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Comparison of Animals Used in Disc Research to Human Lumbar Disc Geometry

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Study Design. Measurement and normalization of disc geometry parameters for several animal models used in disc research.

Objectives. To compare normalized values of disc geometry to the human disc geometry to aid in the selection and interpretation of animal model studies.

Summary of Background Data. Animal models are widely used to study intervertebral disc degeneration and to evaluate disc treatment methods because of the availability of the tissue, the decreased variability between subjects compared with humans, and the feasibility to perform *in vivo* experiments. There is a general lack of comparative data with respect to the human disc analog for animal models.

Methods. The disc height, lateral width, AP width, area, and the nucleus pulposus lateral width, AP width, area, and centroid offset were all measured and normalized by 2 scaling factors, lateral width and disc area, for comparison to human.

Results. The species studied were ranked according to the average percent deviation of the normalized disc height, AP width and nucleus pulposus area from human geometry as: mouse lumbar (12%), rat lumbar (15%), mouse tail (18%), baboon (19%), bovine tail (22%), rabbit (26%), sheep (31%), and rat tail (46%).

Conclusions. This paper provides a reference to compare disc geometries of experimental animal models to the human lumbar disc, to aid both in interpretation of and in planning for experimental disc research, and to provide normalized disc geometry parameters for computational models.

Key words: intervertebral disc geometry, comparative anatomy, animal model, disc degeneration, disc area, disc height. **Spine 2007;32:328–333**

Animal models are widely used to study intervertebral disc degeneration and to evaluate disc treatment methods because of the availability of the tissue, the decreased variability between subjects compared with humans, and the feasibility to perform *in vivo* experiments. Several factors are involved in choosing a particular animal species, such as size, cost, disc geometry, biochemistry, cellularity, and biomechanics. There is a general lack of comparative data with respect to the human disc analog for animal models used to study the disc. Previous studies have evaluated vertebral body anatomy, biomechanics, and *in vivo* disc forces.[1–5] Although these studies provide support for comparison of the human disc to animal discs used as models in the study of human disc degeneration, they are not directly focused on comparison of disc anatomies across species.

A comprehensive comparison of disc geometries from species commonly used for intervertebral disc investigation has not been reported. No study has comparatively evaluated animal disc geometry, including axial cross sections, shape and position of the nucleus pulposus, and relative disc height for the species used in disc research. Furthermore, geometry data for the nucleus pulposus are lacking in the literature for any of the species and little disc height information is available. Therefore, the objective of this study was to measure geometric parameters of the intervertebral disc from several animal species and to normalize these parameters for comparisons with human lumbar disc geometry. Animal species widely used in disc research were evaluated and the measured dimensional data were scaled for comparison across species. The scaled dimensions obtained using these methods permit comparison of mechanical test results and provide scaling for finite element models. Through these comparisons, it is intended to aid both in interpretation of and in planning for experimental disc research.

Materials and Method

Based on their use in experimental models of disc degeneration, the intervertebral disc anatomic geometry was evaluated for eight disc types in 6 animal species. Not every species used in spine research could be included due to cost, availability, and time constraints. Lumbar disc geometry for the baboon, sheep, rabbit, rat, and mouse were evaluated, as well as tail disc geometry of the bovine, rat, and mouse (Table 1). In addition, nondegenerate human discs were evaluated for comparison to the animal species. Wherever possible, the same methods were used for each species; however, the differences in disc size required modifications in some techniques, as noted below. All animal tissues were obtained under approved IACUC protocols.

Adult olive baboon spines were obtained from Southwest National Primate Research Center and Oklahoma Health Sciences Center (Table 1). Adult female Rambouillet-Columbia sheep spines and adult female New Zealand white rabbits were acquired from another experiment unrelated to the spine. Adult bovine tails were obtained from a local abattoir. Retired male breeder Sprague-Dawley rats were acquired from Harlan and adult C57BL/6 male mice were obtained from Jackson Laboratory.

