The Porcine Accessory Carpal as a Model for Biologic Joint Replacement for Trapeziometacarpal Osteoarthritis

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Introduction

Trapeziometacarpal (TMC) osteoarthritis (OA) is one of the most common conditions affecting middle and older aged adults[1]. Given that the opposable thumb is central to all activities of daily living, loss of function has a significant impact on quality of life. Patients with TMC OA are initially managed with activity modification, non-steroidal anti-inflammatory drugs, splinting, and occasionally corticosteroid injections[2]. These conservative treatments often fail in the long term, and many patients will eventually require surgical intervention. However, most of these procedures are destructive, involving removal of all or part of the trapezium, and replacement with tendon, fascia, or an artificial substrate or 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 this study, we explored the porcine accessory carpal (AC) bone as a model for TMC OA, with the goal of using this to evaluate a tissue-engineered biologic joint replacement.

Methods

The forelimbs of skeletally mature Yucatan minipigs under general anesthesia were imaged with a portable 8-slice CT scanner (CereTom, Neurologica). DICOM files were exported and opened in ITK-SNAP[5], where the bones were individually segmented. Using this information, a 3D model was generated in OpenSim, and the relative motion of the AC and normal and shear contact forces were evaluated through a range of flexion angles. Next, five AC bones were isolated from the right forelimbs of adult Yucatan minipigs from an unrelated study. A custom indentation testing setup was used to evaluate cartilage mechanics along the midline of the AC articular surface via stress relaxation tests. The saddle-shaped articular cartilage surface was indented with a 2 mm diameter spherical indenter in three locations (superior, middle, and inferior). Four compressive ramps (10% strain each) were applied, with a 600s relaxation between each step. The equilibrium modulus was calculated from the second step. Samples were then fixed in formalin and imaged via μCT (VivaCT 75, Scanco medical), before and after immersion in Lugol's solution (5% I2, 10% KI in water) to enhance cartilage contrast. DICOMs from the initial scan were imported into ITK-SNAP and the bone was segmented. 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 in order to compute the bone volume and surface features. Scans post Lugol's treatment were manually registered with the bone scan and processed similarly, with the cartilage layer segmented in a semi-automated manner. Cartilage thickness was determined across the 3D object with a grid spacing of 1.25 mm. After imaging, samples were decalcified, processed into paraffin, sectioned, and stained with Safranin O and fast green to visualize cartilage, bone, and fibrous tissue. Statistical analysis was by one-way ANOVA with Tukey's posthoc testing, and Pearson correlation of animal weight against cartilage volume and surface area.

Results

The cartilage surface of the pig AC consists of a main saddle-shape that articulates with the ulnar carpal bone and a secondary facet that interacts with the ulna (Fig 1A-B). The remainder of the bone is embedded in fibrous tissue (Fig 1F). When the unloaded hoof extends, this fibrous tissue sheath goes into tension and causes the AC to articulate slightly distally, resulting in estimated contact forces in the range of 138N compression and 21N shear (Fig 1C). Across five donors, the AC had the same basic shape and geometry, but showed a high degree of inter-subject variation in both shape (Fig 2) and in size (Fig 3B). AC volume (Pearson $r = -0.1065$) did not correlate with animal weight, while cartilage surface area was negatively correlated (Pearson $r = -0.6507$). The average thickness of the AC articular cartilage ranged from 310-420 microns within the contour of the main articulating surface. There was a trend towards greater thickness on the superior and

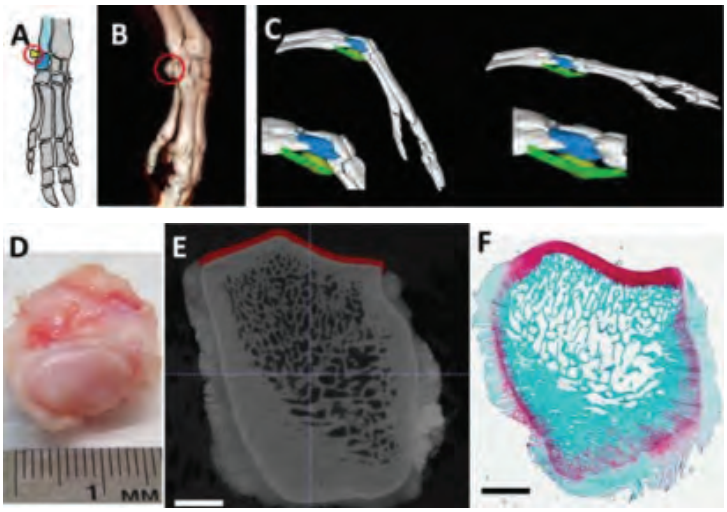

Figure 1. (A) Position of the AC (yellow) with respect to the ulnar carpal (blue) and ulna (light blue); **(B)** CT visualization with the AC identified (red circle); **(C)** OpenSim model showing position of the AC (yellow) relative to the ulnar carpal (blue) in flexion (left) and extension (right); **(D)** Gross view of cartilage surface of the AC; **(E)** μCT slice in ITK-SNAP showing segmented cartilage in red. Scale = 3mm; **(F)** Safranin O/Fast Green stained section of AC. Scale = 3mm.

