Development and Mechanical Characterization of Polycaprolactone-Hydroxyapatite Spinal Cages for Transforaminal Lumbar Interbody Fusion

Trenton Campos[1], Gregory Datto[1], Chet S. Friday[2], Andy Liu[1], Dean Wertz[1], Carlos Mendez Cruz[1], Rashad Madi[2], Michael W. Hast[2], Chamith Rajapakse[1,2]
[1]Department of Radiology, University of Pennsylvania, Philadelphia, PA
[2]McKay Orthopaedic Research Laboratory, Department of Orthopaedics, University of Pennsylvania, Philadelphia, PA
tdcampos@seas.upenn.edu
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INTRODUCTION: Degenerative lumbar spondylolisthesis is a pathological condition characterized by a combination of disc degeneration, facet joint arthritis, and disruption in the lumbar spine's stabilizing structures. This multi-factorial etiology leads to spinal stenosis and arthritis, manifesting clinically as neurogenic claudication and radiculopathy. Initial intervention commonly consists of conservative therapeutic approaches; however, surgical intervention becomes required when conservative measures prove ineffective. In such cases, transforaminal lumbar interbody fusion (TLIF) is performed to decompress and fuse the spine, reducing the pathological vertebral instability [1]. During this procedure, interbody cages made from either titanium or polyetheretherketone (PEEK) and bone graft are utilized. Nonetheless, each cage material presents its own set of postoperative complications: titanium has been linked to complications arising from its elastic modulus mismatch with bone, whereas PEEK has been criticized for its lack of osteointegration [2]. To solve this problem, other materials have been investigated for use in spinal cage development, including polycaprolactone (PCL), a biodegradable polymer with an elastic modulus similar to bone, and hydroxyapatite (HA), which promotes osteogenesis. In this study, we developed several biodegradable, osteogenic PCL-HA spinal cages utilizing a synthetic bioprinting system, which we characterized using a compressive mechanical testing protocol. We hypothesized that the optimal PCL-HA spinal cages were designed with the smallest infill to maximize mechanical properties.

METHODS: *Spinal Cage Design*: All spinal cages were printed with an 80:20 ratio of PCL to HA, which was determined based on two factors: first, the need for slow degradation rates in spinal fusion [3], which is facilitated by high concentrations of PCL; and second, the need for optimal mechanical properties, which was determined based on previous mechanical testing [4]. Various prototypes as depicted in Figure 1 were designed in CAD software (Onshape, PTC). The design shown in Figure 2 was selected for mechanical testing as its size was optimized for TLIF procedures and the graft window was removed as the HA acted as a synthetic bone graft. *Spinal Cage Printing*: Spine cage printing was based on our previously established protocols [4]. To summarize, we utilized a desktop 3D bioprinter (Allevi 2, Allevi) with molecular weight 55,000 g PCL pellets and 10 μM HA powder. Bioink was synthesized via melting of the PCL pellets and subsequent quantitative mixing of the HA powder. After loading the bioink, the printer was heated to 70℃ and set to a pressure of 100 PSI. For extrusion, a 23-gauge needle was utilized at a print layer height of 0.4 mm. A circular acrylic glass slide covered in double-sided tape for proper print adhesions served as the printing surface. *Mechanical Testing*: All spinal cage designs were subjected to mechanical testing to determine which design could best withstand compressive loading in the spine. Samples were tested on a servo-hydraulic mechanical test frame (Instron 8874, Instron) with a 25kN load cell. Samples (n = 10 per spinal cage design) were tested in unconfined compression, with custom aluminum platens connected to a universal joint to ensure normal application of forces. Samples were loaded at a rate of 1 mm/min until the obvious onset of plastic deformation to determine stiffness (N/mm; slope of the linear region of the force-displacement curve) and yield force (N; force at .2% offset strain relative to the linear region). Additionally, cuboid scaffolds (n = 12) with known cross-sectional area were tested to determine the elastic modulus (MPa; slope of the linear region of the stress-strain curve) of the PCL-HA material after printing. Modulus was calculated for these constructs instead of the spinal cages due to the difficulty of calculating the cross-sectional area of the spinal cage designs. All mechanical properties were calculated using custom MATLAB scripts (MATLAB 2022a, MATLAB). Results for stiffness and yield force were evaluated using one-way ANOVA (GraphPad Prism 10, GraphPad) to determine the effect of scaffold design on mechanical properties.

