Zero echo time MR imaging of contrast-agent-enhanced calcium phosphate bone defect filler

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Introduction

Calcium Phosphate Cement (CPC) is a widely used class of bone substitute and scaffold material. A disadvantage of CPC is their similar radiopacity to natural bone, rendering them difficult to visualize in classical X-ray and CT imaging. Conventional MR imaging of bone is in low quality due to the low water content and very short T_2 relaxation time. However the development of ultra-short echo time (UTE) and recently introduced zero echo time (ZTE) MRI were shown to allow for optimal bone visualization. T_2* values determined with UTE sequence showed little difference in T_2* for bone versus CPC, hence these materials are difficult to be separated based on T_2 alone. Therefore the possibilities of contrast agent incorporation to improve differentiation were examined.

Material and Methods

MR imaging was acquired on bone defects repaired by CPC doped with ultra-small particles of iron oxide (USPIO) and gadopentetate dimeglumine (Gd-DTPA), 1% (w/w) and 5% (w/w). Then setting time and compression test were run on these materials to finally decide the formulation for in vivo experiment.

UTE-3D was used for T_1 and T_2*measurements, regions of interest were manually outlined. Variable flip angle method was used for T_1 measurement[1], several images obtained with different echo times were used to measure T_2*.

A circular hole drilled in the femoral condoyle of adult male Wistar rats served as a bone defect model. Bone repair was performed on 2 groups of animals with CPC, doped with 1% (w/w) GD-DTPA or no contrast agent respectively. MRI was performed at 11.7T Biospec (Bruker, Gemrnay) with home-built Helmholtz coil. ZTE MR imaging was acquired with 200 kHz bandwidth, TR=8ms, flip angle=5°, FOV=45*45*45mm, acquisition time ~ 30mins. Animals were scanned right after surgery and 8 weeks later.

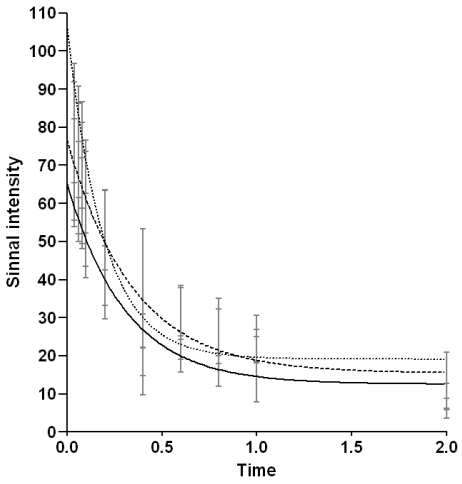
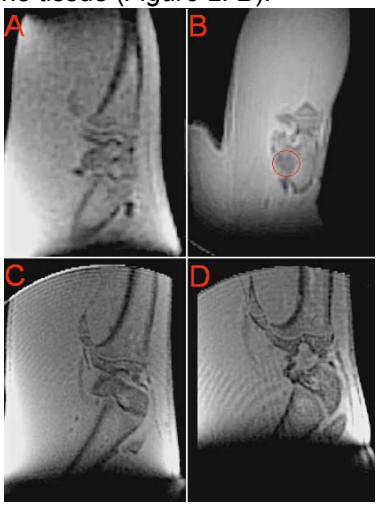


Figure1. Signal intensity plotted versus TE (ms) in UTE acquisition of bone material. Dotted line: fit of bone T_2 decay. Dashed line: T_2* decay of CPCs. Solid line: T_2* decay of Gd-DTPA loaded CPC*

Results

Each formulation resulted in clear visualization of bone filler, with decreased intensity on ZTE imaging of bone samples. The setting times and compression test for different formulations showed unfavorable effect on the solidification and/or mechanical proprieties of CPC, except 1% Gd-DTPA doped cement. Fitting of a mono-exponential decay curve (*Figure 1*) resulted into following T_2* values: bone =340±50μs, CPC=306±77μm, CPC (Gd-DTPA doped) =191±57μs. The T_1 value as follows: bone=474.19±28ms, CPC=537.63±29ms and CPC (Gd-DTPA doped) =336.44±25ms. Negligible contrast between CPC and bone was shown in the in vivo experiment. While the shape and location of contrast agent loaded CPC was clearly seen at the initial scanning point, which appeared to be darker than the surrounding bone tissue (*Figure 2. B*). Furthermore at week 8 it was impossible to differentiate the cement from bone (*Figure 2. D*).



Discussion

For 1% Gd-DTPA, which had no unfavorable effect on the solidification time and mechanical properties, and largely decreased T_2* of the material, was therefore explored in an *in vivo* experiment. Here, the contrast was enhanced at an early stage then disappeared due to material decay and bone regeneration after eight weeks. This indicates that ZTE imaging using Gd-DTPA as a contrast agent is a valid radiation free method to visualize CPC degradation. With improvements on contrast agents and MR imaging technique, the following of CPC degradation and bone regeneration using ZTE in preclinical experiment will become possible.

Figure2. In Vivo MR imaging of repaired femoral condyle defects. A: defect filled with CPC. B: defect filled with Gd-DTPA loaded CPC. C: defect filled with CPC after 8 weeks. D: defect filled with Gd-DTPA loaded CPC after 8 weeks. The red circle shows the Gd-DTPA loaded material.

References: 1.Fram EK et al. Magn Reson Imaging. 1987; 5(3):201-8

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