Maximum Entropy Reconstruction of Correlated Spectroscopy of Human Breast In Vivo

Brian L Burns[1,2], Jon K Furuyama[3], Neil Wilson[3], Nicki DeBruhl[3], Alex Bui[2,3], and M. Albert Thomas[3]
[1]*Biomedical Engineering, UCLA, Los Angeles, CA, United States,* [2]*Medical Imaging Informatics (MII), UCLA, Los Angeles, CA, United States,* [3]*Department of Radiological Sciences, UCLA*

Introduction – The altered metabolism of breast cancer tissues gives rise to changes in metabolite concentrations that are detectable using two-dimensional (2D) Magnetic Resonance Spectroscopy (MRS) [1]. 2D Localized-Correlated Spectroscopy (L-COSY) MRS has been shown to increase the specificity and sensitivity of tumor grade classification when used with traditional techniques, such as Dynamic Contrast Enhanced (DCE)-MRI [1]. However, because of the number of t_1 increments used to construct the indirect spectral dimension (F_1), the L-COSY sequence requires on the order of 25 minutes for 100 t_1 increments and 8 averages [2]. To reduce scan times to a clinically acceptable 12 minutes, only 45 t_1 increments are typically used, but this reduces spectral resolution along F_1. Maximum entropy (MaxEnt) image reconstruction techniques have been used in Nuclear Magnetic Resonance (NMR) to non-uniformly under-sample (NUS) indirect spectral dimensions and then reconstruct the most statistically likely fully-sampled multi-dimensional spectrum [3,4]. This technique can be used to accelerate the collection of 2D L-COSY data *in vivo* by selectively under-sampling along t_1. We show that under-sampling the indirect dimension by ~50% and reconstructing the spectrum using MaxEnt preserves the metabolite diagonal peaks: olefinic fat (UFD), methyl fat (FMETD), and choline (Cho) and the cross peaks: unsaturated fatty acid, right (UFR), unsaturated fatty acid, left (UFL), and triglyceryl fat (TGFR) which have demonstrated clinical importance.

Methods – To qualitatively measure the performance of the MaxEnt reconstruction algorithm on NUS *in vivo* data, fully sampled 2D L-COSY scans of both healthy (n=10) and malignant (n=8) breast tissues were acquired on a 3T Siemens Trio scanner using the following parameters: 1cm^3 voxel size, TR/TE=2s/30ms, 45 t_1 increments, 8 averages, and no water suppression. Both scans were retrospectively under-sampled to 22 lines along the t_1 dimension, apodized along the t_1 and t_2 dimensions, and then reconstructed using the MaxEnt algorithm to 45 lines. MaxEnt is a constrained convex optimization algorithm that uses a variant of the conjugate gradient method to iteratively solve the inverse problem [5]:

$$maximize\ S_{1/2}(f)\ s.t.\ ||F^{-1}Kf - D||_2 <= \sigma \qquad (1)$$

where f is the estimated fully-sampled spectrum at each iteration, F^{-1} is the inverse Fourier transform, K is the NUS matrix, D is the time-domain measured data, σ is the noise standard deviation, and $S_{1/2}(f)$ is the spin-½ entropy of the estimated spectrum [3]. The spectrum with the highest entropy is that which conforms to the uniform distribution and has a flat baseline. Therefore, by maximizing the spin-½ entropy in (1), MaxEnt enforces sparsity of the estimated spectrum in the frequency domain and reduces incoherent aliasing artifacts in the spectrum caused by NUS. The fidelity constraint ensures that peaks in the estimated spectrum must come from the sampled data to within a tolerance of the noise. The reconstruction is performed over both dimensions simultaneously as opposed to a series of 1D reconstructions as implemented elsewhere [4].

