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Static and Dynamic Fatigue Behavior of Topology Designed and Conventional 3D Printed Bioresorbable PCL Cervical Interbody Fusion Devices

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Abstract

Recently, as an alternative to metal spinal fusion cages, 3D printed bioresorbable materials have been explored; however, the static and fatigue properties of these novel cages are not well known. Unfortunately, current ASTM testing standards used to determine these properties were designed prior to the advent of bioresorbable materials for cages. Therefore, the applicability of these standards for bioresorbable materials is unknown. In this study, an image-based topology and a conventional 3D printed bioresorbable poly(ϵ)-caprolactone (PCL) cervical cage design were tested in compression, compression-shear, and torsion, to establish their static and fatigue properties. Difficulties were in fact identified in establishing failure criteria and in particular determining compressive failure load. Given these limitations, under static loads, both designs withstood loads of over 650N in compression, 395N in compression-shear, and 0.25Nm in torsion, prior to yielding. Under dynamic testing, both designs withstood 5 million (5M) cycles of

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compression at 125% of their respective yield forces. Geometry significantly affected both the static and fatigue properties of the cages. The measured compressive yield loads fall within the reported physiological ranges; consequently, these PCL bioresorbable cages would likely require supplemental fixation. Most importantly, supplemental testing methods may be necessary beyond the current ASTM standards, to provide more accurate and reliable results, ultimately improving preclinical evaluation of these devices.

Keywords

Interbody fusion; Bioresorbable cages; Structural properties; Spine fusion; Fatigue properties; ASTM testing

1. Introduction

Over the past two decades, the number of anterior cervical decompression and fusion (ACDF) procedures performed in the United States has more than doubled, increasing from approximately 61,000 procedures in 1993, to nearly 160,000 procedures in 2011[1]. The goal of these procedures is to decompress nerve roots [2], maintain disc height [3], and achieve solid fusion[4, 5], typically through the use of a spinal cage enhanced with biologics that promote bone growth.

In order to achieve fusion, the spinal cage must provide sufficient mechanical strength to withstand the physiological loads placed on the spine [6-8]. Designs composed of nonresorbable materials, such as titanium or PEEK[9, 10], provide the mechanical strength necessary to withstand these loads; however, due to their substantially larger modulus of elasticity compared to the vertebral bodies, stress shielding [11, 12] and implant subsidence into the vertebrae is a significant concern. Alternatively, bioresorbable cages have been developed, in part, to address such concerns[13]; however, the mechanical properties of such devices, especially dynamic fatigue behavior, have not been widely reported. Therefore, the safety of using these cages in the cervical spine, either as stand-alone cages or cages supplemented by additional fixation, has not been established.

Improved 3D printing technologies, which enable fabrication of topology optimized designs, allow for improvements in the mechanical design of scaffolds to withstand typical loads by placing material in critical load bearing paths, but leaving sufficient porosity and permeability for bone ingrowth and biologic delivery [14, 15]. Combining topology design and optimization with 3D printing technologies such as laser sintering, allows for the realization of complex topology designed cages fabricated for resorbable polymers [15, 16]. However, despite the sophisticated 3D printing and optimization capabilities, the effects of these designs and resorbable polymer properties on the structural strength of the implants is not well known. As bioresorbable cages tend to have weaker material properties than their nonresorbable metal and permanent polymer (PEEK and PEKK) counterparts, optimum designs must be utilized to maximize their mechanical and structural strength.

In order to establish the mechanical properties of bioresorbable cages prior to use in patients, spinal cages are typically tested using ASTM standard F2077[17], as mandated by the FDA

special controls guidance document for intervertebral body fusion cages[18]. Thus, these tests are required to obtain FDA approval of spine cages via the 510(k) premarket approval pathway. This preclinical standard was developed to evaluate the compressive, shear, and torsional structural mechanical properties of the devices under both static and dynamic loading conditions. However, this testing standard was initially established for hollow cylindrical and rectangular shapes made of solid nonresorbable materials such as titanium or PEEK, representative of the most common devices available when the standard was initially drafted. Therefore, it is not clear whether these testing methods are equally appropriate for spine cages composed of bioresorbable materials which tend to be more porous and ductile, and vary widely in geometry. This is especially true given that fusion must be obtained with bioresorbable cages to stabilize the cervical spine, as failure to obtain fusion at 1 year with bioresorbable cages would lead to instability. Thus, the 5 million cycles recommended in ASTM F2077 would go well beyond that required for successful spinal fusion. Moreover, while previous studies have measured the properties of bioresorbable materials under various static loading setups[15, 19-22], there has been limited investigation into dynamic and fatigue properties of these implants[23]. In fact, to our knowledge, no previous dynamic fatigue testing under ASTM F2077 of any 3D printed bioresorbable cages has been previously reported.