The intact lumbar spine was radiographed (Model TM30, TREX Medical Corp., Danbury, CT) with the spine oriented

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Table 1. General Information for the Animal and Human Specimens Used in the Study

	n	Age	Weight	Level
Human	3	19, 25, 36 yr	NA	L4–L5
Baboon	3	5–7 yr	26.0 kg	L4–L5
Sheep	3	3.5–5 yr	NA	L4–L5
Rabbit	3	6–8 mo	4.3 kg	L4–L5
Rat: L	3	7–9 mo	490 g	L4–L5
Mouse: L	3	8–9 mo	28 g	L3–L4
Bovine: T	4	1.5–2.5 yr	NA	C2–C3
Rat: T	3	7–9 mo	490 g	C10–C11
Mouse: T	3	6–8 mo	4.3 kg	C9–C10

T indicates tail or caudal disc; L, lumbar disc. Where not denoted, the lumbar disc was measured. NA, not applicable.

laterally, for measurement of disc height. The mouse spines were microradiographed (Model 43855A, Hewlett Packard, Palo Alto, CA) for higher resolution. The spine was then dissected by removing the musculature and the facet joints and sectioned into bone-disc-bone motion segments by cutting through the vertebrae with a band saw. The motion segment was kept semifrozen to prevent swelling. While semifrozen, discs were sectioned in the midaxial plane using a microtome blade. An image of the axial section, including a calibrated scale, was acquired using a high-resolution digital camera (2.6 Megapixel Canon ProShot 90IS, Canon Inc.). Geometry was measured from fixed and stained axial sections for the smaller animals because the nucleus pulposus was lost from the disc during dissection if it was not fixed. In the rabbit, one vertebra was removed with a scalpel, leaving a bone-disc structure, and the disc was stained with hematoxylin and eosin. The disc was then microtomed to obtain a flat surface. For the rat and mouse intervertebral discs, standard 6- to 9-μm-thick sections were prepared and stained with hematoxylin and eosin. Images of the rabbit discs were captured using a Sony digital camera (Exwave HAD) attached to a Leica MZ6 microscope. Images of the rat discs on the histology slides were taken using a scanner (Minolta Dimage Scan Dual II) and images of the mouse discs were taken with a digital camera (Qimaging MicroPublisher 5.0 RTV) attached to a Leica DMLP microscope.

Nondegenerate human spines were obtained from tissue banks under an approved Institutional Review Board protocol. Sagittal magnetic resonance (MR) images were acquired using a T2-weighted pulse sequence with a standard clinical MR scanner (Signa 1.5 T, GE Medical Systems) for measurement of disc height. The spines were dissected into motion segments as described above. The intervertebral discs were dissected from the vertebrae adjacent to the endplate using a scalpel and an image was taken of the disc with a high-resolution digital camera (2.6 Megapixel Canon ProShot 90IS, Canon Inc.).

Image Analysis. Axial and sagittal images were evaluated for geometric parameters using a custom written Matlab program (Mathworks, Inc.). Cross-sectional area, location of the centroid, and lateral and anteroposterior (AP) width of the entire disc and nucleus pulposus were measured from axial images (Figure 1). Disc height was measured from the sagittal images (Figure 2).

Analysis of the axial images was performed by first manually selecting the boundary of the disc edge and the boundary between the nucleus pulposus and the anulus fibrosus (Figure 1). From this input, measurements were automatically made for the cross-sectional area, the centroid of the whole disc and the nucleus, and the distance between the 2 centroids, called y-offset. A positive y-offset represents the nucleus centroid being located more posterior with respect to the disc centroid. Lateral and AP widths were calculated as a line going through the centroid to the disc or nucleus edge, respectively (Figure 1). Analysis of the sagittal images was performed using a similar program by selecting the boundary along the superior and inferior vertebrae and connecting the points at the anterior and posterior height to create the disc space area (Figure 2). From this input, the AP width was calculated at the midpoint of the anterior and posterior height. The average disc height was calculated by dividing the total disc space area by the AP width (Figure 2). The disc height for the mouse, calculated from microradiographs, was previously reported by our laboratory.[6]

Data Analysis. Because of large size differences, a comparison of animal models with the human intervertebral disc can only be done using normalized, nondimensional values. The choice for the parameter by which to normalize the other parameters should be easily acquired and also conserved across species. Two different scaling factors were used for normalization in this study; 1) lateral width, which may be directly measured on an AP radiograph, and 2) the disc cross-sectional area, which eliminates the confounding factor of lateral to AP width ratio and thus may be more likely to be conserved across species. All measured parameters were normalized by both scaling factors. Note that normalizations were performed to achieve nondimensional results, that is, "length" dimensions (*e.g.*, AP width) were divided by the lateral width or by the square-root of the area (also a length dimension) and that "length-squared" dimensions (*e.g.*, disc area) were divided by the square of lateral width or by the actual area. Finally, for comparison to the human, the values of the scaled parameters were further normalized to the human disc.

