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Comparison of porcine brain mechanical properties to potential tissue simulant materials in quasi-static and sinusoidal compression

D. Singh[1], S. Boakye-Yiadom[2], D. S. Cronin[1],

[1]Department of MME, University of Waterloo, 200 University Avenue West, Waterloo, Canada

[2]York University

Corresponding Author: Dr. Duane Cronin
                           Department of Mechanical Engineering
                           University of Waterloo
                           200 University Ave. West
                           Waterloo, Ontario, Canada, N2L 3G1
                           dscronin@mecheng1.uwaterloo.ca
                           (519) 888-4567 x32682

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ABSTRACT

In both finite element and physical surrogate models of head blast injury, accurate material properties of the brain and/or tissue simulants are necessary to ensure biofidelity in predicted response. Thus, there is a need for experimental comparisons between tissue and simulant materials under the same experimental conditions. This study compares the response of porcine brain tissue and a variety of brain tissue simulants in quasi-static and sinusoidal compression tests. Fresh porcine brain tissue was obtained from a local abattoir and tested within 4h post mortem. Additionally, the effect of post mortem time was investigated by comparing samples stored at room temperature and stored frozen (-18°C), at various time intervals. The brain tissue simulants tested were bovine gelatin (3%, 5%, and 10% concentration), agarose gelatin (e0.4%, 0.6%, 0.8% concentration), and Sylgard 527. The experiments were performed using a DMA apparatus (TA Instruments Q800). The quasi-static compression data were fit to Ogden hyperelastic functions so that parameters could be compared. It was found that bovine gelatin at 3% and 5% concentration demonstrated the closest response to brain tissue in quasi-static compression. Conversely, in sinusoidal compression, the agarose gel and Sylgard 527 were found to be in closer agreement with the tissue, than bovine gel. In terms of post mortem time and storage, there was no statistically significant difference detected in the response of tissue samples after 48h, regardless of storage method. However, samples stored at room temperature after 48h appeared to demonstrate a reduction in stiffness.

1.0 INTRODUCTION

A primary challenge in assessing the potential risk for head injury, is the difficulty in measuring the loadings and deformations present in the head and brain during injurious events, especially in living humans. This has been addressed by researchers in a variety of ways, including the use of physical surrogates (Merkle et al. 2009, Ouellet et al. 2017) with corresponding computational models, and computational modeling of the human head and brain (Takhounts et al. 2008, Panzer et al. 2012, Gayzik et al. 2012, Singh et al. 2013, Ghajari et al. 2017). However, the utility of such models depends on the quality of the mechanical properties that define them, and thus underscores the need for accurate mechanical properties of brain tissue and potential surrogate materials.

Most experimental studies on brain tissue have used animal tissues, most prominently porcine or bovine, due to the availability of material test specimens. The properties of porcine brain tissue have been measured previously in tension, compression, and shear at various strain rates (Miller & Chinzei 2002, van Dommelen et al. 2010, Kaster et al. 2011, Prevost et al. 2011a, Prevost et al. 2011b, Zhang et al. 2011, Rashid et al. 2012a, Rashid et al. 2012b, Rashid et al. 2013, Rashid et al. 2014, Falland-Cheung et al. 2018). However, the inherent complexity of the tissue, and many experimental variables including post-mortem time and temperature sensitivity, and regional and directional variation, have prevented a clear consensus. Consequently, the experimental data demonstrates a large variance in the magnitudes of reported properties. For example, a sensitivity study on the viscoelastic properties of the brain tissue in one blast head model found that the predicted strains in the brain varied by an order of magnitude when using the wide range of constitutive properties presented in the literature (Singh et al., 2014).

The issue of post-mortem time is important when conducting experiments on excised tissue samples, since the mechanical properties may change with time. The effect of post-mortem time has been investigated to a limited extent in the literature, and the results have varied from significant softening of tissue response at 45 minutes post-mortem (Metz et al. 1970), to stiffening of tissue response starting from 6h (Garo et al. 2007, Zhang et al. 2011) to 24h (Nicolle et al. 2004) post-mortem, to no significant effects up to five days post-mortem (Darvish & Crandall 2001, Budday et al. 2015). The variation in this data is thought to be due to different sample preparation and storage protocols by different researchers.

The properties of white and gray matter have been distinguished in the literature, with white matter in general characterized as being approximately 30 – 50% stiffer (Pervin & Chen 2009, van Dommelen et al. 2010, Kaster et al. 2011, Jin et al. 2013, Budday et al. 2015, MacManus et al. 2017). Although some computational models distinguish between gray and white matter (Zhang et al. 2004, Ipek et al. 2009, Gayzik et al. 2012, Yang et al. 2014, Ghajari et al. 2017), many established finite element head models do not make this distinction (Horgan & Gilchrist 2003, Deck & Willinger 2008, Takhounts et al. 2008, Ho & Kleiven 2009, Zhao et al. 2017, Migueis et al. 2019). Similarly, most physical models (Merkle et al. 2009, Ouellet et al. 2017) of the brain use a single surrogate material for the brain tissue with no distinction between the gray and white matter. For the purpose of providing mechanical properties for such models, there is a need for characterizing mixed gray/white matter samples.

A variety of brain tissue simulant materials have been proposed in the literature, most commonly gelatins (porcine and bovine), hydrogels, and silicone elastomers. Pervin and Chen (2010)

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reported that agarose gel in 0.4 – 0.6% concentration could be used to simulate brain tissue, although they did not present a quantitative comparison. Falland-Cheung et al. (2018) reported that the apparent elastic moduli of agar gels matched more closely with brain tissue at lower strains, while gelatin matched closer at larger strains, although in both cases the simulant materials were stiffer compared to brain tissue. However, they did not consider strain rates exceeding 1.6 s^{-1}, which limited their conclusions to low deformation rate phenomena.

In summary, the material properties of brain tissue have been characterized, but exhibit a large variance due to experimental considerations, which prevent a direct comparison for evaluating simulant materials. The goal of the current study was to measure and compare the mechanical properties of porcine brain tissue and a variety of surrogate materials using the same experimental conditions, enabling a direct comparison of the materials.

2.0 METHODS

2.1 Preparation of Porcine Brain Tissues

Fresh porcine brain tissues were obtained from a local abattoir in order to serve as a baseline for comparison to the deformation behavior of the tissue simulant materials. Prior to obtaining the fresh porcine brain tissues, ethics approval for the use of animal tissues was received from the University of Waterloo Office of Research Ethics (UW ORE# A-14-11).

The fresh porcine brains were collected approximately 15 minutes post-mortem and tested within 4h. The cerebral hemispheres were received split into right and left halves by cutting along the sagittal plane through the corpus callosum. Each of the cerebral hemispheres were then cut in the

coronal plane, and square sections (20 x 20 mm) were extracted from the anterior and posterior directions of the frontal and parietal lobes of the cerebrum (Figure 1). The square shape of the specimens was chosen because it provided the most dimensional consistency between samples. The specimens excised from the porcine brain were composed of mixed white and gray matter. Excess brain tissues were removed from the square cross sections in order to maintain an approximate specimen thickness of 10±0.5 mm. The actual thickness of each specimen was measured prior to testing. All specimens were prepared at room temperature and saline solution was frequently sprayed on the samples during cutting and before the tests in order to prevent dehydration. The fresh porcine brain tissue was tested at room temperature (22°C) and body temperature (37°C) using an environment chamber, to characterize any differences in the response from temperature.

The effect of post-mortem time (up to 48h) on the mechanical properties of the brain tissues was measured to determine if the properties changed over time when stored at room temperature. In addition, the effect of storage on the tissues was investigated, by comparing frozen specimens with those stored at room temperature. The collected fresh porcine brain tissues were divided into two groups, with the first group stored at room temperature and the second group frozen (-18ºC). Some specimens from each group were tested after 24h, and the remaining specimens were tested after 48h. Both the room temperature stored and frozen specimens were sealed in small plastic containers, without submersion or hydration.

2.2 Preparation of Brain Tissue Simulants

Three different tissue simulant materials (agarose gelatin, bovine gelatin, and Sylgard 527) were obtained and prepared for testing (Figure 2). The concentrations of the simulant materials were chosen based on the expected responses of these materials from previous studies in the literature (Pervin & Chen 2010, Lazarjan et al. 2014, Falland-Cheung et al. 2018). The simulant materials were mixed in a liquid form and then poured into cylindrical polycarbonate molds to obtain good geometry and adequately shaped samples (supplementary images included in Appendix A). For cylindrical samples, the ratio between the initial length and the diameter of the sample is a pertinent parameter. In reference to the ASM Handbook (ASM Handbook, 2000), the length/diameter ratio for soft material compression samples should be less than 2. This was taken into consideration when the molds were designed. For the static compression tests, 10 x 9.5 mm cylindrical molds were designed, while 20 x 9.5 mm cylindrical molds were designed for multi-frequency tests to prevent sample slippage.

Bovine gel with concentrations (w/v) of 3%, 5% and 10% were prepared by dissolving appropriate amount of gelatin powder (Sigma-Aldrich, G9391) in distilled water. The mixture was slowly stirred to minimize entrapment of air until all the gelatin powder dissolved. The molds with the bovine gels were kept in sealed plastic bags to maintain humidity and held at room temperature for 24h for curing. Bovine gelatin is known to exhibit variation in properties with temperature, and is typically used at specific temperatures according to its preparation (Cronin and Falzon, 2011). In this study, the bovine gelatin samples were tested at room temperature (22°C), since this is the typical condition under which brain tissue surrogates are often used in testing. Body temperature (37°C) tests were not undertaken with the bovine gel since this material essentially becomes liquid at this temperature, for the concentrations tested.

Agarose gels with concentrations (w/v) of 0.4%, 0.6% and 0.8% were prepared by dissolving an appropriate amount of powdered agarose (Bio-Rad Laboratories Canada Ltd) in distilled water. The solution was heated to 90-95°C for 15 minutes and stirred continuously to aid dissolution of the powder and prevent bubbling. The molds with the agarose gels were kept in sealed plastic bags to maintain humidity and cured at room temperature for 24h to cure the samples. The agarose gels were tested at both room (22°C) and body temperatures (37°C).

Commercially available PDMS, Sylgard 527 (Dow Corning Corporation) gel was obtained and prepared per the manufacturer's instructions by mixing equal weights of part A and part B and stirred continuously to ensure that the components were thoroughly mixed. The Sylgard samples were cured at room temperature in sealed plastic bags for two weeks before testing at both room (22°C) and body temperatures (37°C). Although the Sylgard 527 was expected to have physical properties similar to the agarose and bovine gels, it tended to stick to the molds and consequently deform during mold release. To help mitigate this, the interior surfaces of the Sylgard 527 molds were lined with plastic wrap. This allowed easier demolding and handling of the cured samples. The plastic wrap was removed prior to testing.

2.3 Mechanical Characterization of Brain Tissue and Simulant Materials

A Dynamic Mechanical Analyzer (DMA, TA Instruments Q800) was used to perform the experiments. To determine the static compression properties of the porcine brain tissues and the prepared tissue simulant materials, a strain rate controlled compression mode was used. The temperature was held constant within an environment chamber, and the strain ramped at a

constant strain rate of 0.01 s^{-1}. The DMA apparatus measured the stress and strain response of the samples corresponding to the quasi-static stress-strain curve.

The viscoelastic properties of the materials were measured in the DMA using a frequency sweep, where sinusoidal deformation is applied at increasing frequencies. The amplitude at which to apply the frequency sweep was determined from the linear viscoelastic strain limit, found to be between 0.20 % - 0.37 % for the materials tested. To determine this amplitude, the samples were placed in the DMA and oscillated at constant frequencies (2 Hz and 50 Hz) while the strain was gradually increased in amplitude. The DMA measured the complex modulus, and the strains at which the modulus began to vary with frequency were identified as the linear viscoelastic strain limit. In the multi-frequency sweep mode tests, the samples were placed in the DMA and oscillated at a constant strain amplitude while the frequency was increased. This information is presented in this paper as complex modulus as a function of frequency.

All of the materials, both tissue and simulant, were tested in quasi-static compression and dynamic mechanical analysis (Table 1).

2.4 Statistical Comparison Methodology for Quasi-Static Compression Results

A methodology for comparing the results of the quasi-static compression tests was employed, that allowed for tests of statistical significance. Each individual experimental stress-strain curve was fit to an Ogden hyperelastic constitutive model (Eq. 1), from which the initial shear modulus could be calculated (Eq. 2). This allowed for a common set of parameters to be compared across the various materials using statistical methods.

$$W(\lambda_1, \lambda_2, \lambda_3) = \sum_{i=1}^{n} \frac{\mu_i}{\alpha_i} (\lambda_1^{\alpha_i} + \lambda_2^{\alpha_i} + \lambda_3^{\alpha_i} - 3)$$ Eq. 1: Ogden Hyperelastic Function

$$G = \frac{1}{2} \sum_{i=1}^{n} \mu_i \alpha_i$$ Eq. 2: Initial Shear Modulus

Where W = strain energy density; $\lambda_{1,2,3}$ = principal stretch ratios; n, μ, α = material constants; G = initial shear modulus.

3.0 RESULTS

3.1 Quasi-Static Compression Testing

The results of the quasi-static compression tests on fresh porcine brain tissue demonstrated a typical hyperelastic response (Fung, 1993) for both room temperature and body temperature responses (Figure 3). The experimental variation in the data was generally on the order of typical biological tissues. The tissue simulants demonstrated similar hyperelastic responses (Figure 4), albeit with less variability. Results for all individual test curves for the tissue simulants are included in Appendix B.

The stress-strain curves for each experiment were fit to the Ogden hyperelastic constitutive equation (Eq. 1). A single term (n=1) model was sufficient for all materials except that agar gels, which required a three term (n=3) model. The resulting curve fits produced R^2 values exceeding 0.99 for all curves. The responses of each material and temperature condition were also averaged, and the average curves were fit using the Ogden model. The Ogden parameters of each individual test and the averaged material responses are included in Appendix C.

