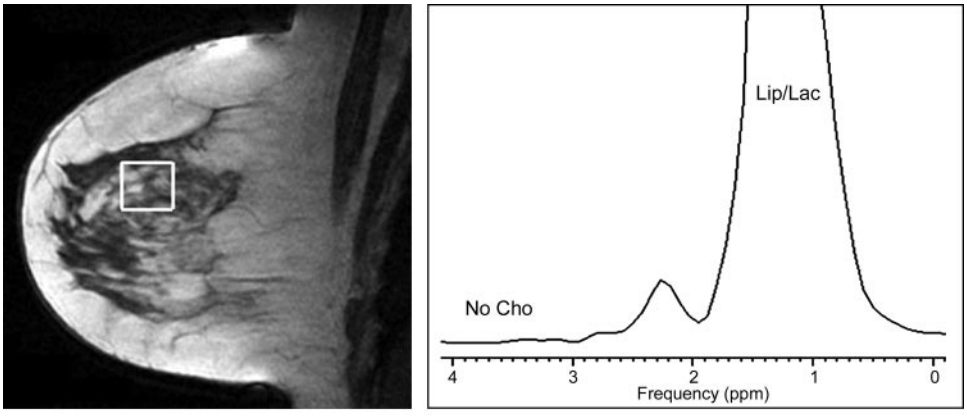
In this article, we review ^{1}H MR spectroscopic technique; discuss and illustrate the potential clinical applications of this modality in the breast (differentiating benign from malignant breast lesions, predicting response to neoadjuvant chemotherapy); and describe the current limitations of ^{1}H MR spectroscopy in this setting.

Technical Considerations

Breast ^{1}H MR spectroscopy is usually performed on a clinical magnet with a field strength of at least 1.5 T. A breast coil is also needed, just as for MR imaging. Spectroscopic sequences are commercially available, but at the present time, a spectroscopist needs to be involved to perform off-line data processing.

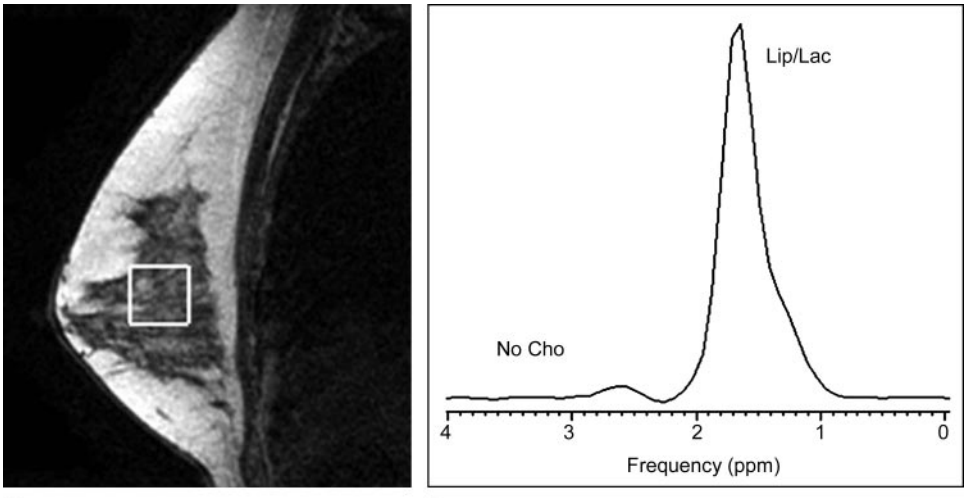
Breast ^{1}H MR spectroscopy has predominantly been performed with a single-voxel technique. This technique is limited to evaluating one lesion at a time. A voxel is placed to encompass the lesion or area of interest. In most single-voxel ^{1}H MR spectroscopic studies of the breast, the point-resolved spectroscopic sequence or a variation thereof is used for data acquisition. One such variation is the incorporation of echo time averaging technique into a regular point-resolved spectroscopic sequence (1). This method reduces the sidebands that result from spurious echoes generated by mobile lipids, which sidebands can obscure the detection of the choline peak. This lipid signal problem arises because of the large amount of fat in the breast. Typical acquisition parameters include an echo time of 135 msec or longer to reduce lipid signal and a repetition time of 1.5–3.0 seconds. The number of signals acquired is usually between 128 and 256, resulting in a net data acquisition time of 3.2–12.8 minutes. An extra 5–10 minutes is needed for preacquisition set-up of ^{1}H MR spectroscopy voxel shimming and water suppression. In cases of multiple suspect lesions in one breast, multivoxel MR spectroscopy is the preferred technique. This technique provides information about the spatial distribution of metabolites and is useful for studying multiple lesions. It can be used to measure multiregional metabolite levels in a data acquisition time comparable to that for a single-voxel study. However, mostly due to difficulty in obtaining good shimming in a relatively large breast region within a reasonable time frame, only a few studies have yielded data of acceptable quality (5,6). For differentiating benign from malignant breast lesions, except for a study in which choline concentration was quantified using water signal as the internal reference (1), the majority of ^{1}H MR spectroscopic studies are based on detection (or nondetection) of the choline peak or its signal-to-noise ratio (SNR) (7).

