Quantitative MRS of Ovaries and Ovarian Masses at 3T: Methodology and Initial Findings

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Introduction: There is a great need for improved imaging biomarkers for ovarian cancer. Proton magnetic resonance spectroscopy has been shown to have clinical value in managing cancers of the brain, breast, and prostate, and it may be useful for diagnosing and monitoring treatment of ovarian cancer. MRS in ovarian cancer is particularly challenging to the highly heterogeneous nature of the disease, which may consist of solid masses, cystic masses, and various combinations thereof. Initial reports have shown that it is possible to detect total choline-containing compounds (tCho), and, less frequently, creatine and glycine (1-3). Additionally, there have been several *in vivo* observations of a resonance at 2.05 ppm that has not been definitively identified, but may have contributions from NAA or sialic acid (1,4). There has also been one report of quantitative MRS choline measurements using water as an internal reference and assuming a fixed water concentration (35mM) (3).

The primary aim of this work is to describe our experience in developing quantitative MRS of normal ovaries and ovarian masses. For this series of spectra – the largest ovarian MRS dataset reported to date – we describe the metabolites observed, quantitative measurements of spectral quality (signal-to-noise and linewidths), and technical challenges encountered. These findings are compared between spectra acquired in cystic masses, primarily solid masses, and normal ovaries. Furthermore, we describe an alternative strategy for quantifying tCho in ovarian masses, based on methods previously developed for breast cancer. This approach measures and corrects for water T_2, and gives concentrations in molal units (mmol/kg-water) rather than molar units (mmol/L). This avoids the need to assume fixed values of water concentration or T_2 relaxation rates, which vary greatly between solid and cystic regions.

Methods: Subjects were recruited to this IRB-approved study in three cohorts: patients about to receive surgery for a primary pelvic mass, patients with recurring ovarian cancer about to begin a new therapy, and healthy female volunteers. All scans were performed on a 3T Siemens TIM system (Siemens, Erlangen, Germany) using the spine and body matrix array receive coils. T_2-weighted anatomical and dynamic contrast-enhanced images were used to guide the MRS voxel placement. Prior to spectral acquisition, the transmit power and shim currents were adjusted using prototype software provided by the manufacturer. All spectra were acquired using an optimized PRESS sequence, without OVS. Respiratory triggering was not used. Water reference scans were acquired with TR=6s and TE=50, 75, 100, 125, 150 ms. Metabolite spectra were acquired from the same voxel, with weak water suppression enabled, and using either fixed TE (TE=125ms, 64-256 averages) or with TE averaging (TE=50-200ms in 64-256 increments). All acquisitions used 1024 complex points and 2 kHz bandwidth.

Spectra were analyzed using semi-automated routines developed in Matlab (Mathworks, Natick, MA). Water T_2 reference scans were fit with a mono-exponential decay to estimate water T_2 and M_0. The single-shot water signal-to-noise (wSNR) was corrected to estimate the theoretical water SNR at TE=0ms. Metabolite spectra were individually phased and frequency-corrected prior to averaging to reduce motion artifacts. SVD-based passband filtering was used to remove resonances outside the 2-4ppm range and reduce baseline distortion. The choline region (3.03-3.43ppm) was fit with a single Voigt lineshape and a linear baseline. Objective detection of tCho required SNR>2, Cramer-Rao estimated standard deviation < 200% of the peak amplitude, and total linewidth>4Hz. The choline:water ratio was then converted to a molal concentration (mmol tCho / kg-water) as described previously for breast MRS (5). After fitting, all spectra and fit results were qualitatively assessed to identify resonances other than tCho, and to assign a data quality score (good, fair, or poor) for each dataset.

Results: An example spectrum is shown in figure 1, and the findings of all 68 spectra are given in table 1. In healthy ovaries, few metabolites were observed due to the small voxel size and difficulty in shimming. The cystic spectra, which included both benign and borderline pathologies, had generally high SNR and narrow linewidths, but few measured metabolites. The solid/mixed group, which included benign, borderline, and malignant pathologies, had generally good quality with acceptable water linewidths and high SNR. A tCho resonance was more commonly detected in spectra with higher than median wSNR (93%) and with linewidths narrow than the median (86%), compared with 55% overall.

Discussion: The tCho quantification strategy proposed here, using water T_2 measurements to estimate M_0, produces tCho levels that are physiologically reasonable and similar to breast MRS. This approach avoid the need to assume fixed water concentration and T_2 values, which is highly variable in ovarian disease. We found that creatine was not observed often enough to be used as a internal reference, as proposed in Ref (1). Many of the lower quality spectra were affected by motion. Based on cine imaging, the predominant source of motion was peristaltic rather than respiratory. Larger voxels also gave worse localization and increased phasing problems.

Conclusion: Acquiring spectra in normal ovaries is feasible but limited by their small size. In masses, spectra from primarily solid regions of masses yielded more metabolic information than cystic regions.

References: 1) Stanwell P et al., Invest Radiol 2008; 2) Booth SJ et al., Gyn Onc 2007; 3) McLean MA et al., MRM 2009; 4) Kolwijck E et al., NMR Biomed 2009; 5) Bolan PJ et al., MRM 2003.
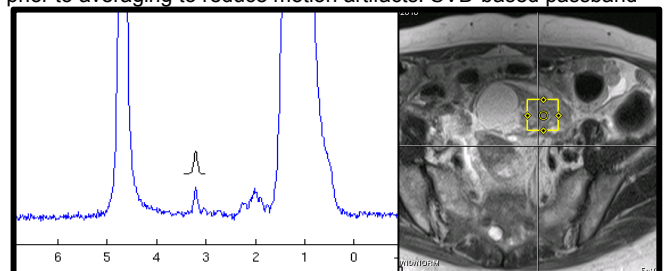
Fig.1 - Example spectrum with fit from a stage IIIC serous carcinoma, [tCho]=0.9mmol/kg, water FWHM=10.5Hz.

	Ovary	Cyst	Solid/Mixed
# Spectra	20	16	32
# Subjects	8	11	20
Quality (good/fair/poor)	7/7/6	5/8/3	24/5/3
Water T2 (ms)	57.3 – 353.7 (81.2)	67.8 – 1302.7 (305.0)	21.7 – 413.3 (76.8)
Water LW (hz)	8.5 – 160.0 (21.7)	5.3 – 29.2 (9.1)	6.3 – 55 (19.1)
Water SNR (wSNR)	107 – 11,460 (2500)	230 – 215,800 (31,700)	190 – 155,800 (9,750)
Voxel size (mL)	1.1 – 9.6 (2.9)	3.4 – 168 (24.8)	1.7 – 89 (9.1)
Cr +	0/14	1/13	4/29
Gly +	0/14	1/13	2/29
2.05ppm +	0/14	1/13	2/29
tCho +	3/14	2/13	20/29
[tCho] (mmol/kg)	0.5, 0.7, 2.5	0.7	0.2 – 3.4 (0.9)

Table 1 - Spectral findings in normal ovaries, cystic masses, and primarily solid masses. Quantitative values are given as ranges, with the median value in parenthesis. Peak detection rates include only spectra of good or fair quality.