The initial shear moduli (Eq. 2) were compared between materials using two tailed t-tests, assuming unequal variance, to test for statistically significant differences (Table 2). The tissue simulants were compared to either fresh room temperature or body temperature brain tissue, corresponding to the temperature at which the simulant was tested. All of the brain tissue groups (temperature, time, and frozen/unfrozen) were compared to fresh room temperature brain tissue.

There was found to be no statistically significant difference in the response of brain tissue at room and body temperatures ($p = 0.061$). All of the agar gels were found to be significantly stiffer than the brain tissue ($p < 0.005$), primarily due to an initial higher stiffness region at low strains evident in their stress-strain responses (Figure 4a, 4b). In comparing the bovine gels to brain tissue, there was found to be no statistically significant difference at 3% ($p = 0.967$) and 5% ($p = 0.197$) concentrations, whereas the 10% concentration bovine gel was stiffer ($p = 0.022$). The Sylgard 527 response demonstrated a statistically significant difference when compared to brain tissue at room temperature ($p = 0.044$), however no statistically significant difference was detected at body temperature ($p = 0.100$).

The responses of brain tissue samples that were stored for 24h at room temperature ($p = 0.784$) or in a freezer ($p = 0.382$) were not found to be significantly different from fresh tissue. At 48h, there was similarly no statistically significant difference between the frozen ($p = 0.916$) and room temperature ($p = 0.085$) stored tissues, although the samples that were stored at room temperature appeared to have softened in their response (Figure 5).

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3.2 Sinusoidal Compression Testing

The complex moduli of the porcine brain tissue demonstrated an increase in magnitude with increasing frequency of oscillation (Figure 6). The DMA apparatus was unable to resolve the phase angle between the inputted and measured output curves during the testing, therefore the storage and loss moduli are not reported. However, the complex modulus, which was a direct measurement based on the applied sinusoidal strain amplitude and the amplitude of the resulting stress, was an accurate and representative measurement of the material response that could be used for a qualitative comparison of the different materials.

The complex modulus of the bovine gelatins was in reasonable agreement with the brain tissue at lower frequencies, up to about 100 Hz (Figure 7a). However, the response at higher frequencies diverged significantly from the brain tissue response (Figure 7b). In contrast to the bovine gel, the complex moduli of the agar gels were in general greater than the brain tissue at lower frequencies, and in reasonable agreement at frequencies greater than 100 Hz (Figure 7c). The viscoelastic response of Sylgard 527 was found to match the porcine tissue response well at both low and high frequencies (Figure 7d).

4.0 DISCUSSION AND CONCLUSIONS

This study measured the quasi-static and sinusoidal compression response of porcine brain tissue and a variety of brain tissue simulant materials using the same methodology. The purpose of the tissue testing was to provide a benchmark upon which to compare the various simulant materials, used for simulating the response of actual brain tissue in physical surrogate head models. The tissue testing also provides additional data that can be used to inform finite element models

through properties that could be implemented in constitutive relationships, although it is acknowledged that further high deformation rate testing is required.

In terms of the quasi-static compression response, the Ogden constitutive models (R^2 values greater than 0.99 in all cases) are used to compare the simulant materials to the brain tissue. The 3% and 5% concentration bovine gels best matched the response of brain tissue in quasi-static compression. These findings were further supported by a simple analysis of calculating the area under the stress strain curves at two discrete strain values: 5% strain and 30% strain (Appendix D). The 5% strain value was chosen because it corresponds generally to the level of strain seen in brain tissue during typical blast-induced mTBI loadings (Singh et al. 2013), and the 30% strain value was chosen because it corresponds to strain injury criteria reported in the literature (Mao et al. 2011, Deck & Willinger 2008, Kleiven 2008).

Two of the tested materials (bovine gel and agar gel) could be created at different concentrations. Although the 3% and 5% bovine gels were representative of brain tissue at room temperature under quasi-static loading, and thus the range of concentrations considered was appropriate, these gels were effectively liquid at body temperature, which may be a limitation in application for physical surrogates if high temperature testing is considered. Bovine gelatin is most commonly used for ballistic testing at the 10%, 4° C and 20%, 10° C concentrations and is known to demonstrate a sensitivity to temperature in the mechanical properties (Cronin & Falzon 2011).

The agar gel was tested in 0.4%, 0.6%, and 0.8% concentrations, all of which were stiffer in comparison to the tissue. Concentrations of agar gel below 0.4% were not tested, and would presumably have a lower stiffness; however, the agar gels demonstrated an atypical initial high stiffness region at small strains, which was not observed in the brain tissue or the simulant materials. This was further evidenced by the need for a three-term Ogden model for the agar gel, while all other materials were adequately fit with a one-term model, thus the agar gel demonstrated a different shape of stress-strain response compared to brain tissue.

The Sylgard 527 was found to be stiffer than brain tissue at room temperature, although there were no statistically significant differences when the materials responses at body temperature were compared. However, there were only two tests measured for Sylgard 527 at body temperature, which limited the ability of the statistical comparison to detect differences in this case.

The porcine brain tissue was also tested at 24h and 48h post mortem, after being stored at room temperature and in cold storage. The time and storage method sensitivity of brain tissue has been reported previously in the literature, but with no clear consensus on the effects (McElhaney et al. 1973, Darvish & Crandall 2001, Budday et al. 2015, Garo et al. 2007, Prevost et al. 2011a, Prevost et al. 2011b, Zhang et al. 2011). In the current study, it was found that there was no statistically significant difference in the quasi-static compression response of brain tissue samples after 48h, regardless of storage method. However, the response of the samples that were stored at 48h at room temperature demonstrated a visible reduction in stiffness when comparing stress strain curves (Figure 5b), demonstrated in part by the relatively smaller p value (0.085) for

this case. The tests for statistical significance used initial shear moduli determined from the

Ogden model parameters. While this provided a common set of parameters that could be

compared across materials, it may not fully capture non-linearities in the material response.

Regardless, these differences indicate that storage methodology should be an important

consideration for researchers undertaking physical experiments with brain tissue.

The viscoelastic properties, presented in terms of complex modulus of the materials were

compared up to an oscillation frequency of 200 Hz. In general, the agar gel and Sylgard 527

demonstrated complex moduli on the same order as the porcine brain tissue, whereas the bovine

gel was significantly higher at frequencies beyond 130 Hz. The DMA apparatus was limited to a

maximum frequency of 200 Hz, so greater frequencies were not tested, although would be

informative.

A limitation of this study was the low number of samples tested; however, the test results were

generally consistent in the shape and magnitude, and were able to demonstrate trends. The brain

tissue samples tested were mixed grey/white matter samples, which provided a more appropriate

benchmark for evaluating the tissue simulants where a single material is used to represent brain

tissue as a whole. However, recent advances in medical imaging and computational efficiency

have seen the development of finite element models that can model distinguish between white

and grey matter in the brain, so future work should isolate and characterize white and grey matter

matter separately. The brain tissue was tested using samples with a square cross-section, due to

the difficulty in creating cylindrical samples of sufficient quality, whereas the tissue simulants

were tested using cylindrical samples from molds. This approach is common in the literature and the effect of test sample shape should be investigated further, particularly at larger deformations.

In assessing the brain tissue simulants, the bovine gelatin produced the most comparable response to brain tissue in quasi-static compression. However, the bovine gelatin diverged from the tissue response for the sinusoidal compression tests, whereas the agar gels and Sylgard 527 were found to be comparable. This highlights a general limitation of physical surrogate models where no single material may achieve correspondence across a range of temperatures and deformation rates, since certain materials can match better in a particular loading condition, and not as well in another. Further, it underscores the importance of loading mode and rate on the choice of simulant material for a particular application. With regards to tissue simulants, there are often other factors, such as bio-compatibility or material longevity, that may be important considerations for the selection of tissue simulants, that were not considered in this work. Future work should focus on high deformation rate characterization of tissue simulants.

CONFLICTS OF INTEREST:

The authors declare no conflicts of interest.

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Appendix A: Supplementary Experimental Setup Pictures

The tissue simulant materials were prepared in polycarbonate molds (Figure A1), and the experiments were performed using a DMA apparatus (Figure A2).

Appendix B: Supplementary Experimental Setup Pictures

The individual test curves in quasi-static compression are presented for the tissue simulants (Figure B1) and the brain tissue stored for 24h and 48h (Figure B2). Figures B1 and B2 present the raw data corresponding to Figures 4 and 5 in the main body of this paper.

Appendix C: Ogden Constitutive Parameters for Quasi-Static Compression Tests

The Ogden hyperelastic constitutive parameters for each experimental quasi-static compression tests are presented for room temperature (Table C1) and body temperature (Table C2). The averaged parameters presented in these tables are Ogden parameters that were fit to the averaged stress-strain curve for each material group. These are distinct from the averages of the parameters themselves.

Appendix D: Comparison of Quasi-Static Data using Areas

The areas under the average quasi-static compression response of porcine brain tissue and the simulant materials at room temperature (Table D1) and body temperature (Table D2).

Figure 1: Exemplar porcine brain tissue samples for room temperature storage at (a) fresh, (b) 24h, (c) 48h, and for frozen and thawed samples at (d) fresh, (e) 24h, (f) 48h (scale dimensions in cm).

Figure 2: Processed and cured tissue simulants for (a) agarose gelatin, (b) bovine gelatin, and (c) Sylgard 527 (scale dimensions in cm).

Figure 3: Quasi-static compression response of porcine brain tissue at (a) room temperature and (b) body temperature

Figure 4: Quasi-static compression response of agar gel at 0.4%, 0.6%, 0.8% concentrations at (a) room temperature and (b) body temperature; (c) bovine gel at 3%, 5%, 10% concentrations at room temperature; (d) Sylgard 527 at room temperature and body temperature. Solid lines are mean curves, and dashed lines are standard deviations.

Figure 5: Quasi-static compression response of porcine brain tissue after (a) 24h and (b) 48h stored at room temperature (22 C) and frozen (-18 C). Solid lines are mean curves, and dashed lines are standard deviations.

Figure 6: Complex modulus vs frequency response of room temperature porcine brain tissue.

Figure 7: Complex modulus vs frequency response of room temperature bovine gel at (a) low frequencies and (b) high frequencies; (c) agar gel; (d) Sylgard 527.

Figure A1: Example of a mold used for preparing the tissue simulants (scale dimensions in cm).

Figure A2: Compression clamps used for the dynamic mechanical analysis testing

Figure B1: Individual quasi-static compression tests of agar gel at 0.4%, 0.6%, 0.8% concentrations at (a) room temperature and (b) body temperature; (c) bovine gel at 3%, 5%, 10% concentrations at room temperature; (d) Sylgard 527 at room temperature and body temperature.