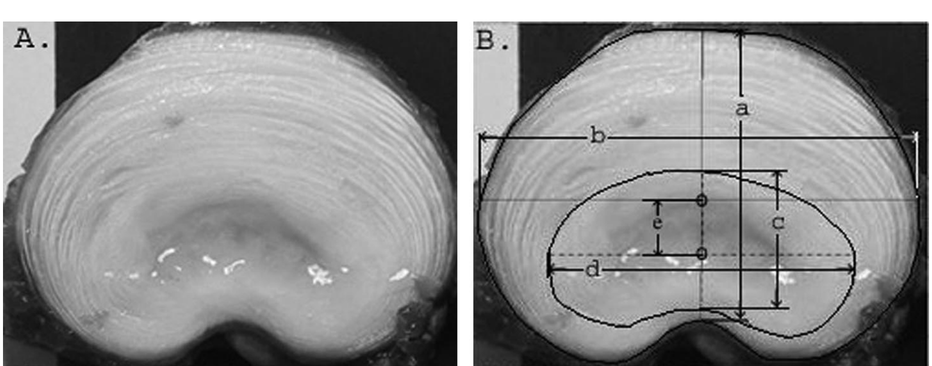

Figure 1. **A**, Image of a baboon L4–L5 disc. **B**, Output image of the same baboon disc with the measured dimensions labeled. The disc centroids are labeled with the "o" and the dimensions are: (a) disc AP width, (b) disc lateral width, (c) nucleus pulposus AP width, (d) nucleus pulposus lateral width, and (e) y-offset of the nucleus pulposus with respect to the disc centroid.

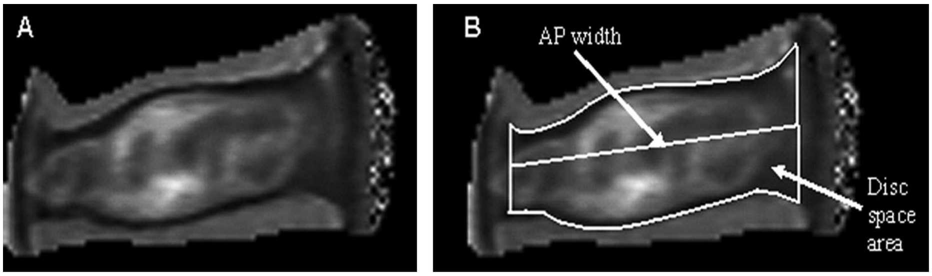

Figure 2. **A**, Image of a lateral radiograph from a baboon L4–L5 motion segment. **B**, Output image of the same baboon motion segment with the measured dimensions labeled. The dimensions are disc AP width and the disc space area. The average disc height is calculated by dividing the disc space area by the AP width.

Results

Representative disc axial cross sections from each animal species are shown in Figure 3, with the discs scaled to match in the lateral width dimension. The directly measured average disc and nucleus pulposus geometry for each species are provided in Table 2. Normalized parameters scaled by the lateral width are provided in Table 3 and normalized further as percent difference from the human value as shown in Figure 4. Normalized parameters scaled by the disc area are provided in Table 4 and normalized further as percent difference from the human value as shown in Figure 5.

The disc height, normalized by the lateral width, is quite different from human for the species studied (Table

