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Introduction: In mouse phenotyping and disease screening, 3D imaging at a high resolution is needed to detect abnormalities and quantify their size and shape accurately without partial-volume effects. This requires scan times on the order of hours per mouse, which has lead us to develop multiple-mouse MRI (MMMRI) to increase throughput in imaging experiments with many mice.
Principles of MMMRI: In our method ${ }^{1}$, up to 19 cylindrically-shielded radiofrequency (RF) coils are closely packed in a hexagonal array (dubbed the Mousehive) within a common gradient set and magnet. For a 3D image, the readout gradient is set along the common long axis of the mice (the z-direction in Figure 1) so they will be spatially encoded identically in that direction. The phaseencoding gradients are applied in the x and y directions over one mouse and their FOVs are tiled across the bore of the gradient through the periodicity property of the discrete Fourier transform. Some mice are not centered in the replicated FOVs and appear aliased in the resulting images (Figure 1), although this can be corrected in post processing. Since the RF coils are electrically shielded and have their own receivers, neither the signal nor the noise in any one coil is affected by the addition of other coils, although any noise or image ghosts from crosstalk can be corrected with SENSE ${ }^{2,3}$. Thus, our multiple-mouse method increases the number of mice in an MRI study by a factor of $N$ (the number of RF coils on separate receivers in the scanner) while preserving the imaging time and SNR achieved for one mouse
Methods and Results: To validate MMMRI, we performed experiments on a 7 Tesla 40 cm bore magnet (Magnex Scientific, Oxford, UK) with a Varian INOVA console (Varian NMR Instruments, Palo Alto, CA) and a 29 cm inner bore gradient set (Tesla Engineering Ltd., Sussex, UK). The system has a custom designed set of multiplexers to switch four transmitters and four receivers between seven shielded many-rung birdcage coils of Varian's Millipede design that we use for brain imaging. We first imaged phantoms in each coil to measure the isolation between channels on the scanner and found it to be better than -47 dB (leading to magnitude image ghosts of only $0.43 \%$ ). The gradient distortion was also measured in each of the coils with grid phantoms and produced an average spatial distortion of about $3 \%$ over each brain-sized FOV. Finally, we imaged the brains of seven live female C3H mice (The Jackson Laboratory, Bar Harbor, ME) injected intraperitoneally 48 hrs prior to imaging with $20 \mathrm{mM} / \mathrm{kg} \mathrm{MnCl}_{2} . \mathrm{Mn}^{2+}$ acts as a T1-shortening contrast agent when it accumulates in neurons in brain structures ${ }^{4}$ and we imaged the mice with a 3D T1-weighted sequence (spin echo, frequency x phase $\times$ phase $=256 \times 128 \times 128=40 \times 20 \times 20 \mathrm{~mm}, \mathrm{TR} / \mathrm{TE}=300 / 8 \mathrm{~ms}$, $\mathrm{NEX}=2$, resolution $=156 \mu \mathrm{~m}$ isotropic) in 2 hours and 45 minutes. The mice were anaesthetized with $1 \%$ isofluorane in oxygen during imaging and heated to $37^{\circ} \mathrm{C}$ with blown hot air.

Discussion: A common slice from each of the seven 3D images of the mice (registered into an identical position) is shown in Figure 2. All seven images from the MMMRI are of a similar high quality and are suitable for phenotyping experiments in the major structures in the mouse brain. They are also the same quality as an image obtained in a single mouse with the same parameters and scan time. Thus, we have substantially increased our throughput in the MMMRI experiment.


Figure 1.

## References:

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