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Evaluation and Prediction of Human Lumbar Vertebrae Endplate Mechanical Properties Using Indentation and Computed Tomography

Current implant materials and designs used in spinal fusion show high rates of subsidence. There is currently a need for a method to predict the mechanical properties of the endplate using clinically available tools. The purpose of this study was to develop a predictive model of the mechanical properties of the vertebral endplate at a scale relevant to the evaluation of current medical implant designs and materials. Twenty vertebrae (10 L1 and 10 L2) from 10 cadavers were studied using dual-energy X-ray absorptiometry to define bone status (normal, osteopenic, or osteoporotic) and computed tomography (CT) to study endplate thickness (μm), density (mg/mm^3), and mineral density of underlying trabecular bone (mg/mm^3) at discrete sites. Apparent Oliver–Pharr modulus, stiffness, maximum tolerable pressure (MTP), and Brinell hardness were measured at each site using a 3 mm spherical indenter. Predictive models were built for each measured property using various measures obtained from CT and demographic data. Stiffness showed a strong correlation between the predictive model and experimental values ($r=0.85$), a polynomial model for Brinell hardness had a stronger predictive ability compared to the linear model ($r=0.82$), and the modulus model showed weak predictive ability ($r=0.44$), likely due the low indentation depth and the inability to image the endplate at that depth (≈ 0.15 mm). Osteoporosis and osteopenia were found to be the largest confounders of the measured properties, decreasing them by approximately 50%. It was confirmed that vertebral endplate mechanical properties could be predicted using CT and demographic indices. [DOI: 10.1115/1.4040252]

1 Introduction

Intervertebral arthrodesis (fusion) is one of the most effective treatment methods for lower back pain due to severe degenerative disk disease, herniation, and other pathologies affecting the disk and intervertebral space [1]. Over 267,000 surgical interventions

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Manuscript received February 9, 2018; final manuscript received May 7, 2018; published online June 21, 2018. Assoc. Editor: James C Iatridis.

of the lumbar and lumbosacral levels are performed annually in the U.S., and this number is expected to climb to 350,000 by 2023 [2,3]. Treatment costs range between \$40,000 and \$54,000 over 2 years [4–6]. Revision surgery is required in 15 to 17% of cases, often doubling the cost [7,8]. Additionally, the loss of disk height due to subsidence (i.e., the device sinking through the endplate) causes loss of correction in approximately 30% of the operated cases [8,9]. In cases of subsidence, the patient often requires additional surgery to restore the original corrected disk height. If left uncorrected, the vertebrae may fuse improperly—leading to further complications and increased pain and cost to the patient.

A stronger understanding of the mechanical properties of the endplate is necessary for the development of effective implant designs that minimize and avoid subsidence. A method to predict mechanical properties such as hardness, stiffness, and modulus would allow clinicians to assess the risk of subsidence and other complications following surgery, which are often due to weak bone and low mechanical strength of the endplate. Additionally, it would permit surgeons to determine the optimal implant placement to avoid areas susceptible to subsidence. It is generally known that the vertebral body is primarily made up of trabecular bone with a thin cortical shell, decreasing the mechanical integrity of the vertebra compared to solid bone. Pores within the bony endplate often decrease its stiffness and strength due to decreased cortical bone thickness [10–12]. Additionally, current implant materials are often orders of magnitude stiffer and stronger than the native bone as guided by current design standards that are focused on minimizing failure of the implant material rather than the bone [13]. Current surgical practices further compound this mechanical property mismatch as the bony and cartilaginous endplates are often debried to elicit bleeding and healing in the intervertebral space during surgery exposing the weaker underlying trabecular bone.

The overwhelming majority of studies investigating endplate mechanical properties have either performed measurements at the microscopic scale or used metrics, which are not directly comparable to implant material properties [14–17]. For example, it is common to measure the modulus of the vertebral endplate bone tissue by nano- and micro-indentations of solid bone microstructures within the endplate [14]. However, properties measured using these techniques do not accurately capture the behavior of the endplate as it relates to its interaction with implants at the macroscopic scale. Rather, at this scale, the structure of the bone has a greater influence on the mechanical integrity of the endplate, and micro-indentation cannot capture the gradients in properties or composite interaction of cortical and trabecular bone regions. The contributing effects of bone defects, endplate thickness, and underlying trabecular bone structure are lost when performing indentation at the microscopic scale. Other studies have investigated the macroscopic properties of the endplate using a 3 mm spherical indenter [15–17]; however, these studies measured properties, such as stiffness, which are not directly relatable to materials used in implants and are dependent on indenter geometry. Although stiffness has thoroughly been investigated in the endplate, it only allows for a general understanding of the endplate structure, whereas characterizing the endplate using traditional mechanical properties such as modulus and hardness would facilitate a direct comparison to implant materials. In previous studies, stiffness was defined as a function of axial load provided by penetration of a 3 mm diameter hemispherical probe through the endplate [16,17]. It was shown that the stiffness is highly variable, ranging from 4.6 N/mm to 390 N/mm across the endplate and is typically higher at posterior and lateral locations. It was also found that whole vertebral body stiffness can be predicted using bone mineral density from computed tomography (CT); however, these models do not account for bone defects, which significantly affect the modulus at the endplate–implant interface [18]. Additionally, stiffness measurements do not account for any time-dependent behavior of the endplate bone, where the combined contributions of elastic, plastic, and viscoelastic responses of the

