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MECHANISMS OF ENERGY DISSIPATION AND RELATIONSHIP WITH TISSUE COMPOSITION IN HUMAN MENISCUS

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Abstract

Objective: The human meniscus is essential in maintaining proper knee joint function. The meniscus absorbs shock, distributes loads, and stabilizes the knee joint to prevent the onset of osteoarthritis. The extent of its shock-absorbing role can be estimated by measuring the energy dissipated by the meniscus during cyclic mechanical loading.

Methods: Samples were prepared from the central and horn regions of medial and lateral human menisci from 8 donors (both knees for total of 16 samples). Cyclic compression tests at several compression strains and frequencies yielded the energy dissipated per tissue volume. A GEE regression model was used to investigate the effects of compression, meniscal side and region, and water content on energy dissipation in order to account for repeated measures within samples.

Results: Energy dissipation by the meniscus increased with compressive strain from ~0.1 kJ/m^3 (at 10% strain) to ~10 kJ/m^3 (at 20% strain) and decreased with loading frequency. Samples from the anterior region provided the largest energy dissipation when compared to central and posterior samples ($p < 0.05$). Water content for the 16 meniscal tissues was 77.9 (C.I. 72.0 – 83.8%) of the

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AUTHOR CONTRIBUTIONS
Research design was conducted by AM, AMAM, TMB, FT and ARJ; data acquisition and analysis was carried out by AM, AMAM and FT; data interpretation involved AM, FT, TMB and ARJ; all the authors were involved in drafting and revising the manuscript, as well as reading and approving its final version.

CONFLICT OF INTEREST
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total tissue mass. A negative correlation was found between energy dissipation and water content ($p < 0.05$).

Conclusion: The extent of energy dissipated by the meniscus is inversely related to loading frequency and meniscal water content.

Keywords

cyclic compression; meniscal dampening; water content; hysteresis

INTRODUCTION

The human meniscus is a semilunar-shaped fibrocartilaginous tissue wedged between the femoral condyle and tibial plateau of the human knee. It is divided into medial and lateral components, and anchored to the tibia via ligamentous meniscal attachments.[1] The primary roles of the meniscus are shock absorption, load distribution, and knee joint stabilization.[2] During everyday joint loading, the meniscus distributes 70 – 99 % of the axial loads on the knee.[3, 4] Accordingly, its primary mechanical function is to protect the articular cartilage of the femur and tibia from excessive stress concentration, which can ultimately lead to knee osteoarthritis.[5]

The shock absorbing function of the meniscus is made possible by its unique composition and structure. The tissue is composed primarily of a fluid phase accounting for more than 70% of the tissue's mass, with the remainder constituting its solid phase.[6] The solid phase consists of a porous matrix made up of mostly collagen and proteoglycans. Collagen fibers are aligned circumferentially and radially to provide tensile stiffness while glycosaminoglycans (GAGs) attached to proteoglycans imbibe the tissue with water to increase tissue stiffness.[7] During mechanical loading of the meniscus, the porous matrix deforms, forcing the interstitial fluid to move through its pores and generate frictional drag.[8] Therefore, the meniscus dissipates energy due to its matrix intrinsic viscoelastic molecular arrangement and its fluid flow friction.[9]

The mechanical response of human[1, 10–14] and animal[15–18] menisci under cyclic loading conditions has been investigated to characterize mechanical parameters associated with dampening (e.g., loss modulus, phase angle, etc.), or to directly measure the energy dissipated by the tissue. It has been shown that energy dissipation of the meniscus varies with the specific loading conditions.[10, 11, 14] It has also been found that the magnitude of the mechanical parameters associated with the dampening function of the meniscus vary across regions within the tissue as well as the region and direction of the applied load (parallel vs. orthogonal to collagen fibers).[1, 10, 15] However, to date, there is still limited information on how the amount of energy dissipated by meniscal tissue is affected by the magnitude of loading strains and frequencies. Furthermore, the relationship between tissue water content and energy dissipation has not been directly investigated. Accordingly, an exploratory study was designed to investigate: (1) the association of energy dissipated by human meniscal tissue with magnitude of compressive strains and frequencies, and (2) possible relationships between the extent of energy dissipated by the tissue and its water content. Knowledge on the mechanism of energy dissipation of the meniscus will aid in a better understanding of the tissue's role in preserving the health and integrity of cartilaginous tissues otherwise subjected to damage and/or degeneration. In addition, characterization of the dissipative properties of the meniscus provides important direction for the development of tissue engineering constructs for the replacement of damaged meniscal tissue.

METHODS

Tissue Preparation:

Eight lateral and eight medial human menisci were obtained frozen from deceased donors. Menisci were visually inspected to determine their degeneration grade, which was deemed normal to moderately degenerated. Donor demographics are reported in Table 1. The menisci were sectioned into central, anterior, and posterior regions. All tissue sections were cut into ~1.5 mm slices in the axial direction using a Compresstome® (VF-200–0Z, Precisionary, Natick, MA). A 5 mm diameter corneal trephine was used to core the slices into 1.53 ± 0.27 mm tall cylindrical samples, see Figure 1a–d. Two adjacent samples were prepared from each meniscus section: one for mechanical testing and the second for tissue water content measurements. All samples were stored frozen at −20°C in phosphate buffered saline until testing.