The purpose of the present study was first, to test and evaluate the applicability of ASTM standard F2077 for the testing of PCL bioresorbable 3D printed spinal cages. Second, the study determined the static and fatigue properties of two different bioresorbable spine cage designs to the extent that the ASTM standard could be applied dependably. The two different cage designs were: 1) a cylindrically shaped design replicating clinically available and conventionally utilized ring-shaped solid cages, and 2) a novel, optimized, rectangular design with porous topology, engineered for simultaneous maximal apparent diffusivity and elastic modulus [15,24]. The standard static and dynamic loading protocols described by ASTM F2077 were implemented and the results of these tests were used to evaluate the effectiveness of the standard. Specifically, we determined the mechanical properties of the PCL cages under standard preclinical testing criteria as a function of loading mode and cage design.

2. Methods

2.1 Materials

Two biodegradable cervical cage designs composed of PCL were tested: (1) a ring-shaped cage (standard ring), which has been designed based on commercially available cervical fusion cages, and (2) a novel, porous, rectangular design (optimized design). The optimized design was created using a modular approach, combining topology optimization for the porous regions with image-based design for the cage shape and serrated fixation ridges. The topology optimization approach, using our previous development [24], designs a unit cell to meet bounds on maximum elastic and diffusivity coefficients at a given volume fraction, with a constraint to match the desired volume fraction. For this case, the volume fraction was fixed at 30%, which, based on known cross-property bounds, yields a bound of 15% of the maximum possible material elastic modulus (290 MPa for laser sintered PCL) and 53%

of the maximum possible diffusivity coefficient [24]. The unit cell is repeated in 3D space and then substituted using image-based design for the main cage body, which has serrated ridges for fixation (Figure 1).

The standard ring-shaped cage measures 15.3 mm in width, 13.7 mm in length, and 6.1 mm in thickness, with a 6.5 mm diameter hole in the center, giving a volume of 614mm³ (Figure 1). The novel, rectangular, optimized design cage is porous with dimensions of 14.7 mm in width, 13.7 mm in length, and 6.9 mm in thickness, giving a volume of 639 mm³ (Figure 1).

The cage designs were fabricated from poly-ε-caprolactone (PCL) (43-50 kDa, Polysciences, Warrington, PA) cut with 4% hydroxyapatite(HA) (Plasma Biotol Limited, UK) using a selective laser sintering approach on an EOS P 100 Formiga system (EOS, Inc, Novi, MI) using approaches we and others previously developed.[16, 25, 26] The PCL was cryogenically milled to have a mean particle size range of 40-60µm with a maximum particle size of 125µm. The milled PCL powder was then combined with hydroxyapatite to produce a 4% w/w blend of HA/PCL. STL files of each design were sliced for manufacturing using RPTools (EOS, Inc, Novi, MI) with a layer thickness of 80 µm. The cages were manufactured in a nitrogen environment and the bed temperature of the SLS system ranged from 52-55 °C. Post-manufacture, the cages were air blasted to remove non-sintered powder.

2.2 Mechanical Testing Characterization

These cages were tested in three different loading scenarios: (1) compression, (2) compression-shear, and (3) torsion, following the protocol described by the ASTM standard F2077-03[17]. Static loading to failure was performed first in order to determine the ultimate loads to use during dynamic testing.

