In-vivo brain fast Rosette Spectroscopic Imaging (RSI) with reduced gradient demands/improved patient comfort and a processing pipeline with automated LCModel quantification, for all acquired voxels

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TARGET AUDIENCE: Researchers and clinicians interested in high-sensitivity fast spectroscopic imaging (SI) and automatic processing of SI data. Researchers and device manufacturers interested in fast data acquisition with decreased strain on scanner gradient system and decreased acoustic noise, for improved patient comfort.

PURPOSE: I) To optimize the 2D/3D Rosette Spectroscopic Imaging (RSI, [1]) with LASER excitation for SI data acquisition with reduced demands on the scanner gradient system and demonstrate it *in-vivo* brain. **II**) To develop a pipeline for automatic SI data processing. **III**) To compare two multi-channel recombination methods, when no calibration scans are collected: the 1st FID point [2] (Met 1) and lowest CRLB (Crammer-Rao Lower Bounds) weighted metabolite [3] (Met 2). **IV**) To compare RSI to conventional phase encoding (PE) CSI: SNR sensitivity $tSNR = SNR/\sqrt{T_{AQ}}$, point spread function (PSF) and spectral information.

METHODS: I) The rosette trajectories are described by $\boldsymbol{k = k_{max} \cdot sin(\omega_1 t) \cdot e^{i\omega_2 t}}$ and they were demonstrated in [1] for highest sensitivity while achieving fastest acquisition for a given spatial resolution (Nx, fov) and spectral width (SW). That implementation uses the highest ω_2 allowed by hardware constraints, to maximize trajectory twist and K-space coverage within a TR, reducing the number of shots needed to fully sample K-t space. By using the setting $\omega_2 = \omega_1$, the demands on the gradient system are significantly reduced (Fig 1), gradient (G) readout strength and slew rate (SR) are constant. A 2D 20x20 RSI acquisition (T_{AQ}=32 sec, TR=1s) and a 3D 20x20x12 RSI acquisition with 8mm isotropic resolution (0.5cm^3, T_{AQ}=5-10min, TR=1-1.5s), with G_{max}=5.8mT/m and S_{max}=45mT/m/ms are demonstrated. 3D RSI data were collected in a BRAINO MRS phantom and *in-vivo*, in 3 healthy controls (HC) and 2 glioblastoma (GBM) patients, on Siemens 3T MR and 3T MR/PET scanners, using a 32-channel head and a 12-channel head-neck coil. **II**) We developed programs to pass reconstructed data to LCModel software [4,5] for automatic quantification of all voxels, and programs to read LCModel output (metabolites ratios, CRLB values, phase-corrected spectra, baseline, etc for all voxels). Spectra were processed in the 4.0-0.2ppm range. **III)** After gridding [6] and reconstruction of data for each channel to a 32x32x16 matrix, the channels are either combined using 1st FID point method [2], or 0th and 1st order phase-corrected with LCModel and combined using the metabolite with best quantification accuracy [3]. Average SNR and CRLB are compared between the two methods for five metabolites (LCModel sums): tNAA (NAA+NAAG), tCr (Cr+PCr), tCho (PCho+GPC), mIns (Ins+Gly) and Glx(Glu+Glc). **IV**) Conventional 2D phase encoded (PE) and 3D elliptical PE (ePE) CSI with same nominal resolution as RSI were collected in phantom and 2D ePE scans were collected in one HC and one GBM patient. Bland-Altman analysis was used to compare 3D RSI and 3D ePE sequences. Included in analysis are all voxels with CRLB<20% for the five metabolites considered. In addition, we calculate the scalar product of the LCModel baseline-subtracted, phase-corrected normalized spectra $\boldsymbol{RSI \cdot ePE}$ in each voxel, for all voxels. A scalar product of 1 represents identical spectral information for the two sequences. PSF was simulated and FWHM/FVHM (Full Width/Volume at Half Maximum) was calculated [7] for all sequences.

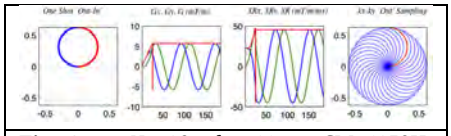

Fig 1:. *Nx=20, fov=16cm, SW=1250Hz Acquisition K-space traj (left), x-,y-gradient waveforms and strength (2nd left), slew rate function (2nd right), K-space coverage.*

