

High resolution MR breast imaging

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Conventional Magnetic Resonance Imaging (MRI) has good sensitivity for detecting very early breast cancers and pre-cancerous conditions, and is therefore an important screening tool for women who are at high risk for breast cancer [1]. However, improvements in specificity are required, particularly given the high sensitivity of MRI [2]. This is an especially difficult problem when MRI detects very small lesions that may or may not be early cancers. Data currently available suggest that for conventional MRI, the specificity for detection of cancers in a high-risk population is between 70% and 80% [3, 4]. However, specificity for detection of early cancers such as Ductal Carcinoma In Situ (DCIS) is as low as 50% [5].

Advances in MRI technology are required to address this problem. Work at the University of Chicago, in collaboration with Philips Healthcare, has developed High Spectral and Spatial resolution (HiSS) MR imaging for improved anatomic and functional imaging of the breast. The results obtained to date demonstrate that HiSS MR images acquired on Philips scanners using Echo-Planar Spectroscopic Imaging (EPSI) have advantages compared to conventional breast images [6-10].

HiSS MR imaging provides a high-resolution spectrum of water and fat signals in each small image voxel [8, 11, 12]. The spatial resolution of HiSS data is equal to that of conventional anatomic images, but additional information related to tissue composition and physiology is available from the detailed lineshapes of water and fat signals in each voxel. For example, deoxyhemoglobin in deoxygenated tumor blood vessels affects resonance frequency and water proton spectral lineshape, and detection of these effects with HiSS can increase sensitivity to tumor neovascularity. Therefore, HiSS provides important new information regarding tissue structure and function.

HiSS MRI should not be confused with the more common biomedical application of spectroscopic imaging to obtain water-suppressed, spatially

resolved spectra of metabolites. HiSS images are acquired without water suppression. Images are produced to represent features of the water and fat line shapes, such as signal peak height, line width, resonance frequency, number of resolved components, asymmetry of the water resonance, and changes in these features following contrast media injection. The resulting images increase the quality of anatomic and functional information that is available from MRI [8, 12].

HiSS images are acquired on a Philips Achieva scanner using a specially designed EPSI pulse sequence that provides spatial resolution of up to 400 microns in-plane and spectral resolution as high as 2.6 Hz. Signals are detected with either a 7- or 16-channel dedicated breast coil. Images of the peak height of the water resonance – referred to here as “water peak height images” – provide excellent morphologic detail.

These images can be T_1 weighted but their primary source of contrast is very strong T_2 weighting without the distortion that typically degrades gradient echo images with long TR. Figure 1 shows slices through a typical water peak height image of a breast with an invasive cancer (arrow, left). This image was acquired with spatial resolution of 500 microns, slice thickness of 1 mm, and spectral resolution of 8 Hz. The strong texture and the absence of fat signal results in clear morphologic detail.

Figure 1, right, shows a Maximum Intensity Projection (MIP) image of four slices, acquired with HiSS, surrounding the slice shown on the right. The connectivity of the parenchyma and blood vessels is more easily visualized in the MIP. Because of the excellent fat suppression in the individual slices, background signal does not accumulate in the water peak height MIP as it does in conventional MIPs.

HiSS is a natural extension of the work of previous investigators, who used low spectral resolution imaging to separate fat and water signals and correct for B_0 inhomogeneity, and

► **Conventional MRI specificity for detecting early cancers like DCIS is as low as 50%.**

► **HiSS MRI not to be confused with biomedical spectroscopic imaging.**

produced substantially improved MR images [13-16]. Recently, advances in MR hardware and software have allowed rapid acquisition of data using EPSI [17, 18] at very high spectral and spatial resolution. This allows resolution of the details of the water and fat line-shapes in each small image pixel [8, 19, 20] with reasonable acquisition times and minimal eddy current distortion.

Work in this laboratory [8, 19-23] and other laboratories [24, 25], demonstrates that HiSS data sets can be used to produce images with significantly improved anatomic detail relative to conventional spin-echo or gradient echo imaging. In the brain, high field data with relatively low spectral resolution can be analyzed in the “time” domain. This produces high-quality images of vasculature and other structures that produce variations in magnetic susceptibility (for example the work of Reichenbach et al. [26], and recent brain imaging at 7T by Duyn et al. at NIH [27]). Hu et al. demonstrated that Susceptibility-Weighted Imaging (SWI) [28] can produce very high quality venograms of the brain.

HiSS is also useful for brain imaging [29]. However, it is more helpful for imaging breast cancers. In breast, because of the large fat content of surrounding tissues and the significant inhomogeneous broadening of the water resonance, it is helpful to acquire data at high spectral resolution and bandwidth, and analyze data in the frequency domain.

