Multi Whole Mouse MR Phenotyping

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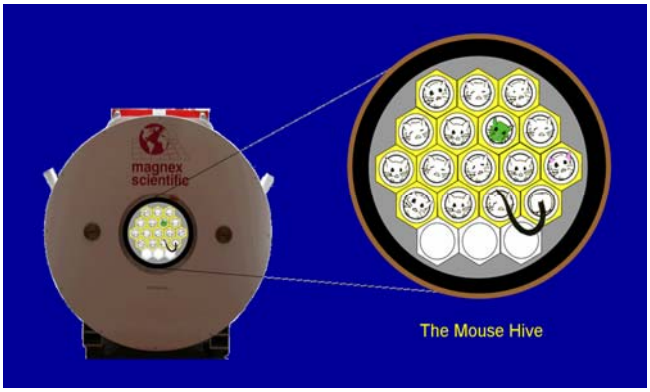
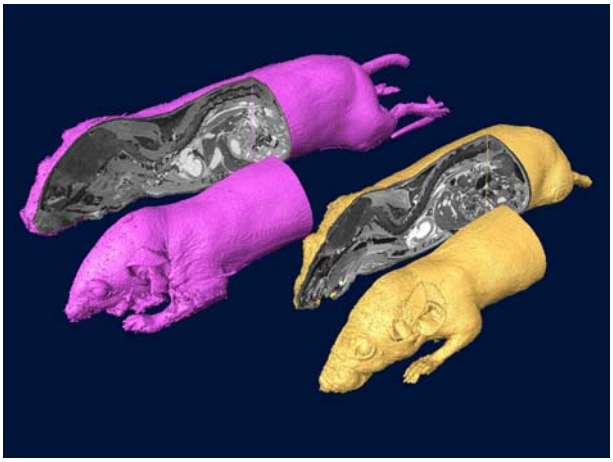
With the complete sequencing of the human and mouse genomes (along with hundreds of other species), there is a major challenge in biomedical science to understand how the detailed information in the genome gives raise to the characteristics of the individual. Elucidation of the genome into phenotype relationship is one of the major challenges in biomedical science of the 21st Century. For mammals, the general features of this relationship are likely to be worked out in the mouse. 99% of the genes in the human are recognizable in the mouse, and mice show many of the symptoms that are characteristic of human diseases. In addition, there are inbred strains of mice and powerful genetic techniques for modifying the mouse genome.

Imaging is a very good way to get a phenotypic overview, and MR imaging is particularly suited for three-dimensional visualization of soft tissues. Thus, MR imaging has a major role to play in phenotyping mice with a variety of genomes. However, these sorts of experiments required high throughput with the capability of imaging thousands of mice over multiple-year experiments. We have developed a multiple-mouse MR imager capable of imaging 16 mice simultaneously in the same magnet and gradient system but with individual spectrometers. Examples of how such images can be used to characterize genetically-modified mice presented.



In addition to high quality and high throughput MR imaging, there is a need for computer automated techniques for three-dimensional data analysis. Methods to extract quantitative measure of statistical differences in the brains of genetically variant mice will be presented. From this sort of analysis comes a new mode of functional MRI which tracks anatomical changes associated with learning and memory.



With the decision of the world-wide consortium to knock out one at a time each of the 23,000 individual genes in a mouse, there will be a high demand for mouse phenotyping. About 30% of these gene knockouts will be embryonic lethal. Thus, MR imaging of embryos will provide important information about the phenotypic differences associated with those knockouts. Experimental methods for addressing MR image-based embryonic phenotyping will be described and compared with alternate competing techniques such as Optical Projection Tomography and X-ray Computed Tomography.

MRI has a new and exciting opportunity to participate in understanding the relationship between genome and phenotype. This opportunity is recognized by an exponentially increasing number of mouse imaging submissions to the ISMRM meeting.