Mechanical Testing:

Experiments were conducted to measure the amount of energy dissipated during one unconfined compression cycle. A uniaxial testing apparatus (Univert, Cell Scale, Waterloo, ON) with a 20 N load cell was used in displacement-control mode to measure sample reaction forces in the axial direction, see Figure 1e. Before testing, the cylindrical samples were thawed and placed on fine sandpaper in the compression chamber to prevent slippage during compression. Each compression cycle had a trapezoidal waveform: compressive displacement increased linearly with time until reaching a plateau; the final compressive strain was held for a time equal to 10% of the total duration of the cycle; subsequently, sample compression linearly decreased to zero, see Figure 1f. Each sample underwent nine compression cycles (3 strain x 3 frequencies). The magnitudes of compressive strain were 10%, 15% and 20%, and the loading frequencies were 0.125 Hz, 0.25 Hz and 0.5 Hz. A rest period (no load applied) of 600 s was applied between two consecutive compressive cycles. Strain magnitudes evaluated are within the range of normal physiological strains[19, 20]. Similarly, the frequencies of compression are representative of activities like walking or squatting.[19, 20] Preliminary testing indicated that such duration of the rest period is sufficient to eliminate any memory of the previous load history in the sample, see Figure 2. All data were recorded at 100 Hz using Labjoy (Version 10.78, Cellscale.com). Energy dissipated during each compression cycle was calculated as the area under the stress-strain hysteresis curve. Data post-processing was conducted via custom code in MATLAB® v2021a (MathWorks, Inc., Natick, MA).

Water Content Measurements:

Water content in menisci samples was measured as the mass fraction with respect to the weight of the hydrated sample (wet weight). Weight measurements were taken with an analytical scale (Model ML104, Mettler Toledo, Columbus, OH). Water content was calculated based on the following equation:[21]

$$\text{Water Content } = \frac{w_{wet} - w_{dry}}{w_{wet}}\% \qquad (1)$$

where W_{wet} is the wet weight and W_{dry} is the 'dry weight' of the sample, measured after lyophilization.

Statistical Analysis:

All data were reported as mean and 95% confidence interval. GEE (generalized estimating equations) regressions were used to determine the association between each of the outcomes with the frequency and magnitude of force of each of the experimental conditions while controlling for tissue region variables. The GEE model was used to account for the repeated nature of measures within combinations of tissue sample and person using an exchangeable correlation structure. Furthermore, the assumption of normality was verified via Q-Q plots on the residuals of the GEE models. P values under 0.05 were considered statistically significant and all analyses were run in R version 4.1.1 using the gee package version 4.13-20.

RESULTS

The amount of energy dissipated at all compression levels and frequencies is summarized in Table 2, and the associated estimates of the GEE coefficients are reported in Table 4. Energy dissipation by meniscal samples significantly increased as the magnitude of compressive strain increased (via 95% CI), see Figure 3. In addition, at each strain level, the amount of energy dissipated decreased when loading frequency was increased (via 95% CI). Comparisons of meniscal location indicated that the extent of energy dissipated by the medial tissue samples was larger, but not statistically significant (via 95% CI), than the lateral menisci. Furthermore, investigation of regional effects for extent of energy dissipation showed that the anterior region had significantly larger dissipation than the central and posterior regions (via 95% CI).

A summary of the water content of the menisci is reported in Table 3. The water content for all 48 meniscal samples was 77.9% (C.I. 72.0 – 83.8%). No statistically significant differences in water content were observed across side of knee or region (via 95% CI), with confidence intervals for the GEE coefficients of the lateral-medial sides, central-anterior regions, and posterior-anterior regions being (−3.74 0.25), (−1.97 1.13), and (−1.67 2.13) respectively. Finally, the tissue water content was negatively correlated to the energy dissipated during compression (via 95% CI), see Figure 4 and Table 4.

DISCUSSION

Several studies have investigated the mechanical behavior of the meniscus under compression.[2, 4, 10, 11, 13, 14, 17, 22–28] However, to best of our knowledge, this is the first study specifically measuring the ability of human meniscal samples to dissipate mechanical energy under a variety of cyclic loading conditions.

The results of this exploratory study show that the extent of energy dissipation is related to the characteristics of the mechanical compressive load. Specifically, the amount of energy dissipated significantly increased with increasing compressive strain, ranging from ~0.1 kJ/m^3 (at 10% strain) to ~10 kJ/m^3 (at 20% strain), see Table 2. Since larger compressions require greater external work to be applied to the tissue, more energy is dissipated within higher strain cycles. Such a magnitude of energy dissipation is comparable to that reported in previous studies: porcine meniscal samples cyclically compressed at 10% and 0.125 Hz dissipated ~0.2 kJ/m^3.[15, 16] Other studies on human meniscal attachments reported that samples cyclically tested in tension at 20% strain and ~0.04 Hz dissipated an amount of energy of one order of magnitude larger than that reported in the current study.[1] This apparent discrepancy should not be surprising since it has been reported that meniscal samples tested in tension dissipate an amount of energy 10-fold larger than that attained when tested in compression.[15] Results also indicate that the extent of energy dissipation was inversely related to loading frequency ($p < 0.05$). This is consistent with previous studies showing that, within the range of frequencies tested herein, the dynamic properties of the meniscus in compression (loss modulus and phase angle) were inversely related to the loading frequency.[10, 11, 13, 14, 21]

Energy dissipated by the medial versus lateral meniscal tissues was not significantly different ($p > 0.05$), see Figure 3. However, on average the medial side dissipated more energy than the lateral menisci, see Table 2. A similar trend was found in previous studies showing that the loss modulus and phase angle are higher in medial meniscal samples when compared to their lateral counterparts.[14, 21] During gait, the highest peak forces are experienced by the medial meniscus,[29] which may help to explain the superior dissipative properties of this tissue compared to the lateral side. It was also found that energy dissipation in the medial meniscus significantly varied across regions ($p < 0.05$): the highest was observed in the anterior region, see Figure 3. Similar results have been reported from dynamic compression studies: the loss modulus and phase angle were the largest for samples harvested from the medial anterior region of the meniscus.[10, 14]

The average water content of the meniscal tissues was 77.9% (C. I. 72.0 – 83.8%), which is within the range of previous measurements.[21, 30, 31] Interestingly, the lateral tissues were on average higher in water content when compared to the medial ones ($p > 0.05$), see Table 3. This result is consistent with previous water content measurements across meniscal sides and regions.[31] Furthermore, the GEE regression analyses showed that the water content was negatively correlated with the degree of energy dissipation ($p < 0.05$). This result is consistent with previous observations correlating water content to the magnitude of the tissue's loss modulus.[10] Increased water content is associated with meniscal degeneration;[31–33] therefore, the dissipating capacity of the tissue likely decreases with the progression of tissue degeneration and may account for the high degree of association between meniscal degeneration and presence of knee OA.

