**Preliminary assessment of dispersion
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spectral and spatial resolution
magnetic resonance images in the
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Abstract. Water resonance lineshapes observed in breast lesions imaged with high spectral and spatial resolution (HiSS) magnetic resonance imaging have been shown to contain diagnostically useful non-Lorentzian components. The purpose of this work is to update a previous method of breast lesion diagnosis by including phase-corrected absorption and dispersion spectra. This update includes information about the shape of the complex water resonance, which could improve the performance of a computer-aided diagnosis breast lesion classification scheme. The non-Lorentzian characteristics observed in complex breast lesion water resonance spectra are characterized by comparing a plot of the real versus imaginary components of the spectrum to that of a perfect complex Lorentzian spectrum, a “dispersion versus absorption” (DISPA) analysis technique. Distortion in the shape of the observed spectra indicates underlying physiologic changes, which have been shown to be correlated with malignancy. These spectral shape distortions in each lesion voxel are quantified by summing the deviations in DISPA radius from an ideal complex Lorentzian spectrum over all Fourier components, yielding a “total radial difference” (TRD). We limited our analysis to those voxels in each lesion with the largest TRD. The number of voxels considered was dependent on the lesion size. The TRD was used to classify voxels from 15 malignant and 8 benign lesions (~2400 voxels after voxel elimination). Lesion discrimination performance was evaluated for both the average and variance of the TRD within each lesion. Area under the receiver operating characteristic curve (ROC AUC) was used to assess both the voxel- and lesion-based discrimination methods in the task of distinguishing between malignant and benign. In the task of distinguishing voxels from malignant and benign lesions, TRD yielded an AUC of 0.89 (95% confidence interval [0.84, 0.91]). In the task of distinguishing malignant from benign lesions, the average radial difference yielded an AUC of 0.90 (95% confidence interval [0.71, 1.00]) and the variance in the radial difference yielded an AUC of 0.84 (95% confidence interval [0.61, 0.99]). We have applied the DISPA spectroscopic analysis method to HiSS data in order to identify and quantify voxels in breast lesions displaying non-Lorentzian characteristics. We have shown that a breast lesion classification scheme based on the absorption and dispersion spectral data obtained from HiSS acquisitions may outperform a similar classifier based on single off-peak component analysis, as it uses shape details of the entire spectrum instead of the magnitude at a single spectral location. © 2015 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.2.2.024502](https://doi.org/10.1117/1.JMI.2.2.024502)]

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1 Introduction

The current paradigm for breast cancer screening and diagnosis employs dynamic, contrast-enhanced magnetic resonance imaging (DCEMRI) to increase the sensitivity and specificity of breast exams. DCEMRI requires the injection of a Gadolinium-based contrast agent and repeated imaging to record the time course of the agent uptake and washout in breast tissue. The data are analyzed to determine local uptake and washout rates, providing insight into the physiology and vascularity of small regions of the breast. In particular, rapid uptake and rapid washout patterns are indicative of the sporadic, abnormal angiogenesis observed in malignant lesions.¹

However, there are risks inherent to Gadolinium-based contrast agents which contraindicate the use of DCEMRI for certain patients (e.g., those with compromised renal function or at risk of allergic reaction).² The insertion of an IV catheter itself comes with the risk of bruising, bleeding, or striking a nerve and can be painful to the patient. As the use of breast magnetic resonance imaging (MRI) is expanded, the use of contrast agents for screening exams in large numbers of women may not be appropriate or practical. Therefore, an imaging technique with similar performance to DCEMRI that does not require contrast injection would be desirable. In this paper, we test a novel approach to the analysis of contrast-free high spectral and spatial resolution (HiSS) MRI for breast cancer diagnosis.

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1.1 HiSS in Lesion Diagnosis

HiSS MRI is an echo-planar spectroscopic imaging (EPSI)^{3,4} sequence that rapidly acquires a series of gradient echo images to sample the proton free-induction decay (FID) every 2 to 4 ms. This provides spectral bandwidth that is adequate to separate water and fat signals. The FIDs are processed to obtain complex proton resonance spectra. These spectra provide anatomic and physiologic detail generally not available from standard MRI exams, such as information on different Fourier components of the water resonance associated with different water compartments (intra- versus extravascular) in the breast tissue.