In practice, even simple pre-contrast water peak height images are very sensitive to morphologic details, including blood vessels. Figure 2 compares HiSS MR images at a spatial resolution of 500 μ in-plane, slice thickness of 1 mm, with conventional fat-saturated images. Lesions are clearly visible and margins and morphology are well defined in the HiSS images, without the need for contrast agents.

Advantages of HiSS images:

Advantages of HiSS images are due to a number of factors:

- more precisely defined anatomy
- improved fat/water separation
- optimal signal-to-noise ratio per unit time
- vascular imaging without contrast agents.

More precisely defined anatomy

Spectral data associated with each k-space point can be used to calculate an “ideal” MRI image, that is, an MRI image obtained in the absence of magnetic susceptibility gradients and chemical shift. This is a significant departure from

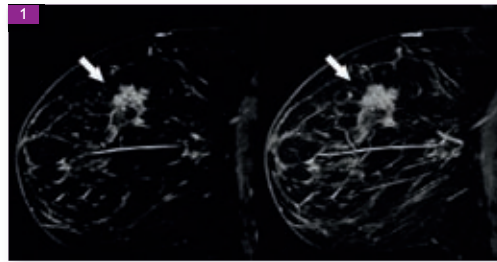


Figure 1. Water peak height image of invasive tumor with DCIS component (left). The fat background is completely suppressed and some blood vessels can be seen near the cancer. Maximum intensity projection of four slices through the lesion is shown on the right.

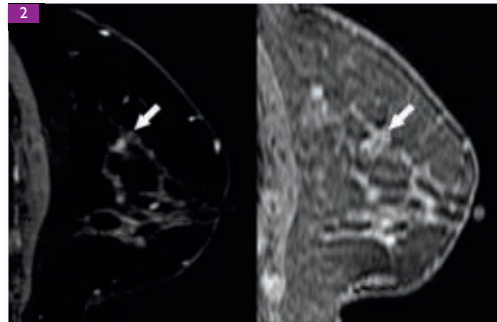


Figure 2. An HiSS water peak height image of an IDC lesion (arrow) is shown on the left. A routine fat-suppressed image is shown on the right, acquired with selective inversion to suppress fat. Visualization of tumor morphology and edges is improved in the HiSS water peak height image.

conventional MRI where spatial and spectral information are mixed together. Improved anatomic detail clearly delineates tumor boundaries and internal structure.

Improved fat/water separation

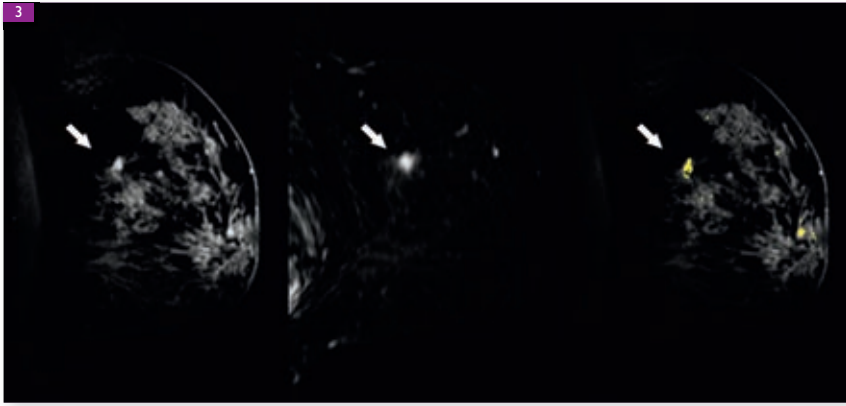
Conventional methods use frequency selective saturation, frequency selective inversion, and related methods to suppress the fat signal. This can reduce the signal-to-noise ratio of the water resonance via magnetization transfer effects or partial inversion of the water resonance. B_0 gradients result in poor fat suppression with conventional methods. HiSS achieves fat suppression by adequately sampling the proton free-induction decay (FID), producing a fat/water spectrum, fitting the fat resonance, and removing it. If the time over which the FID is sampled is optimized (see below) this approach can increase signal-to-noise ratio rather than reducing it.

Optimal signal-to-noise ratio per unit time

Conventional imaging acquires only a single gradient echo. However, optimal signal-to-noise ratio per unit time requires sampling the FID for slightly less than one T_2^* . In fact, since the water resonance frequently is inhomogeneously broadened, evaluation of data in the spectral domain reduces effects of destructive interference between different Fourier components and improves the signal-to-noise ratio associated with longer sampling of the FID.