Some limitations must be noted. This was an exploratory study; therefore, sample size was limited to 8 medial and 8 lateral menisci. Tissue samples were obtained from elderly donors (73.5 ± 6.4 y.o.). Since age-related changes in the composition of the knee meniscus occur,[30, 32, 34] the magnitude of the effects observed in this study may change when applied to other age groups. Additionally, the current study did not account for depth-dependent meniscal energy dissipation. Samples were taken from the central portion of the tissue sections, and no differences across tissue layers were considered. However, we do not expect significant changes in the extent of energy dissipated from samples of different meniscal layers since previous cyclic tensile tests have shown that energy dissipation does not depend on tissue layer.[1] Moreover, it is well known that water, collagen, GAG are fundamental components characterizing the mechanical behavior of the meniscus.[7, 10, 21, 30] However, the current study solely focused on the effect of water content on energy dissipation as previous studies have indicated that, when compared to GAG and collagen, water content has the highest level of correlation to meniscal mechanical properties.[21, 26, 30, 33] Finally, the range of compression frequencies analyzed in the present study only covers a portion of the spectrum of loading frequencies experienced under physiological conditions. Higher loading frequency, such as those experienced at the knee during running or jumping were not investigated and will be addressed in the future.

In summary, the results of this study suggest that the extent of energy dissipated by the meniscus is significantly affected by the loading conditions (compressive strain and frequency) and the meniscal side and region loaded. Moreover, the inverse relationship between amount of energy dissipation and water content suggests that the ability of dissipating energy reduces as the meniscus degenerates. A study conducted on younger tissues could help support this hypothesis. The information hereby reported can be utilized to better understand the dampening role of meniscal tissue under pathophysiological mechanical loading conditions.

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APPENDIX

Hereby, individual data points collected in the study are reported to complement the inferential results. In figure A1, energy dissipation data, for each loading frequency tested, are segregated by tissue type (medial or lateral), region (anterior, central and posterior) and magnitude of compression (10%, 15% and 20%). In figure A2, the energy dissipation is reported in relation to the water content of the samples tested.

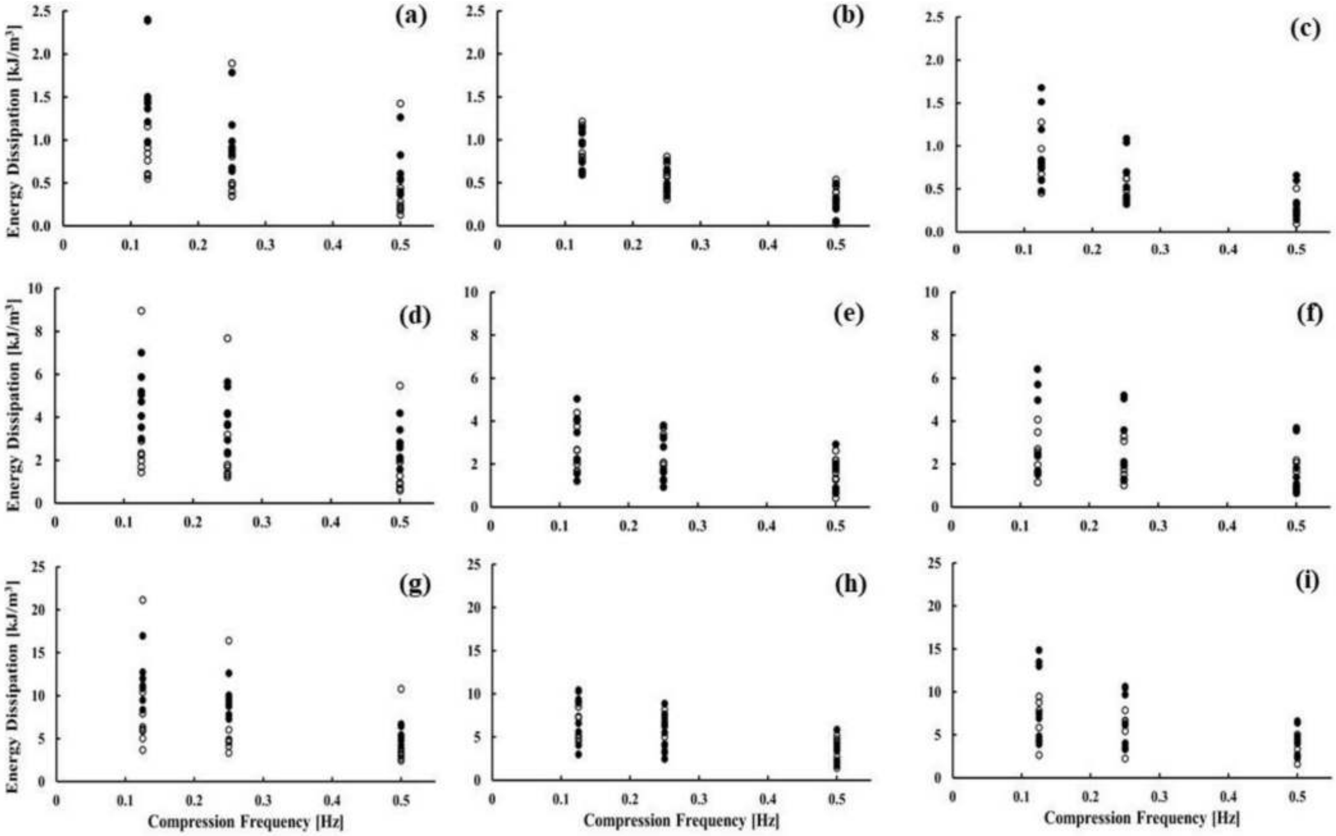

Figure A1:

Energy dissipation vs. compression frequency. Data are segregated by magnitude of compression (10%: a-c, 15%: d-f, 20%: g-i) and regions (anterior: a, d, g; central: b, e, h; posterior: c, f, i). Open circles refer to lateral samples and closed circles to medial ones.

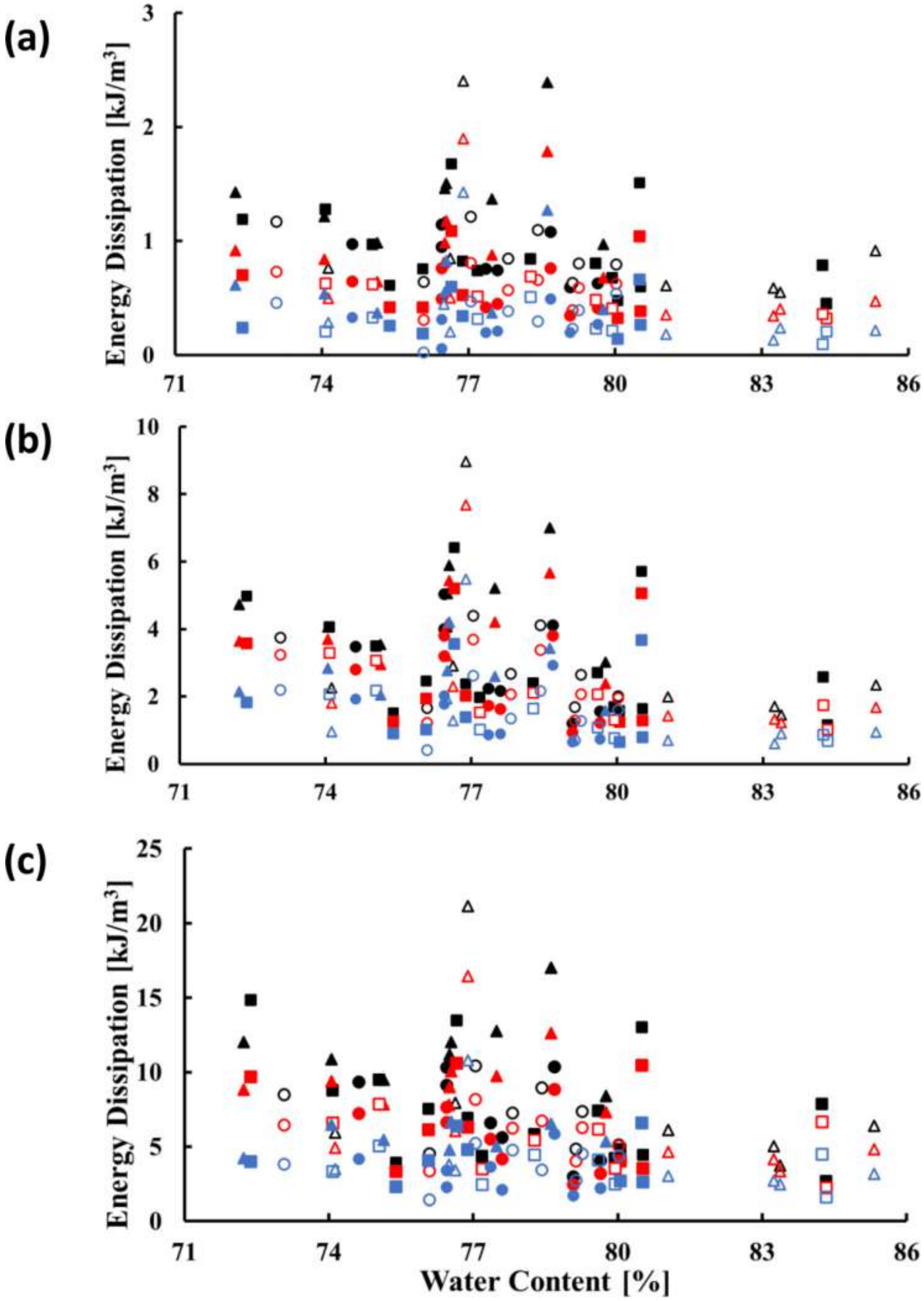

Figure A2:

Energy dissipation vs. water content: (a) 10% compression magnitude; (b) 15% compression magnitude; (c) 20% compression magnitude. Open symbols refer to lateral samples and closed symbols to medial ones. Triangles, circles and squares represent the anterior regions, the central regions and posterior regions, respectively. The colors of the symbols refer to the frequencies of compression: 0.125 Hz (black), 0.25 Hz (red), and 0.5 Hz (blue).