The diagnostic performance of HiSS data in breast lesions has been reported in numerous previous publications. HiSS allows the complete separation of spectral components, leading to single spectral component (e.g., water and fat) images. Water images from HiSS datasets display more complete fat suppression than conventional techniques, providing higher contrast and better lesion demarcation.⁵⁻⁷ In previous studies, the morphological lesion features extracted from HiSS-imaged two-dimensional (2-D) water-peak height images performed similarly to a combination of morphological and kinetic features extracted from three-dimensional (3-D) DCEMRI datasets in the task of distinguishing between malignant and benign lesions.⁸ Water-peak height images showed noninferior performance compared to conventional postcontrast images when assessed using Breast Imaging Reporting and Data System morphologic scores.⁹ Lesion contrast in images of spectral Fourier components that are offset from the peak of the water resonance by several Hertz has also been shown to correlate with cancer, because malignant lesions are often characterized by inhomogeneous broadening of water resonances,^{10,11} and water-peak height HiSS images have compared favorably with conventional images in earlier studies.¹²

Recently, this group analyzed the shape of magnitude spectra from HiSS data and correlated non-Lorentzian characteristics with malignancy^{13,14} or tumor microvasculature.^{15,16} Previous methods^{13,14} involved removal of the Lorentzian characteristics of each water resonance and based malignant versus benign discrimination on the largest residual spectral component. Whereas these showed that noncontrast HiSS data can be valuable in the classification of breast lesions, much of the complex spectral information is discarded when examining single components of the modulus spectra. There are intrinsic advantages to analyzing complex spectral data. A phased absorption spectrum has higher signal-to-noise ratio and displays a sharper peak, without peak broadening associated with computing the magnitude. This should facilitate the detection of spectral deviations or off-peak components that would have otherwise been unresolvable from the magnitude spectrum. The hypothesis underlying this work is that retaining complex spectral information and examining the shape of the entire complex spectrum, as opposed to a single component, should provide a more robust malignant versus benign distinction. We accomplish this by applying a “dispersion versus absorption” (DISPA) analysis technique, pioneered in nuclear magnetic resonance (NMR), to HiSS spectroscopic imaging data.

1.2 DISPA Analysis

One of the first applications of DISPA plots was in the examination of line-broadening mechanisms observed in

radiofrequency, microwave, and nuclear magnetic resonance spectroscopy.^{17,18} Spectral analysis techniques employing such “DISPA” plots were further developed in a series of papers by Roe et al. They demonstrated the use of such plots to distinguish spectral line-broadening mechanisms. For instance, the superposition of two unresolved Lorentzians with different resonant frequencies display different DISPA characteristics from two unresolved Lorentzians of different line width.¹⁹ Also examined were the effects of digitization noise, truncation, saturation, and superimposed peaks with a simultaneous distribution of peak width and position.^{20,21} These papers, while important and innovative, provide only a “qualitative” insight into how to detect and characterize non-Lorentzian features of complex spectra.

One paper in the series developed a “quantitative” method of “linearizing” DISPA circles by examining the DISPA radius as a function of frequency.²² This method allows quantitative assessment of non-Lorentzian characteristics of a complex spectrum. Specifically, a normalized, phased, complex Lorentzian spectrum will form a perfect circle with diameter 1, symmetric about the abscissa, when the values of the real spectrum are plotted on the x -axis and the values of the imaginary spectrum are plotted on the y -axis. Deviations from a perfect circle, differences in the radial directions, suggest the presence of non-Lorentzian spectral components. This method serves as the basis for our analysis of the spectra obtained from HiSS-imaged breast lesions.

2 Materials and Methods

2.1 Data Acquisition and Database

The HiSS acquisition protocol employs a rapidly alternating readout gradient to sample the FID using EPSI. The complex MR signal is recorded using a breastcoil which acquires k -space data in quadrature. This k -space data are reconstructed to form images with two spatial dimensions and one complex spectral dimension via a 3-D Fourier transform. Images corresponding to the magnitude of the water resonance peak in each voxel (“water-peak height images”) were created using in-house software for anatomical reference and lesion segmentation. For a detailed description of the data acquisition and reconstruction algorithm, see Refs. 6 and 12.