2.2.1 Static Loading—Static loading was performed using single-station loading fixtures mounted in an MTS 858 biaxial servohydraulic load frame (MTS, Minneapolis, MN). Six specimens of each design (standard ring and optimized design) were loaded to failure for each of the three static loading modes: static compression, static compression-shear, and static torsion. Each specimen was sandwiched between custom stainless steel plates, containing a groove contoured specifically for each specimen design, secured to the stationary table of the MTS machine. For compression-shear loading, the bottom plate was created to hold the specimen at a 45 degree angle. A compressive or torsional load was applied by the actuator, located above the specimens, via a cylindrical rod resting on a spherical component, which was secured to the top plate (Figure 2) as per ASTM F2077 requirements. For torsional loading, the rod and sphere were rigidly fixed together using a pin and yoke (Figure 2-c). A load was applied at a rate of 0.1 mm/second or 0.1 degree/second, to 3 mm for compression, 7 mm for compression-shear, or 60 degrees for torsion. During torsion testing, a constant axial compressive preload of 100 N was applied throughout testing. Before and after loading, the dimensions of each specimen were measured.

From these tests, the force-displacement and torque-rotation curves were plotted for each of the specimens. The peak of the curve was considered to represent the ultimate force or

torque. However, the static compression tests resulted in continuously increasing force-displacement curves, and therefore, ultimate force could not be determined. Instead, the yield force, at the end of the linearly elastic region, was recorded. Additionally, stiffness and apparent Young's modulus of elasticity were calculated for each specimen.

2.2.2 Dynamic Loading—Dynamic loading was performed using a three-station loading apparatus designed to test three specimens under the same loading conditions. Six specimens of each design, standard ring and rectangular optimized design, were cyclically loaded to failure or 5 million (5M) cycles for each of the three loading modes: dynamic compression, dynamic compression-shear, and dynamic torsion. For compression and compression-shear loading, the design of the three-station loading apparatus included three of the single-station loading fixtures secured to a base plate that rested on a ball joint, allowing for an even distribution of force among the three. For torsional loading, a stacked configuration was used, in which the specimens and plates were stacked linearly. For all tests, separate polyethylene plates were created for each specimen and discarded after use.

For compression loading of both the standard ring-shaped and porous, rectangular-shaped optimized design specimens, three of each design were loaded up to 125% of the yield load, determined by the static loading test, since no clear ultimate load could be established. Next, three of each design were loaded up to 145% of the yield load to provide a reasonable number of fatigue failures. In total, six ring-shaped and six porous optimized rectangular specimens were tested in dynamic cyclic compression.

For compression-shear loading, three of each design loaded to 75% of the ultimate load, determined by the static loading test, and three specimens were loaded to 98% of the ultimate load (total n=6 of each). For torsion loading, three of the six standard ring design specimens were loaded to 40% of the ultimate load, and three specimens were loaded to approximately 60% of the ultimate load (total n=6). Three of the optimized design specimens were loaded to approximately 60% of the ultimate load, and, because these specimens survived the maximum 5M cycles, three specimens were then loaded to 70% of the ultimate load (total n=6). Cyclic loading was applied at a rate of 6 Hz.

Loading was paused twice a day to measure the dimensions of each of the specimens in order to quantify deformation and determine if failure had occurred. Due to the ductile nature of the material, failure was defined as deformation or rotation equal to or greater than the yield values. Specifically, failure during compression loading was defined as a change in thickness of at least yield deformation. Failure during compression-shear loading was defined as a change in length from the anterior edge of the specimen to the posterior edge of the groove in the plate of at least the yield deformation divided by the cosine of 45 degrees. Finally, failure during torsion loading was defined as an increase in rotation, measured between the top and bottom plates without any torque present, of at least yield rotation.

Additionally, a displacement or rotational limit was set in the loading program to stop loading if the specimen deformed to the failure values. Loading was discontinued after the specimen reached failure or 5M cycles. If only one of the three specimens reached failure,

that specimen was removed and a dummy specimen was put in its place and loading was continued. The number of cycles at failure was recorded for each specimen.

2.3 Statistical Analysis

Boxplots were used to present the distribution of each mechanical property for the two tested cage designs. SPSS Statistical Software (SPSS Inc, Chicago, IL) was used to perform independent samples t-tests to compare each of the mechanical properties as a function of the two cervical cage designs (standard ring versus optimized design).