Figure B2: Individual quasi-static compression results of porcine brain tissue after (a) 24h and (b) 48h stored at room temperature and frozen (-18 C).
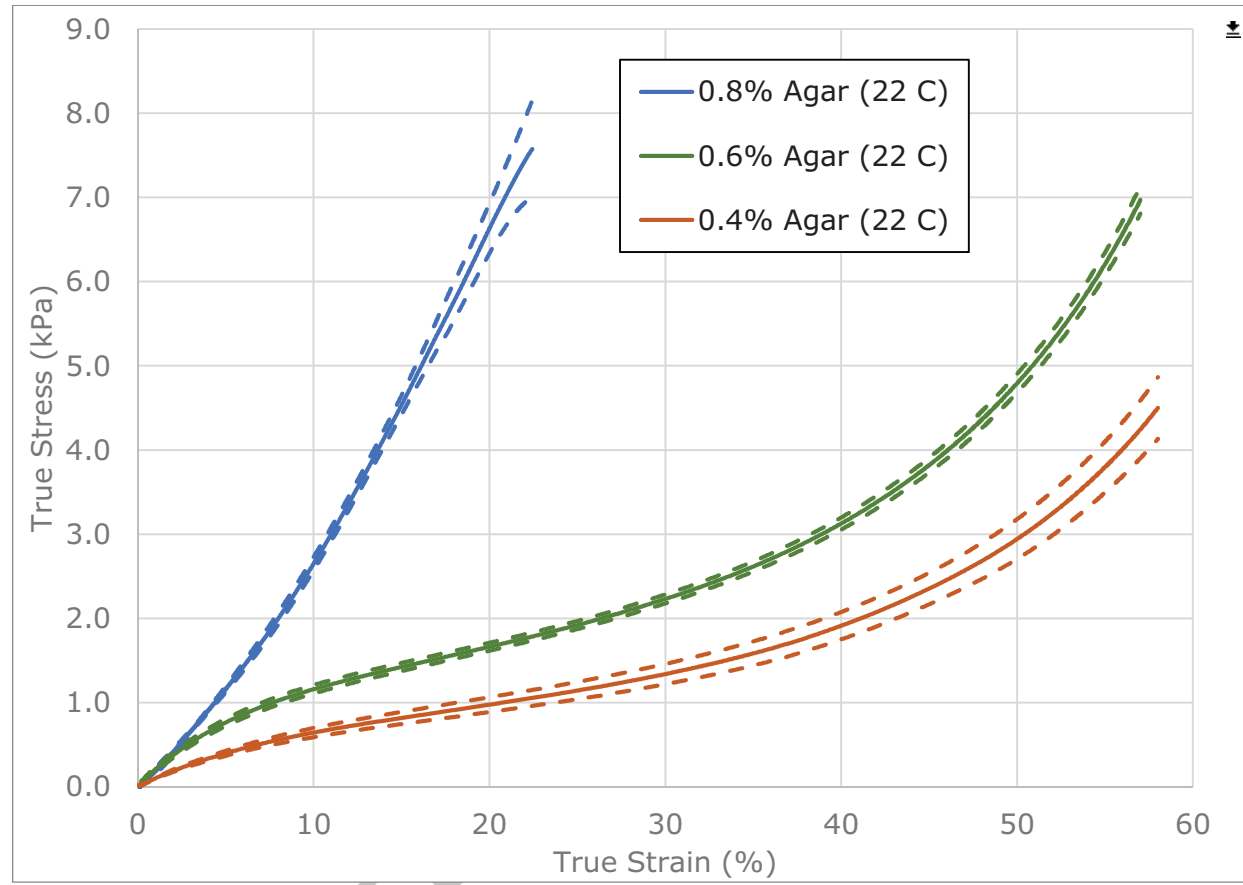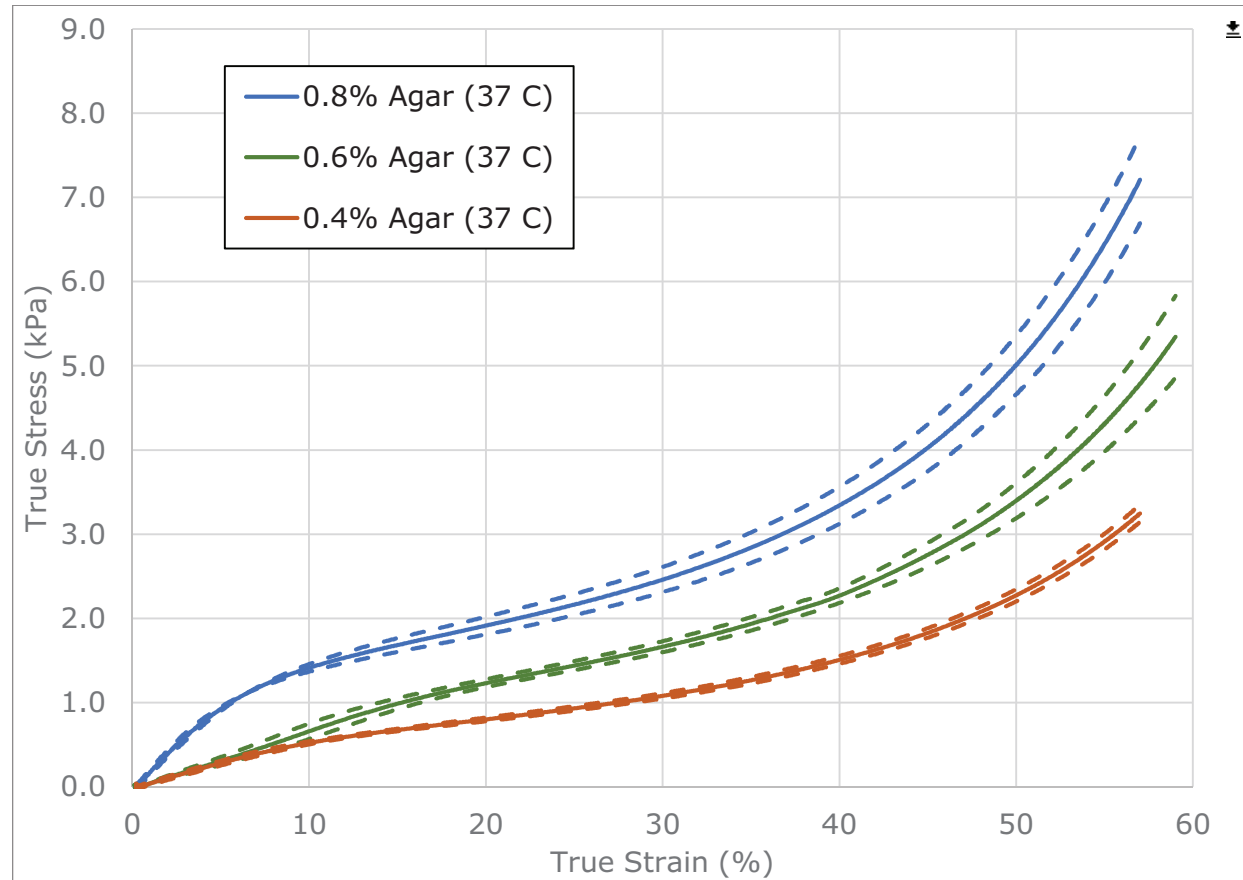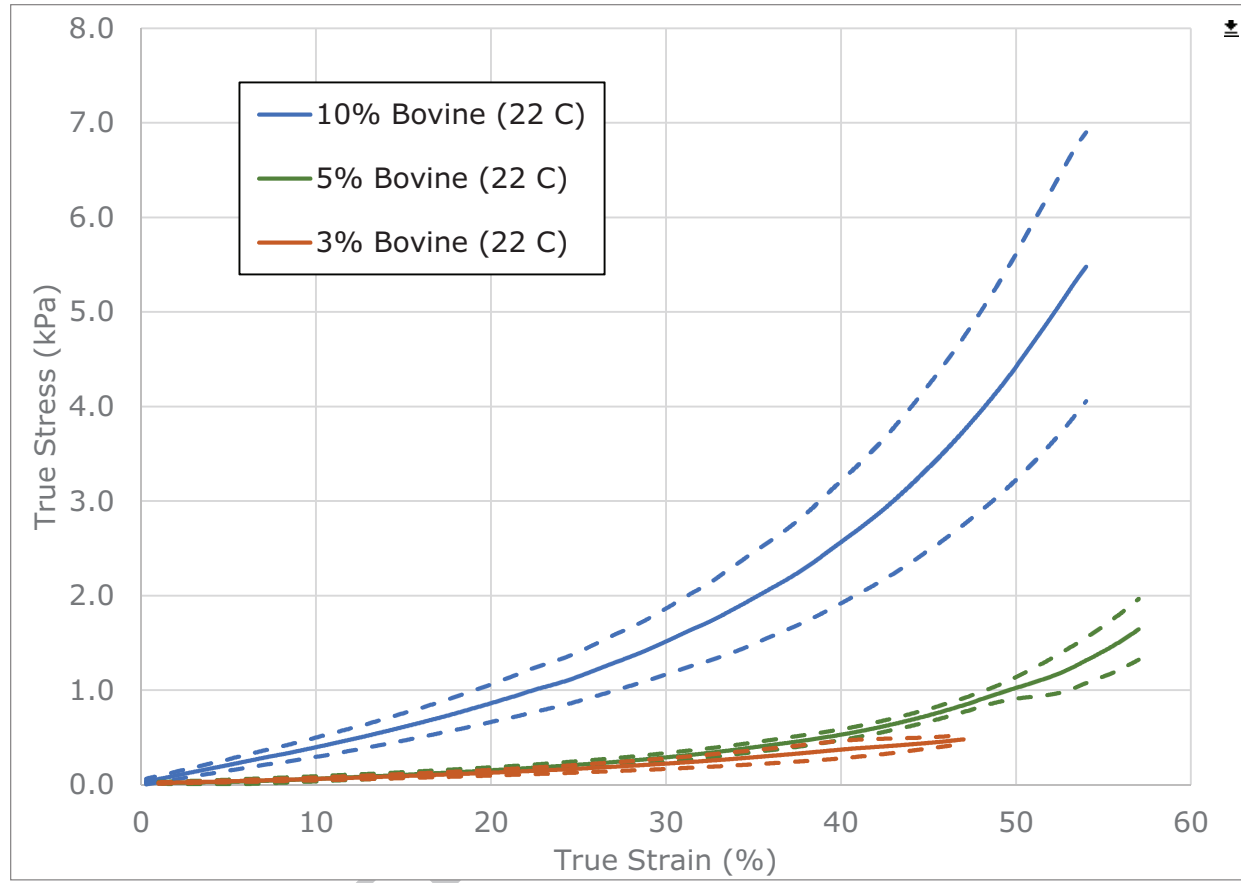
Thermocouple