vertebral bone need to be quantified in order to fully understand the mechanical behavior of the endplate with regard to implant loading. Furthermore, these properties have only been quantified using techniques available for ex situ studies in cadavers, but in order to use the endplate in a clinical setting, a method for predicting the properties of the endplate in vivo is required. A noninvasive method that uses currently available clinical tools and practices is necessary to estimate the properties of the endplate and predict the performance of implants following surgery, as it is not clinically feasible to directly measure the endplate properties of individual patients.

This study will introduce an indentation method to help separate and compare the elastic, plastic, and viscous effects in the vertebral endplate and correlate these effects using predictive parameters from clinical CT and demographic data. The purpose of this study is to develop a predictive model for endplate mechanical properties at a scale relevant to implant design and behavior. Specifically, this study seeks to build predictive mathematical models to predict modulus, stiffness, and Brinell hardness from demographic and radiographic data. Brinell hardness is a measure of the strength of the material as it transitions from elastic to plastic deformation, while Oliver–Pharr modulus captures the elastic response of a material during indentation and allows for visualization of the viscoelastic effects of loading on the bone. Brinell hardness is a very commonly used standard engineering material metric and allows for direct comparison between materials as it is easily quantifiable. The same is true for the apparent modulus as these material properties are often used to directly characterize engineering materials. It should be noted that the modulus, calculated from indentation using the Oliver–Pharr model, and Brinell hardness have not been previously reported for the vertebral endplate. Further, the Oliver–Pharr modulus calculated in this study should be viewed as an apparent or effective modulus, as it is a measure of the overall behavior of a structure’s mechanical properties and allows for direct comparison of the endplate properties to implant materials. Additionally, this study seeks to challenge the current paradigm of implant material and its relationship to bone mechanics.

2 Methods

Whole lumbar spine specimens (T12–S1) from ten cadaveric donors (five male and five female; age range, 44–65 year) with no cardiovascular or degenerative bone disease were obtained from Science Care (Phoenix, AZ) and placed in a -20°C freezer upon delivery. Dual-energy X-ray absorptiometry was performed using a Discovery W DXA instrument (Hologic Inc, Waltham, MA) on whole spines to define bone status and bone mineral density (g/cm^2) of each vertebra. Detailed characteristics of the tested specimens are presented as Sec. S1; Table S1, which is available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection. Then, conventional CT of each spine was performed (see detailed description below).

Each spine was thawed ($0\text{--}4^{\circ}\text{C}$) and the L1 and L2 vertebrae gently separated. Soft tissues and the cartilaginous endplate were carefully removed by dissection with a small scalpel, leaving the bony endplate and cortical shell intact. Twenty vertebrae (10 L1; and 10 L2) were wrapped in wet gauze to prevent drying. During preparation, each tested site was marked according to a Cartesian map (Fig. 1) and photographed to guide the indentation test and CT images analysis; indentation testing was then performed to define stiffness, apparent Oliver–Pharr modulus, maximum tolerable pressure (MTP), and Brinell hardness of both cranial and caudal endplates of each vertebra.

2.1 Computed Tomography. Computed tomography was performed using a Gemini TF 64 (Philips Healthcare, Cleveland, OH) scanner at 120 kVp with a slice thickness of 0.67 mm, interslice spacing of 0.33 mm, and in-plane resolution of 0.68 mm. Regions of interest for analysis at cranial and caudal surfaces of

Fig. 1 Cartesian map of the indentation sites across the vertebral endplate. Indentation sites were defined relative to percentages of the dimensions of the vertebral endplate.

each vertebra were identified according to the Cartesian coordinate system defined in Fig. 1. A detailed method for CT image analysis has been published previously [17]. The following characteristics were defined at each test site: endplate thickness (μm), endplate mineral density (mg/mm^3), mineral density of underlying trabecular bone (mg/mm^3), and presence of endplate defects (e.g., local concavity, fracture, or other defects, which affect the normal anatomy of the endplate) (yes/no). Hounsfield units were converted into bone mineral density (mg/mm^3) using a calibration phantom provided by the manufacturer, which displays known bone mineral densities allowing for direct conversion from Hounsfield units to mg/mm^3 .