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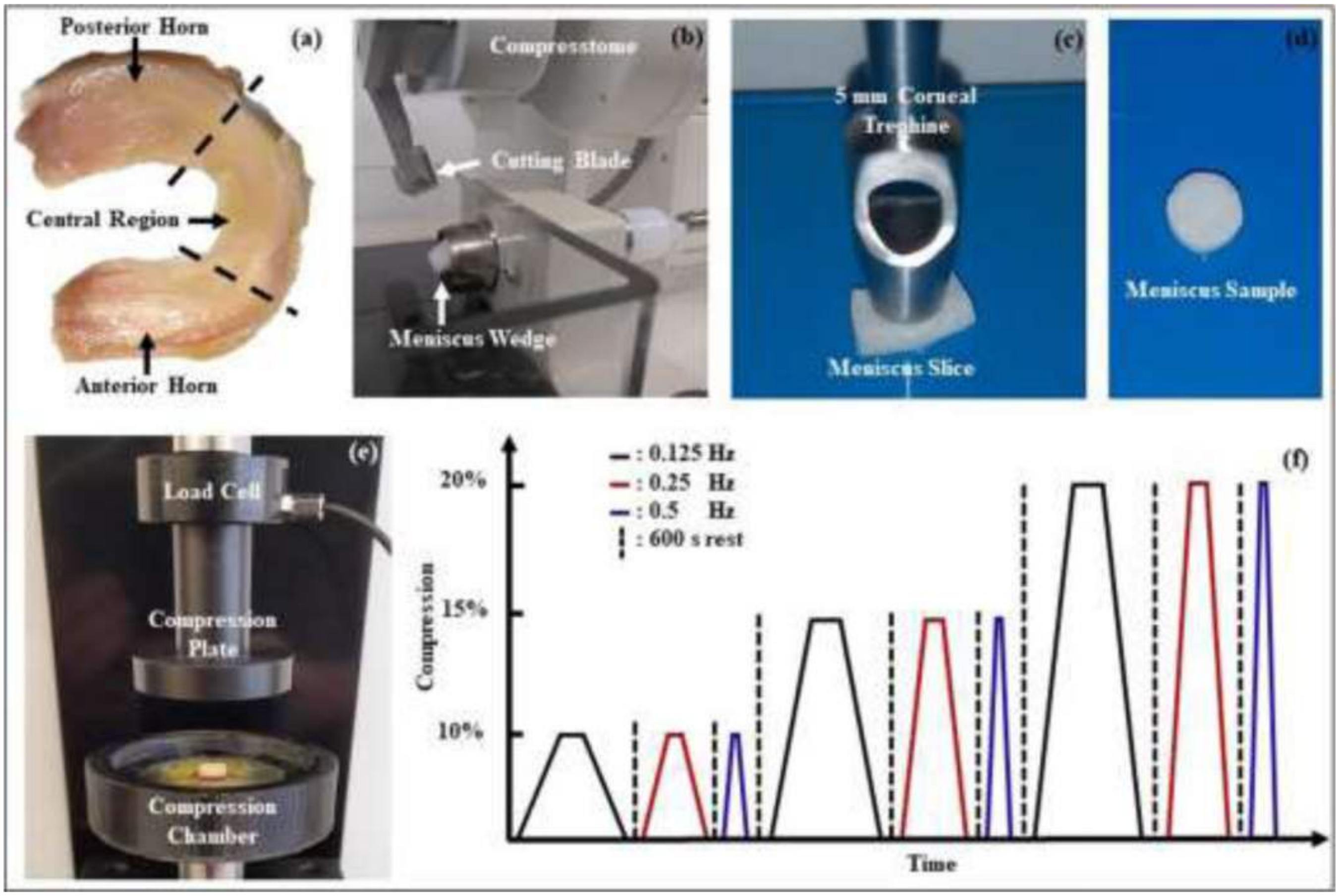

Figure 1:

Experimental procedures: a) samples were obtained from the posterior, central and anterior regions of human menisci; b) meniscal wedges were cut into 1.5 mm slices with Compresstome®; c) a 5mm corneal trephine was used to core the slices into discs; d) representative meniscus sample used in compression experiments; e) customized compression chamber for unconfined compression; f) compression cycles consisted of a series of trapezoidal loading curve with a 600s rest time between each cycle.