Lower clamp

Sample

Upper clamp

Lower clamp
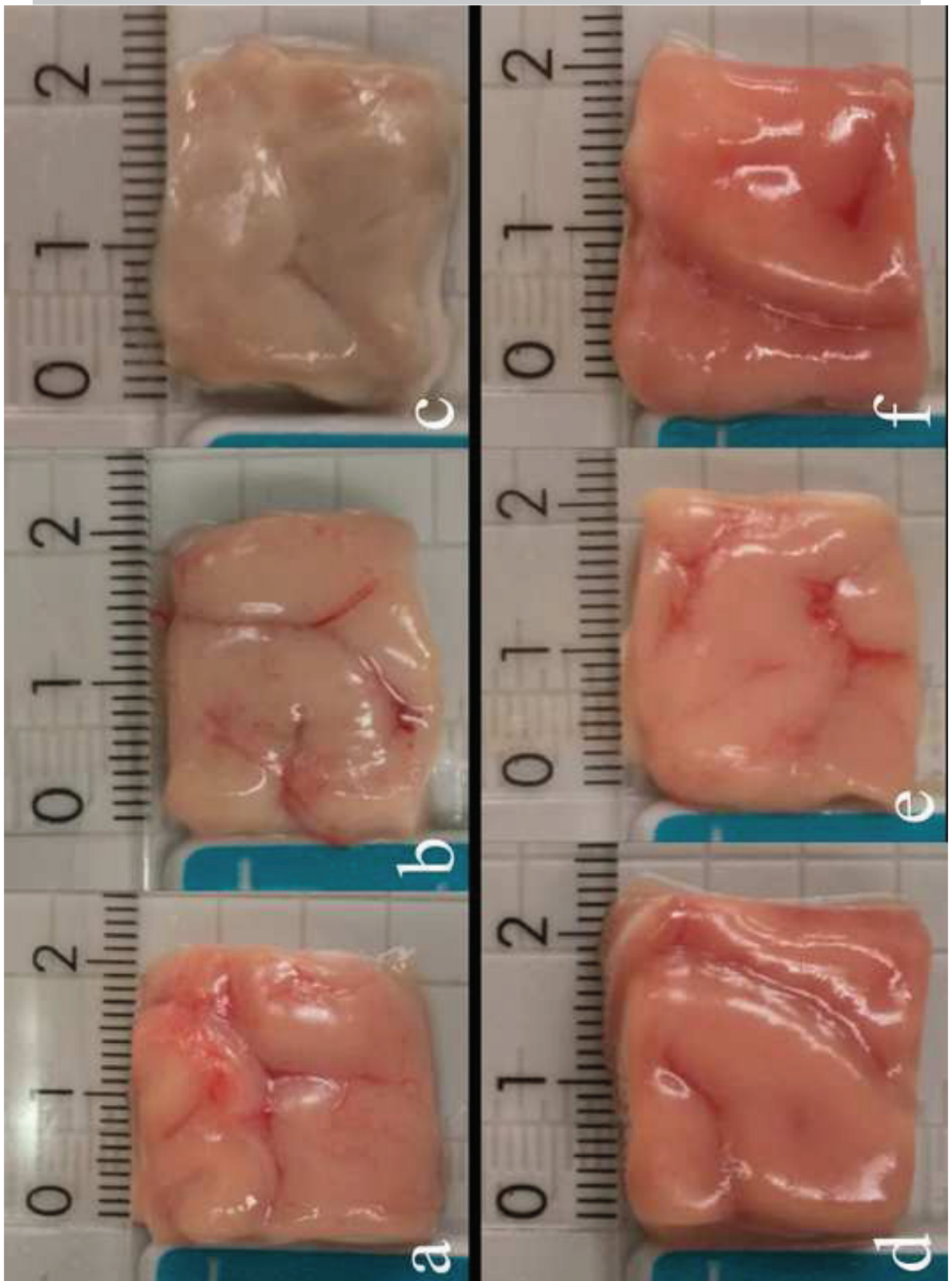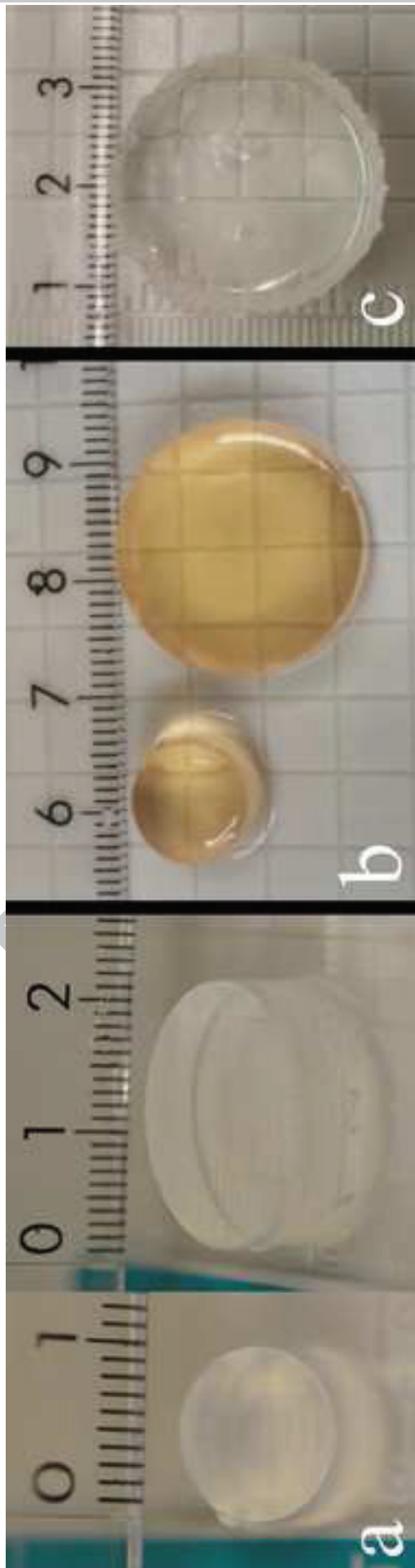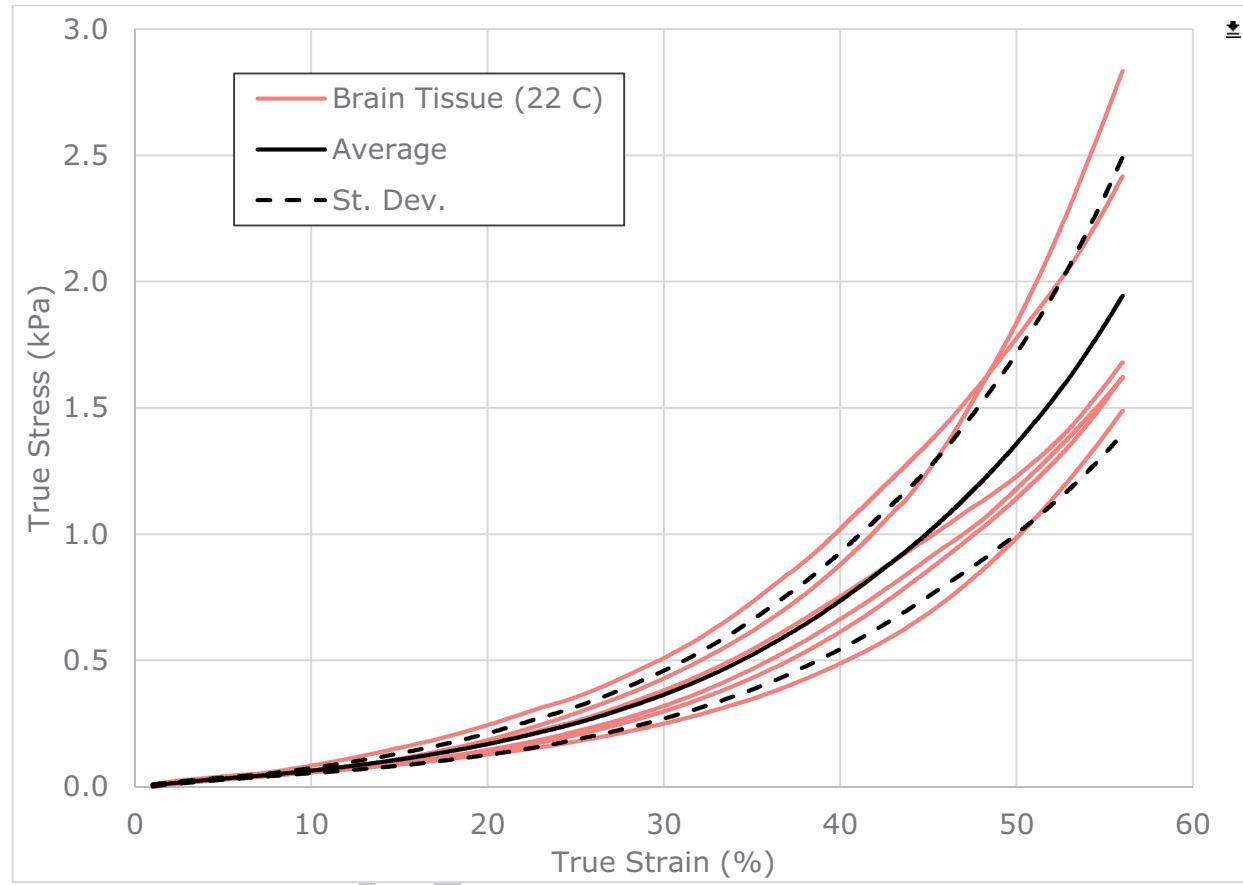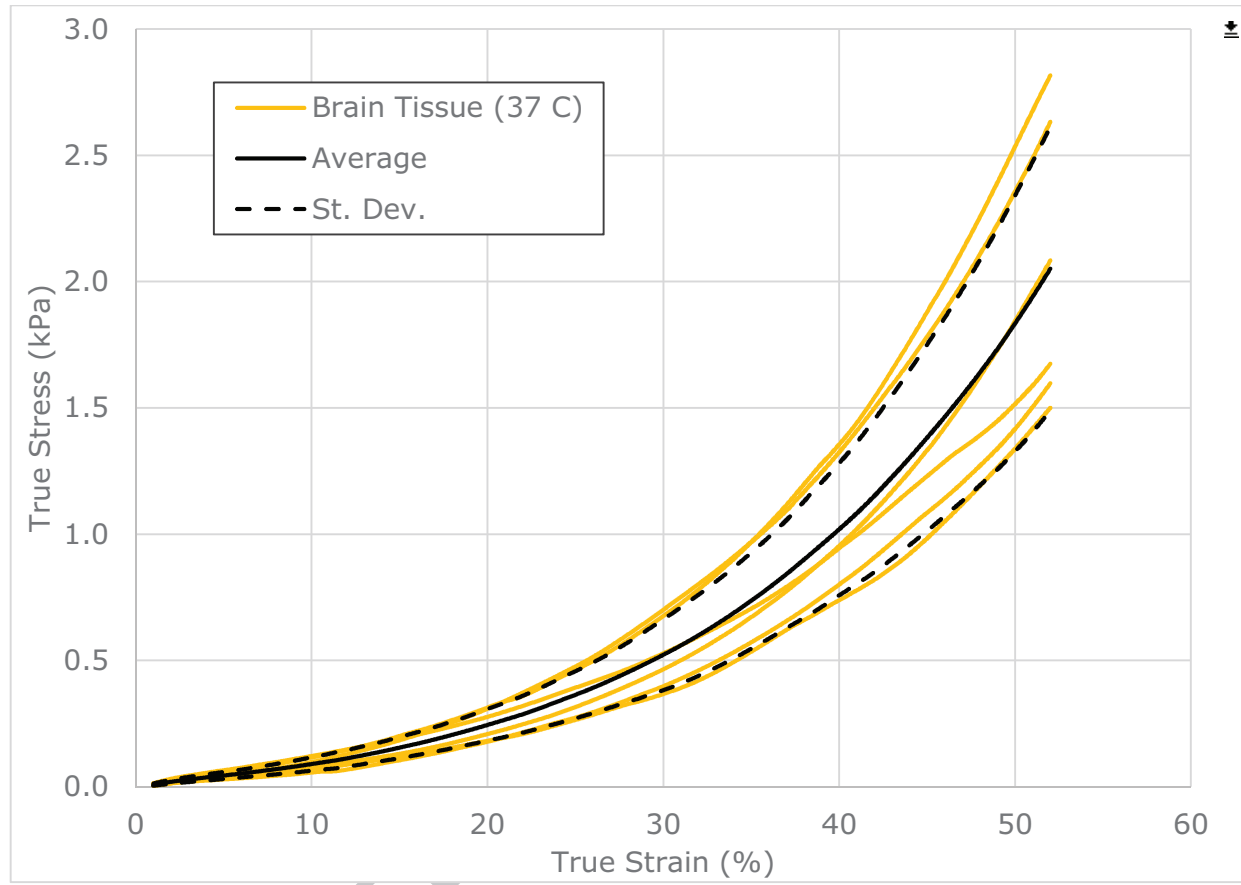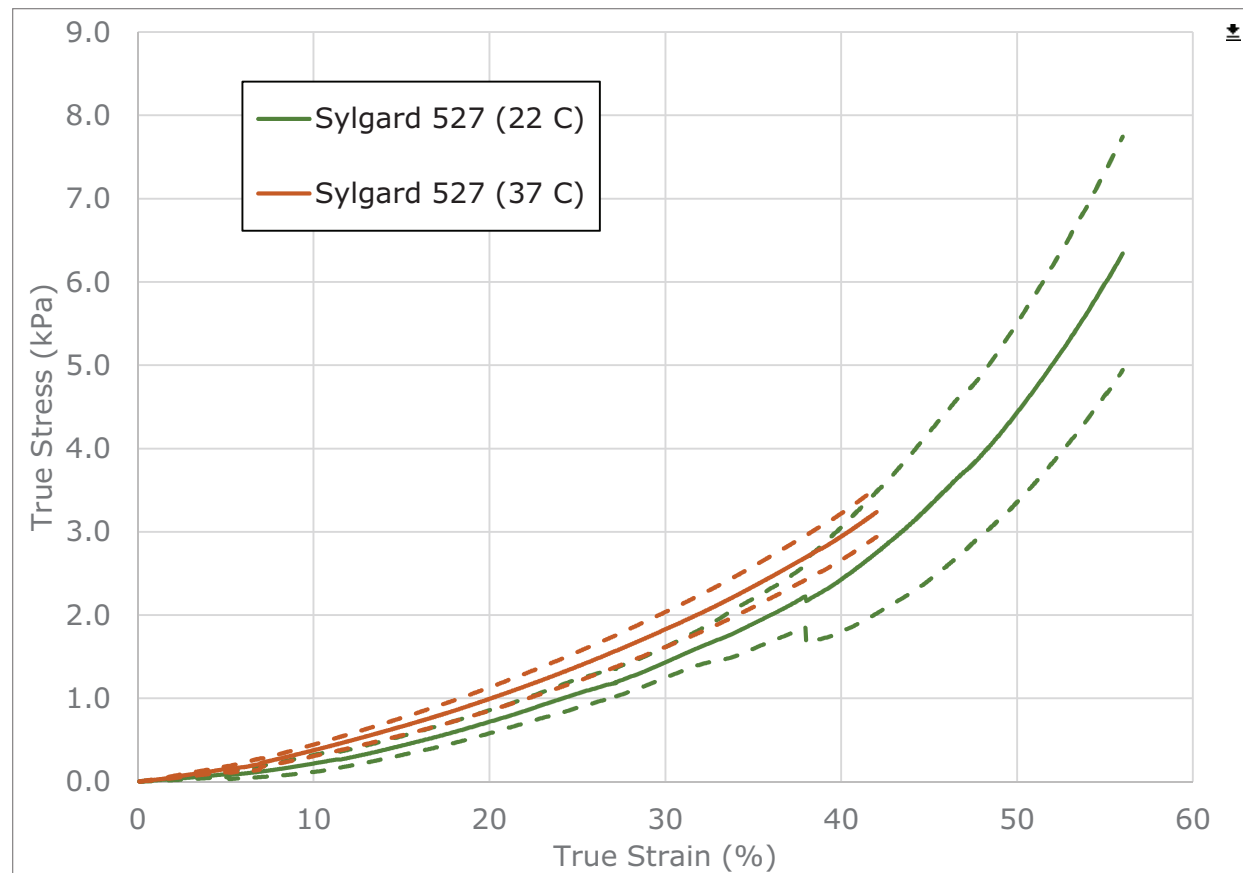