2.2 Indentation Testing. The procedures related to preparation and indentation of the vertebrae closely followed a study by Noshchenko et al. [17]. The endplates were tested in a mechanical testing machine (MTS, Eden Prairie, MN). Eleven sites were tested on each surface using a 3 mm diameter hemispherical aluminum indenter. The indentation test had two stages. The first stage measured the apparent modulus of the endplate surface [19,20]. The endplate was indented to a load of 10 N at a rate of 0.05 mm/s and held for 30 s and then unloaded at the same rate and held for 30 s (Figs. 2(a) and 2(b)). This loading rate was chosen to minimize overshoot during the 10 N holding phase. The second stage then evaluated the stiffness, maximum load, MTP, and Brinell hardness by pressing the probe into the bone at a speed of 0.2 mm/s to a depth of 1.8 mm. Data were recorded at a rate of 10 Hz. This method was chosen to match that of previous indentation studies measuring stiffness [16,17]. This method was also used to measure the stiffness of commonly used materials for spinal fusion cages made from polyetheretherketone (PEEK) and cortical bone rings for comparison of stiffness in a clinical application.

The apparent Oliver–Pharr modulus was calculated using the unloading stiffness after the 10 N holding period [20]. The unloading stiffness was defined as the slope of first four data points, or approximately 30%, of the unloading curve and measured in N/mm (Fig. 2(b)) [21]. Then the resultant modulus, E_r , was calculated as

$$E_r = \frac{\sqrt{\pi}S}{2\sqrt{\pi(2Rh_c - h_c^2)}} \quad (1)$$

where S is the unloading stiffness (N/mm), R is the radius of indenter (1.5 mm), $\pi \approx 3.14$, h_c is the contact depth of the indenter tip, as defined by

$$h_c = h_m - 0.75 \frac{P_m}{S} \quad (2)$$

where h_c is the contact depth, h_m is the probe displacement (mm) at the maximum load of 10 N (Fig. 2(b)), P_m is the load at maximum displacement (10 N), and S is the unloading stiffness (N/mm). Then, the apparent modulus was defined as

$$E_s = \frac{1 - \nu_s^2}{\frac{1}{E_r} - \frac{1 - \nu_i^2}{E_i}} \quad (3)$$

where E_s is the apparent endplate modulus, ν_s is the Poisson's ratio of the endplate, ν_i is the Poisson's ratio of the indenter (0.33), E_r is the resultant modulus, and E_i is the modulus of indenter tip (70 GPa). It should be noted that the Oliver–Pharr method is relatively insensitive to variations in the Poisson's ratio, and the exact value of Poisson's ratio of the endplate is involved to determine; therefore, a constant value of 0.3 was used for all samples in this study [22]. Additionally, it is assumed that during loading, the sample undergoes both plastic and elastic displacement, whereas, during unloading, the sample simply recovers the elastic deformation.

Methods of the maximum load and the MTP assessment are described as Sec. S2, which is available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection. In brief, the maximal load was taken as either the load at which the endplate failed or the load at the maximum indentation depth of 1.8 mm, and MTP was calculated as the maximal load divided by the cross-sectional area of the indenter.

The stiffness was defined as the load at 1 mm of the probe displacement to be in line with methods from previous studies (N/mm; Fig. 2(a)) [17].

Fig. 2 (a) Overall indentation protocol where E is the Oliver-Pharr modulus assessment at the endplate surface; stiffness is the load at 1 mm of probe displacement (N/mm); maximum load was defined as the peak of the load-displacement curve. (b) Oliver-Pharr indentation protocol where S is the unloading stiffness of the curve (N/mm), $P_{\max}$ is the maximum load achieved in this loading step (10 N), and h_m is the maximum indentation depth (displacement) reached in this step (mm).

Brinell hardness was calculated as [23]

$$HB = 0.102 \frac{2F_m}{\pi D(D - \sqrt{D^2 - d^2})} \quad (4)$$

and

$$d = 2\sqrt{h(D - h)} \quad (5)$$

where HB is the hardness in units of Brinell scale, F_m is the maximum load (N), D is the indenter tip diameter (3 mm), h is probe displacement (mm) at maximum load (Fig. 2(a)), and d is the diameter of indented probe tip at the maximum load, defined as a function of the probe displacement Eq. (5), if displacement (h) was < 1.5 mm; and 3 mm, if displacement was ≥ 1.5 mm.

2.3 Statistical Analysis. An analysis of distributions and variance was performed to characterize the studied numeric variables, the Wilcoxon test was applied to evaluate differences between two subgroups and for multiple comparisons (more than two subgroups), Fisher and Tukey-Kramer tests were used [24].

Fig. 3 Representative load-displacement curves for Oliver-Pharr measurements for specimens within the top 10% (404 MPa), top 25% (208 MPa) and bottom 50% (106 MPa) of all test data

Indentation data was pooled across all indentation locations and specimens. Correlations between mechanical, radiographic, and demographic characteristics were defined by the nonparametric Spearman's rank correlation coefficient [24]. Multiple regression analysis was performed to select optimal combinations of the radiographic and demographic parameters to develop a predictive model of studied mechanical properties. Linear and nonlinear approximations were applied and tested using the JMP-7 program (SAS, Cary, NC). Correspondence between modeled and experimental values was defined by Pearson's correlation coefficient (r), coefficient of determination (r^2), root mean square error (RMSE), and p -value [24]. Sensitivity, specificity, and positive and negative predictive values were defined to evaluate diagnostic abilities for each developed model [24].