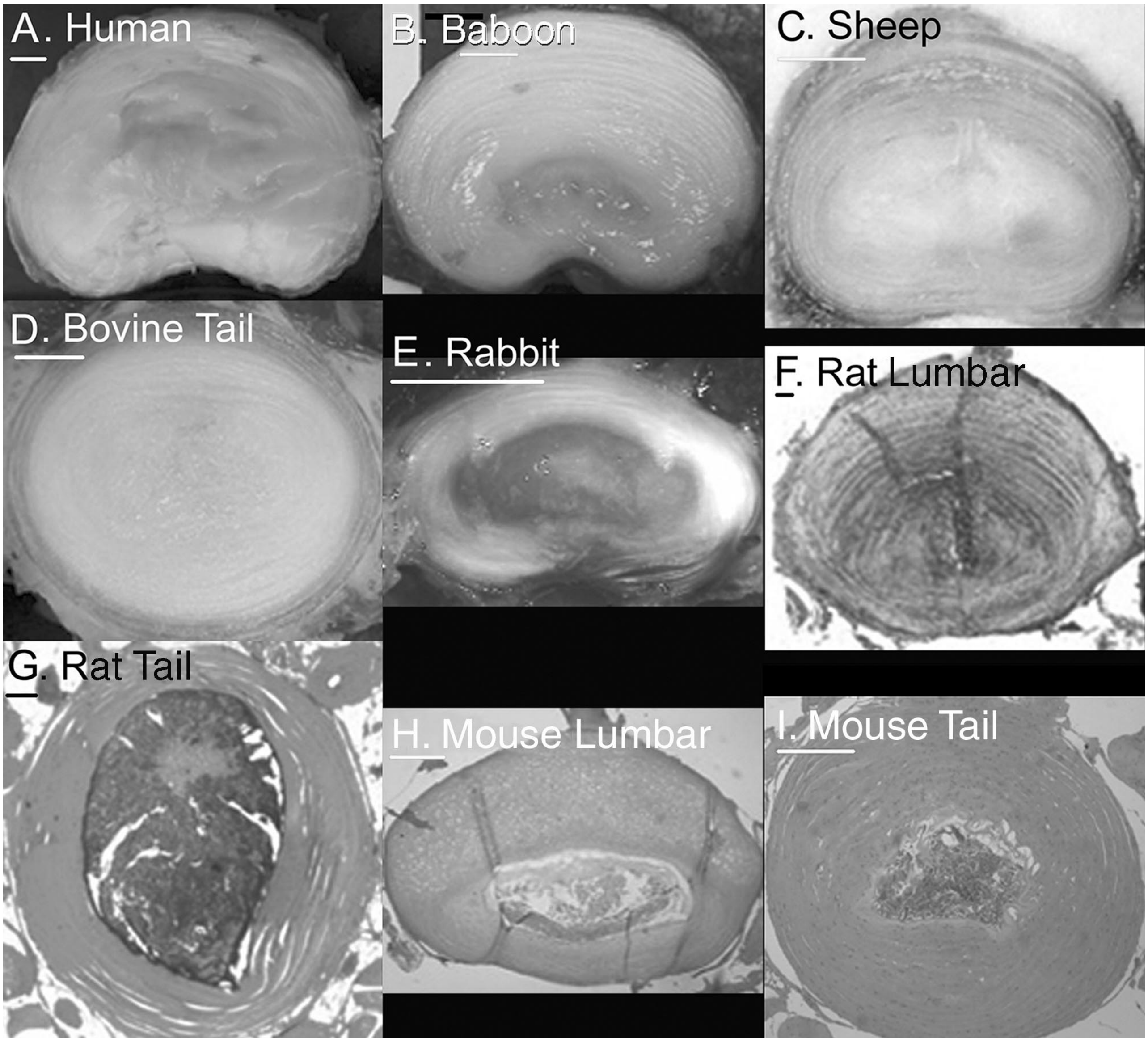

Figure 3. Representative axial cross section from each species scaled by the lateral width. The calibration bar for the human, baboon, sheep, bovine tail, and rabbit is 5 mm, whereas the measure bar for the rat and mouse represents 0.25 mm.