RESULTS: I) Used SR=45mT/m/ms is more than three-fold lower than for fastest RSI [1], spiral SI [8] or echo-planar SI [9] at similar spatial resolutions, and the T_{AQ} of 5 to 10 mins for 3D RSI the same as 3D SSI [8]. **II)** Processing pipeline developed was used to handle all data for comparisons, metabolites/CRLB map generation and display, storage, etc **III)** Recombination Met 2 [3] achieves an average of 8% greater SNR in phantom, and same avergae CRLB as Met 1 [2]; *in-vivo* (for the 5 subjects), Met 2 achieves 3% higher SNR and 3% lower average CRLB than Met 1. **IV**) Bland-Altman agreement (using NAA/Sum, [8]) of 3D RSI and 3D ePE has narrow 95% confidence interval for difference: 13% of mean for unfiltered data (Fig 2) and 6% for Hamming filtered data (not shown). xy-FWHM and FVHM are only 5% and 7% larger for RSI than PE, but much narrower/smaller than for elliptical PE sequence Average scalar product $\boldsymbol{RSI \cdot ePE}$ agreement**,** for 2D in-vivo data in a GBM patient, for N=197 (of 288) voxels with CRLB<20% for all five metabs, is 0.962(+/-0.013) (Fig 3). For 2D, RSI average measured SNR sensitivity in phantom, for all 5 metabs, was found to be 15% greater than for 2D PE, and the normalized sensitivity (***nSNR=tSNR/*FVHM**) ratios $nSNR_{RSI}/nSNR_{PE}$=1.07 and $nSNR_{RSI}/nSNR_{ePE}$=1.12. For the 3D acquisitions, $tSNR_{RSI}/tSNR_{ePE}$=0.49 but, because effective RSI voxel size is 3 times smaller than for ePE, $FVHM_{RSI/ePE}$=0.34 (0.55cm^3/1.60cm^3), $nSNR_{RSI}/nSNR_{ePE}$=1.43. In Fig 4, example *in*-vivo spectra are shown for 2D scans in a GBM patient.

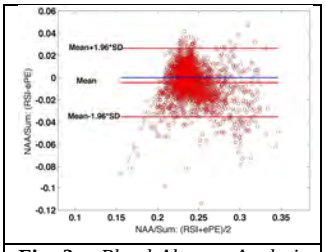

Fig 2:. *Bland-Altman Analysis 3D RSI vs ePE (N=2725/2816)*

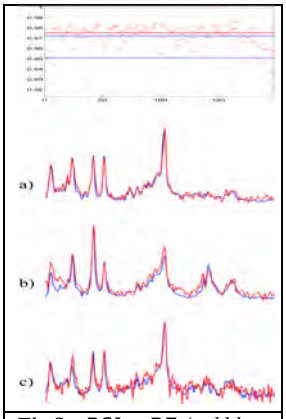

Fig 3:. $\boldsymbol{RSI \cdot ePE}$ *(red,blue; N=197)* ***a)*** *best* ***b)*** *median* ***c)*** *(mean-2*SD) match*

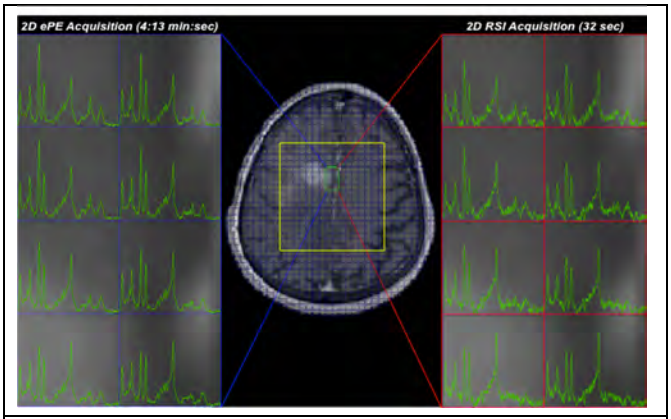

Fig 4: *Center: T1 image for one GBM patient, at 2D SI position. Yellow box: LASER 96x80 mm (AP-RL) excited VOI. Green box: location for sample spectra displayed. 2D RSI & ePE nominal resolution: 8x8x18mm^3*

DISCUSSION/CONCLUSION: When no SI calibration scan is collected/used, channel rescombination as in [3], performed somewhat better (3-8%) than the method in [2], but at significantly longer computational cost and only for spatially (Hamming) filtered data. Automatic processing is necessary for fast SI techniques due to large number of spectra generated (>2K for one 3D RSI scan), and we developed the programs which, with LCModel, form a complete processing pipeline. LASER-RSI is a fast, high sensitivity SI technique which can collect useful 2D data in less than one minute (Fig 4) and high resolution data (0.5cc) in the 3D implementation in 5 to 10 mins. Use of the $\omega_2 = \omega_1$ setting reduces the demands on scanner gradient system (decreasing Eddy currents and frequency drift), which also results in decreased acoustic noise and decreased scanner vibrations, improving patient comfort.

References: [1] Schirda *et al.*, JMRI '09; [2] Brown, MRM '04; [3] Maril *et al.*, JMRI '05; [4] http://www.s-provencher.com/pages/lcmodel.shtml; [5] Provencher, MRM '93; [6] Jackson *et al.*, IEEE Trans Med Imag '91; [7] Zierhut *et al.*, JMRI '09; [8] Andronesi *et al.*, Radiology '12; [9] Posse *et al.*, Radiology '94