For these reasons - while acquisition of HiSS data typically requires longer run times than conventional data - there is significant potential for improved signal-to-noise ratio per unit time and/or increased spatial resolution.

► **HiSS images lesions clearly, defining margins and morphology without contrast agents.**



▲ Figure 3. An HiSS water peak height image of an IDC lesion (left, indicated by arrow) compared to a DCE-MRI subtraction image (middle). Image on the right shows regions of high water spectrum asymmetry in yellow – possibly indicating high deoxyhemoglobin in tumor vessels.

Vascular imaging without contrast agents
Previous work on animal models of cancer in this laboratory demonstrates that HiSS images can be used to map tumor vasculature without the need to inject contrast agents [30]. In tumors, the imbalance between oxygen delivery and oxygen utilization produces high concentrations of deoxyhemoglobin in blood vessels and this leads to frequency shifts and changes in water signal lineshape [31].

Because the spatial distribution of tumor blood vessels is often very heterogeneous within individual image voxels, small subvoxel clumps of deoxygenated blood vessels can produce shoulders or partially resolved components of the water resonance that are reliably detected in high spectral resolution data. The water lineshape (for example, water resonance asymmetry, shoulders or partially resolved components on the water resonance) can be analyzed to produce images of variations in local magnetic susceptibility.

These images are strongly correlated with images of vascular density around tumors produced from Dynamic Contrast Enhanced-Magnetic Resonance Imaging (DCE-MRI) data. For example, Figure 3 compares an image of water resonance asymmetry produced from a HiSS dataset with a “difference image” produced from DCE-MRI data, showing regions with rapid contrast media uptake. The regions around the tumor that have high vascular density as shown on the DCE-MRI difference image also have strong water resonance asymmetry.

HiSS as a DCE-MRI substitute for detecting early breast cancer

New American Cancer Society (ACS) guidelines for screening of women who are at increased risk for breast cancer are likely to significantly increase the number of women receiving MRI screening exams each year [1]. This increases

the importance of new approaches to MRI that increase sensitivity. DCE-MRI is currently the primary tool in MRI detection of breast cancers. Due to their dense and permeable vasculature, breast tumors enhance rapidly and strongly in comparison to normal breast tissue.

While DCE-MRI has obvious advantages, it also has some shortcomings:

- as greater numbers of women are screened with MRI, concerns about nephrotoxicity of contrast agents [32] and other reactions to contrast media become significant.
- diffusive and convective motion of contrast agent molecules blurs tumor edges, handicaps tumor delineation, and morphology assessment. Susceptibility gradients caused by the contrast agent further degrade image quality; particularly at tumor edges where there may be an abrupt change in contrast media concentration. Thus, it would be advantageous for radiologists to examine the “true” morphology of lesions, before contrast agent is injected. In principle, fat-suppressed images can be used for this purpose. However, conventional fat-suppression is often incomplete and image quality is modest.
- DCE-MRI has the highest specificity when acquired with high temporal and spatial resolution – but this is not possible in conventional clinical scans, due to the need to cover both breasts for lesion detection. Temporal resolution is particularly important for detection of DCIS, as shown by Dr. Newstead and co-workers, because DCIS can typically be seen clearly against a dark background in difference images produced from images acquired during the first 30 – 60 seconds after contrast injection [33].
- imaging of tumor morphology and tumor vasculature with HiSS pre-contrast injection may lead to increased diagnostic accuracy.
- HiSS is easily combined with other pulse sequences. For example, the T_2 or apparent diffusion coefficient (ADC) of each component of the water resonance can be measured.

Implementation of HiSS MRI on the Philips Achieva Scanner

Collaboration between scientists at Philips Healthcare, Gyrotools, and the University of Chicago has produced a high-resolution EPSI pulse sequence and data processing software. This is integrated into the Philips Operating system so that HiSS scans and image reconstruction can operate routinely in the clinical environment. Optimization of multislice imaging protocols allows full breast imaging using HiSS with clinically acceptable acquisition times (8 – 12 minutes). Further enhancement

► **New ACS guidelines are likely to significantly increase the number of MRI screening exams.**

of HiSS acquisition speed is expected soon with the development of parallel imaging reconstruction methods for HiSS. Therefore, it is likely that HiSS will provide an important addition to the tools available to radiologists for breast cancer detection and diagnosis.

Acknowledgments

This work was supported by grants from the NIBIB (RO1 EB003108-01), the NCI (R01CA78803), NIH/NCI (P50 CA125183-01) and Philips Healthcare. The authors would like to thank Philips Healthcare for their assistance with this manuscript ■

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