All data were acquired on a 1.5 T Philips Achieva MR scanner (Philips Healthcare, Andover, Massachusetts). Single-slice sagittal acquisitions were performed with in-plane resolution of 1 mm in a 512×256 mm² field-of-view, 2-mm slice thickness, Repetition time = 500 ms, effective Echo time = 90 ms, flip angle = 90 deg, echo train length = 128, spectral resolution/bandwidth = 5.6 Hz/716.8 Hz, and automatic shimming.

The 2-D HiSS image data were acquired for previous studies and were used retrospectively for analysis in this work. Our dataset included 23 lesions from 23 patients with biopsy-proven diagnoses. These lesions included: 15 malignant lesions [8 invasive ductal carcinoma (IDCs) with associated DCIS, 5 IDC, 1 invasive mucinous cancer, 1 adenoid cystic carcinoma], and 8 benign lesions (7 fibroadenomas and 1 fat necrosis). Data for this project were acquired with informed consent from each patient, under an institutional review board-approved protocol and in compliance with the Health Insurance Portability and Accountability Act.

2.2 Lesion Segmentation

Lesion segmentation was performed using an automatic two-class (lesion and nonlesion) fuzzy c-means (FCM) algorithm on a manually drawn, rectangular region of the water-peak height image containing the lesion. The water resonance peak intensity from each voxel of the region of interest (ROI) served as input to the FCM algorithm. Class-membership scores are initially randomly assigned to each voxel as “lesion” or “non-lesion” (summing to 1). The membership scores are then iteratively updated until the interclass variation is maximized and the intraclass variation is minimized. The class prototype with the largest water resonance is then labeled as the “lesion” class. The two-class FCM approach assigns two fuzzy membership scores to each voxel. A voxel’s most likely class will be that which corresponds to a membership score greater than 0.5. To account for noise and class “ties,” we used a more conservative membership score threshold of 0.6 for inclusion in the lesion. Therefore, we considered voxels with a membership score >0.6 in the lesion class to be within the lesion.

2.3 Phase Correction

After excitation, the orientation of the net magnetization vector relative to the reference signal is arbitrary. Misalignment with the reference leads to a combination of the signals from the two 90 deg out-of-phase detector channels, altering the recorded real and imaginary spectra. This “zero-order” phase error will cause a rotation about the origin on a corresponding DISPA plot, illustrated in Fig. 1. Zero-order phase errors are corrected using a linear combination of the real and imaginary spectrum weighted by the sine and cosine of the phase error to produce the corrected spectrum.

NMR spectra often exhibit frequency-dependent phase errors due to resonance offset effects, dead time, and so on. However, in this work, we focus our analysis on the deviation from the Lorentzian shape of the water resonance. The relatively narrow bandwidth occupied by the water peak makes any frequency dependence of the phase error negligible. We therefore correct only the zero-order phase error of each spectrum as follows. For a complex spectrum S with N data points, centered on the water

peak, the phase correction angle θ is calculated by Eq. (1). The corrected spectrum S_c is given by Eq. (2).

$$\theta = \tan^{-1} \frac{\text{Im}[S(N/2)]}{\text{Re}[S(N/2)]}, \quad (1)$$

$$S_c = S e^{-i\theta}. \quad (2)$$

2.4 DISPA Analysis—Total Radial Difference

DISPA analysis involves examining the shape of a complex spectrum by creating a parametric plot of the real versus imaginary components of the spectrum at each frequency location. An arbitrary spectrum will produce a DISPA plot characteristic of the shape of the spectrum, including any distortions or phase artifacts. To examine the spectral shape deviations in HiSS-imaged lesions, we compare the DISPA plot of our observed, phase-corrected complex spectra to the reference circle obtained from a perfect Lorentzian. The DISPA radius r_i at each of 25 spectral locations in the frequency range $[-67.2, 67.2]$, centered on the water peak, is calculated and subtracted from that of a reference circle with $r = 0.5$ [Eq. (3)]. The radial differences are summed in each voxel, representing the TRD [Eq. (4)] for that voxel. Figure 2 illustrates this method with an example spectrum from both a malignant and benign lesion.

$$r_i = \sqrt{(\text{real}_i - 0.5)^2 + \text{imaginary}_i^2}, \quad (3)$$

$$\text{TRD} = \sum_{\text{Bin } i} (r_i - 0.5). \quad (4)$$

We do not include a normalizing term to account for the number of spectral points considered in the TRD calculation, as all water spectra included in this study were acquired at the same spectral resolution and contain the same number of data points. A more general method (e.g., for data acquired at a different spectral resolution) would require appropriate normalization. Note that our method involves only a single feature, i.e., the DISPA radius, which is analytically calculated, and thus no training is involved.