Table 2. Directly Measured Disc Geometry

	Whole Disc				Nucleus Pulposus			
	Height (mm)	Lateral Width (mm)	AP Width (mm)	Area (mm²)	Lateral Width (mm)	AP Width (mm)	Area (mm²)	Offset (mm)
Human	11.3 (0.3)	55.9 (9.4)	37.2 (4.7)	1727 (550)	27.3 (3.2)	20.8 (2.0)	479 (110)	1.17 (0.58)
Baboon	4.45 (1.39)	35.4 (2.3)	22.8 (0.8)	749 (82)	22.7 (1.4)	10.8 (1.3)	242 (50)	3.02 (1.21)
Sheep	3.93 (0.07)	34.5 (2.9)	21.6 (2.1)	676 (122)	27.3 (4.0)	10.4 (1.9)	267 (79)	2.18 (0.59)
Rabbit	1.42 (0.39)	12.7 (0.9)	6.59 (0.19)	73.4 (6.1)	6.95 (0.33)	2.80 (0.51)	18.0 (1.6)	−0.37 (0.22)
Rat: L	0.93 (0.24)	5.79 (0.29)	4.36 (0.16)	20.4 (2.1)	3.13 (0.47)	1.83 (0.45)	5.00 (2.06)	0.51 (0.17)
Mouse: L	0.31 (0.03)	1.84 (0.03)	1.24 (0.11)	1.81 (0.14)	0.95 (0.10)	0.417 (0.089)	0.33 (0.07)	0.106 (0.033)
Bovine: T	6.90 (0.35)	28.9 (2.0)	27.8 (1.3)	622 (71)	18.6 (1.3)	11.4 (1.2)	176 (22)	−0.97 (0.53)
Rat: T	0.94 (0.09)	3.26 (0.62)	3.48 (0.67)	8.86 (3.54)	1.90 (0.33)	2.13 (0.72)	3.30 (1.55)	0.087 (0.062)
Mouse: T	0.24 (0.06)	1.21 (0.18)	1.31 (0.35)	1.19 (0.51)	0.63 (0.14)	0.71 (0.26)	0.35 (0.09)	0.02 (0.01)

Values are mean (SD) for each species.
AP indicates anteroposterior; T, tail or caudal disc; L, lumbar disc. Where not denoted, the lumbar disc was measured.

3). The mouse tail normalized disc height is the only species within 10% of the human disc (Figure 4). For the majority of the species studied, the normalized disc height is less than the human, except for the bovine and rat tail, which are larger than the human (Figure 4). When disc height is normalized by disc area, the results are similar, with the exception of the bovine and rat tail, which appear more similar to the human under this scaling factor (Figure 5).

The disc AP width, scaled by the lateral width (Table 3), is 0.665 for the human lumbar disc. The normalized human lumbar disc AP width is most closely matched, within 10%, by the baboon, sheep, and mouse lumbar discs (Table 3; Figure 4). The rabbit disc has the smallest normalized AP width, since it is the most elliptical in shape among the animal models analyzed. The 3 tail discs have a large normalized AP width, due to the circular shape of the intervertebral discs in the tail.

The nucleus pulposus area, scaled by the disc area, for the human is 28%, and the bovine and mouse tail discs are most similar to human, within 10% (Table 4; Figure 5). The nucleus area scaled by disc area for the sheep and rat tail are larger than human and the mouse lumbar is smaller than the human (Figure 5). The offset of the nucleus pulposus centroid for the human is 1.17 mm posterior to the disc centroid and the nucleus of most animal species is also positioned posterior, while the rabbit and the bovine tail nucleus centroid are located more anterior with respect to the disc centroid (Table 2). The nucleus pulposus offset, scaled by lateral width, is very small for the human disc (0.02) compared with the animal models (Table 3).

■ Discussion

The primary objective of this study was to compare normalized values of disc geometry from several animal species to the human intervertebral disc geometry to aid in the selection and interpretation of animal model studies. To select a species that best represents human geometry, the 3 normalized parameters deemed to be most functionally relevant are the disc height scaled by lateral width, the AP width scaled by lateral width, and the nucleus pulposus area scaled by disc area. The species studied were ranked according to the average percent deviation from human geometry for these 3 parameters as: mouse lumbar (12%), rat lumbar (15%), mouse tail (18%), baboon (19%), bovine tail (22%), rabbit (26%), sheep (31%), and rat tail (46%).

A second objective of this study was to determine the scale values for each geometric parameter for use in finite element models and to compare mechanical experiments across species. The geometry of the disc is important to take into consideration when analyzing mechanical data. The