3. Results

3.1 Static Loading

Overall, the structural properties of the cages were significantly affected by cage geometry and design. Specifically, the standard ring design had significantly higher compressive stiffness (Figure 3), ultimate compressive-shear force (Figure 4), and compressive-shear yield force (Figure 5), as compared to the optimized porous, rectangular design. The optimized design had a larger compressive yield force than the ring design; however, this was not significant. Additionally, both designs withstood over 4000 N of compression without ultimate failure (Figure 6). Representative failed specimens for each of the testing modes is shown in Figure 7.

The optimized cervical cage performed better in torsion testing, resulting in a significantly higher torsional stiffness (Figure 3), ultimate torque (Figure 4), and yield torque (Figure 5), compared to the standard ring design.

3.2 Dynamic Loading

For the dynamic compression tests, both the standard ring and the optimized design specimens were loaded to 125% of their yield load and to 145% of their yield load (Table 1). During the testing to 125% yield load, all three of the ring design specimens survived the maximum of 5M cycles without failure, and two of the three porous design specimens survived 5M cycles, with one specimen reaching failure at 4.0M cycles. When loaded to 145% yield load, all of the standard ring and optimized design specimens experienced failure at an average of 1.5M and 0.5M cycles, respectively.

For compression-shear dynamic testing, both the ring and the optimized design specimens were loaded to 75% and 98% of their ultimate load. All specimens survived the 5M cycle limit during both loading scenarios.

During dynamic torsion testing, the first set of three standard ring design specimens were loaded to 40% of their ultimate load and survived the 5M cycle limit. The next set of three were then loaded to 60% of their ultimate load and experienced failure at an average of 1.5M cycles. The first set of three optimized design specimens were also loaded to 60% of their ultimate load and all survived the 5M cycle limit. The next set was therefore loaded to 70% of their yield load and reached failure at an average of 2.0M cycles.

4. Discussion

The aforementioned loads and results were determined by applying the typical preclinical standard for testing interbody devices, that is, ASTM F2077[17]. However, several difficulties were encountered throughout testing, highlighting aspects of the standard that may need improvement. First, during static compression testing, the load continually increased with increasing deformation. Therefore, the test was stopped immediately prior to impingement of the testing fixture and, as a result, no ultimate force could be determined. With a typical nonresorbable design, such as one composed of a harder material, or one designed with large encapsulated voids in transverse cross sections, an ultimate force would be reached prior to fracture and/or catastrophic failure of the device; however, with softer materials, such as PCL, this may not occur. Therefore, alternative methods must be developed to establish the ultimate compressive load of these implants. Another difficulty with the testing methods was defining the failure displacement/rotation for dynamic testing. As discussed, and unlike other implant designs, the designs tested in the present study showed gradual deformation under applied loads. Therefore, as the failure criteria, we chose the yield displacement/rotation; however, no direct specimen measurement can be acquired at this point during testing. Instead, actuator displacement/rotation is relied on for the deformation acquired from the load-displacement curves; however, this does not account for error in the machine or movements within the testing apparatuses. Moreover, this relies on firm and definite fixation of the implant within the fixture plates, a difficulty which has been recognized in discussions of nonstandard implant designs and materials[37].

Overall, the two cage designs maintained mechanical integrity at over 650 N in compression, 395 N in compression-shear, and 0.25 Nm in torsion. Additionally, the structural properties were significantly affected by cage geometry, as each design provided advantages in different testing modes. Specifically, under static loading, the traditional ring shape design provided higher strength in compression-shear, with a significantly larger yield force and ultimate force, compared to the novel optimized, porous, rectangular design. Meanwhile, the optimized design was stronger in compression and torsion. Under dynamic compression testing, both designs demonstrated similar results, surviving 5M cycles of loading at 125% of the yield load. Under dynamic torsion, however, the optimized design demonstrated better long-term performance, surviving 5M cycles at 60% of the ultimate load, compared to only 1.54M cycles for the traditional ring design.