Breast ^{1}H MR spectroscopy has several drawbacks. Prior contrast material–enhanced MR imaging is usually required for lesion localization and MR spectroscopic voxel placement. The accumulation of contrast agent in the lesion can affect ^{1}H MR spectroscopic quality due to T2* broadening effect (8). Also, the time required (including preacquisition adjustment) is relatively long (10–25 minutes) and the spatial resolution poor. Fine tumor heterogeneity cannot be assayed. It is difficult to achieve sufficient simultaneous suppression of water and lipid resonances, making it difficult to quantify choline concentration. Thus, the majority of ^{1}H MR spectroscopic studies are non- or semiquantitative. Furthermore, because of the difficulty of detecting weak choline signal from a small lesion within a reasonable time frame in a clinical setting at 1.5 T, the sensitivity of ^{1}H MR spectroscopy in detecting breast malignancy drops dramatically when the lesion is less than 2 cm in diameter (9). With expected improvement in SNR, higher-field-strength (eg, 3-T) MR imagers may allow ^{1}H MR spectroscopic investigation of smaller lesions with high sensitivity within a reasonable time frame. Higher field strength will also improve spectral resolution, which means better separation between water, choline, and fat peaks. This im-



a. b.

Figure 1. **(a)** Sagittal non-fat-suppressed T1-weighted MR image (repetition time msec/echo time msec = 6.4/3.1) of the right breast, obtained in a 65-year-old woman with a history of pseudoangiomatous stromal hyperplasia in the left breast, shows normal glandular parenchyma and fat. **(b)** Magnified spectrum illustrates a high lipid *(Lip)* peak, but no choline *(Cho)* resonance peak is observed at a frequency of 3.2 ppm. *Lac* = lactate.



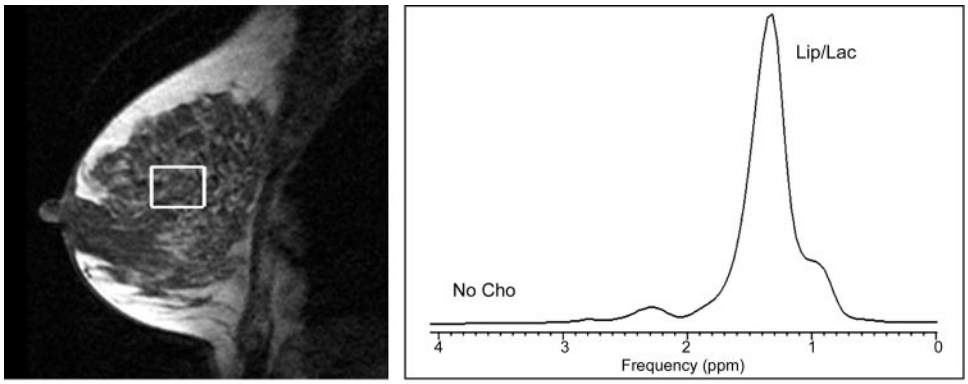
a. b.

Figure 2. **(a)** Sagittal non-fat-suppressed T1-weighted MR image (6.4/3.1) of the left breast, obtained in a 47-year-old woman during week 2 of the menstrual cycle, shows normal glandular parenchyma and little fat. The patient had undergone lumpectomy in the contralateral breast for cancer discovered at screening breast MR imaging performed owing to the patient's high risk. **(b)** Magnified spectrum illustrates a high lipid *(Lip)* peak, but no choline *(Cho)* resonance peak is observed at a frequency of 3.2 ppm. *Lac* = lactate.

proved resolution would allow improved spectral quality and less obscuration of the choline peak by either the water peak or the fat peak.

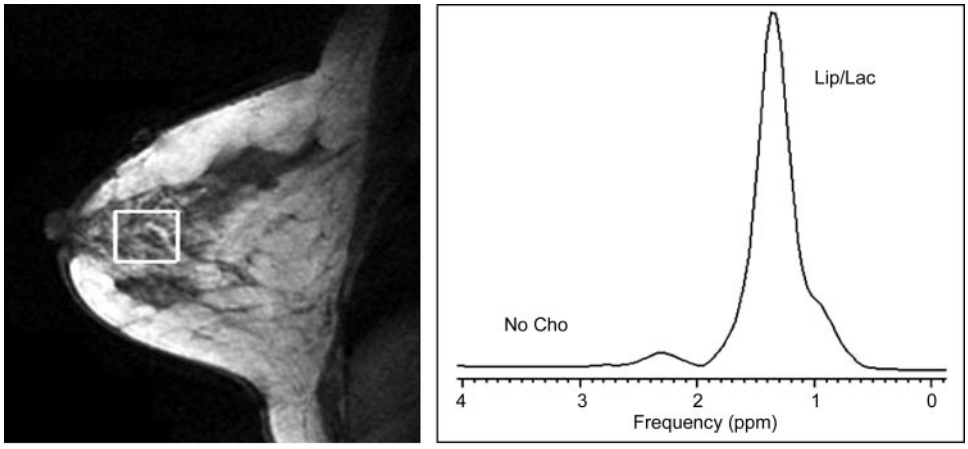
Evaluation of Normal and Lactating Breast Parenchyma

Normal glandular parenchyma of the breast does not consistently demonstrate a choline resonance peak that can be detected at 1.5 T. At our institution, we conducted a small prospective study in which we performed ^{1}H MR spectroscopy in 27 patients undergoing screening breast MR imaging (10). We included both pre- and postmenopausal patients as well as patients at different stages of the menstrual cycle (Figs 1–5). All of these patients have undergone imaging or clinical follow-up for a year, with none having developed any abnormality at the site of spectroscopy. All areas where the voxel was placed and ^{1}H MR spectroscopy was performed had MR imaging characteristics of normal breast parenchyma without evidence of suspect enhancement. We did not detect any choline in normal breast tissue at 1.5 T.



a. b.

Figure 3. **(a)** Sagittal non-fat-suppressed T1-weighted MR image (6.4/3.1) of the left breast obtained in a 53-year-old woman shows normal glandular parenchyma. The patient had undergone lumpectomy for cancer in the right breast that was discovered at screening breast MR imaging performed owing to the patient's high risk. **(b)** Magnified spectrum illustrates a high lipid *(Lip)* peak, but no choline *(Cho)* resonance peak is observed at a frequency of 3.2 ppm. *Lac* = lactate.