Table 3. Parameters Normalized to the Disc Lateral Width

	Whole Disc				Nucleus Pulposus			
	Height	Lateral Width	AP Width	Area	Lateral Width	AP Width	Area	Offset
Human	0.202	1.0	0.665	0.553	0.488	0.372	0.153	0.021
Baboon	0.126	1.0	0.645	0.598	0.641	0.305	0.193	0.085
Sheep	0.114	1.0	0.626	0.568	0.791	0.301	0.224	0.063
Rabbit	0.112	1.0	0.519	0.455	0.547	0.220	0.112	−0.029
Rat: L	0.161	1.0	0.753	0.609	0.541	0.316	0.149	0.088
Mouse: L	0.169	1.0	0.674	0.535	0.524	0.227	0.097	0.058
Bovine: T	0.239	1.0	0.962	0.745	0.644	0.394	0.211	−0.034
Rat: T	0.288	1.0	1.067	0.834	0.583	0.653	0.311	0.027
Mouse: T	0.198	1.0	1.083	0.813	0.524	0.587	0.241	0.003

Where not denoted, the lumbar disc was measured. Note that normalizations were performed to achieve nondimensional results, that is, "length" dimensions (*e.g.*, AP width) were divided by the lateral width and "length-squared" dimensions (*e.g.*, disc area) were divided by the square of lateral width.
AP indicates anteroposterior; T, tail or caudal disc; L, lumbar disc.

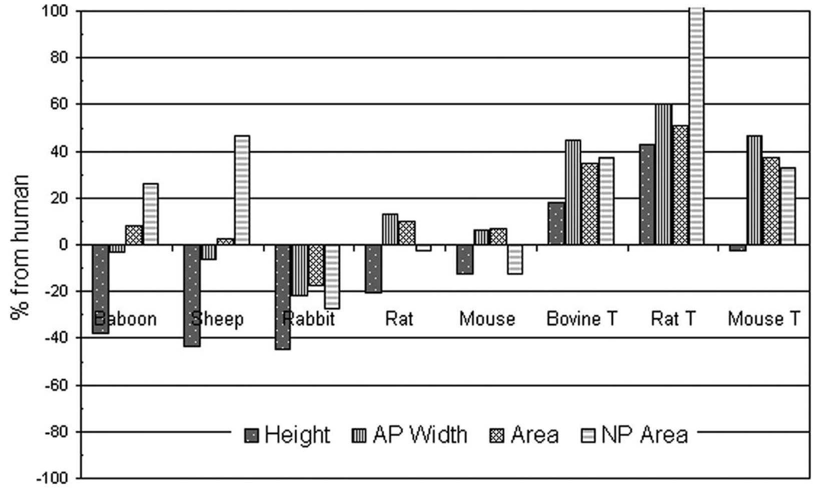

Figure 4. Scaled parameters normalized to lateral width, and further normalized to the human disc.

normalized parameters in Table 3 can be used to compare animal data to the human intervertebral disc. Using the same dimension for all normalizations allows for conversion from one parameter to another and from animal to human models. However, the choice of scaling factor is important, and in this study we present the results for 2 scaling factors: lateral width and disc area. Lateral width has the advantage of being readily measured on AP radiographs. Disc area has the advantage of removing potential bias due to the AP-lateral width ratio, and based on Figure 5 may be better conserved across species.

While there are limited geometric data in the literature, in general the parameters measured in this study are comparable to previous studies of animal disc geometry. Although we found no previously reported values of the baboon lumbar disc geometry, an anatomy study in the baboon cervical spine found the baboon to be approximately 50% of the human spine, consistent with our values of 60%.[7] Bovine dimensions were consistent with previous reports of height (4–6 mm) and lateral width (20–25 mm).[8] Adult sheep disc geometry for lateral width (30 mm), AP width (20 mm), disc height (4.3 and 3.6 mm), and disc area (475 mm^2) are comparable to the values in the present study.[5,9] The variations are reasonable and likely represent differences in age, sex, or strain of sheep studied. The disc height for the rabbit measured in this study is within one standard deviation to the disc height measured in previous studies.[9,10]

Values for human intervertebral disc geometry vary widely in the literature and depend on age, sex, and level. The human discs in this study had disc area within a standard deviation of previous literature reports (1560 mm^2).[6] The moderately higher area in this study may be due to the small population or to an improved method of calculating disc area. Instead of approximating the area of the disc by assuming an elliptical shape (area = $\pi/4*W*D$, where W = lateral dimension and D = AP dimension), the custom-written program used here calculated the actual area within the entire cross section. The disc height was similar to previously reported values, based on a summary of the literature (10.9 mm).[6] The lateral and AP dimensions measured using the current methods are also similar to values measured in previous studies.[6,11–14]