The modeling of stiffness was performed using the previously published equation [17]

$$E(e) = -2.2 + 0.94y + 0.0045(y - 74.8)^2 \quad (6)$$

where $E(e)$ is a modeled equivalent of the stiffness (N/mm), and y is a function of radiographic and demographic characteristics defined as

$$y = -360.8 + 0.11X_1 + 0.255X_2 + 0.025X_3 + X_4 - 0.07X_5 \quad (7)$$

where X_1 is the endplate thickness (μm), X_2 is the density of the endplate (mg/mm^3), X_3 is the adjacent cancellous bone apparent density (mg/cm^3), X_4 is the existence of endplate defects or herniation parameter (yes, -5.5 ; no, $+5.5$), and X_5 is the age of the donor (years). These equations were determined using multiple regression analysis with demographic and radiographic measures. The correspondence between indentation results in this study and stiffness predicted by these equations was measured in this study.

3 Results

3.1 Apparent Modulus. Representative indentation results used to calculate the apparent Oliver-Pharr modulus are shown in Fig. 3; these three curves represent the behavior seen from the top 10%, top 25%, and bottom 50% of the specimens with respect to the apparent modulus values of all tests. For all samples, there was a slight drop in force due to overshoot as the machine reached 10 N, which was adjusted for during the 30 s hold using the machine's built-in proportional-integral-derivative controller. Overall, samples with a higher modulus experienced less creep deformation during the 10 N hold compared to samples with a

Table 1 Distribution of mechanical characteristics of the tested sites (indentation test)

Distribution statistics	Stiffness (N/mm)	Oliver–Pharr modulus (MPa)	Brinell hardness (BH)	Max tolerable pressure (MPa)
10th percentile	113.6–333.7	324.4–760.6	1.75–3.99	14.0–31.7
15th percentile	72.4–113.5	237.3–324.3	1.19–1.74	9.8–13.9
25th percentile	48.6–72.3	171.4–237.2	0.82–1.18	6.7–9.7
Median	48.6	171.4	0.82	6.7
Mean	61.8	194.7	0.98	7.9
Standard deviation	44.6	95.0	0.63	4.9
Standard error of the mean	2.1	4.5	0.03	0.2
95% confidence limits				
Lower	57.6	185.9	0.91	7.4
Upper	65.9	203.6	1.03	8.3

lower modulus. The maximum indentation depth at load 10 N ranged from 0.01–1.2 mm, with the mean value 0.07 ± 0.11 mm, and the median 0.04 mm. The apparent modulus ranged from 50–761 MPa, having a right-skewed distribution with a mean of 194.7 ± 95 MPa and median of 171.4 MPa. For the samples tested, 50% were <171 MPa and 90% were <324 MPa (Table 1). The following factors significantly ($p \leq 0.002$) decreased modulus: osteoporotic or osteopenic status of the vertebrae, and female sex (Table S2, which is available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection). Bone status had the strongest correlation to apparent modulus, with the mean modulus being 244.9, 198.3, and 145.5 MPa for normal, osteopenic, and osteoporotic bone, respectively.

3.2 Stiffness. Representative curves used to calculate stiffness measured from testing are shown in Fig. 4. These curves are also compared to PEEK and cortical bone tested in the same manner, materials commonly used to create spinal fusion cages. It can be seen that both PEEK and cortical bone show noticeably higher stiffness than the strongest tested endplates. The endplate stiffness measurements had a right-skewed distribution ranging from 2.5–333.7 N/mm. The mean value was 61.8 ± 44.6 N/mm, and the median was 48.6 N/mm. Fifty percent of tested sites had stiffness <48.6 N/mm, and 90% <113.6 N/mm (Table 1). The following factors were significantly ($p \leq 0.004$) linked with decreased stiffness: osteoporosis or osteopenia; the presence of endplate defects; cranial/caudal vertebral surface; anterior or medial locations across endplate; and sex (Table S3, which is available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection). The most influential factor in stiffness was again the

Fig. 4 Representative stiffness curves for the Common spinal cage materials and vertebral endplates. The two bottom curves are representative of the top 10% of tested endplates and the top 50%, respectively. PEEK and cortical bone are shown to be significantly stiffer than even the stiffest endplates.

bone status resulting in 115.7, 56.9 and 37.7 N/mm for normal, osteopenic, and osteoporotic bone, respectively.