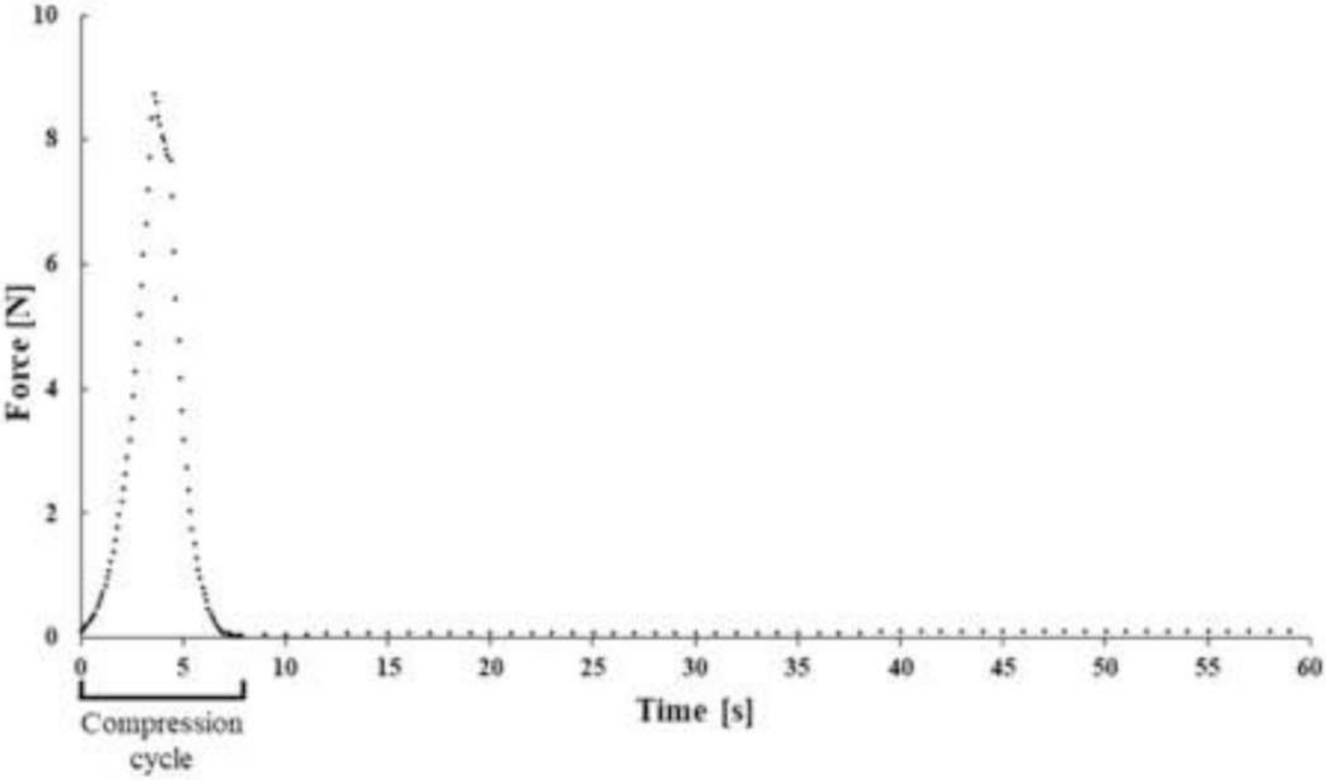

Figure 2:

Representative force response during a cycle of 20% compression strain at a frequency of 0.125 Hz. The equilibrium force recovers to pre-compression levels within the allotted 600s rest time.

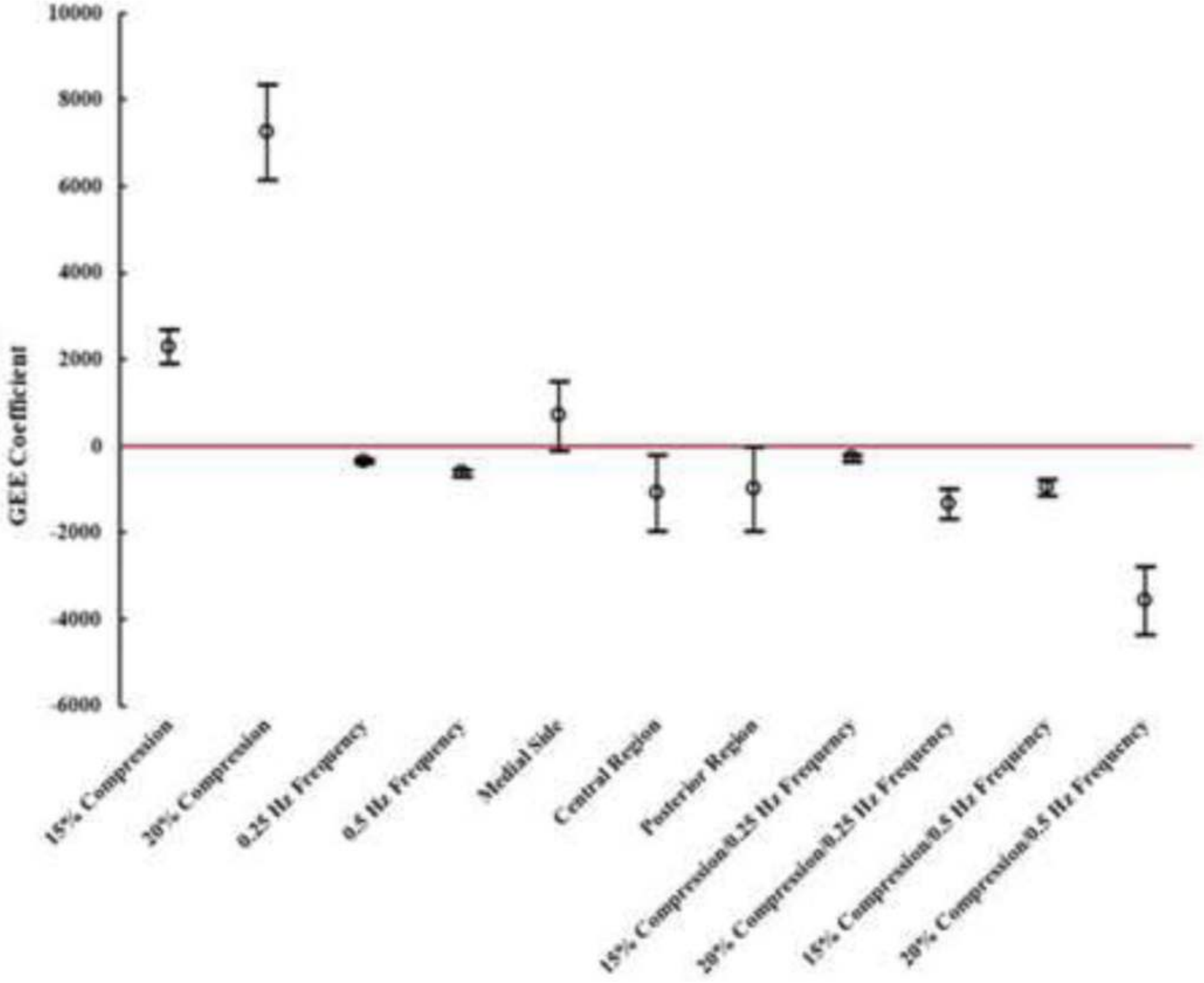

Figure 3:

GEE regression model coefficients of energy dissipation comparisons across compression levels, compression frequencies, meniscal side, and meniscal regions. All comparisons were conducted with respect to the case of 10% compression strain, 0.125 Hz compression frequency, lateral side, and anterior region. Bars in the diagram represent the 95% confidence interval of the coefficient.