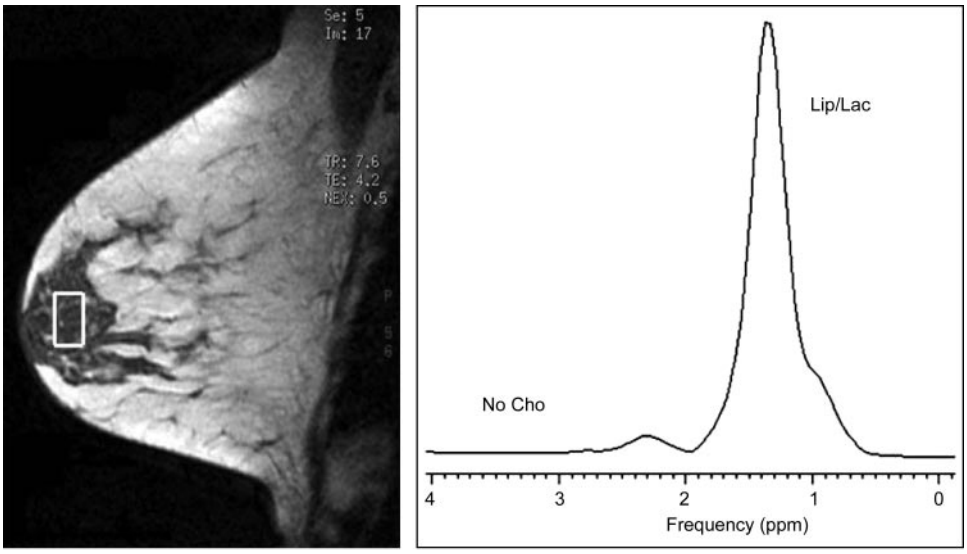
a. b.

Figure 4. **(a)** Sagittal non-fat-suppressed T1-weighted MR image (6.4/3.1) of the left breast obtained in a 56-year-old woman shows normal glandular parenchyma and little fat. The patient had undergone lumpectomy for atypical ductal hyperplasia that was discovered at screening breast MR imaging performed owing to the patient's high risk. **(b)** Magnified spectrum illustrates a high lipid *(Lip)* peak, but no choline *(Cho)* resonance peak is observed at a frequency of 3.2 ppm. *Lac* = lactate.

A group in Australia studied 43 asymptomatic volunteers, including three lactating mothers, at 1.5 T (4). A resonance in the choline spectral region (3.2 ppm) was observed in all three mothers, but three false-positive resonances were also seen in the remaining 40 (nonlactating) volunteers. Choline signal has also been documented in the lactating breast by other groups (11,12). Limited data exist, but at higher field strengths, choline signal can be detected in normal breast tissue, increasing the need for quantification of choline concentrations (3). The amount of choline detected in normal breast tissue at higher field strengths has been less than in malignant lesions.

Differentiating Benign from Malignant Breast Lesions

Studies have demonstrated that MR imaging can help detect otherwise occult breast cancers, and this modality is playing an increasingly important role in the clinical setting, including a role in screening high-risk women (13–15). Because of the lack of standardization of technique and interpretation, the specificity of MR imaging has been variable from center to center, but overall its specificity has been relatively low, resulting in a considerable number of benign biopsies (16–18). Improving the positive predictive value (PPV) of MR imaging–based biopsy recommendations would improve the acceptability and cost-effectiveness of this imaging technique.



a. **b.**

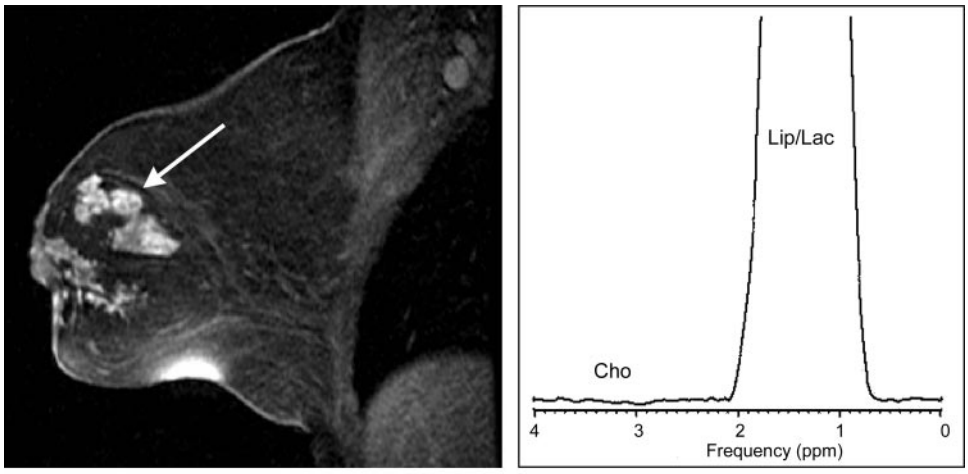
Figure 5. **(a)** Sagittal non-fat-suppressed T1-weighted MR image (6.4/3.1) of the left breast obtained in a 68-year-old woman shows normal glandular parenchyma and fat. The patient had undergone contralateral lumpectomy for breast cancer that was discovered at screening breast MR imaging performed owing to the patient's high risk. **(b)** Magnified spectrum illustrates a high lipid *(Lip)* peak, but no choline *(Cho)* resonance peak is observed at a frequency of 3.2 ppm. *Lac* = lactate.