3.3 Brinell Hardness. The Brinell hardness distribution was right-skewed ranging from 0.07–3.99, the mean was 0.98 ± 0.63 , and the median was 0.82; 50% of measures were <0.82 and 90% were <1.75 (Table 1). The following factors were significantly ($p \leq 0.043$) linked with decreased hardness: osteoporosis or osteopenic bone status; endplate defects; cranial/caudal vertebral surface; anterior or medial locations across the endplate; and female sex (Table S4, which is available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection). The largest contributing factor to the variation of Brinell hardness was again bone status, with hardness values of 1.77, 0.93, and 0.53 for normal, osteopenic, and osteoporotic bone, respectively.

3.4 Maximum Load and Maximum Tolerable Pressure. The maximum load showed a right-skewed distribution ranging from 6.7–442 N with mean value = 73.5 ± 61.6 N and median value = 54.1 N. The probe displacement at the maximal load (depth at which resistance was maximal) ranged from 0.4–1.8 mm with a mean value of 1.1 ± 0.4 mm. The maximum tolerable pressure ranged from 0.6–31.7 N/mm², having a right-skewed distribution with a mean value of 7.9 ± 4.9 N/mm² and a median of 6.7 N/mm². 50% of values were found to be <6.7 N/mm² (Table 1).

3.5 Correlation Between Studied Characteristics. Statistically significant correlations existed between the measured mechanical properties (Table 2). The strongest correlations were found between MTP and Brinell hardness ($r^2 = 0.98$). A more detailed analysis is presented as Sec. S4, which is available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection. All studied mechanical characteristics had statistically significant ($p < 0.001$) correlations with radiographic (endplate thickness, endplate density, underlying cancellous bone apparent density, and bone mineral density) and demographic (age, and weight) indices (Table 3).

No statistically significant correlations were found with patient height for any of the mechanical properties. It was found that the strongest predictor for endplate stiffness was endplate thickness, with a correlation coefficient of 0.71. For Brinell hardness, the strongest predictor was found to be endplate density ($\rho = 0.64$). Apparent Oliver–Pharr modulus only showed weak correlations with all of the radiographic and demographic indices. Additionally, it was found that the volumetric underlying cancellous bone mineral density provided a stronger correlation to the properties than areal bone mineral density from dual-energy X-ray absorptiometry, both for stiffness and Brinell hardness.

3.6 Modeling Mechanical Characteristics Using Radiographic and Demographic Measures. Correspondence between the experimental and modeled values of stiffness was strong, (Fig. 5) with a correlation, $r = 0.85$; coefficient of determination,

Fig. 5 Correspondence between the predictive stiffness model and stiffness measured from indentation testing. Stiffness was modeled as a function of endplate thickness, endplate density, adjacent cancellous bone density, existence of endplate defects, and patient age according to Eqs. (6) and (7). The stiffness model showed a correlation of $R^2 = 0.72$ with the measured endplate stiffness from indentation.

$r^2 = 0.72$; and RMSE of 17.5 N/mm; $p < 0.001$. Using the model as a method to diagnose sites with stiffness < 125 N/mm had the following predictive values: sensitivity, 97%; specificity, 91%; positive predictive value, 99%; negative predictive value, 70% (Table S5, which is available under the “Supplemental Materials” tab for this paper on the ASME Digital Collection). Analysis of discrepancies over two RMSE (± 35 N/mm) showed that 25 of 26 cases overestimated the stiffness when an endplate with relatively high average thickness and density had lacunarities, visible as black spots in enhanced contrast images, explaining the decreased negative predictive value of the model [17].

A correlation between modeled and experimentally measured Brinell hardness is shown in Fig. 6. Brinell hardness was predicted using endplate thickness and density, existence of endplate defects, and patient weight, which showed the strongest correlations with the mechanical property (Table 3; Table S4, which is available under the “Supplemental Materials” tab for this paper on the ASME Digital Collection). Multiple linear approximation

Fig. 6 Correspondence between predicted hardness and hardness measured from indentation testing. Brinell hardness was modeled as a linear and polynomial model using endplate density, endplate thickness, the presence of and endplate defect, and patient weight. The linear fit used the equation $y_{BH} = -2.9 + 0.002X_1 + 0.0011X_2 + 0.008X_4$, where y_{BH} is the linear approximation of Brinell hardness, X_1 is the endplate mineral density (mg/mm^3), X_2 is the endplate thickness (μm), X_3 is the presence of an endplate defect or herniation (yes/no = ± 0.1), and X_4 is patient weight (kg). The polynomial fit was described by the equation $Y_{BH} = 0.06 + 0.85 y_{BH} + 0.36 (y_{BH} - 0.98)^2$, where Y_{BH} is the polynomial approximation of Brinell hardness, and y_{BH} is the linear approximation obtained from the first equation. The linear fit showed a correlation of $R^2 = 0.64$ while the polynomial fit showed a correlation of 0.68 with the measured hardness values.

showed significant correspondence to the experimental data with correlation $r = 0.80$; coefficient of determination $r^2 = 0.64$; RMSE, 0.38 BH; $p < 0.001$ (Fig. 6). However, analysis revealed a nonlinearity which was well described by a polynomial equation

Table 2 Spearman's correlation between studied mechanical characteristics

Indices of distribution	Stiffness (N/mm)	Oliver–Pharr modulus (MPa)	Brinell hardness (BH)	Maximum tolerable pressure (MPa)
Stiffness (M/mm)	1.0	0.47	0.81	0.78
Oliver–Pharr modulus (MPa)		1.0	0.67	0.69
Brinell hardness (BH)			1.0	0.98

Note: p -value for all correlations, < 0.001 .