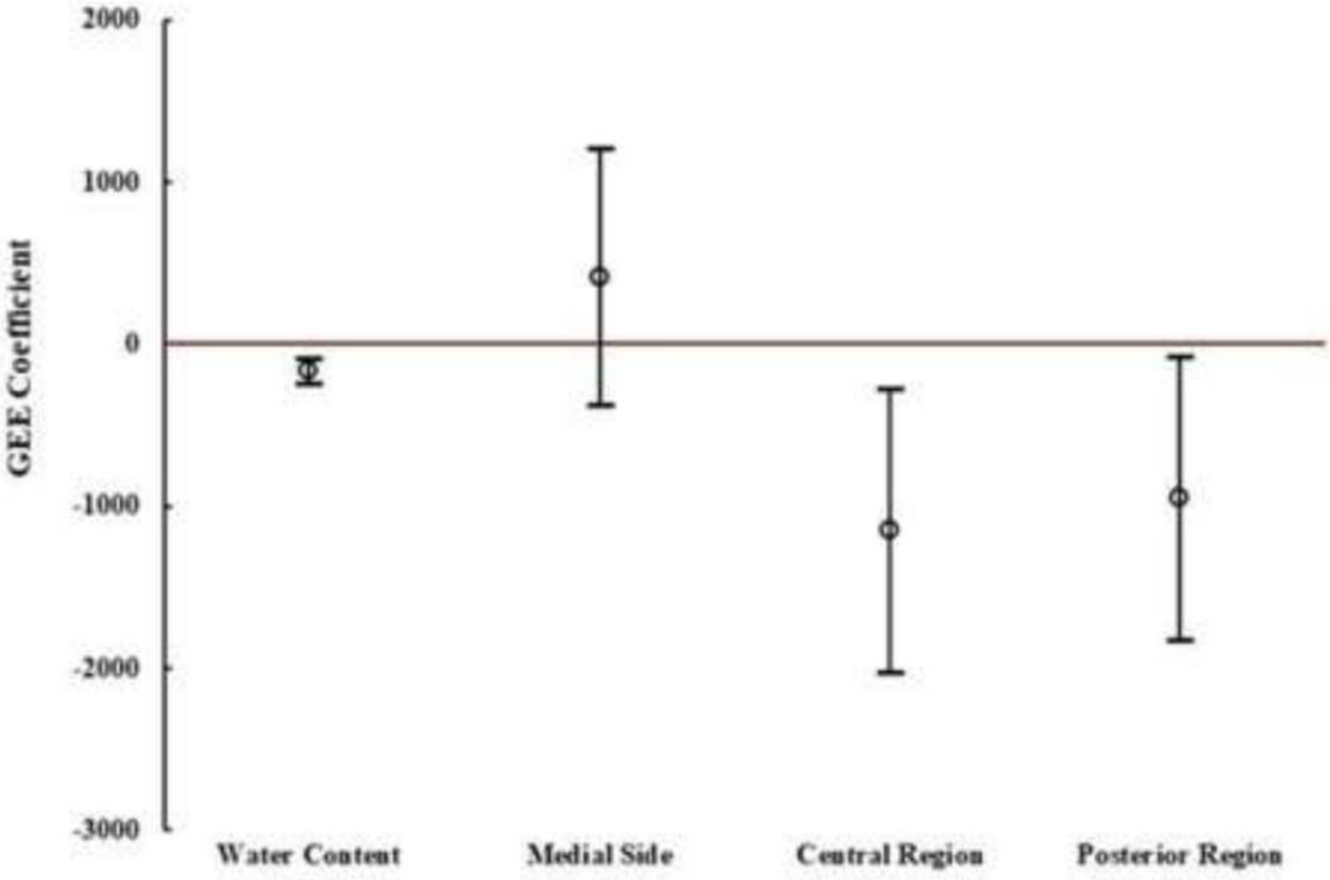

Figure 4:

GEE regression model coefficients of energy dissipation association with water content for all meniscal sides and regions. Bars in the diagram represent the 95% confidence interval of the coefficient.

Table 1:

Demographics of meniscal donors. Medial and lateral columns refer to the meniscal side used for experiments.

Donor	Medial	Lateral	Age	Gender
1	x		30	F
2	x		66	F
3	x	x	67	M
4	x	x	63	M
5	x	x	67	M
6	x	x	77	M
7	x	x	72	M
8	x	x	77	F
9		x	52	M
10		x	59	F
Average			**63.0**	
Standard Deviation			**13.9**	

Table 2:

Average and 95 % confidence interval of energy dissipated by the meniscus samples during each compression cycle expressed as kJ/m^3. Data are segregated by meniscal sides and regions. Combined data include all the regions of the lateral and medial menisci.