Findings in Selected In Vivo Single-Voxel ^{1}H MR Spectroscopic Studies Performed on 1.5-T Imagers

Study*	Malignant Lesions	Benign Lesions	Sensitivity (%)	Specificity (%)	True-Positive Findings	True-Negative Findings	False-Positive Findings	False-Negative Findings	PPV (%)
Roebuck et al (19)	10	7	70	86	7	6	1	3	88
Kvistad et al (11)	11	11	82	82	9	9	2	2	82
Cecil et al (20)	23	15	83	87	19	13	2	4	90
Yeung et al (21)	24	6	92	83	22	5	1	2	97
Jagannathan et al (12)	32	14	81	86	26	12	2	6	93
Tse et al (22)	19	21	89	100	17	21	0	2	100
Huang et al (7)	18	12	100	87	18	8	4	0	82
Bartella et al (23)	31	26	100	88	31	23	3	0	91
Total	168	112	87†	87†	149	97	15	19	90†

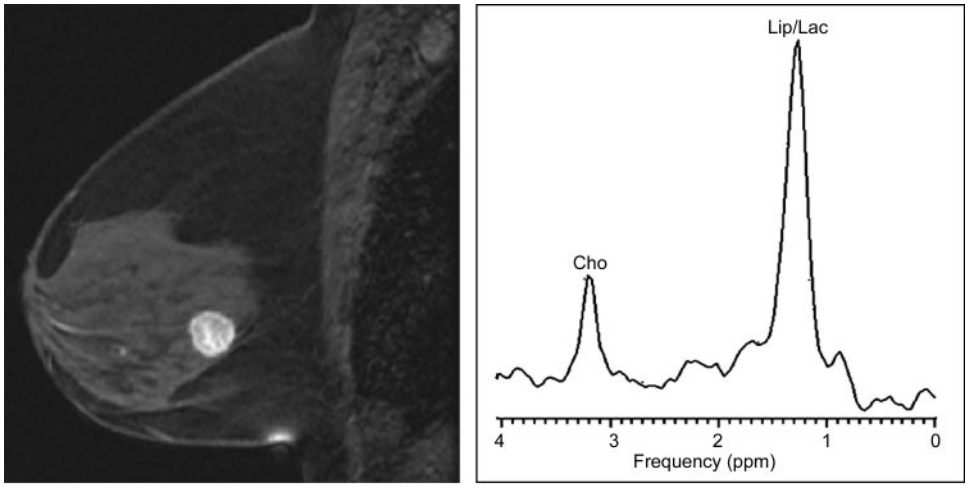
*Numbers in parentheses indicate reference numbers.
†Average percentage.

^{1}H MR spectroscopy has been suggested as an adjunct to breast MR imaging to improve the specificity of the latter technique. Prior studies performed on 1.5-T MR imagers have reported sensitivities of 70%–100% and specificities of 67%–100% for breast MR spectroscopy (Table). Multiple in vivo ^{1}H MR spectroscopic studies aimed at improving discrimination between benign and malignant breast lesions have been conducted at several centers (1,6,7,11,19–22,24,25). In a study that we conducted at our institution (23), breast ^{1}H MR spectroscopy had a sensitivity of 100% and a specificity of 88%, comparing



a. **b.**

Figure 6. Benign fibrosis and ductal hyperplasia (true-negative findings) in a 43-year-old woman who presented with a new palpable mass in the right breast. **(a)** Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) demonstrates a 4.2-cm irregular mass (arrow). A voxel was placed around the mass. **(b)** Magnified spectrum shows no positive choline *(Cho)* resonance peak, with only a noise level at a frequency of 3.2 ppm. *Lac* = lactate, *Lip* = lipid. MR-guided biopsy followed by surgical excision revealed benign fibrosis and ductal hyperplasia. (Fig 6 reprinted, with permission, from reference 23.)

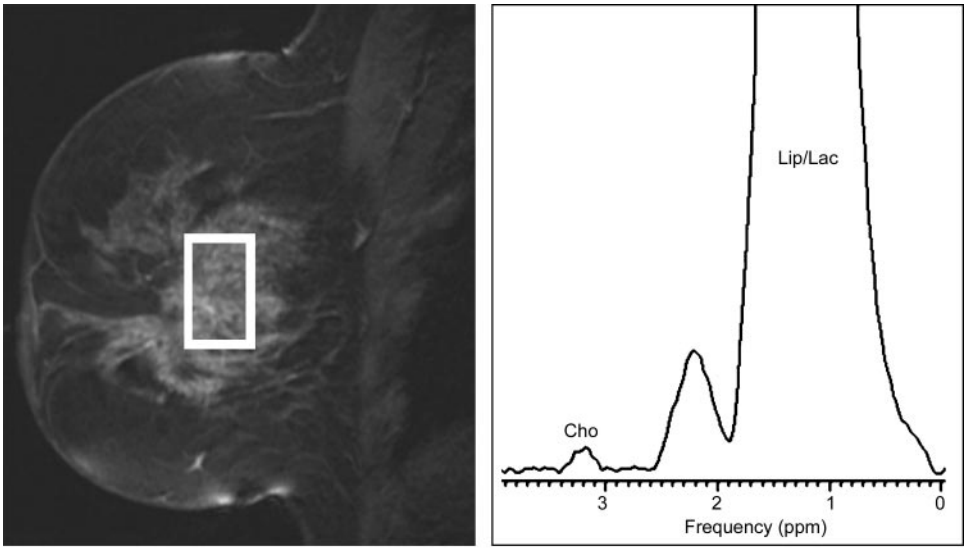


a. **b.**

Figure 7. Mammographically detected, biopsy-proved invasive ductal carcinoma (true-positive finding) of the left breast in a 52-year-old woman. **(a)** Sagittal fat-suppressed T1-weighted MR image (6.4/3.1) obtained immediately after the intravenous injection of gadolinium-based contrast material shows a 1.5-cm rim-enhancing mass. A voxel was placed around the mass. **(b)** Magnified spectrum illustrates a positive choline *(Cho)* resonance peak at a frequency of 3.2 ppm with an SNR greater than 2. *Lac* = lactate, *Lip* = lipid. (Fig 7 reprinted, with permission, from reference 23.)

