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Impact of Data Quantity

Seiferheld, Bo Eitel; Andersen, Michael Skipper

Sensitivity Analysis of Cartilage Creep Material Properties Prediction in Unconfined Compression: Impact of Data Quantity

Bo E. Seiferheld[1*] and Michael S. Andersen[1]

[1]Department of Materials and Production, Aalborg University, Denmark
*Ph.D. student. bes@mp.aau.dk

INTRODUCTION
Osteoarthritis (OA), a prevalent and debilitating disease, involves progressive cartilage loss and altered joint features [1]. This has pushed advancements in cartilage tissue engineering for treatment and healing. Mechanical testing is crucial in the evaluation, but inconsistent testing techniques, across studies, leads to data misinterpretation and impede meaningful comparisons [2]. A recent review emphasized the need for 1 MPa creep stress with >60-min relaxation. Therefore, this study aims to assess the impact of data quantity on cartilage creep material property predictions, offering guidance for creep testing time modes.

METHODS
Ex vivo unconfined compression creep experiments were conducted using cylindrical 6-mm diameter, full-thickness cartilage samples (n = 11) extracted from bovine knees. An Instron material testing machine (Model 5944) performed creep experiments in a force-controlled setting with a preload of 0.05 MPa. After 15 minutes of preload, to reach baseline thickness and even out irregularities [3], a force ramping rate of 0.25 MPa/s reached the creep load of 1 MPa within 4 seconds. Creep load was maintained for 5 hours with continuous force and displacement recording at 10 Hz.

Experimental creep strain was split into six-time intervals (30, 60, 120, 180, 240 and 300 minutes) and fitted to two different models: (1) a standard linear solid model in Kelvin form and (2) a standard linear solid model with the elastic modulus (E_1) constrained and directly determined from the raw data. The creep equation [4] is as follows:

$$\varepsilon(t) = \frac{\sigma_0}{E_1} + \frac{\sigma_0}{E_2}\left(1 - e^{\left(-\frac{t}{\tau}\right)}\right) \qquad (1)$$

where ε is creep strain at time t, under constant stress, σ_0. E_1 is the initial elastic modulus, E_2 is the steady state elastic modulus and τ is the time constant for equilibrium. MATLAB 2022b was used for a nonlinear least-squares curve-fitting.

RESULTS AND DISCUSSION
The samples exhibited a baseline thickness of 2.06 ± 0.56 mm and reached a mean strain of 0.59 ± 0.06 at creep equilibrium. The initial strain following the ramp-up to the creep load averaged 0.14 ± 0.06, with an associated elastic modulus of 7.12 ± 2.62 MPa. All samples reached a well-defined equilibrium, as evidenced by less than 0.6 microns of deformation over one minute, achieved after 124 ± 23 minutes of loading, with a corresponding strain of 0.56 ± 0.06, only 5% deviating from the final creep strain.

The results highlight a noteworthy observation: Model 1 tends to gradually overestimate E_1 with optimiser bias toward fitting the viscous component, ultimately improving model fit. However, this inclination brings the solution closer to E_2 and τ. Conversely, Model 2 exhibits a fitting bias towards the linear elastic region, resulting in an underestimation of the viscous properties.
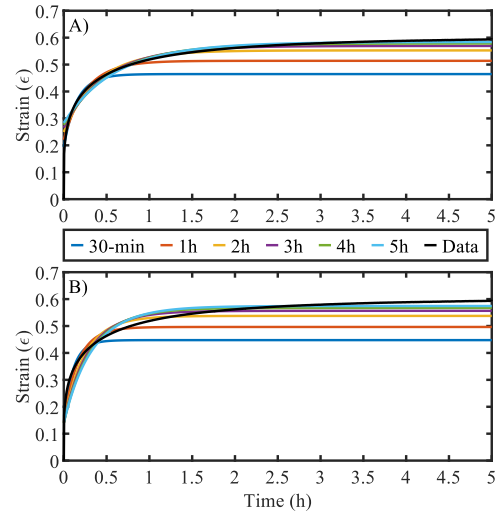

Fig. 1 Predicted strain based on six different time intervals with model 1 (A) and model 2 (B) and corresponding ground truth data in black.

CONCLUSIONS
For unconfined creep testing, it is advisable to maintain the stress for at least 2 hours to acquire sufficient information for model fitting. Lastly, setting a clear criterion for defining equilibrium and enrolling only those samples that meet this criterion are recommended.

REFERENCES
1. Glyn-Jones et al. *The Lancet* **386**: 376-387, 2015.
2. Patel et al. *Tissue Eng Part C Methods* **25**: 593-608, 2019.
3. Athanasiou et al. *J. Ortho Res* **9**: 330-340, 1991.
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Table 1 Cartilage material properties at different time intervals with the corresponding R^2 values.

	Model 1				Model 2		
	E_1 (MPa)	E_2 (MPa)	τ (sec)	R^2	E_2 (MPa)	τ (sec)	R^2
30-min	5.64 ± 1.59	3.75 ± 0.47	565 ± 87	0.72 ± 0.08	3.31 ± 0.40	395 ± 73	0.62 ± 0.08
60-min	4.87 ± 1.26	3.46 ± 0.39	943 ± 124	0.86 ± 0.05	2.85 ± 0.31	614 ± 112	0.75 ± 0.07
120-min	4.25 ± 0.99	3.33 ± 0.35	1464 ± 226	0.94 ± 0.02	2.55 ± 0.27	892 ± 168	0.85 ± 0.05
180-min	3.97 ± 0.86	3.32 ± 0.34	1818 ± 338	0.96 ± 0.01	2.43 ± 0.26	1066 ± 214	0.89 ± 0.04
240-min	3.80 ± 0.79	3.34 ± 0.33	2075 ± 429	0.97 ± 0.01	2.37 ± 0.26	1184 ± 251	0.91 ± 0.04
300-min	3.69 ± 0.75	3.35 ± 0.32	2265 ± 500	0.97 ± 0.01	2.33 ± 0.27	1268 ± 279	0.92 ± 0.03