2.5 Voxel Elimination and Discrimination

The underlying hypothesis of this work is that voxels from cancerous lesions contain high concentrations of deoxyhemoglobin and other sources of magnetic susceptibility gradients which lead to large deviations in the voxel’s DISPA radii and that these radii may be a marker for cancer. However, as noted in previous work,^{10,11,13,14} the magnitudes of non-Lorentzian features observed in malignant lesions are often less homogeneous than those from benign lesions. Specifically, voxels from malignant lesions tend to contain a wider range of off-peak component magnitudes, and there is a large overlap of the off-peak magnitudes from malignant and benign voxels. Because of this overlap, including all voxels for analysis yields poor discrimination between malignant and benign lesions, with an AUC close to 0.5. In previous work, a “voxel elimination” step was applied to each lesion which discarded voxels in which off-peak non-Lorentzian components were small, in order to focus the analysis on the largest off-peak components in each lesion. A similar voxel elimination step was performed in this work to

Fig. 1 Effects of zero-order phasing errors on the complex spectral components and the corresponding dispersion versus absorption (DISPA) plot. Shown is a complex Lorentzian peak located at the central frequency. The series of plots on the top correspond to the spectrum with no phasing errors, as evidenced by the alignment of the DISPA plot with the x-axis. The series of plots on the bottom show the effects of introducing a 150 deg constant phase error, resulting in the complex spectral components showing severe distortion and the DISPA plot being rotated by 150 deg.

Fig. 2 Left to right: Example complex spectrum, its corresponding DISPA curve, and the radial difference at each spectral location, from a voxel in an IDC lesion (top) and a fibroadenoma (bottom). The DISPA plots show a reference circle corresponding to a perfect Lorentzian lineshape. The spectrum from the malignant lesion shows greater shape distortion, as evidenced by the larger total radial difference (TRD) shown.

emphasize voxels with high radial deviation. We retained for analysis the 10% of voxels in both malignant and benign lesions with the largest radial deviations, while keeping no fewer than 10 voxels from small lesions and no more than 50 voxels from the largest lesions. These thresholds were identified empirically for this dataset to demonstrate potential malignant/benign distinction and were not acquired through rigorous optimization.

The voxel-based DISPA radial difference was evaluated in terms of its ability to distinguish voxels from malignant lesions and voxels from benign lesions. In addition, the summary features of lesion mean and lesion variance of the radial difference, both after voxel elimination, were evaluated in terms of their ability to distinguish malignant lesions from benign lesions.

2.6 Evaluation and Statistical Analysis

Three methods were used to evaluate the malignant versus benign discrimination task after selecting the 10% least Lorentzian-shaped voxels from each lesion: voxel-based discrimination using the TRD calculated in each voxel after voxel elimination and lesion-based discrimination using both the mean and variance of the TRD calculated in each lesion. Each discrimination task was assessed using the area under the receiver operating characteristic curve (ROC AUC)^{23,24} and the 95% confidence interval of the AUC as performance metrics. To calculate the 95% confidence interval, the standard error of the AUC was computed, which measured the degree to which our data fit a binormal model. The (assumed symmetric) confidence interval was then calculated as $(\text{AUC} - 1.96 \cdot \text{SE},$

$\text{AUC} + 1.96 \cdot \text{SE})$. All data processing was performed using MATLAB (The MathWorks, Inc., Natick, Massachusetts) and ROC-Kit (University of Chicago, <http://metz-roc.uchicago.edu/>).