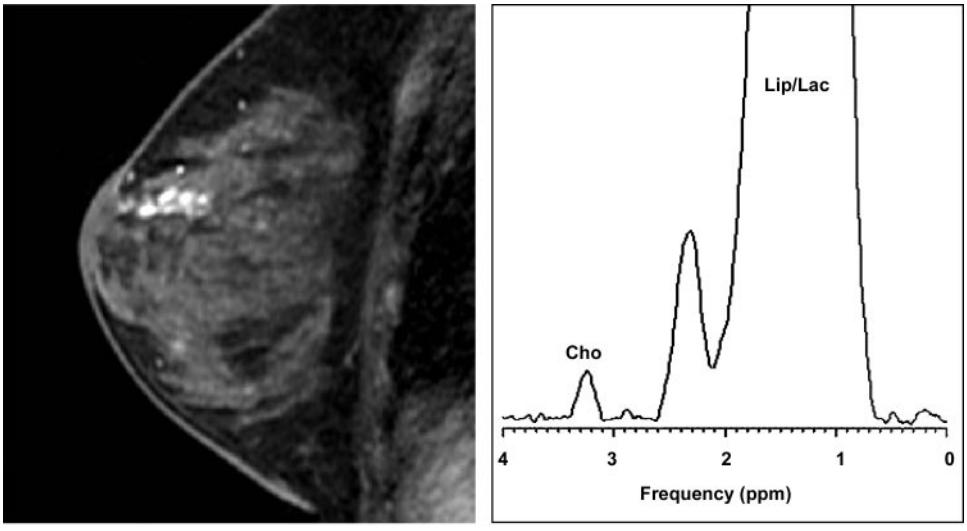
favorably with the results of prior reports that made use of this technique. The use of ^{1}H MR spectroscopy as an adjunct to breast MR imaging would have significantly ($P < .01$) increased the PPV of biopsy from 35% to 82% and might have obviated biopsy in 57% of the 40 lesions with unknown histologic features, with none of the cancers being missed. These data suggest that ^{1}H MR spectroscopy may be a useful supplement to breast MR imaging, reducing the number of benign biopsies without compromising the diagnosis of breast cancer (Fig 6).

All cancers in the study described in this article were identified at ^{1}H MR spectroscopy; there were no false-negative findings. A choline peak was identified at ^{1}H MR spectroscopy in a variety of cancer histologies, including 16 invasive cancers (infiltrating ductal, infiltrating lobular, and infiltrating mixed ductal and lobular carcinoma) (Fig 7) and one ductal carcinoma in situ (DCIS).



a. **b.**

Figure 8. Fibroadenoma and fibroadenomatoid changes (false-positive findings) in a 43-year-old woman with biopsy-proved DCIS. A suspect lesion was detected at MR imaging performed to determine disease extent. **(a)** Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) shows regional clumped enhancement in the outer portion of the left breast. **(b)** Magnified spectrum illustrates a choline *(Cho)* resonance peak with an SNR greater than 2. *Lac* = lactate, *Lip* = lipid. Excision revealed fibroadenoma and fibroadenomatoid changes. (Fig 8 reprinted, with permission, from reference 26.)

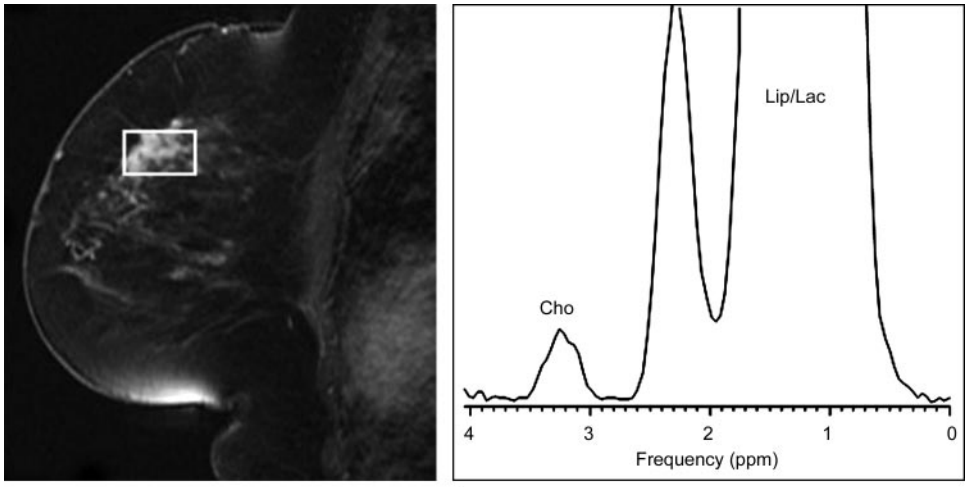


a. **b.**

Figure 9. Chronic inflammatory lesion with atypia (false-positive findings) in a 51-year-old woman with a positive family history of breast cancer. The patient presented with a suspect lesion that had been detected at screening breast MR imaging performed owing to the patient's high risk. **(a)** Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) of the left breast shows ductal clumped enhancement in the retroareolar region. A voxel was placed around the area of enhancement. **(b)** Magnified spectrum illustrates a positive choline *(Cho)* resonance peak with an SNR greater than 2. *Lac* = lactate, *Lip* = lipid. Excision of the lesion demonstrated an atypical chronic inflammatory lesion. (Fig 9 reprinted, with permission, from reference 23.)

