Title: Heart Imaging in Mice
Thursday May 12th, 5:40 pm
Session: "Mouse imaging: How to do it fast, cheep, and better"

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Mouse models of cardiovascular disease play an extremely important role in cardiovascular research. While echocardiography remains the dominant imaging platform to image phenotype in mice, MRI has an extremely valuable role to play. Over the last few years we have seen significant advances in all aspects of cardiac MRI in mice. In keeping with the theme of the session we will focus here on techniques that have: 1) Made MRI of the mouse heart simpler and faster, 2) cheaper and more efficient, and 3) more robust and powerful.

Cardiac MRI in mice should ideally be performed at a field strength of 7T or higher and with a gradient of greater than 600 mT/m. The most common reason for inadequate image quality on these high-end systems is the failure to use RF coils tailored for cardiac imaging. A high-end small animal MR system such as this is obviously a major investment and it is thus appropriate to investigate alternative platforms. 1 Tesla "benchtop" MRI scanners have been recently introduced and offer some intriguing high-throughput possibilities. These systems have an extremely small footprint and could likely compete with echocardiography for rapid and convenient screening of some models. These systems will likely also prove extremely useful in the development of Gd-based contrast and molecular imaging agents, since the r1 of Gd at 1T is significantly higher than it is at 7T.

The use of clinical (1.5 and 3 Tesla) scanners to perform cardiovascular MRI in mice has also been reported by several groups. It should be realized, however, that clinical scanners have gradients in the 50mT/m range and that this can impose limitations on spatial and/or temporal resolution during cine imaging. Sequences with high intrinsic SNR such as balanced SSFP work best. Screening of novel contrast and molecular imaging agents can also be performed on these systems.

Given the large cost and footprint of high-end small animal imaging systems a need does exist to increase throughput on these systems. Systems with multiple receive channels, supporting parallel acquisition, are now available. In addition, the use of multi-element cardiac arrays to support parallel acquisition of the heart in mice has been reported and appears promising. Improved gradient performance is also allowing new readouts (spiral and EPI) to be performed in the mouse heart. For instance, single shot echo planar imaging (EPI) of the mouse heart was recently reported. A full image with 0.25 mm in-plane resolution can be acquired in 11ms with this technique. Single shot EPI requires no physiological gating and supports robust realtime cine MRI of the mouse heart. Filtering the data with a principal component analysis approach has been shown to reduce the noise in these realtime images significantly, and without blurring or loss of sharpness. The use of this EPI technique in mice requires an ultra-high performing gradient (1500 mT/m) but provides the possibility of screening cardiac function in mice within a matter of minutes.

The value of high-end platforms can also be increased by the ability to support more sophisticated imaging and provide novel readouts of cardiac pathophysiology. Over the last years we have seen, amongst others, new techniques introduced to produce robust T1 and T2 maps of the myocardium in

mice, measure myocardial mechanics, perform first pass perfusion, measure flow, and image myocardial fiber architecture. In several areas, the sophistication of cardiac MRI in mice has now surpassed that of humans on clinical systems. Examples of this include arterial spin labeling (ASL) and diffusion MRI tractography of the mouse heart. ASL in mice benefits from the high myocardial blood flow in mice (3-5 times greater than in humans) and the lengthening of T1 at high field strengths. Robust quantitative measurements of myocardial perfusion can be obtained using the FAIR approach. Several strategies to deal with the effects of respiration have also been developed and further improve the accuracy of the technique.

Two-dimensional diffusion tensor MRI (DTI) has been performed in humans in vivo. However, robust tractography of the heart requires high resolution and isotropic 3D diffusion data to be acquired. A cardiorespiratory-gated 3D diffusion-encoded EPI sequence has recently been developed on a high-end small animal scanner, and allows this to be done. Imaging was performed at 9.4T with a 1500 mT/m gradient. This allowed motion compensated diffusion gradients with short durations to be used, and allowed high b-values (degree of diffusion encoding) to be obtained using a spin echo EPI readout with a relatively short TE. Three dimensional DTI tractography of the entire mouse heart in vivo could be performed in 30-40 minutes. The in vivo tractograms compared extremely favorably with those acquired ex vivo.

In summary, cardiac MRI in mice continues to evolve in many spheres including spectroscopy, sophisticated high-end imaging techniques, and high throughput 1 Tesla benchtop systems. Over the last several years the cardiac imaging community has thus met the challenge of imaging the mouse heart “faster, cheaper and better”.