Despite the routine application and recommended use of ASTM F2077 for interbody spacers by the FDA Intervertebral Body Fusion device guidance document in 510(k) premarket applications, the results have not been widely reported in the literature. For the lumbar spine, studies have reported the ultimate compressive loads of various cages (manufactured with PCL, 70/30 PLDLLA, titanium alloys, and carbon reinforced polyetherimide) ranging from 1,250 N to 9,800 N[15, 21, 27, 28]. Results for cervical cages, however, are less common. Timmer *et al* [29] reported the ultimate compressive load of allograft and PPF/PPF-DA cages, with ultimate loads of more than 13,000 N. In the present study, the ultimate compressive load could not be determined due to limitations of the testing standard coupled with the material properties and mechanical behavior of PCL based cage designs. Specifically, as static compression was applied, the load continually increased as the

specimen continually compressed; however, no fracture or catastrophic failure occurred prior to the test being stopped to prevent impingement of the fixture plates. While the ultimate load could not be determined, all specimens from both cage designs withstood loads of more than 4,000 N prior to the end of the test without fracture.

The yield force in compression for both cage designs, however, was significantly smaller than reports of PEEK and PMMA cages. Brenke *et al*[30] reported compressive yield loads of 8,396 N and 10,598 N for PEEK and PMMA cervical cages, with the ultimate loads presumably much larger. In the present study, the yield loads in compression were 660 N and 847 N for the ring-shaped and optimized porous designs, both smaller than either PEEK or PMMA cages; however, both PEEK and PMMA have significantly stronger raw material properties as compared to PCL. Specifically, the bulk ultimate compressive strength of PCL has been reported as 38.7 MPa, while the 0.2% offset yield strength is 12.5MPa[31], significantly less than PEEK and PMMA, which have compressive strengths of 160 MPa[32] and 80-124 MPa, respectively. Moreover, the designs in the present study were highly porous, decreasing their yield strength.

Clinically, in order to achieve successful fusion, the cage must maintain its mechanical integrity under physiological loading.[6-8] Moroney *et al*[33] estimated that, during typical bending of the spine, *in vivo* compressive loads range from approximately 120-1200 N in the cervical spine. In comparison, the traditional ring-shape design and the optimized, porous, rectangular design cages tested in the present study had compressive yield loads of 660 N and 847 N, respectively. As these yield loads fall within the mid-upper range of potential physiological loads, these cage designs may not be strong enough as stand-alone cages in the cervical spine. However, it should be noted that failure loads of the intact cervical spine have been reported within the 120-1200 N physiological range as well. For example, the compressive strength of the cervical spine has been reported to range from approximately 850-4230 N[34, 35], and the elastic limits ranging from 300-2010 N[35]. Truumees *et al*[36] reported endplate failure of cadaveric cervical vertebrae at 754 N. However, without the complete structural support provided by additional fusion hardware, it is difficult to determine how much strength is required by cages alone.

The static compression-shear results in the present study are generally consistent with previous reports of PMMA cages. Brenke *et al*[30] reported a compression-shear yield strength of 804.9 N in stand-alone cervical PMMA cages, and a compression-shear stiffness of 1228 N/mm. In comparison, the compression-shear yield loads of the cages tested in the present study ranged from 397-646 N, and stiffness ranged from 493-610 N/mm. Typical *in vivo* anterior-posterior shear loads, the same loading direction as the compression-shear tests, have been estimated to range from 0-135 N[33], substantially smaller than both the yield and ultimate shear loads with the designs in the present study. The designs, therefore, may be strong enough to withstand the typical shear loads in the cervical spine.

The current study demonstrated the significant effect of design on the static failure and dynamic fatigue failure of resorbable interbody fusion cages. To our knowledge, this is the first report of dynamic fatigue results performed as per ASTM F2077 for 3D printed resorbable cages. Although finite element studies can be used to estimate stiffness of

topology designs, variations in manufacturing quality from the 3D printing process (laser sintering in this case), including layering induced anisotropy, potential variations in bonding between layers, and variations in heat distribution, make it extremely difficult to predict fatigue behavior. Therefore, there is critical need for fatigue testing of resorbable materials to assess how design affects long term fatigue behavior.