The small sample size used in each animal species is a study limitation and is not intended to represent the overall population but to describe relative differences between the animal species and the human intervertebral disc. However, size differences between species were quite large, so that the relative observations reported here remain valid. There are also limitations in measur-

Table 4. Parameters Normalized to the Disc Area

	Whole Disc				Nucleus Pulposus			
	Height	Lateral Width	AP Width	Area	Lateral Width	AP Width	Area	Offset
Human	0.272	1.345	0.895	1.0	0.657	0.501	0.277	0.028
Baboon	0.163	1.293	0.835	1.0	0.829	0.395	0.323	0.110
Sheep	0.151	1.327	0.831	1.0	1.050	0.400	0.395	0.084
Rabbit	0.166	1.482	0.769	1.0	0.811	0.327	0.245	−0.043
Rat: L	0.206	1.282	0.965	1.0	0.693	0.405	0.245	0.113
Mouse: L	0.230	1.368	0.922	1.0	0.717	0.310	0.182	0.079
Bovine: T	0.277	1.158	1.114	1.0	0.746	0.457	0.283	−0.039
Rat: T	0.316	1.095	1.169	1.0	0.638	0.716	0.372	0.029
Mouse: T	0.220	1.109	1.201	1.0	0.581	0.651	0.297	0.003

Where not denoted, the lumbar disc was measured. Note that normalizations were performed to achieve nondimensional results, that is, "length" dimensions (*e.g.*, AP width) were divided by the square-root of the area and "length-squared" dimensions (*e.g.*, disc area) were divided by the area directly.
AP indicates anteroposterior; T, tail or caudal disc; L, lumbar disc.

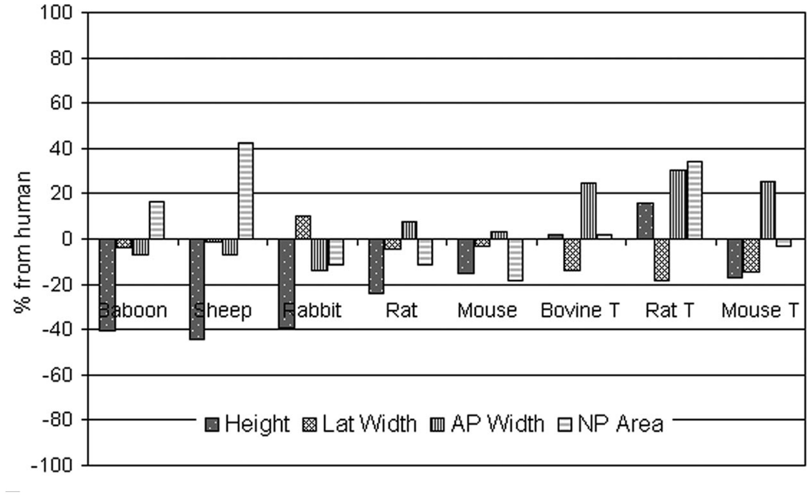

Figure 5. Scaled parameters normalized to disc area, and further normalized to the human disc.

ing the nucleus pulposus area of the human lumbar intervertebral disc due to the lack of a defined boundary between the nucleus pulposus and the anulus fibrosus. While only nondegenerate discs were used for this study in order to improve the nucleus-anulus distinction, this boundary was still difficult to delineate.

■ Conclusion

This study measured disc geometry from several animal species and compared values with the human intervertebral disc geometry for use in the selection and interpretation of animal model studies. With regard to the geometric parameters of the disc height, AP width, and nucleus pulposus area, we conclude that the mouse and rat lumbar, and mouse tail discs are the closest representation of the human lumbar intervertebral disc geometry. In addition to selecting animal models, these results will also be useful for scaling between animal and human disc mechanics, particularly within computational models.

■ Key Points

- Disc geometry for the baboon, sheep, bovine, rabbit, rat, and mouse was measured, normalized, and compared with human disc geometry.
- Based on disc height, the AP width, and the nucleus pulposus, the animals were ranked in decreasing order as: mouse lumbar, rat lumbar, mouse tail, baboon, bovine tail, rabbit, sheep, and rat tail.
- This paper provides a reference to compare disc geometries of experimental animal models to the human lumbar disc, to aid both in interpretation of and in planning for experimental disc research.
- This study will be useful for scaling between animal and human disc mechanics, particularly within computational models.

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