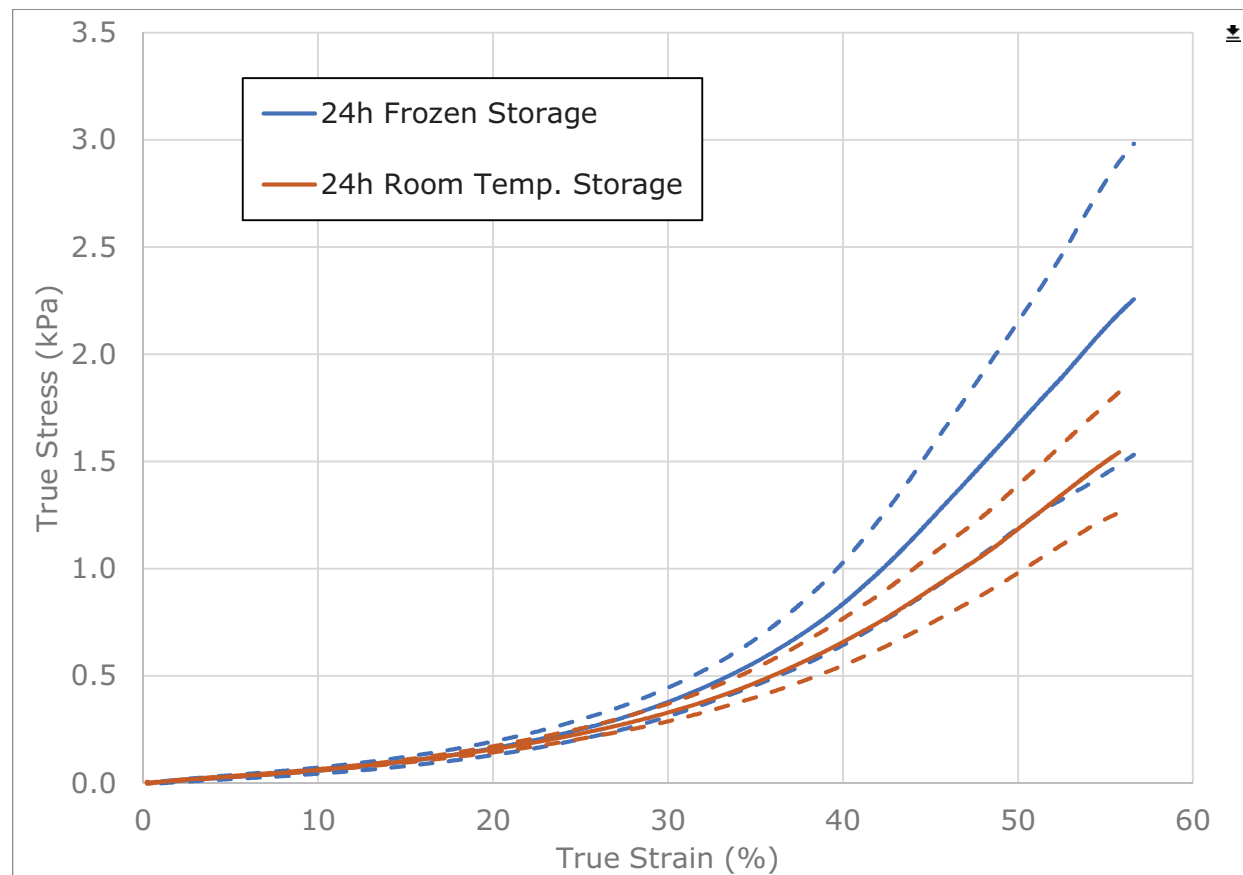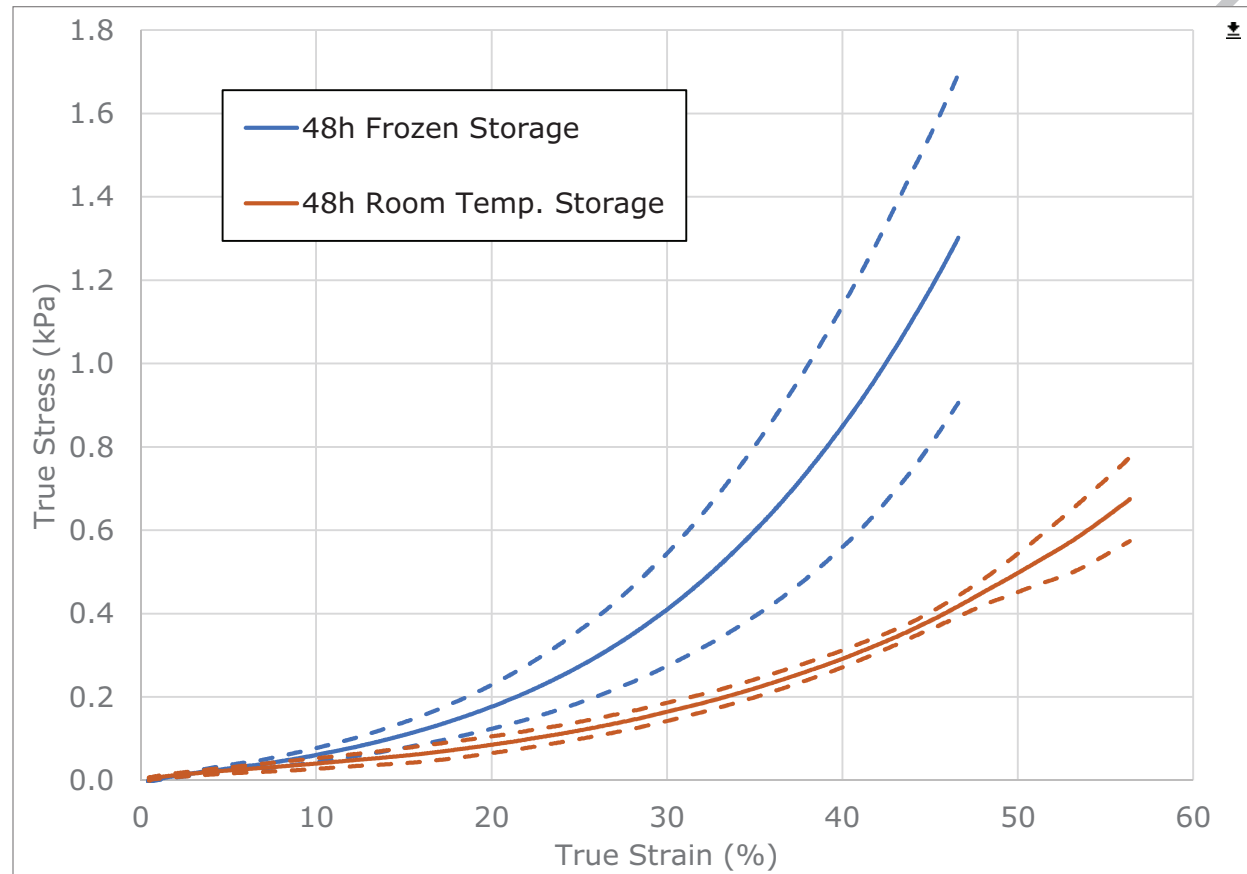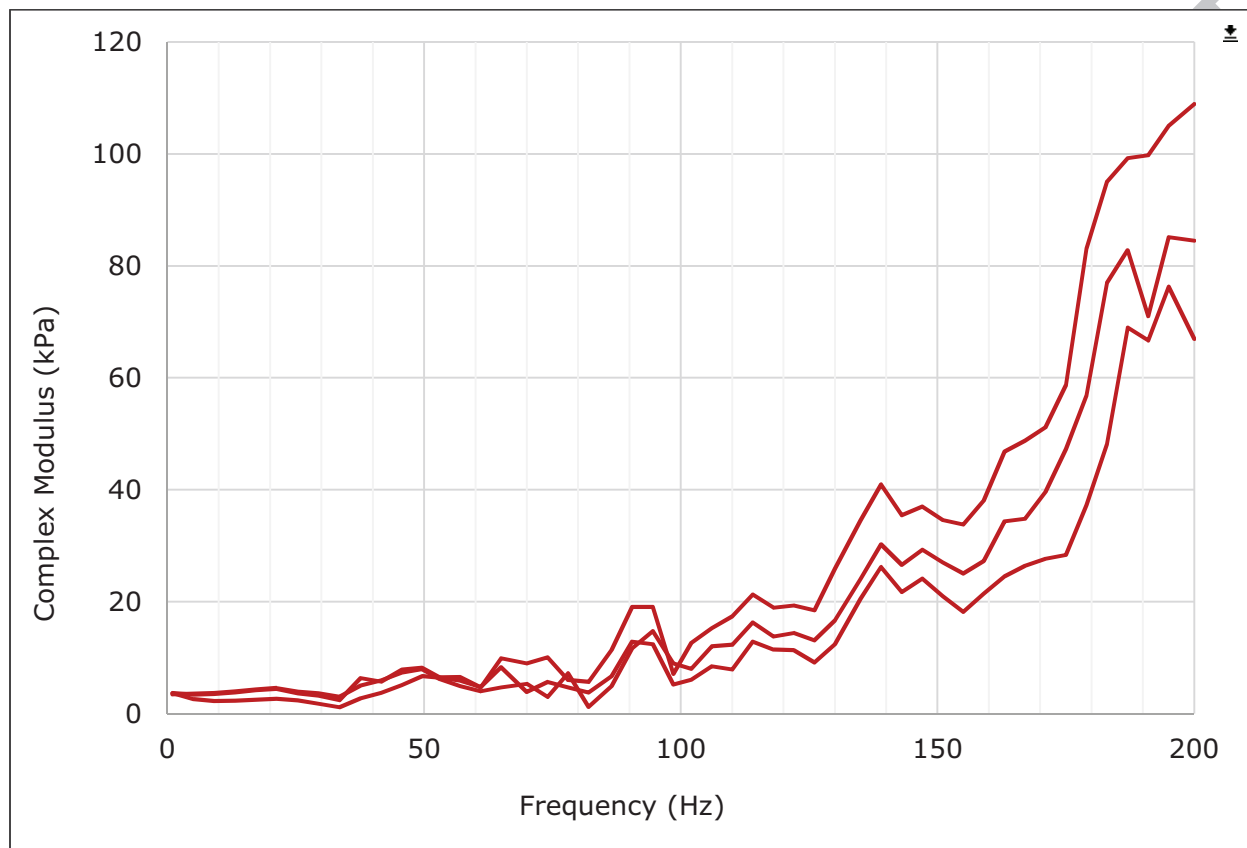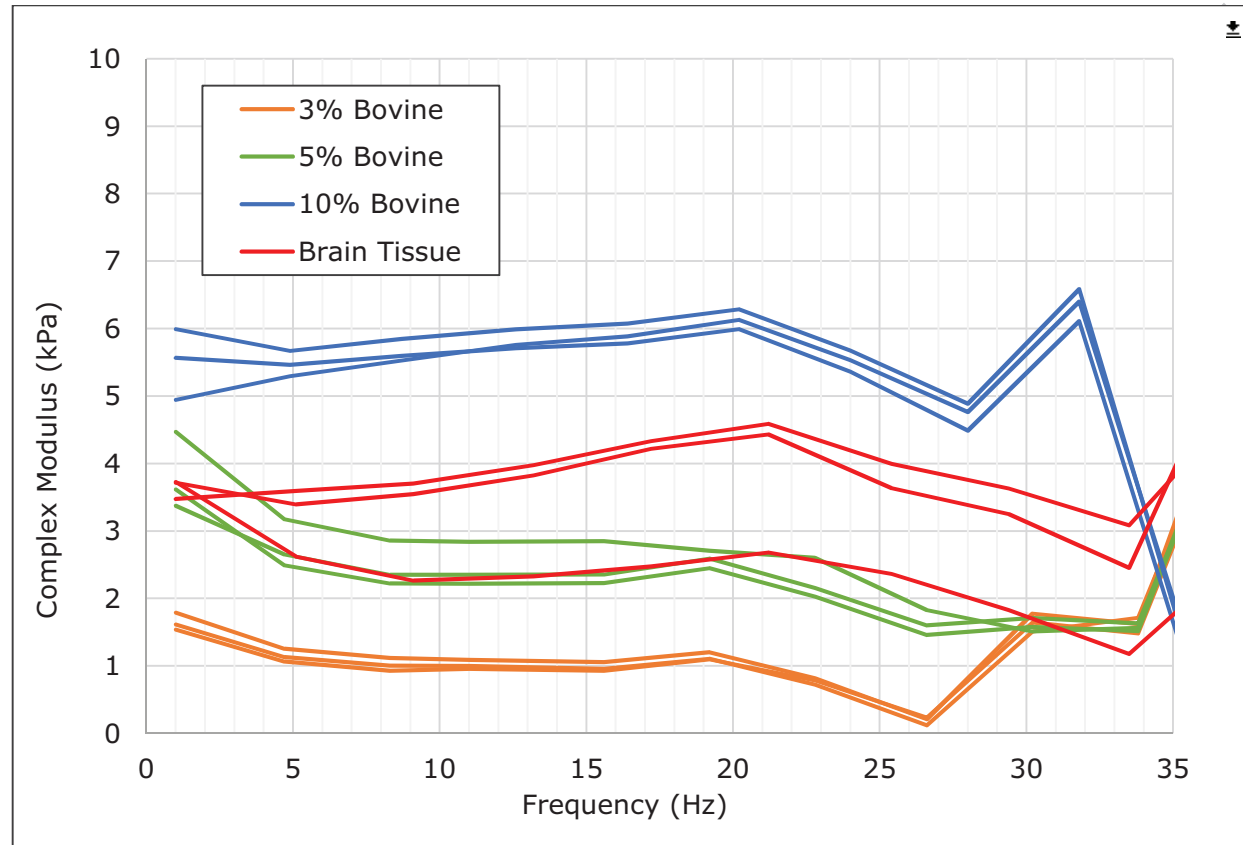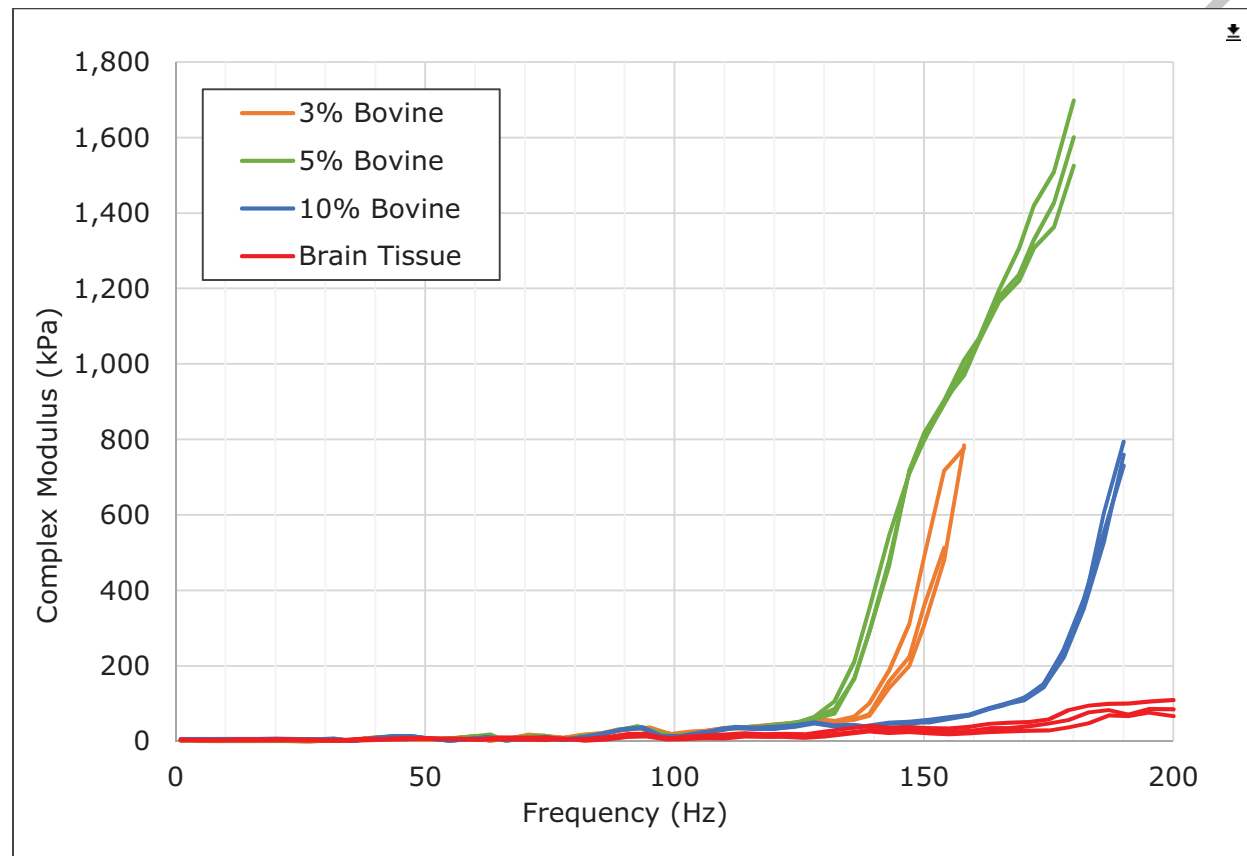