Engineered Anatomic Implants Restore Geometry and Load Transfer in the Porcine Accessory Carpal Joint

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Introduction

Trapeziometacarpal (TMC) osteoarthritis (OA) is one of the most common conditions affecting middle and older aged adults.[1] Many patients will eventually require destructive surgical intervention, involving removal of all or part of the trapezium, and replacement with tendon, fascia, or an artificial implant.[2] While effective at reducing pain, these procedures compromise grip strength and, in some cases, result in subsidence and disfigurement of the hand.[2] Efforts to replace articular cartilage (and bone) with living, functional tissue have matured substantially over the last two decades,[3] as has technology for generating constructs that can match the anatomical complexity and geometry of native articulating surfaces.[3,4] For these technologies to progress towards translation, appropriate large animal models are required. In our previous work, we identified the porcine accessory carpal (AC) as a potential model for TMC OA, given its multiple similarities.[5] We designed a tissue engineered implant for the articulating surface of the AC (consisting of a PCL foam bone integrating portion, and a hydrogel cartilage articulating surface) and demonstrated the feasibility of its implantation in a living animal.[6] Here, we standardized our design and fabrication protocol to build patient-specific implants and evaluated our ability to recreate the geometry and load transfer across the native AC.

Methods

Construct design and fabrication

Clinical CT images of three forelimbs of skeletally mature Yucatan minipigs were obtained with a portable 8-slice CT scanner (CereTom, Neurologica). From these, the AC bones were segmented using ITK-SNAP[7]. For each, a surface mesh was exported and opened in MeshLab (ISTI), where the mesh was smoothed and simplified. This mesh was imported into Solidworks (Dassault Systèmes) and a 3D object was created. The articulating surface was translated normally 500 μm and the resulting shell became the "cartilage" of the implant. Next, a plane was defined parallel to and ~3mm deep from the top of the bone; this plane was used to remove the bottom portion. Finally, a 2mm wide by 5mm deep "keel" was added to the bottom of the bone to enable subsequent fixation. A positive mold of both the bone only and composite implant was then designed and 3D printed. To fabricate elastomeric negative molds, Sylgard 184 (polydimethylsiloxane, PDMS) was prepared at a 10 parts monomer to 1 part curing agent ratio, poured over the 3D printed designs, degassed, and allowed to cure at 40°C overnight. Poly(ε-caprolactone) (PCL) was dissolved in chloroform at 20% wt/vol and mixed with NaCl crystals sieved to ~106 μm with inclusion of Zirconium nanoparticles for radio-opacity. The slurry was poured into the mold and the solvent was evaporated. The units were demolded and the salt was leached. A 30% solution of poly(ethylene glycol) diacrylate (PEGDA) containing 0.05% Lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) photoinitiator was added to the bone and cartilage composite mold, the PCL "bone" portion was added, and the hydrogel was polymerized using UV light at 380nm for 10 minutes to form a 'cartilage' cap on the implant.

Geometry measurement

The thickness of the designed cartilage surface of each implant was measured in Solidworks on a grid spacing of 1.25 mm and compared with previously generated thickness maps based on native AC cartilage. Each of the three animal-specific implants was scanned via μCT (μCT50, Scanco medical), and the results were segmented, cleaned, and imported into Solidworks and compared to the original designs.

Joint biomechanics

In each of the three forelimbs, an incision was made and a TekScan iScan 6900 pressure sensor was inserted into the joint space between the AC and the ulnar carpal. The carpus was extended through a range of angles from 90 degrees to 0° while contact forces were measured. Next, composite AC constructs were implanted. A reciprocating saw was used to remove the surface of the AC and a 2mm burr to create a slot in the remaining bone matching the keel on the construct. After implantation, TekScan measurements were repeated. T-tests at 0° compared force and contact area pre- and post-op, with $p < 0.05$ indicating significance.

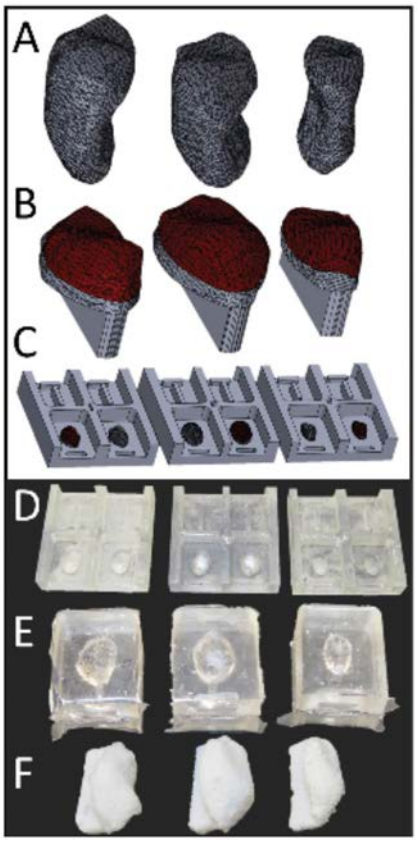

Figure 1. (A) Renderings of 3 AC bones from CT data. **(B)** Designed AC implants with cartilage in red. **(C)** Design of positive molds of the three implants. **(D)** 3D printed positive and **(E)** cast PDMS negative molds. **(F)** Resulting PCL foam constructs.