Table 3 Spearman's correlation (ρ) of mechanical characteristics with radiographic and demographic indices

Radiographic and demographic indices	Stiffness (N/mm)		Oliver–Pharr modulus (MPa)		Brinell hardness (BH)	
	ρ	p -value	ρ	p -value	ρ	p -value
Endplate thickness (mm)	0.71	< 0.001	0.28	< 0.001	0.59	< 0.001
Endplate density (mg/mm^3)	0.67	< 0.001	0.33	< 0.001	0.64	< 0.001
Underlying cancellous bone density (mg/mm^3)	0.49	< 0.001	0.24	< 0.001	0.46	< 0.001
Bone mineral density (g/cm^2)	0.38	< 0.001	0.30	< 0.001	0.45	< 0.001
Age (yr)	0.26	< 0.001	0.23	< 0.001	0.44	< 0.001
Weight (kg)	0.31	< 0.001	0.38	< 0.001	0.50	< 0.001
Height (cm)	0.01	0.740	0.13	0.101	0.06	0.141

Fig. 7 Correspondence between predicted apparent modulus and apparent modulus measured from indentation testing. Apparent Oliver–Pharr modulus was modeled using endplate density, presence of endplate defects, and patient weight. Modulus was modeled using the equation $E = -71.35 + 1.57X_1 + X_2 - 0.092X_3$, where E is the linear approximation Oliver–Pharr modulus (MPa); X_1 is the patient weight (kg); X_2 is the presence of an endplate defect or herniation parameter (yes/no = ± 19.3), and X_3 is the endplate mineral density (mg/mm³). The linear model showed a correlation of $R^2 = 0.19$.

providing a better fit to the experimental data: $r = 0.82$; $r^2 = 0.68$; and RMSE, 0.36 BH ($p < 0.001$) (Fig. 6). Using the polynomial model to diagnose sites with Brinell hardness with a cutoff of < 1.5 had sensitivity, 95%; specificity, 65%; positive predictive value, 94%; negative predictive value, 69% (Table S5, which is available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection). Analysis of discrepancies that exceeded 2 RMSE (± 0.72 BH) showed significant ($p = 0.04$) predominance of overestimation (17 of 22), corresponding with lower specificity and negative predictive value.

Apparent modulus was modeled using patient weight, existence of endplate defect, and endplate density using multiple linear regression modeling. A correlation of 0.44; coefficient of determination, $r^2 = 0.19$; and RMSE, 85.3 MPa ($p < 0.001$; Fig. 7) were found for the correspondence between the experimental and modeled values. Using the model to diagnose sites with modulus < 200 MPa as positive, the diagnostic capability for apparent modulus had sensitivity, 77%; specificity, 63%; positive predictive value, 76%; and negative predictive value, 64% (Table S5, which is available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection). Analysis of discrepancies that exceeded 2 RMSE (± 171 MPa) showed predominance of underestimation (16 of 19 cases, $p = 0.02$). Bland–Altman analysis of modeling for all three properties is shown in the supplement (Figs. S1–S3, which are available under the “[Supplemental Materials](#)” tab for this paper on the ASME Digital Collection). Hardness and stiffness models showed good correspondence with no significant bias; however, the modulus model showed a consistent negative bias for higher measured modulus, indicating that the model tends to under-predict modulus.

4 Discussion

The purpose of this study was to develop a predictive model for regional mechanical properties at a scale relevant to implant design and behavior using radiographic and demographic patient data. Stiffness, apparent Oliver–Pharr modulus, MTP, and Brinell Hardness were evaluated across normal, osteopenic, and osteoporotic endplates (10 L1 and 10 L2 vertebrae) and demonstrated a