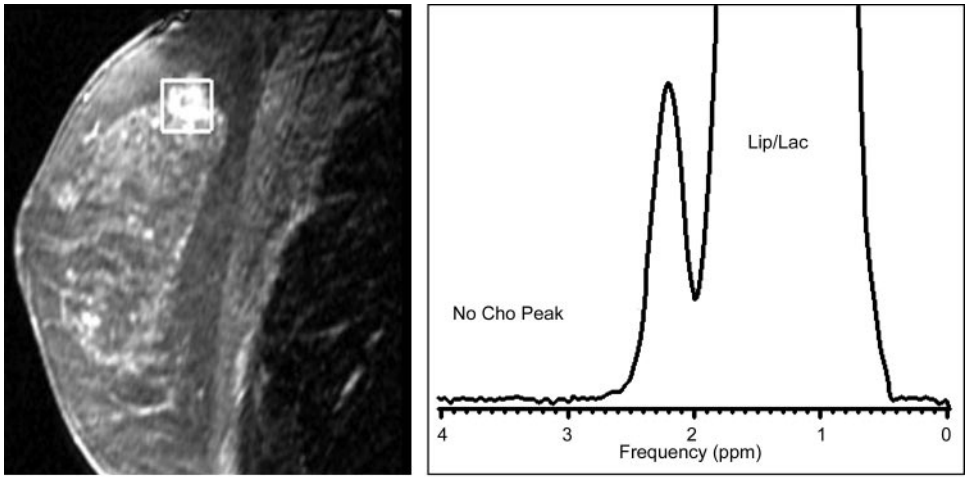
The latter lesion is of interest in light of prior reports suggesting that DCIS may not always demonstrate a choline peak (19,24). Further study involving more DCIS lesions is essential.

This study included three false-positive findings: a fibroadenoma and fibroadenomatoid changes (Fig 8), a chronic inflammatory lesion with atypia (Fig 9), and atypical ductal hyperplasia with columnar cell alteration. A false-positive choline peak has previously been reported with a fibroadenoma (11,21); to our knowledge,



a. **b.**

Figure 10. Palpable, mammographically detected, biopsy-proved invasive lobular carcinoma (true-positive finding) in the left breast of a 56-year-old woman. **(a)** Sagittal fat-suppressed T1-weighted MR image (6.4/3.1) obtained immediately after the intravenous injection of gadopentetate dimeglumine shows a 5-cm area of regional clumped enhancement in the 12-o'clock axis. **(b)** Magnified spectrum illustrates a choline *(Cho)* resonance peak at a frequency of 3.2 ppm with an SNR greater than 2. *Lac* = lactate, *Lip* = lipid. (Fig 10 reprinted, with permission, from reference 26.)

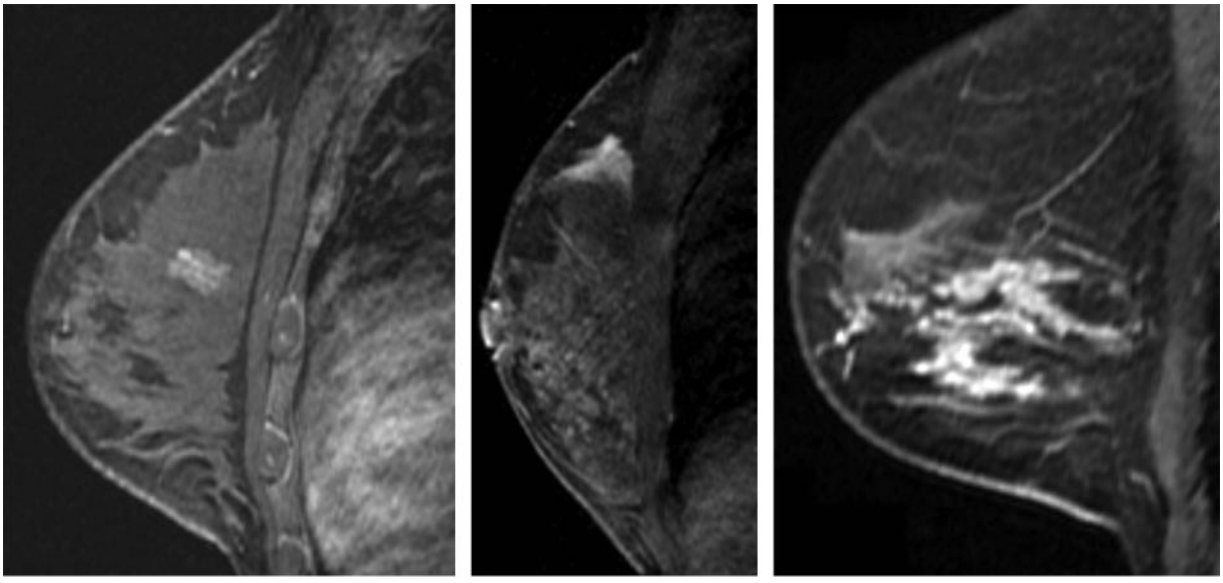


a. **b.**

Figure 11. Non–mass-enhancing lesion (true-negative finding) in a 38-year-old woman with a *BRCA1* gene. A suspect lesion was detected at screening MR imaging. **(a)** Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) obtained on day 11 of the menstrual cycle shows focal clumped enhancement in the upper inner portion of the left breast. **(b)** Magnified spectrum illustrates a high lipid *(Lip)* peak, but no choline *(Cho)* resonance peak is observed at a frequency of 3.2 ppm. *Lac* = lactate.

however, no choline peak has been reported with the other two lesions, although the number of published series on single-voxel breast ^{1}H MR spectroscopy is limited. In view of the presence of atypia in these two lesions, excision would have been the standard of care. Further work is necessary to evaluate the prevalence and characteristics of false-positive findings at ^{1}H MR spectroscopy.