RESULTS: Testing of the various spinal cage designs showed that the 3mm-grid spinal cage design resulted in the highest stiffness (4420 +/- 186.9 N/mm) compared to the 4mm-grid (3514 +/- 538.9 N/mm, $p < 0.0001$) and the 4mm-ZigZag (3149 +/- 222.9 N/mm, $p < 0.0001$) (Figure 3A). Similarly, the 3mm-grid resulted in the highest yield force (2672 +/- 164.2 N) compared to the 4mm-grid (1885 +/- 386.1 N, $p < 0.0001$) and the 4mm-ZigZag (1681 +/- 94.52 N, $p < 0.0001$) Figure (3B). There were no significant differences observed between the 4mm-grid and 4mm-ZigZag designs for stiffness or yield force. Testing of the cuboid constructs determined that the modulus of the printed PCL-HA material was 255.9 +/- 34.35 MPa.

DISCUSSION: Mechanical testing revealed that the 3mm-grid design produced the strongest spinal cage, with the highest stiffness and yield force values. Because of these superior mechanical properties, the 3mm-grid spinal cage is likely the best suited for use in TLIF procedures, given its ability to handle high-magnitude compressive forces like those in the spine. Additionally, the average yield force of the 3mm-grid is 1172 +/- 164.2 N greater than the forces used to model in vivo loading of the anterior column [3], and its stiffness value is closest to optimized TLIF cages [3]. Another important finding is that the modulus of PCL-HA printed material falls within the reported mid-range of human trabecular bone (120-450 MPa) [3], with 10 - 3000 MPa being the entire range [5]. This similarity could enable this spinal cage to replicate the loading environment of the spine. One limitation is that, although the 3mm-grid design is strongest, it is likely due more to the fact that this design had a higher infill percentage (and thus, more material printed into the scaffold than the other groups) and less due to overall impact of the geometrical pattern. Future work with PCL-HA spinal cages involves taking DICOM medical imaging files and converting them to STL files with subsequent bioprinting to custom-fit cages to the patient's vertebrae, allowing for more optimal patient outcomes. In the body, the scaffold undergoes point loading due to the flat surfaces on the top and bottom of the scaffold, increasing the likelihood of cage subsidence, which a custom-fit cage prevents, making the stress data more representative of those in vivo conditions. Additionally, further work will be done to vascularize our spinal cages. Bone is porous and vascularized, and having pathways within our scaffolds with vascularized cells will make scaffold osteointegration more efficient. Alginate-gelatin hydrogels will be utilized to culture endothelial cells and vascularize them within the scaffold framework.

SIGNIFICANCE / CLINICAL RELEVANCE: This spine cage is an alternative design for TLIF cages which are generally the preferred mode of spinal fusion over other methods. Current spine cages are different from the modulus of bone or lack osteointegrative properties, whereas our scaffolds align more closely to the modulus of bone and the osteogenic properties of hydroxyapatite allow for fully synthetic cages that forgo the need for bone grafts.

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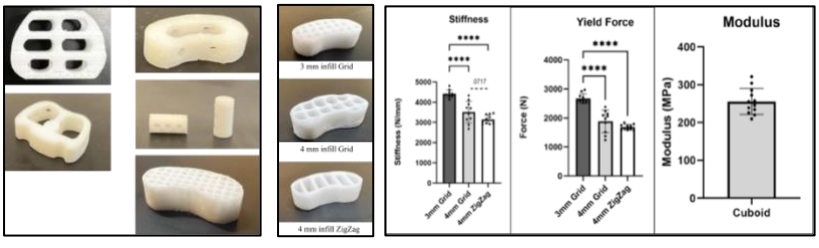

Figure 1. Initial spine cage prototypes. **Figure 2.** Different infill geometries for optimal scaffold. **Figure 3.** Data collected from different scaffold geometries