Design and Characterization of A Set Of MRI Histology RF Coils Dedicated to Standardized Slide Sections

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Introduction: Preclinical studies predominantly rely on the use mice as subjects to test and validate novel MRI techniques. One of the major challenges encountered in validating the MRI findings is the lack of accurate co-registration with histology. Meadowcroft *et al.*[1,2] proposed an original design of a histological coil that permits direct MR imaging of histological tissue samples; enabling for the first time very precise correlation between *ex vivo* MRI and histology using optical microscopy. In the present study, we designed and tested a set of three histological coils based on the same principles and examined the sensitivity limits achievable at 7-Tesla. The dimensions of the three coils were chosen to accommodate each, a standard off-the-shelf cover-slip commonly used for tissue examination under a microscope with a size range enabling the imaging of any mouse organ. Our approach was motivated by the gain in sensitivity achieved through the optimization of the filling factor by tightly fitting the cover-slip while maintaining a homogeneous rf B1 field coverage for the tissue section of interest. Several mouse organ were examined spanning from the olfactory bulb to the liver, one of the largest organ.

Material and Methods: Tissue sectioning: Histology slices of different mouse organs were sectioned using a LEICA CM3050S Cryo-sectioning machine with slice thickness ranging from 30µm to 60µm. The slices were conserved in Cryo-Protectant and kept under -80°C. MRI sample preparation: Each tissue section was immersed in a 5cm diameter petri dish containing either a buffer solution or a buffer doped with 5mM Gd-DTPA (using the passive staining method [3]) in order to boost the MRI signal. Prior to tissue soaking, the buffer containing dish is degassed using a vacuum chamber for 30-min. In presence of the tissue, the dish is then placed in a shaker rotating at 1.5Hz during an additional 30-min. to wash out all the impurities. The hydrated tissue slice is subsequently mounted on a #1 glass cover-slips (glass thickness for each ~130-170µm) and then surrounded with hydrophobic Fomblin (Solvay Solexis Inc., Thorofare, NJ) to prevent dehydration. A second cover-slip is then used to sandwich the tissue prior imaging resulting in an overall thickness that should be less than 400-µm for a tissue section reaching 60µm thickness. The standard sizes of cover-slips available from the vendors were chosen based on the size of the organ of interest. The physical dimensions of the three coils were then designed accordingly to fit optimally any of the cover-slip as summarized in Table 1. MRI: All experiments were performed on a 7-T Bruker micro-MRI system, interfaced to a 200-mm horizontal bore magnet (Magnex Scientific, Yarnton, UK) equipped with an actively shielded gradient coil (Bruker BGA-9S; ID 90-mm, 750-mT/m gradient strength, 100-µs rise time) interfaced to a Bruker Biospec console. Unless noted otherwise, all the acquisition parameters of the MRI sequence were as follow: 2D single slice Multi-Gradient Echo (8 echoes, TE: 3.2-ms, ES: 5.2-ms), TR: 300-ms, Flip Angle was adjusted empirically to maximize SNR (Ernst Angle) in each experiment depending on the sample preparation. Both matrix and FOV were varied depending on the dimension of the samples leading to an in-plane resolution ranging from 50-µm to 60-µm The bandwidth was maintained constante (293Hz/pixel). The number of averages was chosen to keep the SNR higher than 30 (Mean Signal[sample]/Std Dev.[background noise]) with scanning time ranging from 1 to 8 hours.

Results and Discussion:

Table 1

Coil	Physical Dimension of the probe LxWxD (mm)	Effective volume of the radiating RF within the coil (mm^3)	Accessible Volume by the cover-slips LxWxD (mm)	Dimension of Effective RF field accessible by sample LxWxD (mm)	Reference and dimension of standard Cover-slip #1 LxW (mm)	Mouse Organs	Matrix
Small	28.0x10.5x0.6	117.6	14.0x10.5x0.4	10.0x8.0x 0.1	Gold Seal® (ref.:3312) 24x12	olfactory bulb, eyeball, spinal cord, etc..	256x256
Medium	40.0x26.0x0.6	416.0	26.0x26.0x0.4	20.0x20.0x0.1	Fisherfinest® Premium (ref.:12-548-5M) 24x50	brain's cortex, kidney, spleen, heart	256x256
Large	50.0x47.0x0.6	940.0	26.0x47.0x0.4	20.0x43.0x0.1		Liver, Lung	512x1024

