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Magnetic resonance in tissue engineering

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It is a pleasure to introduce this group of articles building on our Sunrise Course, 'Magnetic Resonance in Tissue Engineering', at the Honolulu Meeting of the International Society of Magnetic Resonance in Medicine in 2009, focused on the applications of MRI and MRS to tissue engineering. Even in this small set of articles, the variety of approaches available, and their potential for greatly improving the noninvasive evaluation of tissue, is truly impressive.

The use of ferromagnetic particles for cell labeling is now an accepted technique. However, the MR signal voids caused by the resulting susceptibility effects are often difficult to unambiguously assign to the incorporated labels as opposed to imaging artifacts, native tissue features or air bubbles. The paper by Haddad addresses this issue in a very clever way, by combining standard T_2^* -weighted MR images with temperature-sensitive imaging, with the heating of the particles produced by an external alternating magnetic field. The technique is successfully demonstrated in phantoms and in a living mouse.

The paper by Ramaswamy is also based on ferromagnetic cell labeling. A protocol is established for tracking cell migration in the cardiovascular system using pulmonary vascular cells. This work combines modern cell biology technology, to assess labeling efficiency, with highly sensitive MRI for the localization of labeled cells. Results obtained in both gels and cellular preparations are presented.

The specificity of available MR measures of tissue characteristics is a focus of the article by Cheng *et al.*, in which seeded and unseeded acellular bladder tissue matrices were evaluated by several MR techniques. The ultimate goal of this line of investigation is to establish tissue engineering-based therapeutics for bladder dysfunction. Again, this work applies several important MR techniques, including multiexponential diffusion and transverse relaxation measurements, as well as extensive correlations between MR outcomes and cellularity.

Jeffries and Macdonald provide a particularly comprehensive review of the bioartificial liver. They first describe a variety of appropriate bioreactors. An interesting set of multinuclear studies is then presented; they are individually targeted to appropriate features of the system. They include ^{31}P spectroscopy for bioenergetics, metabolism and oxygen distribution by ^{19}F , ^{13}C analysis to assess glycogen production, and structural and flow analysis using the proton nucleus. These all have wide-reaching potential for tissue engineering settings quite apart from the particular bioreactor systems discussed.

Bowles *et al.* present work targeted at the major medical problem of intervertebral disc degeneration. This remarkable study presents an approach to the creation of a tissue-

engineered disc that exhibits circumferential alignment of collagen surrounding an engineered nucleus pulposus, and shows results following implantation of the construct into the L4/LS disc space of the rat after extraction of the native disc. Results are obtained over a 16-week post-implantation period using, among other techniques, micro-computed tomography and anatomical MRI.

Musculoskeletal tissue, in particular, serves a mechanical role. Although it is reasonable to suppose that adequate mechanical function would follow from adequate biochemical composition and morphology, the paper by Othman *et al.* addresses this issue in a more direct fashion. After a comprehensive introduction to the subject, MR elastography studies of osteogenic constructs implanted into mice are presented. These results illustrate the correlation between mechanical properties and mineralization.

The work of Weber *et al.* is a further illustration of the wide variety of MR experiments that can be applied to engineered tissue. Applicable solid-state NMR spectroscopy techniques are first reviewed, and then used to investigate extracellular matrix formation in bone implants. An effective combination of ^{31}P and ^{13}C studies is presented, allowing for the detection and characterization of the inorganic and organic components of the tissue, respectively. Both structural and dynamic information is obtained.

Finally, the paper by Reiter *et al.* continues my group's efforts to develop more sensitive and specific MR approaches for the evaluation of cartilage. Multiexponential transverse relaxation analysis is applied to identify collagen- and proteoglycan-associated water pools, and a relatively unbound water pool. Differences are clearly seen between these results in engineered tissue as compared with previously presented results for explants. MR parameters are then used to identify stages of tissue development through the use of the support vector machine formalism.

The above articles represent an exciting body of work and, when seeking potential authors for this volume, it was encouraging to find such excellent scientists working in MR applications to tissue engineering. However, the manner in which advances in the assessment of growth and development of engineered tissue will lead to improved products and better clinical outcomes remains incompletely defined. Certainly, building on the body of *in vitro* work, a greater emphasis on studies of the morphology, composition and performance of engineered tissue after placement into the target site in animals and humans would be a major step forward. With its unparalleled ability for noninvasive analysis, MR will likely play a pivotal role in this ongoing effort. We look forward to further advances with great enthusiasm.