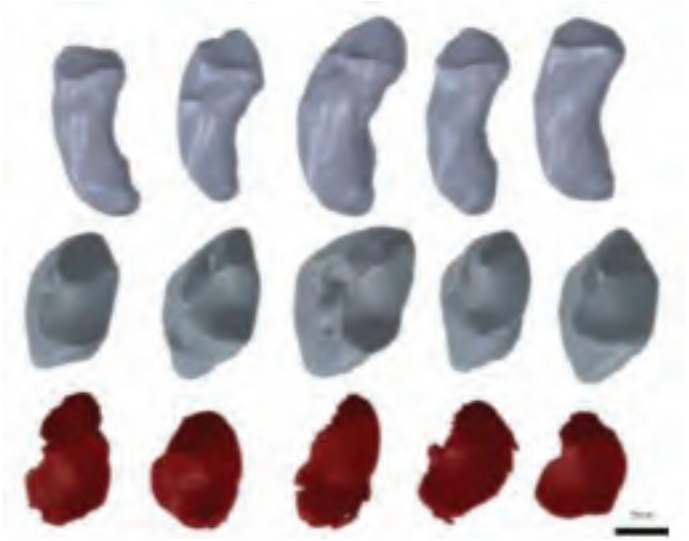

Figure 2. Solidworks models of five AC bones and the corresponding cartilage surfaces (in red). Scale = 5mm.

middle regions compared to the inferior region (Fig 3A). Interestingly, there was more variation in the size and shape of the cartilage surface than there was in the thickness. The equilibrium modulus in the superior, middle, and inferior regions was 1.17 +/− 0.20, 1.63 +/− 0.16, and 1.54 +/− 0.12 MPa, respectively (Fig 3C), with the superior region trending softer than the middle and inferior regions (p=0.14).

Discussion

We evaluated the geometric, histologic, and mechanical properties of the accessory carpal bone and cartilage in a Yucatan minipig model. This bone and articulating surface bears anatomic similarities to the human TMC in terms of its saddle-shaped cartilage surface as well as its load bearing function. While there was variation in geometry between subjects, several trends emerged. Specifically, the superior aspect was thicker and softer, while the inferior aspect was thinner and stiffer. These data provide benchmarks for the generation of anatomic models and living engineered replacements for the AC cartilage and bone[4]. The consistency in cartilage thickness suggests that CT rendering, using a clinical scanner, may provide sufficient resolution for implant generation, a priori, without the need for high resolution scanning of isolated tissue. This will enable ex vivo production and maturation of engineered constructs on an individualized basis. Having established these principles, future studies will focus on the creation of anatomic molds to create engineered bone coupled to an engineered articular cartilage surface. Ultimately, these engineered osteochondral units will be used for biologic joint resurfacing of the AC in a large animal model, advancing the state of the art in the treatment of TMC osteoarthritis

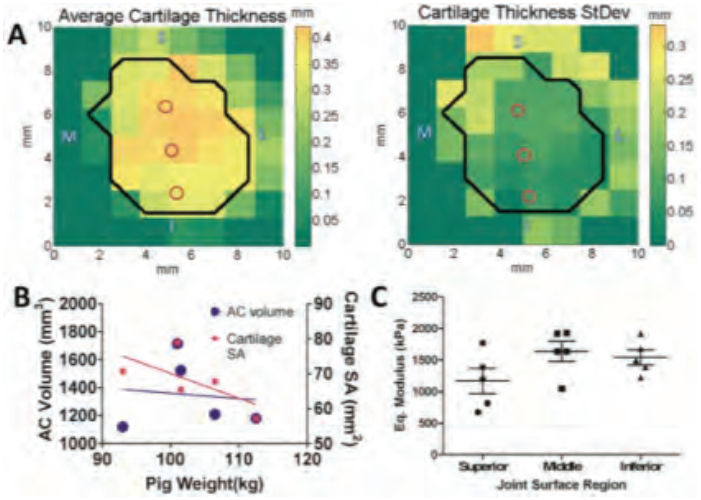

Figure 3. (A) Average (left) and standard deviation (right) thickness maps of the main articulating surface overlaid on top of a profile indicating the average cartilage perimeter (black line). Indentation test location indicated by red circles; **(B)** Correlation analysis of animal weight and cartilage volume and surface area; **(C)** Equilibrium modulus at three locations along the midline of the AC articular cartilage. N = 5, p = 0.14.

Significance

This study defined the anatomic and mechanical features of the porcine AC bone and cartilage, a first step in the development of a large animal model to rigorously evaluate biologic resurfacing strategies for the treatment of TMC osteoarthritis.

Acknowledgements

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