Compression	**10%**			**15%**			**20%**		
Frequency	**0.125 Hz**	**0.25 Hz**	**0.5 Hz**	**0.125 Hz**	**0.25 Hz**	**0.5 Hz**	**0.125 Hz**	**0.25 Hz**	**0.5 Hz**
Combined (n=48)	**0.99 (0.17–1.81)**	**0.65 (0–1.29)**	**0.37 (0–0.88)**	**3.29 (0–6.59)**	**2.68 (0–5.52)**	**1.72 (0–3.82)**	**8.25 (0.89–15.61)**	**6.58 (1.10–12.06)**	**4.07 (0.73–7.41)**
Medial (n=24)	***1.08 (0.38–1.93)***	***0.71 (0.26–1.37)***	***0.41 (0.04–0.91)***	***3.71 (0.78–7.03)***	***3.04 (0.54–5.86)***	***1.97 (0.21–4.03)***	***9.23 (1.87–16.44)***	***7.29 (1.70–12.61)***	***4.32 (1.27–7.46)***
Anterior (n=8)	1.42 (0.60–2.23)	0.99 (0.32–1.66)	0.62 (0.06–1.17)	4.81 (2.45–7.17)	4.01 (1.95–6.07)	2.70 (1.17–4.22)	11.72 (7.02–16.42)	9.35 (6.40–12.30)	5.57 (3.90–7.25)
Central (n=8)	0.86 (0.48–1.24)	0.54 (0.24–0.84)	0.26 (0.03–0.49)	2.98 (0.46–5.50)	2.40 (0.28–4.51)	1.48 (0–2.97)	7.32 (2.01–12.62)	5.73 (1.57–9.90)	3.19 (0.64–5.74)
Posterior (n=8)	0.96 (0.13–1.78)	0.62 (0.06–1.17)	0.34 (0–0.67)	3.34 (0–7.05)	2.71 (0–5.79)	1.73 (0–3.98)	8.65 (0.47–16.83)	6.78 (1.10–12.47)	4.21 (1.16–7.25)
Lateral (n=24)	***0.90 (0.15–1.65)***	***0.58 (0–1.19)***	***0.34 (0–0.85)***	***2.86 (0–5.94)***	***2.32 (0–5.01)***	***1.48 (0–3.49)***	***7.27 (0.29–14.26)***	***5.87 (0.58–11.15)***	***3.81 (0.35–7.27)***
Anterior (n=8)	0.98 (0–2.10)	0.66 (0–1.61)	0.39 (0–1.18)	3.21 (0–7.72)	2.58 (0–6.54)	1.60 (0–4.57)	8.34 (0–18.51)	6.52 (0–14.26)	4.12 (0–9.12)
Central (n=8)	0.90 (0.48–1.33)	0.59 (0.28–0.89)	0.35 (0.05–0.65)	2.87 (0.86–4.88)	2.37 (0.62–4.12)	1.55 (0.15–2.95)	7.14 (3.22–11.06)	5.81 (2.95–8.67)	3.81 (1.54–6.08)
Posterior (n=8)	0.82 (0.38–1.26)	0.51 (0.26–0.75)	0.26 (0.04–0.49)	2.51 (0.78–4.24)	2.02 (0.54–3.51)	1.29 (0.21–2.38)	6.34 (1.87–10.81)	5.27 (1.70–8.83)	3.51 (1.27–5.75)

Table 3:

Composition of tissue samples expressed as mass fraction of water as a percentage of the tissue’s wet mass, see equation (1). Combined data include all the regions of the lateral and medial menisci. Data are reported as mean and 95% confidence interval.

Meniscal Side/Region	**Water Content (%)**
Combined (n = 48)	**77.9 (72.0 – 83.8)**
***Medial* (n = 24)**	***77.0 (72.1 – 81.5)***
Anterior (n = 8)	76.3 (71.8 – 80.8)
Central (n = 8)	77.5 (74.5 – 80.5)
Posterior (n = 8)	76.9 (72.0 – 82.6)
***Lateral* (n = 24)**	***78.8 (72.2 – 85.4)***
Anterior (n = 8)	79.6 (72.1 – 87.2)
Central (n = 8)	77.6 (73.5 – 81.7)
Posterior (n = 8)	79.1 (72.1 – 86.0)

Table 4:

GEE regression model coefficients of energy dissipation association with loading conditions, and tissue region and composition. The first set of coefficients is related to association with compression levels, compression frequencies, meniscal side, meniscal regions; the second set refers to association with water content for all meniscal sides and regions. All comparisons were conducted with respect to the case of 10% compression strain, 0.125 Hz compression frequency, lateral side, and anterior region.

Association with loading conditions and tissue region

Variable	*Estimate (95% C.I.)*	*p-value*
10% Compression	*baseline*	
15 % Compression	2297.61 (1896.83 2698.39)	< 0.01
20 % Compression	7261.64 (6165.69 8357.58)	< 0.01
0.125 Hz Frequency	*baseline*	
0.25 Hz Frequency	−340.29 (−381.54 −299.03)	< 0.01
0.5 H Frequency	−618.48 (−693.29 −543.67)	< 0.01
Lateral Meniscus	*baseline*	
Medial Meniscus	701.47 (−103.39 1506.35)	0.09
Anterior Region	*baseline*	
Central Region	−1079.82 (−1972.71 −186.93)	0.02
Posterior Region	−983.90 (−1944.68 −23.12)	0.04
15 % Compression/ 0.25 Hz Frequency	−265.66 (−345.18 −186.15)	< 0.01
20 % Compression/ 0.25 Hz Frequency	−1332.95 (−1675.07 −990.82)	< 0.01
15 % Compression/ 0.5 Hz Frequency	−943.96 (−1137.70 −750.23)	< 0.01
20 % Compression/ 0.5 Hz Frequency	−3565.06 (−4357.75 −2772.38)	< 0.01

Association with water content across tissue regions

Variable	*Estimate (95% C.I.)*	*p-value*
Water Content	−163.40 (−239.41 −87.39)	< 0.01
Lateral Meniscus	*baseline*	
Medial Meniscus	416.19 (−377.86 1210.26)	0.30
Anterior Region	*baseline*	
Central Region	−1148.25 (−2018.65 −277.85)	< 0.01
Posterior Region	−946.12 (−1817.93–74.30)	0.03