Enhancing lesions at MR imaging that lead to referral for biopsy are described as either mass enhancing or non–mass enhancing. Non–mass



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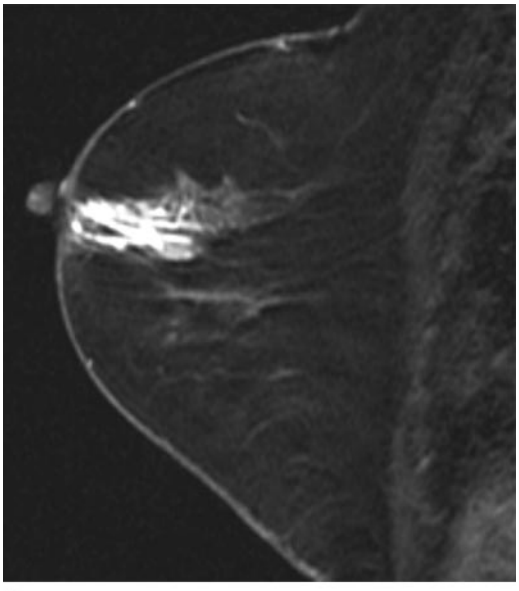


d.

Figure 12. Spectroscopy of non–mass-enhancing lesions. **(a)** A suspect lesion was detected at screening in the left breast of a 20-year-old woman with a positive family history of breast cancer. Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) shows focal clumped enhancement in the upper inner quadrant of the left breast. A voxel was placed around the area of enhancement. Spectroscopy did not demonstrate a choline resonance peak. MR-guided biopsy showed fibroadenomatoid change and breast parenchyma. **(b)** Benign findings in a 43-year-old woman with a family history of breast cancer (sister, age 41 years) who presented with nipple discharge and breast pain. Mammography showed dense breasts without suspect findings. Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) of the right breast demonstrates unilateral regional enhancement at the 12-o'clock position. A voxel was placed around the area of enhancement. MR spectroscopy did not demonstrate a positive choline resonance peak. MR-guided biopsy showed benign breast parenchyma. **(c)** DCIS in a 57-year-old woman who presented with bloody nipple discharge from the right breast. No malignant findings were seen at mammography. Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) of the right breast demonstrates segmental clumped enhancement of the entire lower outer quadrant. A voxel was placed around the area of enhancement. Spectroscopy demonstrated a positive choline resonance peak at a frequency of 3.2 ppm with an SNR greater than 2. MR-guided biopsy and subsequent mastectomy revealed extensive DCIS with a high nuclear grade. **(d)** Fibrocystic change and ductal hyperplasia in a 60-year-old woman with a history of lumpectomy of the right breast for DCIS. Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) of the left breast shows ductal clumped enhancement in the retroareolar region. A voxel was placed around the area of enhancement. No choline resonance peak was detected at spectroscopy. Excision revealed fibrocystic change and ductal hyperplasia. (Fig 12 reprinted, with permission, from reference 26.)

enhancement, defined as "enhancement of an area that is not a mass," may involve different-sized areas, with internal enhancement that is discrete from normal enhancing breast parenchyma (26). Non–mass enhancement has been described in benign hormonal changes and other benign entities but may also occur in malignancies (27,28). Biopsy is often necessary to differentiate benign lesions with non–mass enhancement from cancer (Figs 10–12). However, few data have

addressed the application of breast ^{1}H MR spectroscopy to lesions with non–mass enhancement. Our preliminary data show that the information obtained at ^{1}H MR spectroscopy may decrease the number of biopsy recommendations for benign lesions with non–mass enhancement. In our study, use of ^{1}H MR spectroscopy as a supplement to breast MR imaging would have significantly increased the PPV of biopsy for MR imaging–detected lesions with non–mass enhancement from 20% to 63% and would have obviated biopsy in 68% of lesions (29).

Teaching Point

This hypothesis has also been evaluated at higher field strengths; at 4 T, a retrospective, blinded-observer performance study of 55 individuals was conducted. Performing ^{1}H MR spectroscopy in addition to MR imaging improved sensitivity and specificity for all four readers and also improved interobserver agreement (3). These preliminary results are very promising, although again, larger studies are needed for further evaluation.

Predicting Response to Neoadjuvant Chemotherapy

Neoadjuvant chemotherapy, also known as preoperative, induction, or primary chemotherapy, is administered prior to a definitive surgical excision. It is typically administered to patients with locally advanced disease or large primary tumors. These patients include those with stage 3 and stage 4 disease with isolated ipsilateral supraclavicular adenopathy but no distant metastases (30). Downstaging of disease may be achieved with neoadjuvant chemotherapy, allowing surgical excision of inoperable lesions. Neoadjuvant chemotherapy may allow breast conservation in patients who would otherwise require mastectomy. It can also help identify patients who are resistant to standard chemotherapy as indicated by the lack of response of the primary tumor and may serve as a surrogate for assessing the response of micrometastases and ultimately enhance patient survival.

An early pilot study has shown that with a 1.5-T magnet, a change in the total choline concentration was observed after the completion of neoadjuvant treatment, a finding that was confirmed with pathologic analysis (12). A small group of 14 patients were evaluated in this pilot study, and detection of choline was used as the quantification method. A more recent pilot study was performed on a 4-T system. In this study, 13 patients with locally advanced cancer were evaluated *(a)* before receiving their first chemotherapy dose, *(b)* 24 hours after the first dose, and *(c)* after the fourth dose. ^{1}H MR spectroscopy was able to help detect a change in the choline concentration from baseline within 24 hours of administration of the first dose of neoadjuvant chemotherapy. This change had a positive correlation with the change in final lesion size, with a statistical significance of $P = .001$.

Teaching Point

These results are indeed revolutionary, since ^{1}H MR spectroscopy would be able to help predict clinical response in patients undergoing neoadjuvant chemotherapy within 24 hours of their receiving the first dose. These results suggest that the addition of ^{1}H MR spectroscopy may offer a substantial advantage over MR imaging alone in the prediction of response to neoadjuvant chemotherapy (31) and may ultimately enhance patient survival. Larger studies are being designed to further evaluate these preliminary data.

