Magnetic Resonance Imaging Characterization of Drug Delivery Bioceramics

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Introduction:

In recent years, biomaterials implanted into the body for repair or reconstruction of tissues have demonstrated increasing potential in regenerative medicine and adjunctive therapies. One such application is the use of porous bioceramics[1] (which may be inert, bioactive or resorbable) as enhanced localized drug delivery devices, offering alternative delivery routes and release mechanisms.[2] Conventional drug delivery systems such as capsules and pills release the drug immediately into the system, and the remaining drug in the carrier is released at a decreasing rate in an approximately first order manner (with the exception of continuous intravenous delivery).

Bioceramics with tailored microstructure have potential as long-term and/or variable rate drug delivery vehicles, with properties finely tuned for the particular problem. The success of these materials depends upon the ability to optimize the microstructure in terms of pore size, porosity and surface area so as to release compounds at the appropriate stages of healing.

Fundamental research in this area requires concurrent studies in two areas: 1) measurements of how the microstructure of a specific degradable/resorbable bioceramic varies with space and time, and 2) direct experimental measurements of how this particular microstructure effects the impregnation and release of potential compounds.

Methods:

We have previously demonstrated the application of Nuclear Magnetic Resonance Imaging (MRI) to studies of the microstructural properties of ceramics.[3-5] In the current experiments, we apply MRI to the spatial mapping of fluid density (proportional to porosity) [5], relaxation times (proportional to surface-to-volume ratio) [6] and diffusion co-efficient (related to pore connectivity) [4] in several bioceramic materials. These methodology validation studies were performed at 2-T in a 30 cm horizontal bore imaging system, using a TecMag spectrometer. Measurements performed on resorbable materials were done using a Bruker 11.7-T vertical bore system equipped with 700 mT/m gradients.

Results:

MR imaging/diffusometry/relaxometry data were obtained from a variety of (non-degradable) porous glasses and metal oxide ceramics with spatially homogeneous microstructure. By cross-comparing these results with "conventional" testing methods, we were able to validate our ability to accurately determine pore properties such as porosity, pore size, connectivity, surface chemistry, surface area and pore shape.[3, 4]

Figure 1 shows the results of MR imaging of fluid impregnated in two porous ceramics created so as to have spatially modified pore properties. The space varying microstructure introduced during fabrication of both a co-fired ZnO ceramic composite and two surface-treated Y-TZP ceramics (35% & 40% bulk porosity) is readily apparent in the images.

We are currently applying these methods to the study of calcium polyphosphate bioceramics. *In vitro* measurements of pore phase evolution during material degradation, and corresponding studies of the temporal evolution of the drug elution behaviour are used to evaluate these materials as implantable drug delivery devices.

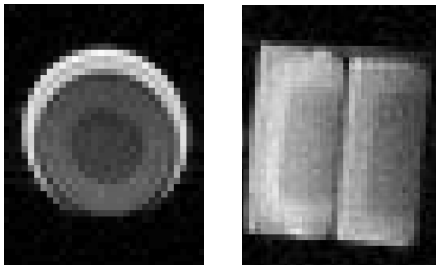

Figure 1. MR Image of fluid density in a bi-phase co-fired ZnO ceramic composite (left) and two surface modified Y-TZP ceramics with varying porosity. Images demonstrate the sensitivity of MRI to initial compaction pressure (ZnO materials) and surface treatment (Y-TZP materials). A high intensity ring of free fluid is visible above the ZnO material.

Conclusions:

MR imaging, in combination with relaxation time and diffusion mapping, is highly useful as a non-invasive and non-destructive method for directly measuring the evolution in both the pore structure and drug elution properties of bioceramics, with the potential for the techniques developed to be applied directly to *in vivo* studies of these materials in small animal models.

References:

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