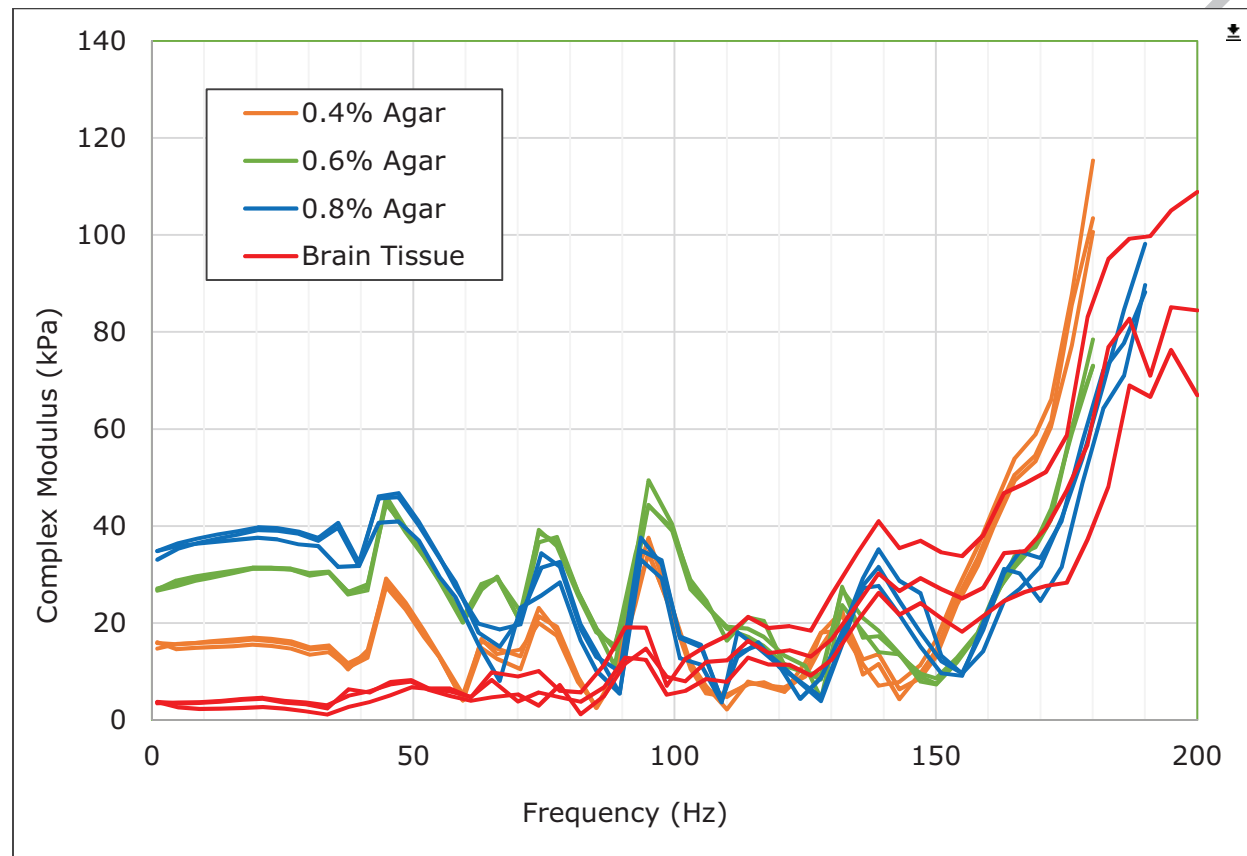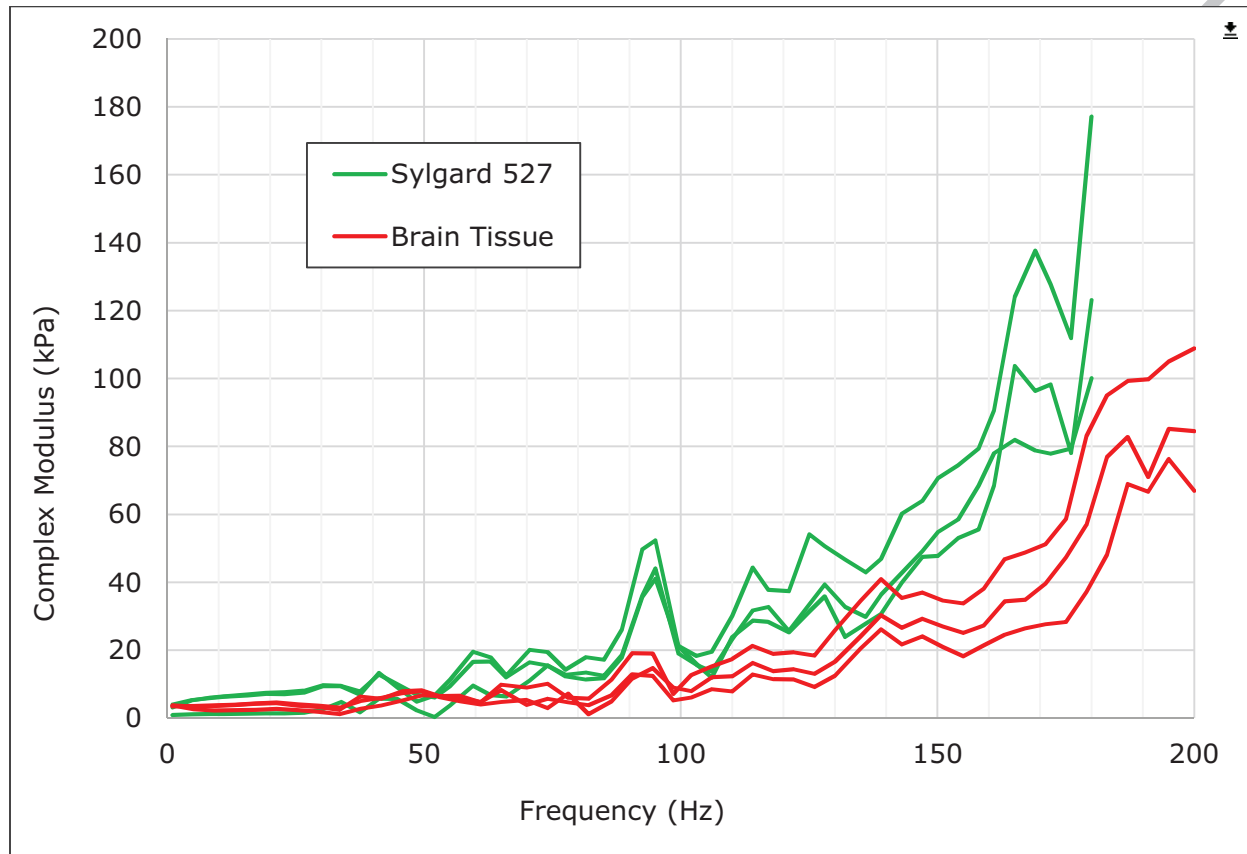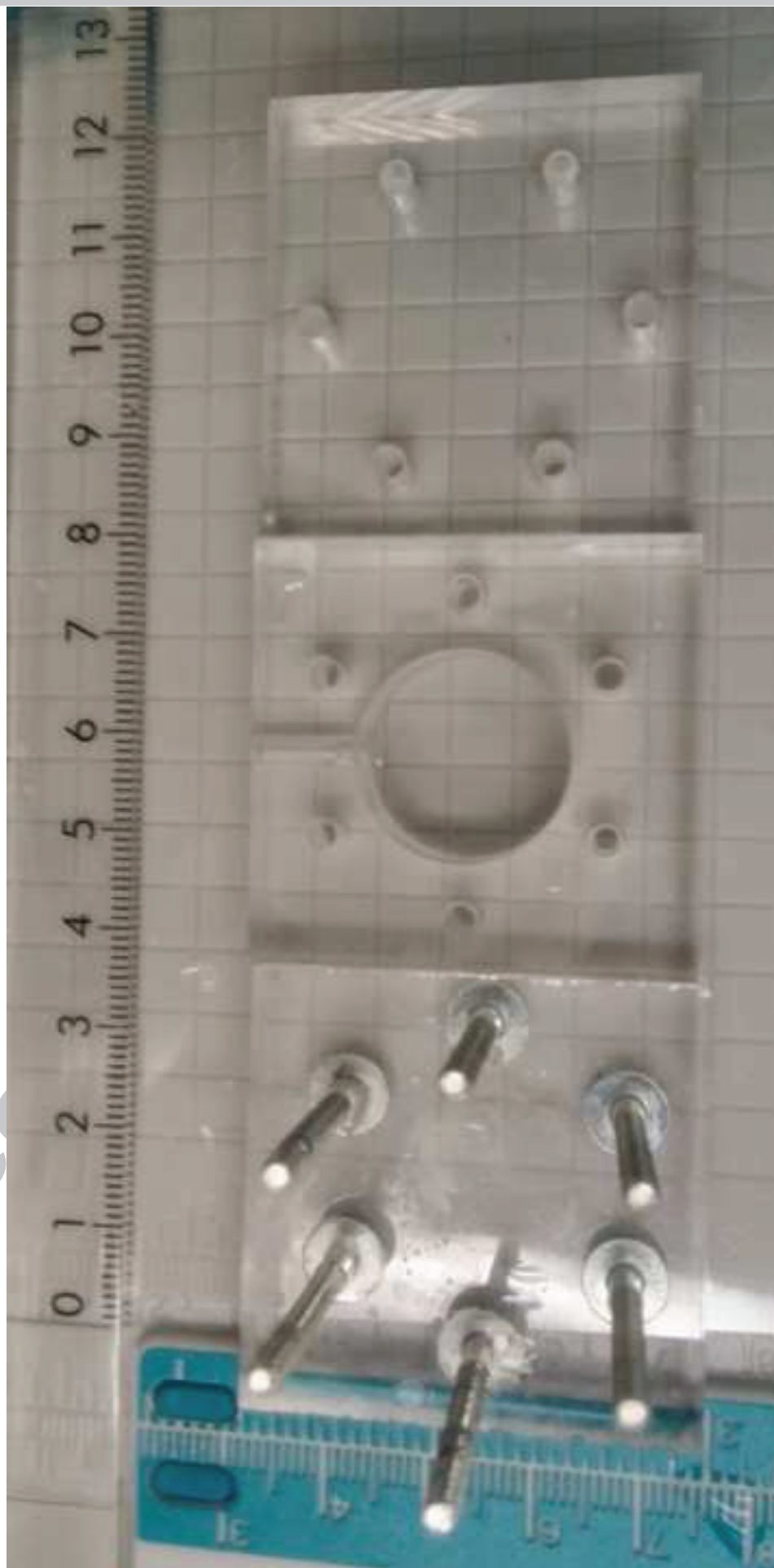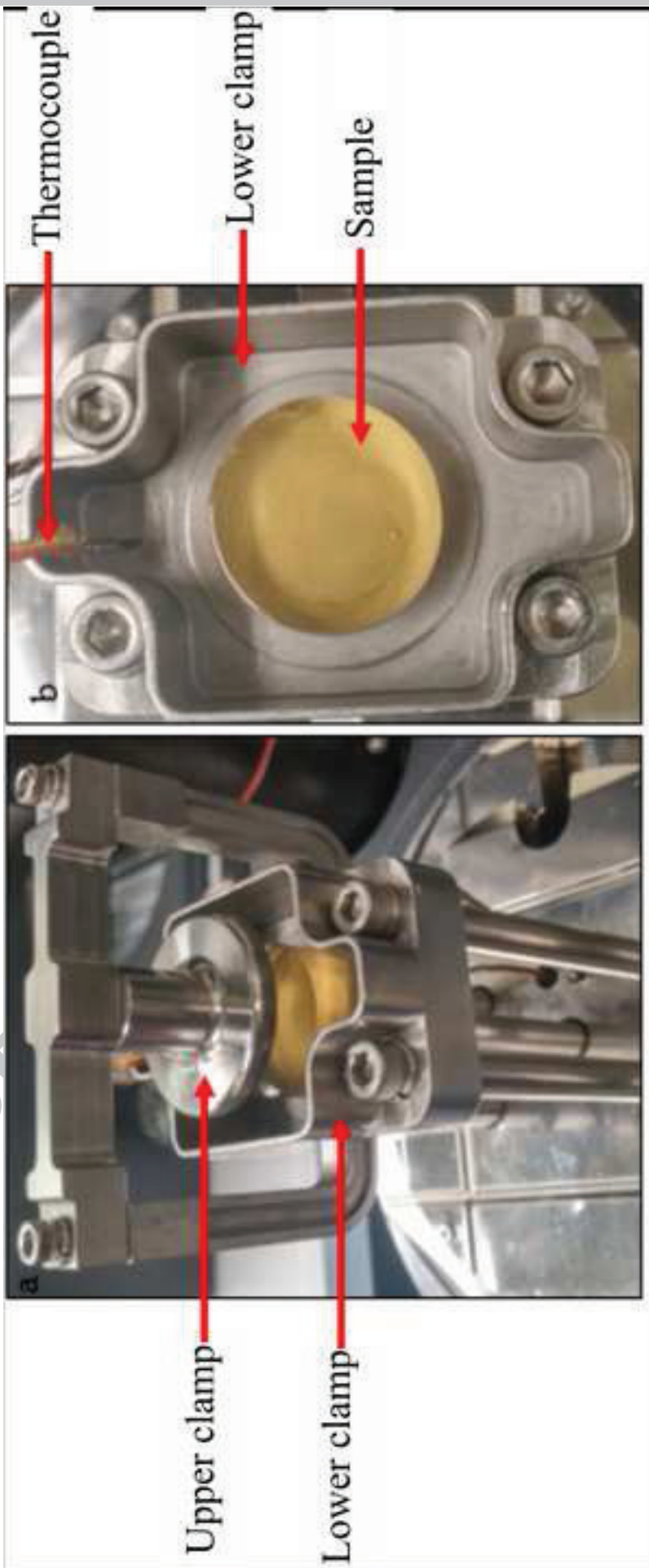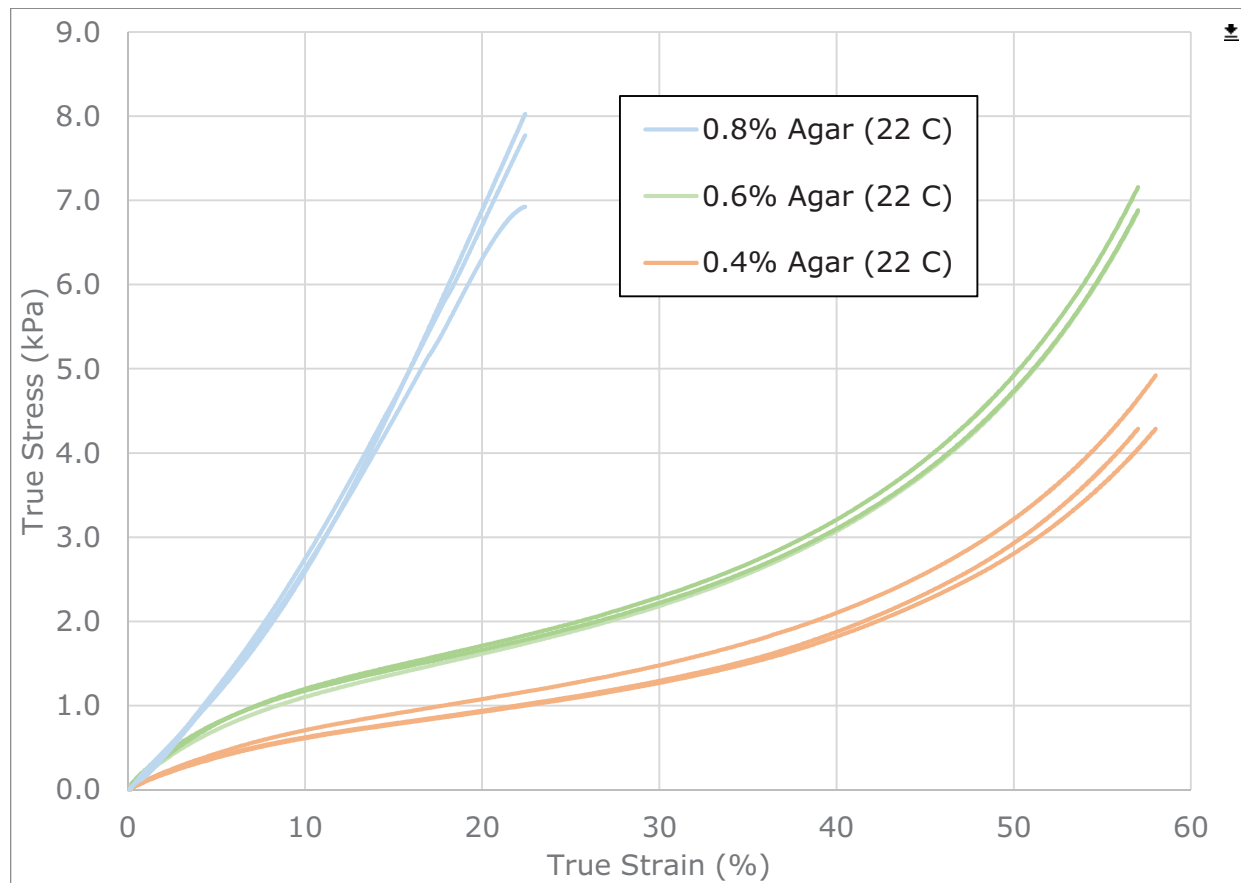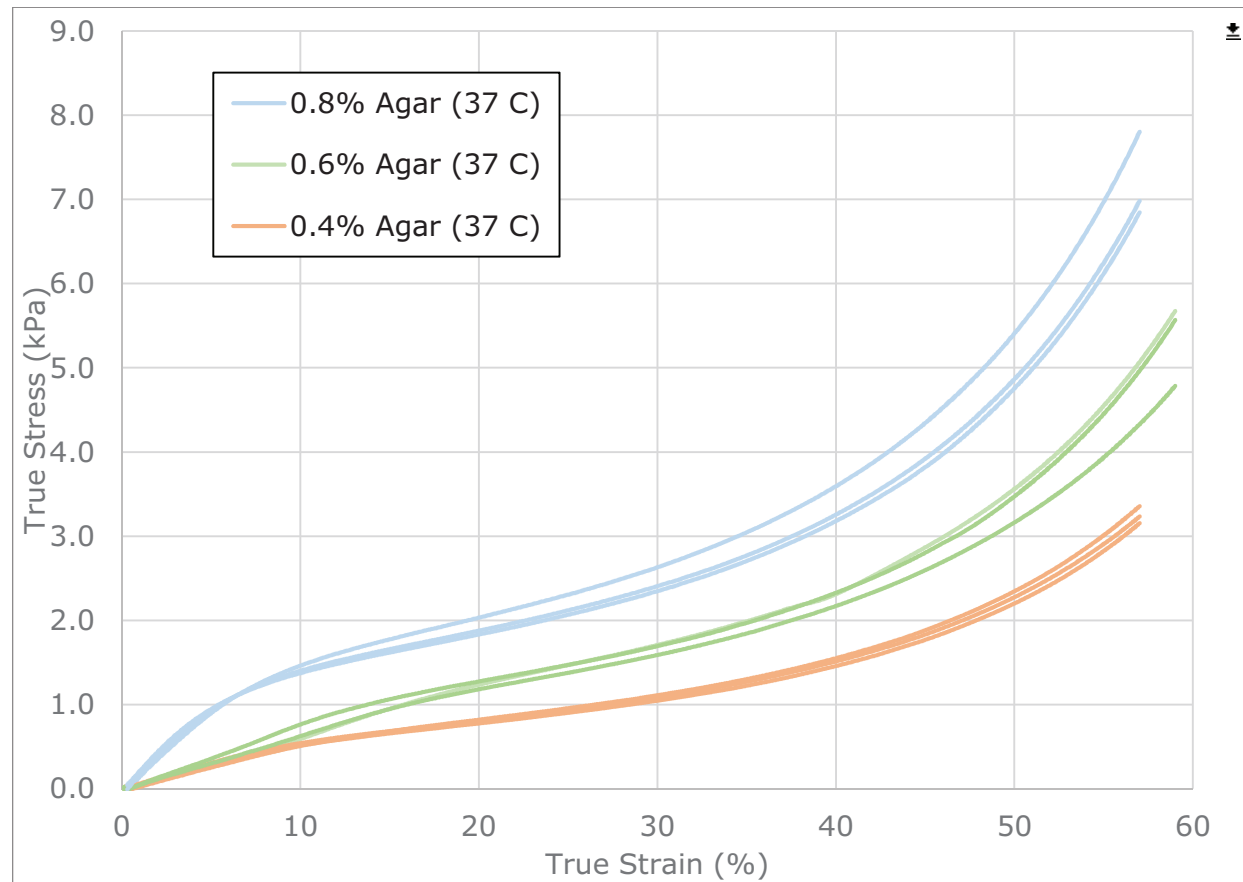