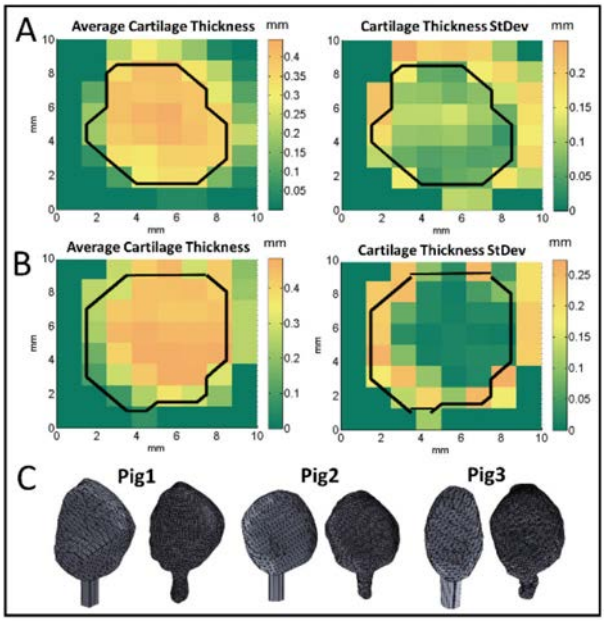

Figure 2. (A) Average (left) and standard deviation (right) of cartilage thickness of 8 native porcine ACs. The black line represents the average cartilage profile. **(B)** The same thickness maps as in **(A)** but for the designed implants for 3 individuals. **(C)** The design (left) and fabricated PCL implant as determined from μCT imaging (right) of each of the three individuals

Results

Starting from clinical CT, we designed animal-specific implants to replace the surface of the AC and molds with which to fabricate them (Fig. 1). Our design technique resulted in a cartilage thickness of ~400-500 μm throughout, much like the native tissue (Fig. 2A-B). Scanning the fabricated constructs by μCT showed that they faithfully reproduced the designs. In the joint loading experiments (Fig. 3), in all preoperative trials, as the limb was extended from 90° to full extension, force and contact area remained close to 0N until the joint approached 0° at which point the average force rose to 21.6N and the average contact area rose to 74.2mm^2. Post-implantation, a similar loading pattern was observed, with force averaging 21.5N and contact area averaging 72.0mm^2.

Discussion

In this study, we expanded on our previous work[5,6] by creating a robust protocol for fabricating biphasic constructs for replacing the osteo-articular surface of the porcine AC bone matched to the geometry of a specific animal's joint. The hydrogel portion of said constructs faithfully recreated the cartilage thickness profile of the native AC and the PCL foam portion restored the original geometry of the bone. Importantly, there was more variation in the size and shape of individual ACs than in the thickness of the cartilage, and

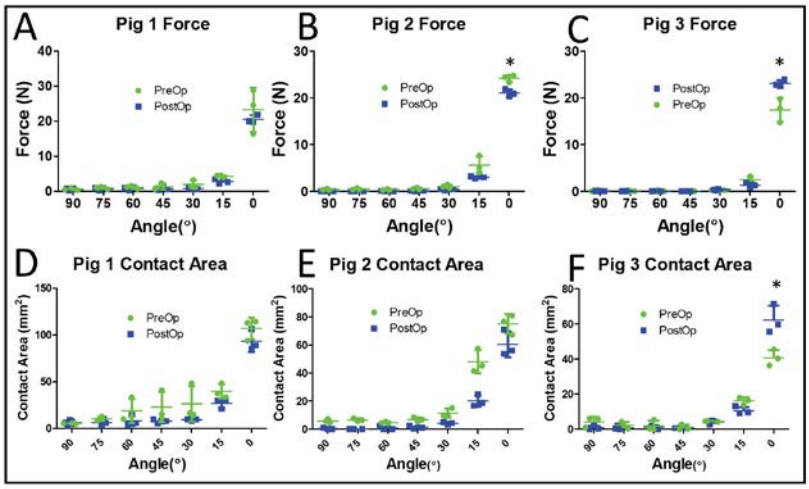

Figure 3. (A-C), Force measurements across flexion angles for each of 3 pigs before and after implantation of composite implant; **(D-F)**, contact area of same.

so knowing the shape of the bone from clinical CT enables us to reasonably approximate the cartilage without the need for contrast agents. When animal-specific constructs were implanted into the forelimb *ex-vivo*, they restored the loading patterns of the joint. Future steps are to evaluate the long-term function of cell seeded osteochondral implants (with a stem cell-laden hydrogel cap to form a cartilage layer) as well as implantation of patient-specific constructs in a living animal to evaluate their long-term efficacy *in vivo*.

Significance

This study refines an approach to design and fabricate of patient-specific implants, furthering the goal of total biologic resurfacing for the treatment of TMC OA in humans.

Acknowledgments

The National Institutes of Health, the Orthopaedic Research and Education Foundation, and the Department of Veteran's Affairs supported this work.

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