wide range of properties, with the standard deviations of each property being between 49% and 72% of the mean values. It is important to note that this is the first study to look at mechanical properties to help separate elastic, plastic, and time-dependent effects during loading by using this set of properties. The resulting “apparent” or “effective” mechanical properties provide a measure of structural behavior of the endplate on a length scale relevant to bone–implant interactions. In particular, these properties can be used to guide the design of interbody fusion cages that aim to minimize the mismatch in material behavior between the implant and adjacent bone. As stated previously, current implants rely on solid materials designed to avoid fracture under physiological loading. However, in this study, we found that even the strongest endplates had stiffness values far below those of commonly used implant materials. The Oliver–Pharr modulus was introduced as a method to capture an elastic measurement of the composite structure of the endplate in order to directly compare it to the moduli of common materials. Though this study focused on many different properties of the endplate, in all cases, it was found that current implants materials have mechanical properties orders of magnitude higher than those of native endplate bone. The authors believe that this study demonstrates that a drastic shift is needed in the discussion of material properties with regards to implant design. The endplates measured in this study showed apparent moduli significantly lower than those measured in previous research as it evaluated modulus at a scale, which includes the structural effects of endplate defects and underlying bone density. Current implants not only are significantly stiffer than the surrounding bone but also have teeth and other protrusions, which can cause stress concentrations. These concentrations combined with the low apparent modulus of the endplate are cause for concern and future designs should account for this during development. Further, previous studies demonstrated have shown the use of softer materials such as poly-L-lactic acid in lumbar cages reduces subsidence under axial loading as well as in vivo. This study aimed to quantify the properties of the endplate as well as develop a method for their prediction, which demonstrated the reasoning and mechanism leading to subsidence in these studies.

The current study results concerning mean values and distributions of maximal load, MTP, and stiffness corresponded with previously published data suggesting significant repeatability and high likelihood that the same results can be obtained in different populations with identical anthropometric characteristics [16,17]. For example, the model correlation to indentation tests for stiffness in this study ($r = 0.85$, $n = 447$) and the previous study by Noshchenko et al. ($r = 0.87$, $n = 1056$) were not significantly different ($p = 0.173$). Furthermore, the current study defines standardized mechanical indices attributed specifically to elastic and plastic properties and elucidates confounders that contribute to their high variability. In particular, it was found that apparent modulus varied significantly between osteoporotic, osteopenic, and normal bone, with a twofold difference between the osteoporotic and normal bone in terms of elastic response. This is indicative that poor bone density (i.e., low bone mineral density and increased bone porosity) will significantly decrease the modulus of the vertebral endplate. This result is in agreement with previous studies which found that subsidence correlates significantly with osteoporotic status [25,26]. However, in this study, the osteoporotic status of the bone was used as a direct predictor of mechanical properties rather than a general quantification of risk of subsidence, allowing for additional comparison to implant material properties. Additionally, several studies have shown subsidence to occur as a time-dependent injury rather than acutely, occurring between 0.25 and 8 months after surgery [27]. This may occur due to a combination of factors, including mechanical creep, resorption of underlying bone tissue by osteoclasts, and/or local failure of the endplate. The mechanical characteristics modeled via CT imaging can be used as indices of the time dependent response of bone to loading during fusion reflecting risk of subsidence or other complications such as vertebral fracture or correction loss. It can

Table 4 Mechanical characteristics of materials used for intervertebral implant manufacturing

Mechanical characteristic	Material	Source of data	Details of material sample	Indices
Stiffness/(N/mm)	CPTi/Ti alloys	Literature [17,30]	Interbody cage	3200
			Surgical rods	1900–2700
	PEEK	Current study	Interbody cage	509–819
			Raw material	1365–1368
	Cortical bone	Literature [17]	Allograft ring	500–1600
Brinell hardness (HB)		Current study	Allograft ring	611–1674
	CPTi/Ti alloys	Literature [31]	NS	223–653
	PEEK	Literature	NS	NS
		Current study	Interbody cage	10–12
			Raw material	21
Oliver–Pharr modulus (GPa)	Cortical bone	Current study	Allograft ring	8–25
	Ti/Ti alloys	Literature [32]	Cylindrical specimens	80–140
	PEEK	Literature [33]	Specimens for NIT	4–16
	Cortical bone	Literature [33,34]	Specimens for NIT	15–26

Note: CPTi/Ti—commercially pure titanium or titanium alloys; PEEK—polyetheretherketone; NIT—nano-indentation test; NS—none-specified; Allograft ring—tibial and femoral specimens.

be confirmed by the creep response shown in Fig. 3 that decreased modulus allows for more rapid creep. In the case of the osteoporotic bone shown on the far right with lowest apparent modulus (106 MPa), the indenter crept significantly more than that of the normal bone over 30 s. It was found that after 30 s of holding, the creep rate was constant, and did not increase. No other properties measured in this study captured the time-dependent characteristics of the vertebral endplate.

Stiffness in this study, unlike modulus, measured both the plastic and elastic responses of bone to loading as the indentation stresses the endplate beyond fracture. Therefore, it can provide an index to predict subsidence caused by permanent bone deformation. Previous studies have shown that the endplate contributes significantly to the indentation stiffness of the vertebra; however, the underlying cancellous bone contributes approximately 20% of the stiffness, indicating that stiffness is still dependent on the underlying bone density and structure, unlike modulus [28]. As such, it may provide a more accurate predictor of subsidence.