3 Results

3.1 Voxel-Based Performance

After eliminating those voxels in each lesion with complex line-shapes that most closely match a perfectly phased Lorentzian, we find that the remaining voxels from malignant lesions contain complex spectra with larger DISPA radial deviations than voxels from benign lesions. The distributions of TRD for each voxel included in this study (~500 voxels) are shown in Fig. 3. ROC analysis performed on the TRD in each voxel yields an AUC of 0.89 (95% confidence interval [0.84, 0.91]) for the task of differentiating benign from malignant lesions. ROC curves are shown in Fig. 4.

3.2 Lesion-Based Performance

The malignant versus benign discrimination performance of both the mean and variance of the TRDs from each lesion was tested. The AUC generated from the average TRD in each lesion is 0.90 (95% CI [0.71, 1.00]). The AUC generated from the variance of TRD in each lesion is 0.84 (95% CI [0.61, 0.99]). The ROC curves generated for the task of classifying malignant from benign lesions based on average TRD and variance of TRD are presented in Fig. 4.

Fig. 3 Distributions of total DISPA radial differences in voxels from all malignant and benign lesions included in this study, both (a) before voxel elimination and (b) after voxel elimination. These figures illustrate the separation of voxels from malignant and benign lesions that occurs as a result of eliminating voxels with the lowest magnitude TRD in each lesion (with a change in AUC from 0.62 to 0.89).

Fig. 4 ROC curves summarizing the performance of the DISPA TRD in distinguishing voxels originating from malignant lesions and those originating from benign lesions and the performance of the average and variance of the radial difference in distinguishing malignant from benign lesions.

4 Discussion

The deviations from Lorentzian spectral shape observed in this study are likely the result of the blood oxygen-level dependent effect, wherein changes in the concentration of paramagnetic deoxyhemoglobin cause local variations in magnetic susceptibility.²⁵ Regions of dense neovasculature observed in tumors often exhibit relatively high concentrations of deoxygenated blood, associated with inhomogeneous non-Lorentzian broadening of local water resonances.¹⁶ The results of this work support

these earlier findings and demonstrate the differences in the degree of spectral-shape deviations observed in malignant and benign lesions.

Our previous work found that malignant lesions contain many voxels displaying relatively large-magnitude off-peak components.¹⁴ The analysis in that work, however, was performed on the magnitude spectrum and focused on a single component of the spectrum in each voxel. While this resulted in good diagnostic performance, this approach did not account for effects of tumor vasculature on multiple components of the water resonance. Aggressive tumor growth is associated with disorganized angiogenesis,²⁶ creating blood vessels of random orientation following tortuous paths. The shift in resonance frequency due to bulk magnetic susceptibility effects varies in accordance with the orientation of a blood vessel relative to the main magnetic field and the concentration of deoxyhemoglobin.²⁷ These two combined phenomena produce deviations from the Lorentzian lineshape at multiple spectral components. Therefore, the method used here to analyze spectral lineshape, which evaluates the water resonance lineshape at multiple frequencies, may represent the microenvironment of a tissue voxel more accurately than analysis of a single spectral component. Use of multiple spectral components for lesion distinction may be responsible for the relatively high AUC values reported here.

We further improved our sensitivity to non-Lorentzian features by analyzing complex spectral data rather than the magnitude data used in previously published work.¹⁴ Magnitude spectra are constructed by summing the real and imaginary parts in quadrature. This increases the overall line width of the spectrum, which can make low-amplitude spectral components close to the main resonance unresolvable from the main peak making lineshape analysis difficult. We avoided these problems by using the complex real and imaginary components of the spectra when analyzing the lesion discrimination performance of HiSS data.

The relative complexity of malignant tumor microvasculature and its effects on HiSS MRI-detectable spectral components suggests that spectral analysis may be valuable in distinguishing

malignant from benign tumors. Our hypothesis for this work was that, by examining additional spectral shape information, the data derived from HiSS acquisitions can be used as a more accurate breast lesion classifier than in previous work. We report similar voxel discrimination ROC AUC as our previous work.¹⁴ This is intuitive, as any voxel that contains a large, single non-Lorentzian component would be expected to display a large spectral shape distortion, and vice versa. Discrimination results for individual voxels were discussed to provide a rationale for using TRD as a diagnostic tool. However, in this pilot study, TRDs from entire ROIs were used to discriminate between benign and malignant lesions. In future work, we will test whether maps of individual voxels that display malignant characteristics are clinically useful, i.e., whether the spatial distribution of the TRD in each lesion provides diagnostically useful information. Despite the correlation between HiSS voxel features from the DISPA approach and the previously published method, the current method is more promising for lesion distinction than the previously published method, based on the larger lesion-based AUC (0.90 versus 0.83).