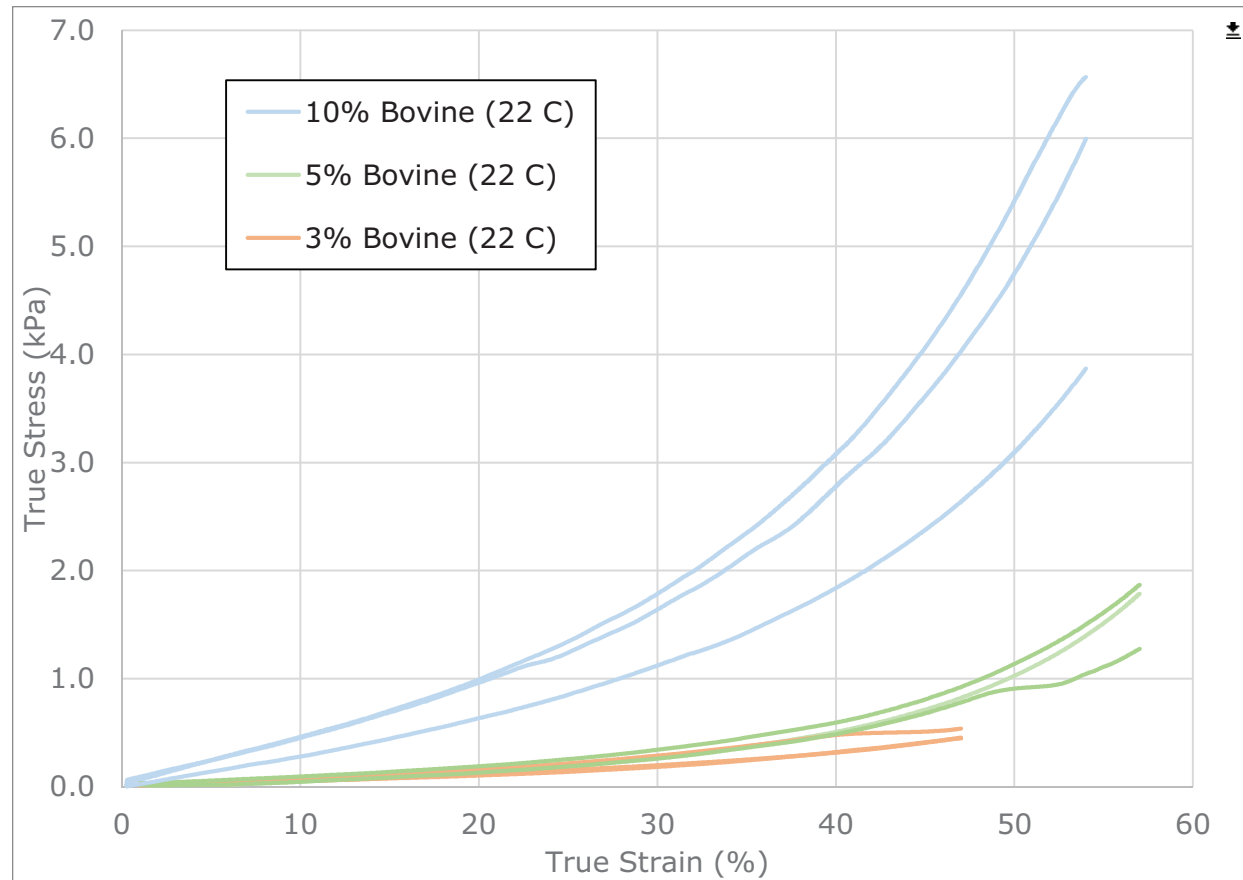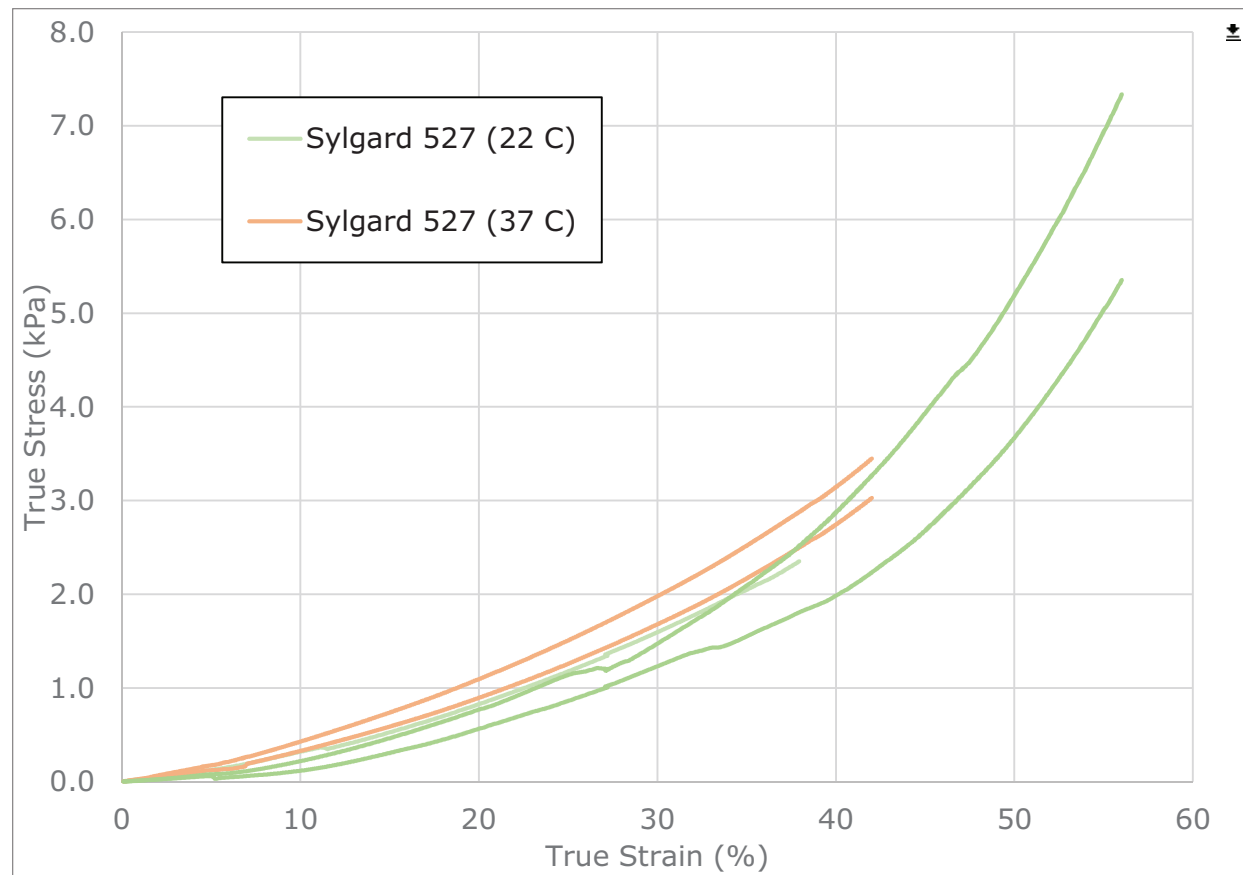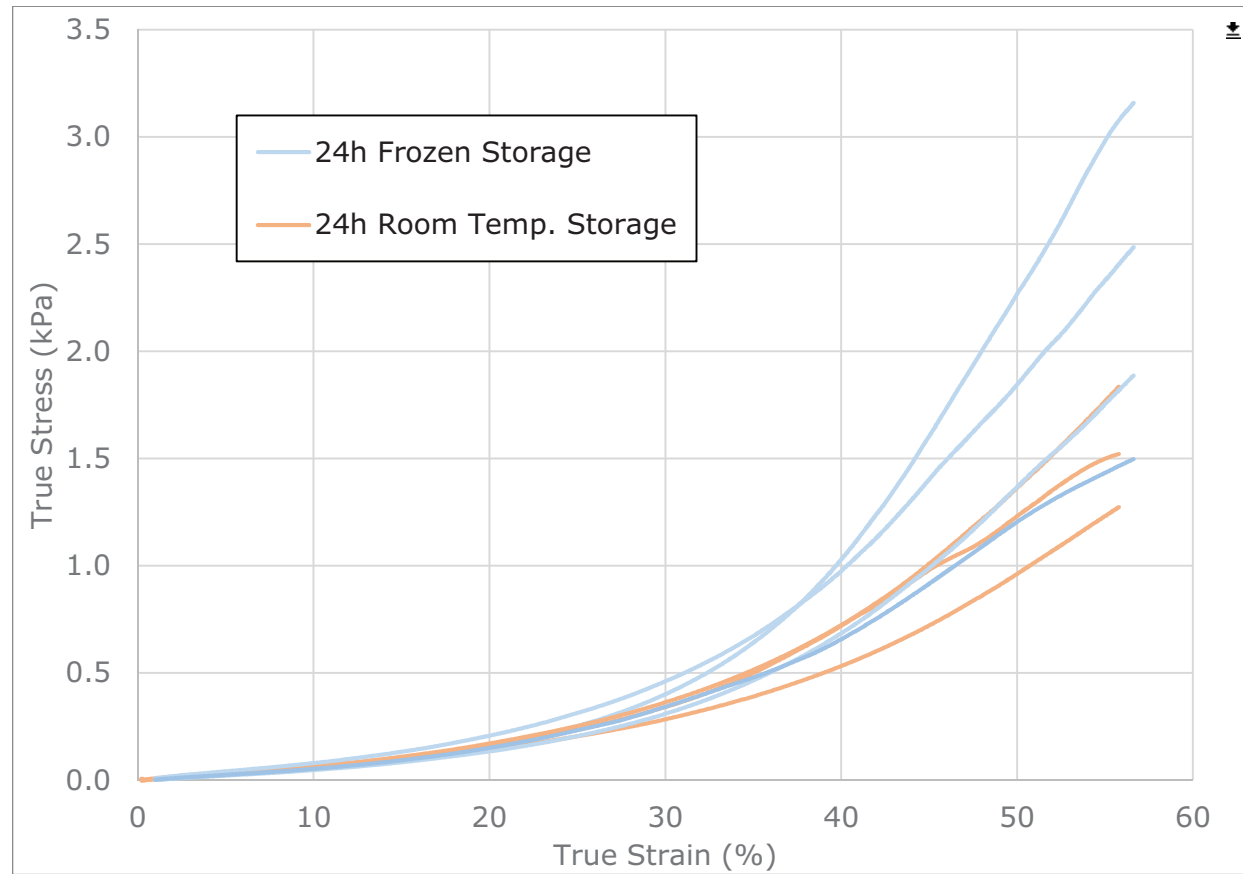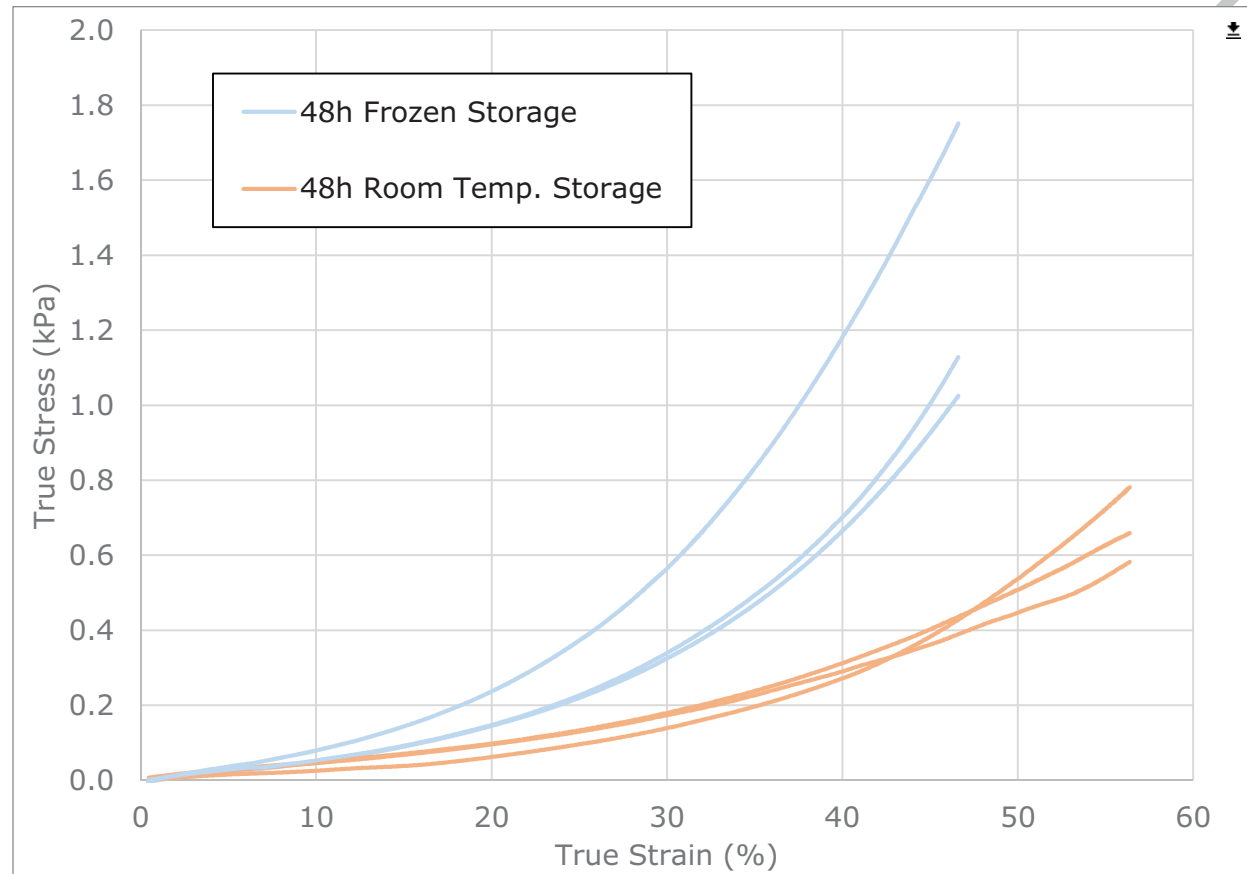
Table 1: Test matrix of tissue and simulant materials and test modes

