Tissue repair differentiation using T2 multicomponents: investigation in tissue-engineered bone regeneration

M. Beaumont[1], M. G. DuVal[2], Y. Loai[3], W. A. Farhat[3], G. K. Sándor[2], and H-L. M. Cheng[1,4]

[1]The Research Institute and Diagnostic Imaging, The Hospital for Sick Children, Toronto, Ontario, Canada, [2]Department of Oral and Maxillofacial Surgery, University of Toronto, Toronto, Ontario, Canada, [3]Division of Urology, The Hospital for Sick Children, Toronto, Ontario, Canada, [4]Department of Medical Biophysics, University of Toronto, Toronto, Ontario, Canada

INTRODUCTION

Tissue repair plays a key role in successful tissue regeneration and involves various simultaneous processes (1). In bone regeneration, bone growth in a defect occurs only in the absence of early fibrous scar formation or collapse of surrounding tissues into the defect (2). In this study, a tissue-engineered construct is inserted into a defect in the rabbit calvarium to provide a 3-dimensional resorbable scaffold that maintains a space for bone growth. Multicomponent T2 measurements are performed to characterize and differentiate tissue repair from normal construct resorption.

METHODS

Two critical size (i.e. non-spontaneous healing) calvarial defects (15mm in diameter) were created surgically in each of five New Zealand rabbits. One defect was grafted with a tissue-engineered soft-tissue construct fortified with 10ng/g of VEGF; the other side was left void. Animals were imaged 3, 6 and 12 weeks after surgery on a 1.5T GE scanner (EXCITE). Construct localization was achieved using a multi-echo gradient echo sequence: TR=118.5 ms, 16 equally spaced TEs=[2.6-34.4] ms, FA=20°, bandwidth (BW)=63.8 kHz, 6 slices (SL= 3 mm), matrix=256×192, FOV=10×10 cm^2, number of averages (NEX)=2. Echo times were chosen to achieve fat signal alternation based on in-phase and out-of-phase effects. Multicomponent T_2 quantification was performed with an 80-echo CPMG sequence: TR/TE=2500/11.4 ms, FA=90°-180°-180°, BW=15 kHz, single slice (SL=5 mm), matrix=256×128, FOV=10×10 cm^2, NEX=2.

All analyses were performed using Matlab (v.7.0). Fat was identified on multi-echo gradient-echo images (due to characteristic signal alternation) and subsequently excluded in the delineation of the construct or scar tissue. Regions of interest (ROIs) for the construct or scar were defined on the first echo of the multicomponent T2 images (Fig.1). The mean signal in the ROI was calculated at each echo time to yield a T2 decay curve, from which T2 component values and fractions were determined using a nonnegative least square method. All results are presented as mean ± standard deviation. Statistical analyses were performed using a Student's t-test.

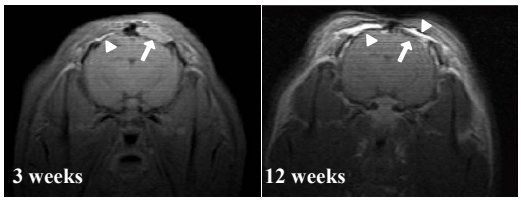

Fig.1: Evolution of the size of the construct (arrows) between week 3 and week 12. Scar tissue appears very bright on T2 images (arrowheads).

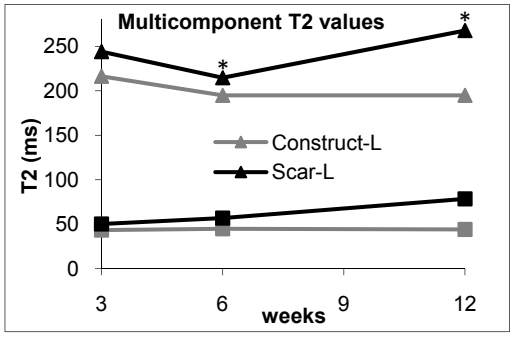

Fig.2: Evolution of the long (triangles) and short (squares) T2 components in the construct (gray) and the scar tissue (black). * P < 0.05 construct versus scar tissue

RESULTS

Fig.1 shows an example of T2-weighted images from the first echo of the CPMG echo train at 3 weeks and 12 weeks post-surgery. The construct presented a hyperintense periphery relative to the core. Its size decreased with time while the bright layer got thicker (it was confirmed to be fibrous tissue with histology; results not shown). The void defect showed an earlier appearance and a thicker layer of fibrous tissue. Fig.2 compares the evolution of the two T2 components in the construct and the scar. For both tissues, the two components T2 values were relatively stable with time. No significant difference was found in t

he short T2 values while the long T2 value was greater in the scar than in the construct. Fig.3 shows the changes in the long component fraction: the construct exhibited a significant and continual increase throughout the 12 weeks, and the scar tissue reached a plateau after 6 weeks with constantly higher values compared to the construct.

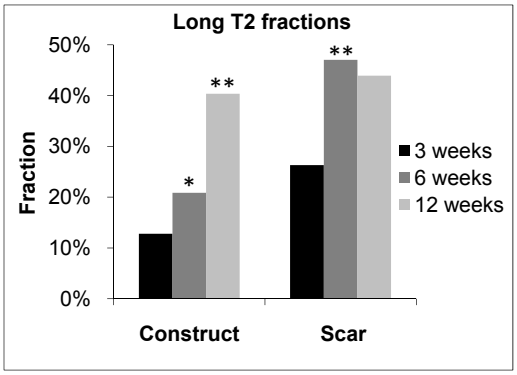

Fig.3: Evolution of the long T2 fraction in the construct and the scar tissue. * P<0.05, ** P<0.01 Different from the previous.

DISCUSSION AND CONCLUSIONS

This study shows that multicomponent T2 can distinguish and monitor different tissue repair processes. Unlike conventional MRI techniques, multicomponent T2 measurement can provide more specific information on structural and biochemical changes that occur during scar tissue formation and construct resorption. Although both the tissue-engineered construct and fibrous tissue are composed mainly of collagen, they can be distinguished based on their unique evolutions in the reparation process on multicomponent T2 data (Fig.3). As previously reported in studies investigating multicomponent T2 in collagen-based tissues (3,4), the short T2 component is associated to the water tightly bound to the collagen fibers and the long T2 component represents the free or loosely bound water. The evolutions of water component fractions clearly indicate that the resorbable construct underwent a continual loss of structure associated with tissue degradation, with an increasing fraction of free water and decreasing collagen content. In contrast, newly formed scar tissue exhibited an early, high and stable long T2 fraction, consistent with the disorganized structure of scar tissue and a very bright MR signal (Fig.1). The distinction of scar from construct is important for localizing where successful bone regeneration may occur. Future work will focus on more detailed investigation of time-course biochemical and histological changes underlying scar formation and construct resorption.

REFERENCES: (1) Axhausen. J Bone Joint Surg Am 1956; 38-A:593. (2) Clokie et al. J Cranofac Surg 2002; 13:111. (3) Webb et al. MRM 2003; 49: 638. (4) Reiter et al. MRM 2009; 61: 803.