This work examined the same data as Ref. 14; therefore, several of the limitations of that study are applicable. Data were acquired at 1.5 T, and as a result, spectral dispersion and spatial resolution are limited. In addition, acquisition times were long (>2 min/slice), leading to motion artifacts. The current HiSS protocol includes bilateral, full-breast acquisition and sensitivity encoding to decrease acquisition time,²⁸ with a field strength of 3.0 T. Unfortunately, insufficient data have been acquired using new methods, to allow meaningful evaluation of DISPA.

Our limited HiSS dataset of 23 lesions was sufficient to assess the use of the DISPA spectral analysis technique in breast lesion classification, although additional patient data would increase the confidence of our results. A greater number of cases would also allow a more definitive comparison between the current method and that in previously published work. Currently, only limited conclusions can be made about the superiority of a particular method, as our limited sample size yields overlapping 95% confidence intervals for the results of both studies.

5 Conclusion

The DISPA technique has previously been applied to qualitatively and quantitatively evaluate characteristic complex spectral distortions due to various sources of line-broadening and phase-error. We have applied this spectroscopic analysis method to HiSS data in order to identify and quantify voxels in breast lesions displaying non-Lorentzian characteristics. We have shown that the absorption and dispersion spectral data obtained from HiSS acquisitions can enhance the performance of a breast lesion-classification scheme. Examining the full complex spectrum provides advantages over single off-peak component analysis, as it uses shape details of the entire spectrum not available when focusing on a single location of the magnitude spectrum.

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References

1. M. J. Paldino and D. P. Barboriak, "Fundamentals of quantitative dynamic contrast-enhanced MR imaging," *Magn. Reson. Imaging Clin. N. Am.* **17**(2), 277–289 (2009).
2. P. H. Kuo et al., "Gadolinium-based MR contrast agents and nephrogenic systemic fibrosis," *Radiology* **242**(3), 647–649 (2007).
3. P. Mansfield, "Spatial mapping of the chemical shift in NMR," *Magn. Reson. Med.* **1**(3), 370–386 (1984).
4. R. V. Mulkern and L. P. Panych, "Echo planar spectroscopic imaging," *Concepts Magn. Reson.* **13**(4), 213–237 (2001).
5. X. Fan et al., "Fat suppression with spectrally selective inversion vs. high spectral and spatial resolution MRI of breast lesions: qualitative and quantitative comparisons," *J. Magn. Reson. Imaging* **24**(6), 1311–1315 (2006).
6. M. Medved et al., "The effect of varying spectral resolution on the quality of high spectral and spatial resolution magnetic resonance images of the breast," *J. Magn. Reson. Imaging* **18**(4), 442–448 (2003).
7. M. Medved et al., "Clinical implementation of a multislice high spectral and spatial resolution-based MRI sequence to achieve unilateral full-breast coverage," *Magn. Reson. Imaging* **28**(1), 16–21 (2010).
8. N. Bhooshan et al., "Potential of computer-aided diagnosis of high spectral and spatial resolution (HiSS) MRI in the classification of breast lesions: HiSS MRI CADx in breast lesion classification," *J. Magn. Reson. Imaging* **39**(1), 59–67 (2013).
9. M. Medved et al., "Non-contrast enhanced MRI for evaluation of breast lesions: comparison of non-contrast enhanced high spectral and spatial resolution (HiSS) images versus contrast enhanced fat-suppressed images," *Acad. Radiol.* **18**(12), 1467–1474 (2011).
10. M. Medved et al., "Fourier component imaging of water resonance in human breast provides markers for malignancy," *Phys. Med. Biol.* **54**(19), 5767–5779 (2009).
11. M. Medved et al., "Fourier components of inhomogeneously broadened water resonances in breast: a new source of MRI contrast," *Magn. Reson. Med.* **52**(1), 193–196 (2004).
12. M. Medved et al., "High spectral and spatial resolution MRI of breast lesions: preliminary clinical experience," *Am. J. Roentgenol.* **186**(1), 30–37 (2006).
13. A. M. Wood et al., "Classification of breast lesions pre-contrast injection using water resonance lineshape analysis," *NMR Biomed.* **26**(5), 569–577 (2012).
14. W. A. Weiss et al., "Residual analysis of the water resonance signal in breast lesions imaged with high spectral and spatial resolution (HiSS) MRI: a pilot study," *Med. Phys.* **41**(1), 012303 (2014).
15. S. Foxley et al., "Quantitative analysis of water proton spectral lineshape: a novel source of contrast in MRI," *Phys. Med. Biol.* **53**(17), 4509 (2008).
16. S. Foxley et al., "Sensitivity to tumor microvasculature without contrast agents in high spectral and spatial resolution MR images," *Magn. Reson. Med.* **61**(2), 291–298 (2009).
17. A. G. Marshall and D. C. Roe, "Dispersion versus absorption: spectral line shape analysis for radiofrequency and microwave spectrometry," *Anal. Chem.* **50**(6), 756–763 (1978).
18. D. C. Roe, A. G. Marshall, and S. H. Smallcombe, "Dispersion versus absorption: analysis of line-broadening mechanisms in nuclear magnetic resonance spectrometry," *Anal. Chem.* **50**(6), 764–767 (1978).
19. A. G. Marshall, "Spectroscopic dispersion vs. absorption. A new method for distinguishing a distribution in peak position from a distribution in line width," *J. Phys. Chem.* **83**(4), 521–524 (1979).
20. A. G. Marshall and D. C. Roe, "Dispersion vs absorption (DISPA): Effects of digitization, noise, truncation of free induction decay, and zero-filling," *J. Magn. Reson.* **33**(3), 551–557 (1979).
21. A. G. Marshall and R. E. Bruce, "Dispersion versus absorption (DISPA) lineshape analysis. Effects of saturation, adjacent peaks, and simultaneous distribution in peak width and position," *J. Magn. Reson.* **39**(1), 47–54 (1980).
22. R. E. Bruce and A. G. Marshall, "Linearized dispersion:absorption plots for spectral line-shape analysis," *J. Phys. Chem.* **84**(11), 1372–1375 (1980).
23. C. E. Metz, "Basic principles of ROC analysis," *Semin. Nucl. Med.* **8**(4), 283–298 (1978).

