Pre-clinical feasibility study of a novel implant for treatment of a cartilage defect in the medial femoral condyle

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INTRODUCTION:
The advent of modern cartilage repair techniques is expanding the development of restorative concepts. A challenging aspect of cartilage restoration continues to be the need to reliably restore a continuous articular surface capable of weight bearing functions. Based on reconstructive device concepts, previous investigations have explored the use of several different materials ranging from alloys [1,2] to polymer composites [3]. Current research into this device concept continues to demonstrate potential benefits [4], but has potential limitations relating to biologic fixation. Based on previous investigations into porous-coated implant topology [5], a novel non-resorbable articular matrix ceramic was developed to test the feasibility of replacing a region of degenerated or damaged cartilage in a large pivotal preclinical model. The device produced from this ceramic is monolithic in form with a highly polished submicron articular surface and interconnected porous structure exhibiting approximately 60% porosity. Two primary hypotheses were tested: (1) The use of a ceramic articulation surface, as part of a regional replacement of cartilage, has no damaging effects on natural articular cartilage. (2) A composite ceramic implant with a macroscopically porous topology and conical geometry can provide immediate fixation and promote secure long-term bone adaptation.

MATERIALS AND METHODS:
Fifteen (15) large male mongrel dogs were used for the study (31.9kg ± 4.7kg). The animals were assigned to the following groups: Unoperated Controls, UC (n=2); Controls, day 0, (n=3); 12 weeks post surgery, (n=3); 24 weeks post surgery, (n=7). Dogs not assigned to the UC group underwent a bilateral implantation of the ceramic device (fig. 1). Specifically, after exposure, articular cartilage and underlying subchondral bone of the region of interest on the medial femoral condyle were removed with a series of custom guides and drills to produce a defect that exactly matched the footprint of the implant and shape of the implant cones. The implant was then press-fit by hand into the excavated region, while ensuring that the articular surface was flush with the existing articular cartilage. After soft tissue closure with resorbable sutures and skin staples, postoperative radiographs were taken to verify placement of the implant. The animals were allowed full weight-bearing and normal cage activity immediately following surgery and appeared fully weight bearing within 2 h. In addition to free cage activity, each dog was allowed 30 min/day for free roaming in a larger area.

RESULTS:
Due to a lax patella, one animal from the 24-wk group had to be euthanized at week 4. All other animals showed no lameness to their hindlimbs following surgery for the entire duration of the experiment. Gross cartilage observation showed no differences in Collins cartilage score between Controls, 12-wk and 24-wk. The UC group had a lower score compared to all other groups. Results from the Safranin O intensity for the UC and 12-wk group indicate that for both groups, the top third of the cartilage had a lower intensity than both the middle and bottom for both the medial and lateral tibial plateau. No differences were found in intensity between the UC and 12-wk groups at any level. Ingrowth measurements for the 12-wk group indicate that in-growth was achieved at 12 weeks (19.5% ± 3%). Pull-out tests showed an increase in maximum load at pullout for both the 12-wk (331N ± 124N), and 24-wk group (235N ± 193N) relative to the Control group (8N ± 7N). In addition, the performance of the implant ceramic matrix does not appear to be affected by hydrothermal instability or low temperature degradation. Localized changes in chemical composition of the cartilage of the tibial plateau are currently being examined with Raman spectroscopy.

DISCUSSION:
We have found that the use of a novel ceramic implant as a replacement for a focal cartilage defect leads to implant fixation within 12 weeks and does not cause significant degradation in opposing articular cartilage. The lower Collins score in the UC group may yield information relating to surgical exposure for cartilage repair surgery. In summary, the use of a ceramic implant appears to be an effective cartilage replacement, which may increase the therapeutic options for focal cartilage lesions.

REFERENCES:

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Figure 1: (A) Implant at dissection 24 weeks post surgery. (B) SEM image of AP-axis cross-section of implant.

Once euthanized, each animal had one hindlimb (tibial plateau + femoral condyle) assigned to histological examinations, while the other hindlimb was used for Raman spectroscopy and subsequent biomechanical pull-out tests. Upon dissection, the articular cartilage of the medial/lateral tibial/femoral articular surfaces was scored using the Collins score [6].

The hindlimbs assigned to histology were fixed in 10% NBF. The tibial plateau for this group was embedded in paraffin and sectioned transverse to the AP-axis (7μm thick). Sections from the center of the medial and lateral tibial plateau were stained with Safranin O for cartilage evaluation. Specifically, the strain intensity was quantified using light microscopy and ImageJ for 3 locations within each section: the top, middle and bottom third of the cartilage thickness (articular edge to subchondral bone). Within each animal, the intensities were normalized to the intensity of the bottom 1/3 of the lateral tibial plateau (set to 100).

The histology-assigned medial femoral condyle containing the implant was embedded in PMMA and sectioned along the AP-axis (360μm thick). The center section of the implant was carbon coated for Scanning Electron Microscopy (SEM) analysis of bone in-growth into the implant cones (fig. 1B). Bone in-growth data is presented as the average of the two cones within each animal.

The distal femur assigned for pull-out was embedded in PMMA and had the cartilage immediately medial and lateral to the implant removed using a drill shaping tool. This was done in order to ensure that a custom clamp could be situated underneath the implant articular ridge. A multi-directional vice was used to vertically align the specimen in a MTS testing machine for a uni-directional tensile pull-out test. The pull-out test was performed at a rate of 1 mm/min.

Upon completion of the pull-out test, one implant from each group was randomly selected for evaluation of low-temperature degradation by measuring the percent monoclinic phase transformation of the implant using x-ray diffraction.

A student’s t-test was used for comparisons between groups. Significance was defined as p≤0.05. Data are presented as average ± standard deviation. This work was approved by the University Committee on Use and Care of Animals at the University of Michigan.

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