Current Limitations of Breast ^{1}H MR Spectroscopy

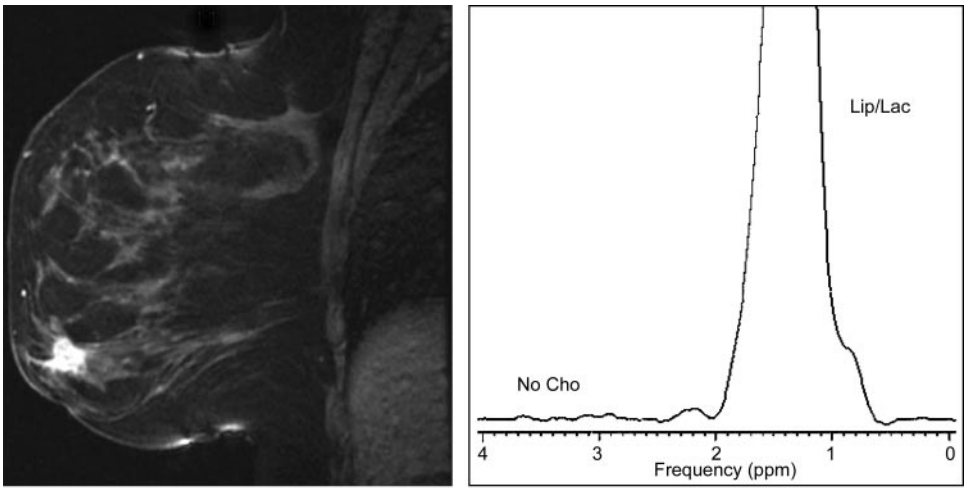
Research concerning breast ^{1}H MR spectroscopy is rapidly expanding, and more and more exciting data are being reported. Considerable progress has been made: This technique is now well tolerated by patients in the clinical setting, with acquisition times of approximately 10 minutes. At present, however, breast ^{1}H MR spectroscopy—although promising—is not ready for clinical use.

As mentioned earlier, the single-voxel technique, which is the most commonly used technique, allows only one lesion to be examined at a time. In addition, the lesion must be around 1 cm^3 in size for the data to be meaningful. In breast evaluation, we often have to perform biopsy on much smaller lesions, and overcoming this limitation would be extremely important. Most of the time, more than one lesion is questioned on an MR image, so the ability to evaluate multiple lesions or even the whole breast is something that we certainly hope to achieve in the future.

Teaching Point

Patients with a hematoma or a metallic clip must be excluded, since inhomogeneities of the magnetic field are produced that affect spectroscopy, which must be performed in a very homogeneous magnetic field. Patient motion also affects this technique, so that short acquisition times are essential (Fig 13). A spectroscopist is still needed because off-line data processing must

Teaching Point



a. **b.**

Figure 13. Biopsy-proved invasive ductal carcinoma in the left breast of a 57-year-old woman. **(a)** Sagittal contrast-enhanced fat-suppressed T1-weighted MR image (6.4/3.1) obtained immediately after the intravenous injection of gadopentetate dimeglumine shows a 1.4-cm irregular enhancing mass. **(b)** Magnified spectrum illustrates no choline *(Cho)* resonance peak at a frequency of 3.2 ppm. *Lac* = lactate, *Lip* = lipid. Patient motion during the examination is the most likely reason for the false-negative result.

be performed (off-line processing software is manufacturer dependent, not standardized); a more automated method would make MR spectroscopy similar to any other MR imaging sequence, allowing it to be performed by the MR imaging technologist and making it much easier to incorporate into the daily clinical routine.

Several groups are currently looking at cases of DCIS, but data on the ability of ^{1}H MR spectroscopy to help detect these lesions as well as the atypical lesions are still limited. Although all types of invasive cancers have been detected with ^{1}H MR spectroscopy, larger studies are still needed to further evaluate these preliminary data (32).

Conclusions

^{1}H MR spectroscopy appears to have a bright future in the field of breast imaging. Its role in differentiating benign from malignant lesions and in improving the specificity of breast MR imaging may result in fewer breast biopsies. Moreover, in the setting of monitoring response to neoadjuvant chemotherapy, the results to date have been extremely promising. Overcoming the current limitations of ^{1}H MR spectroscopy is primarily a technical challenge. We hope that interest in this technique continues to grow, thereby encouraging technologic advances and participation in clinical trials around the world. Large multicenter trials are increasingly needed and represent a vital step in the establishment of this technique in the clinical setting.

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Proton (^{1}H) MR Spectroscopy of the Breast

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Page S242
The diagnostic value of ^{1}H MR spectroscopy in cancer is typically based on the detection of elevated levels of choline compounds, choline being a marker of active tumor (2).

Page S250
In our study, use of ^{1}H MR spectroscopy as a supplement to breast MR imaging would have significantly increased the PPV of biopsy for MR imaging–detected lesions with non–mass enhancement from 20% to 63% and would have obviated biopsy in 68% of lesions (29).

Page S250
^{1}H MR spectroscopy was able to help detect a change in the choline concentration from baseline within 24 hours of administration of the first dose of neoadjuvant chemotherapy.

Page S250
The single-voxel technique, which is the most commonly used technique, allows only one lesion to be examined at a time. In addition, the lesion must be around 1 cm^3 in size for the data to be meaningful.

Page S250
Patients with a hematoma or a metallic clip must be excluded, since inhomogeneities of the magnetic field are produced that affect spectroscopy, which must be performed in a very homogeneous magnetic field. Patient motion also affects this technique, so that short acquisition times are essential (Fig 13).