Resorbable materials by nature have lower stiffness, strength, and fatigue resistance than permanent materials. This fact, combined with the need for strategically placed porosity, permeability, and surface area to deliver biologics and allow bone ingrowth under the tissue, places even greater emphasis on the need for topology design and optimization to achieve the right balance between load bearing and porosity. Characterizing this balance requires more fatigue testing like that performed in the current study. Finally, it will also be critical to study not only how the initial design affects fatigue, but also how design affects the coupling between degradation and fatigue, and bony ingrowth and fatigue. These tests will require developments of new tests and models for fatigue of degrading materials as well as controlled *in vivo* tests that produce scaffolds constructs with tissue that can be fatigue tested.

The present study is the first to our knowledge reporting the fatigue properties of bioresorbable 3D printed PCL cages for the cervical spine. While the cage designs tested in the present study may not be strong enough as stand-alone devices as currently constructed, the results provide a stepping stone for future research in the field. However, further testing on a larger number of specimens would be beneficial in order to draw more substantial conclusions about fatigue strength of bioresorbable cages and differences in cage designs. Additionally, future testing will be performed to systematically test various geometries to identify the ideal structure for applications in the cervical spine. Additionally, the fatigue properties of the bioresorbable cages will be determined as a function of bony ingrowth and cage degradation. Currently, the effects of these properties on the fatigue life of bioresorbable spine cages are unknown. Furthermore, the testing will be expanded to involve testing of the cages in a wet, physiological environment, as compared to the dry testing performed in the current study.

5. Conclusion

The difficulties in determining failure criteria for bioresorbable spine cages using the current ASTM testing standards suggest that additional testing methods may be necessary to provide more accurate and reliable results, in order to improve the preclinical evaluation of these devices. To our knowledge, this is the first study to report the mechanical fatigue properties of bioresorbable PCL cages for cervical spine fusion. Cage design and geometry had a definite effect on both the static and fatigue properties, as the two PCL cage designs tested in the present study each demonstrated advantages in different testing modes. However, the present cage may be strong enough to function when used along with supplemental fixation hardware, such as rods and screws. In order to achieve optimal cage designs to be used in the cervical spine, future testing is essential to fully define the material and structural mechanical properties of PCL cages. Furthermore, alternative geometries must be explored,

and the effects of other factors, such as bony ingrowth and degradation, on the fatigue properties of the cages must be established.

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Figure 1.

Topology optimized cage cervical fusion cage design (a-c) and conventional cylindrical type cervical fusion cage design. (a) Optimized design of unit cell with volume fraction limit of 30% to match 15% of base PCL elastic modulus and 53% of maximum possible diffusion for mass transport. (b) Global shape of cervical cage insert with ridges for fixation to avoid expulsion. Darker grey areas for where optimized unit cell will be substituted. (c) Final optimized cage design including the addition of a plate fixation region. (d) Conventional cylindrical cervical cage design with a center hole for bone graft to enhance fusion and small teeth for fixation to avoid expulsion.

Figure 2.
Static testing set-up for: A) compression, B) compression-shear, and C) torsion loading.

Figure 3.

Calculated stiffness values of each cervical cage design during static compression, compression-shear, and torsion loading.

Figure 4. Ultimate loads of each cervical cage design during static compression-shear and torsion loading

Figure 5. Yield loads of each cervical cage design during static compression, compression-shear, and torsion loading.

Figure 6.

Representative load-displacement curves for each of the two cage designs in A) static compression and B) static compression-shear, and a representative torque-rotation curve for each of the two cage designs in C) static torsion.

Figure 7.
Representative photos of each of the two cage designs in the initial (untested) conditions, and following failure during static testing in compression, compression-shear, and torsion.

Table 1

Dynamic testing results: average number of cycles at failure and standard deviation, rounded to the nearest half cycle.

	Ring Design (Set 1)	Ring Design (Set 2)	Novel, Rectangular Design (Set 1)	Novel, Rectangular Design (Set 2)
Compression				
Load (% of yield load)	125	145	125	145
Cycles (million)	5.0(0.0)	1.5(0.5)	4.5(0.5)	0.5(0.0)
Compression-Shear				
Load (% of ultimate load)	75	98	75	98
Cycles (million)	5.0(0.0)	5.0(0.0)	5.0(0.0)	5.0(0.0)
Torsion				
Load (% of ultimate load)	40	60	60	70
Cycles (million)	5.0(0.0)	1.5(0.0)	5.0(0.0)	2.0(0.5)