Small MRI Scanners

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Motivation Imaging researchers have witnessed an explosion of interest over the last five years in small animal imaging. Many different applications are contributing to this surge in interest. Pharmaceutical companies now desire faster, less expensive and more predictive drug testing in mice. Serial imaging studies promise to reduce the total number and cost of mouse imaging studies, in particular cancer tumor volume estimates. Molecular biologists are ready to translate their genetic manipulation experiments from *in vitro* gel studies to much more complex *in vivo* animal experiments. They would like to have fast, inexpensive, sensitive, localized chemical tests to measure the outcome of these *in vivo* experiments. Biologists rely on exquisitely sensitive *in vitro* experiments including biofluorescence detection, immunohistochemistry stains, and light microscopy. These optical techniques are significantly more challenging when light is highly scattered, as in the *in vivo* mouse model. Hence, over the last decade, researchers have revamped each of the traditional radiological imaging modalities and invented new modalities to address these new questions. The interest in this area is noticed in the growth in the last few years of the Society for Molecular Imaging. Only three years old, the conference already has 900 members spanning nuclear medicine, ultrasound, optical methods, MRI, x-ray, and other methods.

As further evidence of this interest, a slew of small companies have developed imaging systems dedicated to small animal imaging. These include micro PET (Concorde Microsystems, Knoxville TN), micro CT (many, including Enhanced Vision System, London, Ontario, acquired by GE Healthcare), micro ultrasound (Visualsonics, Toronto) Xenogen (Luciferase Bioluminescence, Alameda, CA), microMRI (many, in Mangetic Resonance Technology, Tsukuba, Japan). In many ways this effort was foreshadowed by Richard Feynman's 1959 APS talk "There is plenty of room at the bottom," which actually focused more on high resolution biological imaging than the more oftenquoted motivation for MEMs intsrumentation.

There is now a very healthy competition between the various imaging modalities to support this new imaging application. As in human medical imaging, it seems likely that multiple modalities will find niche applications. In fact, many pharmaceutical companies and universities are creating their own animal imaging centers that rival radiology departments in scope if not size.

In this talk, I will focus on micro MRI, which offers good resolution (25 micron) when compared with more sensitive micro PET (1 mm), and superior soft tissue contrast when compared to micro CT. Unlike the other modalities, MRI is sensitive to the local chemical environment (through T1, T2 and diffusion), and can provide excellent images of blood flow and blood oxygenation, especially with intravascular contrast agents. A particularly exciting area of small animal imaging is targeted cell tracking. Here, MRI has shown significant impact despite lacking the sensitivity of PET. Cell tagging approaches include targeted relaxation agents and magnetic nanoparticles. MRI can now image single cells *in vivo*. Applications are emerging for imaging injected stem cells. Stem cell therapy has shown promise for treating both Parkinson's and Alzheimers disease. Stem cell imaging could be very helpful as a "debugging tool" while developing or optimizing biodelivery methods.

Engineering Challenges for MRI micro Scanners There are significant engineering challenges to creating a cost effective, high quality small animal scanner. Currently, small animal scanners are built by the vendors Varian or Bruker, and they are fairly expensive, high field systems, often between 4.7 T and as high as 18.8 T. At more than US$1 million, a high field MRI mouse scanner is often significantly more expensive than micro-CT, or micro-PET. This is partially due to the small market size but also due to the complexity of the system. Two of the most costly components in the system are the main magnet and the system console. The magnet requires extraordinary precision (1 part per million variation in field strength), and the console requires extraordinary software flexibility and hardware precision. Moreover, from a biologist's point of view, MRI scanners are far too complex to operate compared with other modalities, very difficult to site, and somewhat expensive to operate (e.g., cryogens, software upgrades).

There are several promising new engineering approaches to micro MRI systems. Here I will mostly focus on the mouse MRI scanner, and human extremity (feet, knee, wrist) imaging. These could greatly expand both biological and human applications.

There are significant advantages when scaling down an MRI scanner. While current density increases for superconducting or resistive magnets, the overall costs are reduced. For mouse imaging, permanent magnets (Nd- FeB especially) scale down very favorably. A small company in Japan (MRT, Inc) working with Sumitomo Special Metals has produced a 1.0 T desktop MRI mouse scanner. Their system is relatively low cost, and fairly simple to site since the safety perimeter is within a centimeter of the magnet. While high field magnets are the norm for small animal imaging, researchers can obtain excellent quality images of mice at 1.5 T (Brian Rutt) using RF and gradient coils tailored to mouse MRI. Fortunately, gradient coils (which determine the speed of imaging) scale very favorably with size, so high speed imaging is feasible on small animal scanners. In fact, most mouse scanners can scan an order of magnitude faster than human scanners.

A significant technical obstacle for low cost small animal MRI is the challenge of the complexity of reprogramming hundreds of pulse sequences for each new scanner. An open source pulse sequence and console movement (akin to Linux) may allow small companies to flourish in the small but growing animal imaging market.

There are several nonconventional micro- MRI approaches being investigated around the world. For ultrasmall imaging, the microcoil work at the University of Illinois of Andrew Webb et al., (home of the Nobel Laureate, Paul Lauterbur), has shown enormous improvements. For mouse imaging, Magnetic Resonance Technology of Tsukuba, Japan has shown the potential of low cost Halbach style permanent magnets. For human extremity imaging, my group at Stanford has pioneered a field cycling imaging approach using two pulsed resistive magnets to get the best of both high field and low field MRI. We have constructed a midfield human knee scanner for which the total magnet costs are about $30,000. Preliminary wrist images are promising. Our approach also shows potential for new contrast mechanisms including protein selective imaging through Nitrogen-Hydrogen cross-relaxation. Texas A&M and others have developed a low cost, high speed MRI scanner that exploits the RF sensitivity profile to perform the image encoding rather than more common gradient encoding.

Conclusions Imaging systems development has enjoyed a rennaisance recently with the intense interest in imaging small animals. Many pharmaceutical companies have already bought their own MRI scanners. There are many exciting applications that will require significant engineering innovation and development, perhaps paralleling the two decades of research on whole body human MRI. There are several promising technologies on the horizon that may make MRI less expensive, easier to work with. and bring this noninvasive imaging technology to nonspecialists.

Keywords:

MRI: Magnetic resonance imaging, a noninvasive method of imaging humans and animals. About 3 percent of all medical imaging studies are performed with MRI, which is known for its superior soft tissue contrast, and non-invasiveness. Currently it is the modality of choice for human studies in the head, spine, and joints. It also enjoys great popularity for research imaging studies, including breast, fMRI, and mouse imaging. Drawbacks include relatively long scan times (few minutes), high cost ($2 million), difficulty siting, and a claustrophobic environment.

NdFeB: Neodymium Iron Boron, one of the strongest rare earth permanent magnets available, has recently become popular for desktop small-animal MRI and NMR scanners. Permanent magnets scale down with size more favorably than resistive or superconducting magnets.

NMR: Nuclear magnetic resonance, the fundamental basis for MRI, NMR is a spectroscopic technique relating molecular position to resonant frequency when the liquid is placed in a very uniform, strong magnetic field. This has been used by chemists to elucidate chemical structure more than five decades.