# Correlation of 16.4T mouse models with serial blockface and immunohistochemical imaging

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**Target Audience:** Correlative MRI and histology, mouse brain atlasing, stereotaxy, validation of the cellular correlates of gadolinium enhanced MRI sequences. **Introduction:** Atlases integrate data from differing modalities and provide stereotaxic localisation. Improvements in MRI and gradient strength have led to enhanced resolution; the best current atlases in mouse are that of Ullmann et al and Dorr *et al*[3]. The resolution of current atlases is approaching histological clarity and as such in this project we examine the histological correlates of gadolinum enhanced T1 imaging. This will potentially allow us to develop and validate new MRI imaging "stains" that directly correlate to cellular morphometry.

**Method:** 18 mice were perfused with 4% paraformaldehyde and 0.1% Magnevist®. Brains were incubated in 0.1% Magnevist/PB for 4 days, placed in Fomblin and imaged at 16.4T using a 15 mm SAW coil. MRI was acquired using a 3D GE sequence with TR/TE/FA= 50ms/12ms/30°, 82 KHz spectral bandwidth and 8 to produce $T_1$/$T_2$*-weighted images at 30µm$^3$ isotropic resolution. [7]. **Blockface Imaging:** The brain is then removed from Fomblin cleaned and sectioned on a Leica vibratome, 35MP images were taken for each slice with a Nikon D800E DSLR and 200mm micro lens. Images are then post-corrected and re-aligned to create a 3D block of data. **Immunohistochemistry**: Floating 100µm thick sections from the vibratome are then immunolabelled, mounted, imaged using an automated slide scanner (Zeiss Metasystems) and reconstructed to a contiguous 3D block and matched to the MRI and blockface imaging.

**Results:** A representative tri-planar view of the existing MRI model is shown in Figure 1. Figure 2 shows the resulting blockface and histology images for a single section (of approximately 300 for full brain coverage).

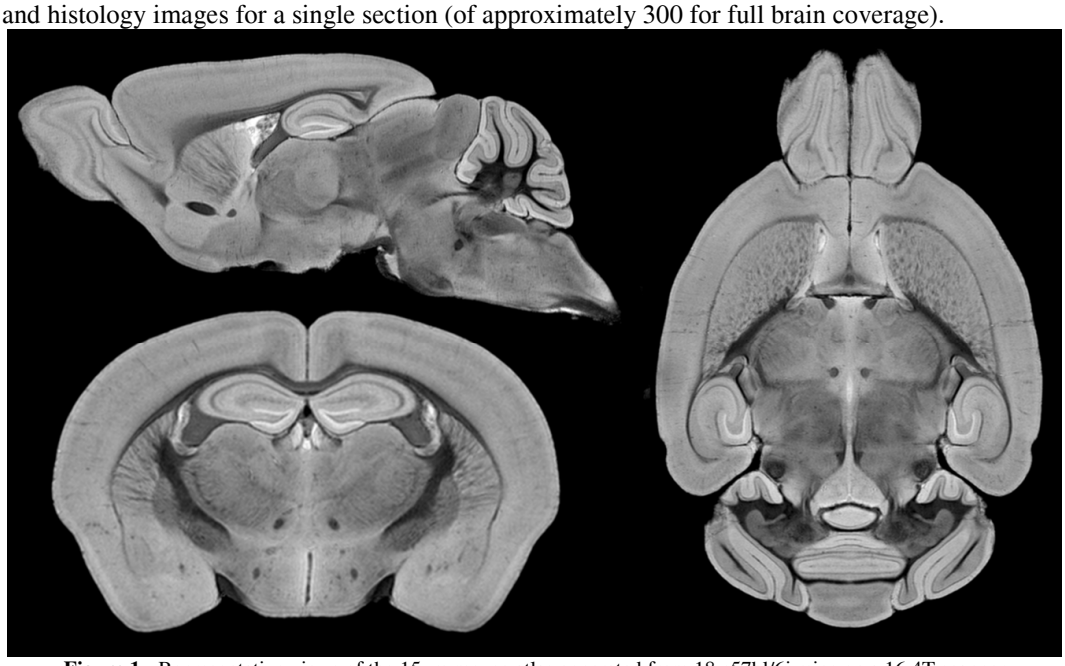

**Figure 1 -** Representative views of the 15um mouse atlas generated from 18 c57bl/6j mice on a 16.4T scanner

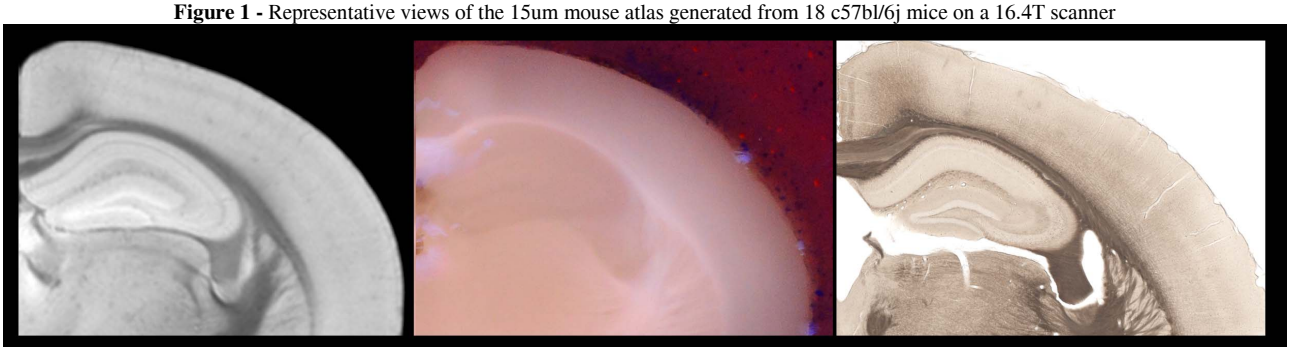

**Figure 2 -** Left: 16.4T micro-MRI (15um voxel size), Centre: block face imaging, Right: IHC staining via slide scanner.

**Conclusion:** Serial sectioning of the same tissue as used in uMRI is possible with careful preparation and shows good correlation to the MRI signal and structure. The MRI and histological data will be made available at http://www.tissuestack.com/ reconstruction code is available on github.org as part of MINC in the volgenmodel package. The MRI models and segmented structures[4] are available from www.imaging.org.au

***1.*** *Franklin, K. B. J. & Paxinos, G. The Mouse Brain in Stereotaxic Coordinates. Vol. 3 (2007).* ***2.*** *Watson, C. & Paxinos, G. Chemoarchitectonic Atlas of the Mouse Brain. (2010).* ***3****. Dorr, A. E., et al. High resolution 3D brain atlas using an average MRI of 40 adult C57Bl/6J mice. Neuroimage* ***42****, 60-69 (2008)* ***4****. Ullmann et al http://dx.doi.org/10.1016/j.bbr.2011.03.031 (2013).* ***5****. Fonov, V. et al. Unbiased average age-appropriate atlases for pediatric studies. Neuroimage* ***54****, 313-327 (2011).* ***6****. Grabner G et al. Symmetric Atlasing and Model Based Segmentation. LNCS 4191, 58-66 (2006).* ***7****. Janke A et al.15um average mouse models in Waxholme space from 16.4T 30um images. ISMRM 2011 Melbourne.*