High spatiotemporal resolution for molecular imaging with BIRDS

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INTRODUCTION We recently showed that pH and/or temperature maps of rat brain can be obtained within minutes using ***B***iosensor ***I***maging of ***R***edundant ***D***eviation in ***S***hifts (BIRDS) method. The BIRDS method is based on the strong dependence of temperature and pH on the proton chemical shifts from complexes between lanthanide ions (e.g., Tm^{3+}) and macrocyclic chelates of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetra (methylene phosphonate) or $TmDOTP^{5-}$ and 1,4,7,10-tetraazacyclododecane-1,4,7,10- tetramethyl-1,4,7,10-tetraacetate or $TmDOTMA^{-}$ **[1,2]**. Using these two agents, BIRDS with high speed 2D chemical shift imaging (CSI) at 11.7T allows a spatial resolution of ~10 μL in the rat's cerebral cortex. However many applications of BIRDS require whole brain coverage and much higher spatial resolution. To that end, we developed a ~1 μL spatial resolution 3D CSI method where the temporal resolution is kept at 5 minutes using *reduced k-space spherical encoding*. We discuss details of some in vitro results with $TmDOTMA^{-}$ as the agent for temperature mapping.

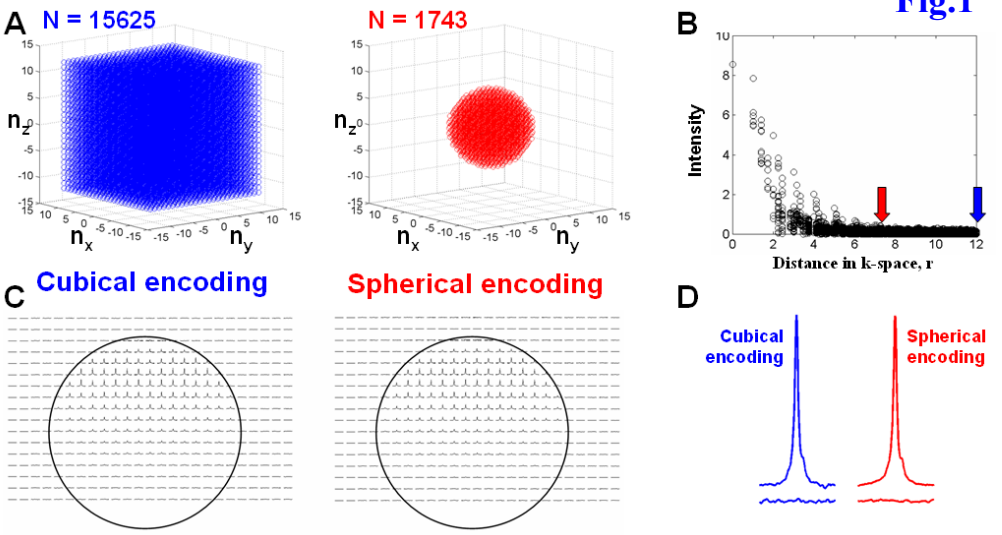
MATERIALS AND METHODS The 25×25×25 3D CSI data of a phantom containing 5 mM $TmDOTMA^{-}$ **(Fig. 1)** were obtained on a modified 11.7T horizontal-bore spectrometer using a ^{1}H resonator/surface coil RF probe. A single-banded refocused 90^{0} Shinnar-Le Roux (SLR) RF pulse of 40 kHz bandwidth and 205 μs was used for selective excitation of the $TmDOTMA^{-}$ methyl group. The data was acquired with a TR of 5 ms and a field of view (FOV) of 25×25×25 mm^3. The spectra were line broadened (300 Hz), phased (zero order), and baseline corrected (first order). Two 3D CSI maps were obtained using the same CSI acquired dataset. One 3D CSI map was obtained using all 25×25×25 (=**15625**) cubical encoded steps **(Fig. 1A, left)**, whereas the other was obtained using **1743** spherical encoded steps **(Fig. 1A, right)**.

RESULTS A cubical 25×25×25 3D CSI dataset requires 15625 encoding steps, where the steps in each direction of k-space (n_x, n_y and n_z) are incremented sequentially by 1 from -12 to 12 **(Fig. 1A, left).** Thus, each encoding step (n_x, n_y, n_z) can be characterized by a distance r to the center of k-space given by

$$r = \sqrt{n_x^{\,2} + n_y^{\,2} + n_z^{\,2}} \qquad [1]$$

The analysis of spectra obtained for each of the 15625 encoding steps before spatial 3D Fourier Transformation indicate that the intensity of the $TmDOTMA^{-}$ methyl group resonance decrease as the distance r to the center of k-space increases **(Fig. 1B).** Moreover, the encoding steps corresponding to larger r values have negligible contribution to the total signal **(Fig. 1B)**, and thus they can be neglected. Based on these results, we determined a cutoff value of 7.4 for r (indicated by a red arrow in **Fig. 1B**). Thus, the number of encoding steps can be decreased from 15625 to 1743, corresponding to encoding steps for which $r \leq 7.4$ **(Fig. 1A, right)**. To asses the effect of the reduction in the number of acquired steps on the signal of CSI voxels, we generated two different 3D CSI maps, one obtained with 15625 cubical encoding steps **(Fig. 1C, left)** and the other with 1743 spherical encoding steps **(Fig. 1C, right)**. The results show that there is no significant difference between the signal intensities in the voxels of the two 3D CSI maps **(Fig. 1D)**.

Fig.1



DISCUSSION To date, for BIRDS we acquired 2D CSI data of a 4 mm slice using 16×16 encoding steps with field of view of 2.56×2.56 cm, a TR of 11 ms and 100 steps for averaging, resulting in total acquisition times of 5 minutes and a spatial resolution of ~ 10 μL **[1,2]**. In the current study we demonstrate the feasibility of obtaining a 3D CSI dataset with a spatial resolution of ~1 μL within 5 minutes, using 1743 spherical encoding steps, a TR of 5 ms and 32 averages. The lower number of averages for the 3D CSI experiment will be compensated by the acquisition of the signal from the whole brain. For the 2D CSI experiment, the signal was acquired only from a 4 mm slice, thus requiring a larger number of averages. These results demonstrate a significant improvement in the spatiotemporal resolution of BIRDS which has numerous applications for physiological imaging in rodent brain studies.

REFERENCES

[1] Coman D, Trubel HK, Rycyna RE, Hyder F. (2009) Brain temperature and pH measured by ^{1}H chemical shift imaging of a thulium agent. *NMR Biomed.* 22:229-239;
[2] Coman D, Trubel HK, Hyder F. (2009) Brain temperature by Biosensor Imaging of Redundant Deviation in Shifts (BIRDS): Comparison between $TmDOTP^{5-}$ and $TmDOTMA^{-}$. *NMR Biomed.* (in press)

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