Based on the effective rf field volume estimated from the dimension of our coils, a 3x increase in sensitivity was expected for the small coil (SHC) and 1.5x for the medium coil (MHC) both relative to the large coil (LHC). This was inferred from the expected improvement in filling factor. Experimental measurement using an identical tissue sample for the three coils were as follow: 3.6x for the SHC and 1.3x for the MHC both relative to the LHC. Figure 1 illustrates sections obtained from various mouse organs with corresponding histology section using a flat bed scanner. MRI and corresponding optical microscopy examples were all obtained from fresh fixed tissue section immersed in buffer solution without any prior tissue staining, unless noted otherwise. In (A) an echo-averaged horizontal MRI of a 30-µm olfactory bulb section acquired with the SHC coil (in-plane: 50-µm, T_{IM}=2-hrs) shows various regions identified by the corresponding histology (B) as follow: (1) olfactory ventricle, (2) combines the internal plexiform layer, granule cell layer and ependymal layer, (3) mitral cell layer, (4) external plexiform layer, (5) glomerular layer, (6) olfactory nerve layer. (C) MRI of a 60-µm coronal section of a brain obtained from an Alzheimer's amyloid β mouse model and stained with congo red dye to help indentify the plaques in red staining. The image was obtained using the MHC coil (in-plane: 60-µm, T_{IM}=2-hrs) showing an excellent match with histology where the (1) cortex and (2) hippocampus can be easily identified. Importantly, dark spots seen in the MRI closely match congo red stained plaques in (D) confirming previous findings [2]. A congo red stained section from the same mouse brain was this time immersed in 5-mM GdDTPA doped buffer boosting the resulting MRI signal (E) while reducing by half the imaging time (MHC, in-plane: 60-µm, T_{IM}=1-hrs) and improving plaque detection closely matching histology (magnified view not shown) as previously demonstrated in full ex vivo brain [3]. The same paramagnetic staining technique (5-mM GdDTPA) was tested in a mouse kidney section where the T2*-weighted MRI (G) obtained from an intra-dual-echo averaging (MHC, in-plane: 60-µm, T_{IM}=1-hrs) shows a clear delineation of the (1) Cortex, (2) Medulla and (3) Pelvis as confirmed corresponding histology section. Image in example (I) shows a 60-mm liver section in buffer acquired with the largest of the three coilsrequiring to extend the acquisition time (LHC, in-plane: 60-µm, T_{IM}=8-hrs) with an excellent match with histology (J).

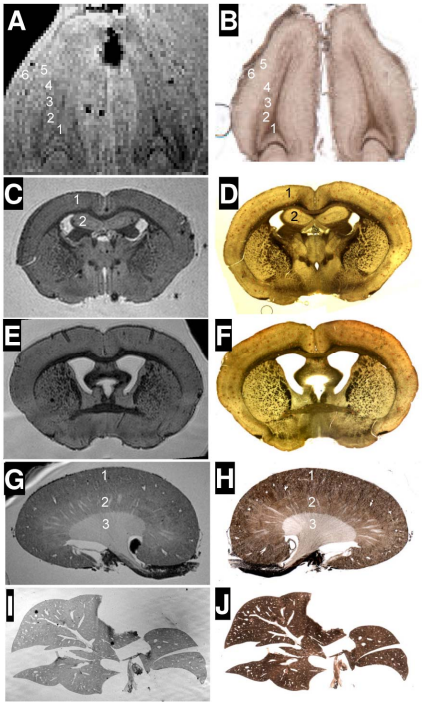

Figure 1

Conlcusion and future direction: Large tissue samples (FOV=20-mmx40-mm) can be imaged in less than 8-hours with the largest coil with a minimum 60-µm section (in-plane: 60-µm). Under similar conditions, tissues that can fit a FOV=10-mmx8-mm could be acquired in less than 2-hours using the smallest coil we have designed. Doping the buffer solution with 5-mM GdDTPA leads to 2.4x gain in SNR enabling the possibility to acquire tissue section as thin as 10-um thickness in 8-hours when combined with our smallest histology coil.

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