			Test Temp.	QS Compression	DMA
Tissue	Fresh		22 °C	X	X
			37 °C	X	
	Room Temp. Storage	24h	22 °C	X	
		48h		X	
	Frozen Storage	24h	22 °C	X	
		48h		X	
Simulants	Agarose Gel	0.4 %	22 °C	X	X
		0.6 %		X	X
		0.8 %		X	X
		0.4 %	37 °C	X	
		0.6 %		X	
		0.8 %		X	
	Bovine Gel	3 %	22 °C	X	X
		5 %		X	X
		10 %		X	X
	Sylgard 527	1:1	22 °C	X	X
			37 °C	X	

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Table 2: Comparison of initial shear moduli (kPa) of tissue and simulants, quasi-static compression. Bolded rows indicate materials that were not found to be significantly different than porcine brain tissue.

Material; Test Temp.	Initial Shear Moduli	Mean	Stdev	t stat	t crit	p	
Brain, Fresh; Room Temp.	0.149, 0.233, 0.173, 0.149, 0.290, 0.102	0.183	0.068	-	-	-	
Brain, Fresh; Body Temp.	**0.358, 0.326, 0.203, 0.193, 0.206, 0.353**	**0.273**	**0.080**	**-2.11**	**2.23**	**0.061**	*
Agar, 0.4%; Room Temp.	3.459, 3.009, 3.009	3.159	0.260	-19.50	4.30	0.002	*
Agar, 0.6%; Room Temp.	5.729, 5.410, 5.777	5.638	0.199	-46.06	4.30	0.000	*
Agar, 0.8%; Room Temp.	6.542, 6.475, 6.066	6.361	0.257	-40.86	4.30	0.000	*
Agar, 0.4%; Body Temp.	2.370, 2.426, 2.555	2.450	0.095	-34.17	2.78	0.000	**
Agar, 0.6%; Body Temp	3.716, 3.147, 3.020	3.294	0.371	-13.95	4.30	0.005	**
Agar, 0.8%; Body Temp.	6.963, 7.014, 6.929	6.968	0.043	-162.84	2.37	0.000	**
Bovine 3%; Room Temp.	**0.259, 0.135, 0.159**	**0.185**	**0.066**	**-0.04**	**2.78**	**0.967**	*
Bovine 5%; Room Temp.	**0.155, 0.095, 0.153**	**0.134**	**0.034**	**1.43**	**2.37**	**0.197**	*
Bovine 10%; Room Temp.	0.742, 1.105, 1.064	0.970	0.199	-6.68	4.30	0.022	*
Sylgard 527; Room Temp.	0.784, 1.038, 0.582	0.801	0.228	-4.59	4.30	0.044	*
Sylgard 527; Body Temp.	**1.159, 1.486**	**1.322**	**0.231**	**-6.29**	**12.71**	**0.100**	**
24h Frozen; Room Temp.	**0.122, 0.117, 0.202, 0.164**	**0.151**	**0.040**	**0.92**	**2.31**	**0.382**	*
24h RT Stored; Room Temp.	**0.191, 0.176, 0.155**	**0.174**	**0.018**	**0.29**	**2.54**	**0.784**	*
48h Frozen; Room Temp.	**0.141, 0.144, 0.248**	**0.178**	**0.061**	**0.11**	**2.57**	**0.916**	*
48h RT Stored; Room Temp.	**0.064, 0.134, 0.133**	**0.111**	**0.040**	**2.00**	**2.37**	**0.085**	*

* compared to Brain, Fresh, Room Temp.

** compared to Brain, Fresh, Body Temp.

Table C1: Ogden constitutive parameters for quasi-static tests, room temperature (22 C)

	Sample	μ_1 (kPa)	α_1	μ_2 (kPa)	α_2	μ_3 (kPa)	α_3	R^2
	1	0.0297	10.003					1.000
	2	0.0529	8.796					0.998
	3	0.0360	9.607					0.999
Brain Tissue	4	0.0259	11.530					0.999
	5	0.0627	9.243					0.999
	6	0.0188	10.783					0.999
	avged	0.0359	9.974					1.000
	1	15.4007	4.175	-85.1580	2.465	124.2856	1.227	0.999
Agar 0.4%	2	14.3488	4.112	-76.0200	2.438	114.0308	1.161	0.999
	3	14.3488	4.112	-76.0200	2.438	114.0308	1.161	0.999
	avged	14.1926	4.172	-78.3868	2.463	114.4730	1.224	0.999
	1	21.0729	4.242	-134.4647	2.378	215.0950	1.124	0.999
Agar 0.6%	2	24.7470	4.117	-133.5332	2.430	203.9226	1.145	0.999
	3	22.0145	4.284	-138.1663	2.454	204.2251	1.255	0.999
	avged	21.2796	4.286	-133.7226	2.454	197.5722	1.256	0.999
	1	-1011.5782	-0.942	704.8624	-2.403	-189.6379	-3.973	1.000
Agar 0.8%	2	-877.1788	-0.700	452.1174	-2.202	-107.5442	-3.665	1.000
	3	-40.9765	4.095	247.7661	2.400	-427.4240	0.970	1.000
	avged	-804.0027	-0.875	491.9450	-2.359	-119.6480	-3.925	1.000
	1	0.0859	6.035					0.991
Bovine 3%	2	0.0356	7.600					0.998
	3	0.0464	6.872					0.998
	avged	0.0548	6.724					0.999
	1	0.0311	9.956					0.995
Bovine 5%	2	0.0170	11.211					0.997
	3	0.0338	9.023					0.997
	avged	0.0263	10.069					0.998
	1	0.1868	7.945					0.998
Bovine 10%	2	0.2610	8.470					0.999
	3	0.2601	8.180					0.998
	avged	0.2353	8.241					0.998
	1	0.1643	9.538					1.000
Sylgard 527	2	0.2592	8.005					0.998
	3	0.1238	9.405					0.997
	avged	0.1625	9.191					0.999

Table C2: Ogden constitutive parameters for quasi-static tests, body temperature (37 C)

	Sample	μ_1 (kPa)	α_1	μ_2 (kPa)	α_2	μ_3 (kPa)	α_3	R^2
	1	0.0753	9.516					1.000
	2	0.0648	10.051					1.000
	3	0.0416	9.748					0.999
Brain Tissue	4	0.0399	9.666					1.000
	5	0.0393	10.495					1.000
	6	0.0873	8.092					0.999
	avged	0.0561	9.619					1.000
	1	6.5930	4.646	-52.3193	2.620	67.2644	1.653	0.999
Agar 0.4%	2	9.6438	4.239	-55.6074	2.495	79.5392	1.292	0.999
	3	11.0286	4.119	-58.9094	2.444	89.0026	1.164	1.000
	avged	9.3443	4.288	-55.6284	2.516	77.9710	1.344	0.999
	1	9.2323	4.759	-82.6341	2.637	105.0313	1.727	0.998
Agar 0.6%	2	6.1242	5.046	-69.4298	2.702	84.0703	1.939	0.997
	3	5.8320	4.885	-57.1729	2.677	71.0632	1.838	0.999
	avged	6.6500	4.942	-69.4763	2.677	85.8730	1.859	0.998
	1	26.6291	3.929	-159.8095	2.114	402.5729	0.614	0.999
Agar 0.8%	2	29.6134	4.129	-164.4139	2.429	254.7633	1.143	0.999
	3	38.8447	3.680	-179.7193	2.164	421.5542	0.616	0.999
	avged	23.2556	4.142	-152.7434	2.234	299.5139	0.864	0.999
	1	0.3030	7.649					0.999
Sylgard 527	2	0.4179	7.112					0.999
	avged	0.3590	7.361					0.999

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Table D1: Comparison of areas under quasi-static stress-strain curves of tissue and simulants at room temperature

	Area at 5% strain	Percent Difference from Brain Tissue	Area at 30% strain	Percent Difference from Brain Tissue
Brain Tissue, Fresh	0.117	0%	4.162	0%
Agar 0.4%	1.107	842%	23.411	462%
Agar 0.6%	2.179	1755%	40.581	875%
Agar 0.8%	2.705	2202%	136.350	3176%
Bovine 3%	0.032	-73%	2.745	-34%
Bovine 5%	0.146	24%	4.228	2%
Bovine 10%	0.524	346%	19.538	369%
Sylgard 527	0.216	84%	16.109	287%

Table D2: Comparison of areas under quasi-static stress-strain curves of tissue and simulants at room temperature

	Area at 5% strain	Percent Difference from Brain Tissue	Area at 30% strain	Percent Difference from Brain Tissue
Brain Tissue, Fresh	0.099	0%	5.634	0%
Agar 0.4%	0.603	506%	18.582	230%
Agar 0.6%	0.728	633%	27.311	385%
Agar 0.8%	2.395	2309%	46.891	732%
Sylgard 527	0.288	190%	19.938	254%