Results and Discussion – Figures 1A and 1B show the 2D L-COSY spectra of the fully sampled and ~50% MaxEnt reconstruction of the NUS healthy breast tissue, respectively. As can be seen, the major diagonal and cross peaks present in healthy fatty breast tissue are present in both spectra. The peak locations, line shapes, and amplitudes of the NUS data are roughly equivalent to the fully sampled data; however a slight loss in spectral resolution along F_1 is evident by the elongation of the UFR peak in the MaxEnt reconstruction. There is no corresponding loss in resolution along F_2. Figures 2A and 2B show 2D L-COSY spectra of the fully sampled and the ~50% reconstruction of the NUS malignant fatty breast tissue, respectively. The presence of water in fatty breast tissue is an indicator of breast cancer, and because of its high concentration, its broad line-width obscures many of the cross-peaks seen in Figure 1. However, the UFR cross-peak is clearly visible in figures 2A and 2B, and the MaxEnt reconstructed peak is comparable to the fully sampled peak, even in the presence of noise. The Cho diagonal peak in figure 2, which is a sign of increased metabolic activity and malignancy, is fully resolved in the MaxEnt reconstruction and shows good agreement with the peak in the fully sampled spectrum.

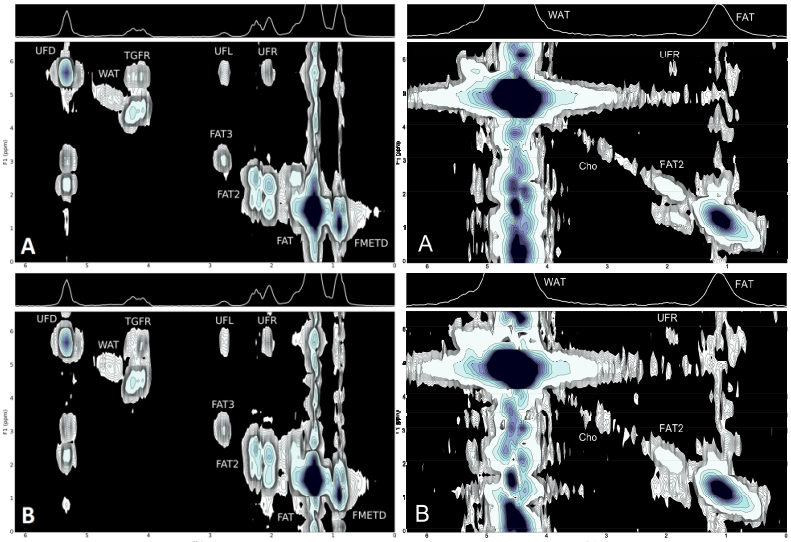

Fig 2: *in vivo* 2D L-COSY spectra of a 25 year old healthy fatty breast tissue **(A)** fully sampled along t_1 **(B)** 50% reconstruction along t_1

Fig 2: *in vivo* 2D L-COSY spectra of a 55 year old malignant tumor in fatty breast tissue **(A)** fully sampled along t_1 **(B)** 50% reconstruction along t_1

Conclusions – We have shown that it is possible to under-sample the L-COSY sequence by up to ~50% and reconstruct *in vivo* spectra from as few as 22 t_1 lines that show similar spectral characteristics to spectra from fully sampled data. This acceleration translates into a sub-6 minute scan time if 8 averages are used and increases the potential use of MRS for breast cancer screening in the clinic. If increased spectral resolution is needed, the MaxEnt reconstruction is not limited to 45 t_1 points and can reconstruct many more NUS points than what was used in these experiments.

References – [1] Lipnick, et al., NMR Biomed. 2010; 23: 922-930 **[2]** Thomas, et al., Mag. Res. Med. 2001; 46:58-67 **[3]** Daniell & Hore, J. Mag. Res. 1989; 84: 515-536 **[4]** Hoch & Stern, 1996, Wiley-Liss, New York **[5]** Skilling & Bryan, Mon. Not. Roy. Astr. Soc. 1984; 211: 111-124

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