The studied endplate mechanical indices had significant correlations with different characteristics such as: (1) radiographic (endplate thickness, endplate density, underlying cancellous bone density, bone mineral density); (2) demographic (age and sex); and (3) physiologic (weight). Interestingly, the mechanical characteristics are proportional to the patient's weight, the endplate thickness, and densitometric indices of the vertebra corresponding to Wolff's law, which states that greater physiological demands on the bone will produce a more robust structure due to bone adaptation [28]. Multiple regression analysis confirmed previous findings that mechanical properties of the lumbar vertebral endplates can be approximated by combinations of radiographic indices obtained by conventional CT, despite low resolution as well as variable demographic (age) or physiologic (weight) indices [17]. In particular, stiffness and Brinell hardness can be approximated most accurately (Figs. 4 and 5) with some tendency to overestimate. Apparent modulus can be defined less precisely (Fig. 6) with a tendency to underestimate because the relatively low resolution of the conventional CT does not allow accurate assessment of density and roughness at the endplate surface. As subvoxel level measurements were not possible using our methodology, the endplate bone density and lacunarities could not be captured at the endplate surface where the modulus measurement is performed, leading to the decreased accuracy of the modulus model. Of note, the diagnostic value of these approximations is relatively high for diagnosis of the softest sites across endplates with low stiffness (<125 N/mm), low hardness (<1.5 BH), and low apparent modulus (<200 MPa), (Table S5, which is available under the "Supplemental Materials" tab for this paper on the ASME Digital Collection) allowing for the use of these predictive models as a diagnostic tool to predict relatively weak bone. Additionally,

it was found that volumetric endplate density was a stronger predictor of mechanical performance than areal bone mineral density for all measured properties. This phenomenon has been described in previous studies, as the volumetric density accounts for three-dimensional structure rather than the two-dimensional measurement of areal bone mineral density [29].

Results of the current study are in agreement with previous findings that the mechanical properties of lumbar vertebrae endplate show a right-skewed distribution [16,17], with a predominance of relatively weak sites with low MTP, low apparent modulus, and Brinell Hardness comparable with the hardness of soft wood (1.6 BH). The average mechanical characteristics of vertebral endplates are significantly lower than that of the most commonly used interbody implant materials such as titanium or titanium alloys, cortical bone allografts (femoral or tibial rings), and PEEK (Table 4). In the case of apparent modulus, the endplate showed a measured modulus at least ten times lower than the various materials on average. It is possible that using materials tailored to the distribution of material properties across the endplate would decrease the risk of subsidence; however, further research is needed to fully understand the effects of using such a material. Theoretically, the large differences seen in mechanical properties between the endplate and current implant materials suggest high risk of endplate damage resulting from interaction with such implant types [35]. Results of this study suggest that the demonstrated approach could be used in clinical practice as an in vivo diagnostic procedure for patient-specific selection of implant and surgical planning. Additionally, this study found that osteoporotic patients are significantly more susceptible to creep-induced subsidence, indicating additional planning is required when performing fusion in such cases. Finally, the high stiffness of current surgical materials compared to vertebral bone requires further research into more compliant materials for implantation in spinal fusion to better distribute load across the endplate and reduce stress concentrations. Other methods of reducing excessive endplate loading could include the use of posterior fixation (e.g., pedicle screws and rods) to transfer additional load to the posterior spine rather than the endplate or augmentation of the vertebra using bone cement.

One limitation of this study was the relatively low resolution from CT imaging, preventing analysis of radiographic indices at the endplate surface at the scale of the Oliver–Pharr indentation depth (≈ 0.15 mm), limiting the accuracy of the apparent Oliver–Pharr modulus modeling. However, the image resolution used in this study is comparable to that available using CT imaging of patients. Therefore, the ability of CT-based indices to predict endplate stiffness shows promise for potential clinical applications. Further, the whole lumbar spines were imaged *ex situ*, and thus are not surrounded by other muscle and organs

which could affect image quality; however, using proper reconstruction filters should minimize this effect.

5 Conclusions

The mechanical properties of the lumbar vertebral endplates are variable across the surface, with a right-skewed distribution. These properties are also significantly decreased by osteoporosis and osteopenia when compared to normal bone.

- (1) The studied mechanical properties showed significant correlations with radiographic and demographic characteristics. Bone status (osteoporosis and osteopenia) showed the greatest effect on all properties, causing decreases between 30 and 50%.
- (2) Using a combination of radiographic and demographic indices allows for the prediction of vertebral endplate mechanical properties. Model correlations (r^2) were found to be 0.72, 0.68, and 0.19 for stiffness, hardness, and apparent modulus, respectively.

Acknowledgment

The authors thank Ramesh Karki who provided computed tomography scanning of the specimens and the reconstruction of images. They also thank Ryan Anderson for his contribution to mechanical testing.

Funding Data

- The current study was funded by National Institutes of Health grant 1R21AR065713. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors also received financial support through the State of Colorado Biological Discovery and Evaluation Grant Program (AWD-144059).

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