24. A. R. van Erkel and P. M. T. Pattynama, "Receiver operating characteristic (ROC) analysis: Basic principles and applications in radiology," *Eur. J. Radiol.* **27**(2), 88–94 (1998).
25. S. Ogawa and T.-M. Lee, "Magnetic resonance imaging of blood vessels at high fields: In vivo and in vitro measurements and image simulation," *Magn. Reson. Med.* **16**(1), 9–18 (1990).
26. D. W. Siemann, "The unique characteristics of tumor vasculature and preclinical evidence for its selective disruption by tumor-vascular disrupting agents," *Cancer Treat. Rev.* **37**(1), 63–74 (2011).
27. K.-C. Chu et al., "Bulk magnetic susceptibility shifts in NMR studies of compartmentalized samples: use of paramagnetic reagents," *Magn. Reson. Med.* **13**(2), 239–262 (1990).
28. M. Medved et al., "Echo-planar spectroscopic imaging (EPSI) of the water resonance structure in human breast using sensitivity encoding (SENSE)," *Magn. Reson. Med.* **63**(6), 1557–1563 (2010).

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Milica Medved has extensive experience in MRI data acquisition and analysis. Her work focuses on several areas, the most important being development of HiSS MRI for clinical applications, mainly breast cancer imaging. Other areas include development of quantitative MRI methods, such as quantitative dynamic contrast enhanced MRI (DCEMRI), e.g., for antiangiogenic anticancer therapy assessment and diffusion weighted imaging (DWI), especially in prostate.

Gregory S. Karczmar has developed new approaches to functional and anatomic magnetic resonance imaging for over 30 years and has focused on applications of MRI to cancer, particularly breast and prostate cancer. He has developed innovative approaches to DCEMRI, diffusion-weighted imaging, and HiSS MRI for noncontrast imaging of breast cancer. He is director of MRI research at the University of Chicago and an expert in translational quantitative imaging research.

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