

Accepted Manuscript

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PII: S1742-7061(17)30388-4

DOI: <http://dx.doi.org/10.1016/j.actbio.2017.06.024>

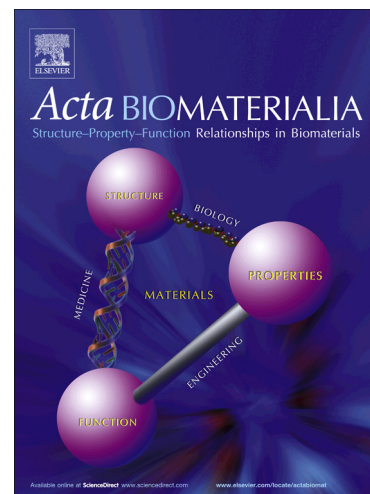
Reference: ACTBIO 4945

To appear in: *Acta Biomaterialia*

Received Date: 3 March 2017

Revised Date: 3 June 2017

Accepted Date: 15 June 2017



Please cite this article as: Budday, S., Sommer, G., Haybaeck, J., Steinmann, P., Holzapfel, G.A., Kuhl, E., Rheological characterization of human brain tissue, *Acta Biomaterialia* (2017), doi: <http://dx.doi.org/10.1016/j.actbio.2017.06.024>

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Rheological characterization of human brain tissue

S. Budday^a, G. Sommer^b, J. Haybaeck^{d,e}, P. Steinmann^a, G.A. Holzapfel^{b,f}, E. Kuhl^g^aDepartment of Mechanical Engineering, University of Erlangen-Nuremberg, 91058 Erlangen, Germany^bInstitute of Biomechanics, Graz University of Technology, 8010 Graz, Austria^cInstitute of Biomechanics, Graz University of Technology, 8010 Graz, Austria^dDepartment of Neuropathology, Medical University of Graz, 8036 Graz, Austria^eDepartment of Pathology, Otto-von-Guericke University Magdeburg, 39120 Magdeburg, Germany^fNorwegian University of Science and Technology, Faculty of Engineering Science and Technology, 7491 Trondheim, Norway^gDepartments of Mechanical Engineering & Bioengineering, Stanford University, CA 94305, USA**Abstract**

The rheology of ultrasoft materials like the human brain is highly sensitive to regional and temporal variations and to the type of loading. While recent experiments have shaped our understanding of the time-independent, hyperelastic response of human brain tissue, its time-dependent behavior under various loading conditions remains insufficiently understood. Here we combine cyclic and relaxation testing under multiple loading conditions, shear, compression, and tension, to understand the rheology of four different regions of the human brain, the cortex, the basal ganglia, the corona radiata, and the corpus callosum. We establish a family of finite viscoelastic Ogden-type models and calibrate their parameters simultaneously for all loading conditions. We show that the model with only one viscoelastic mode and a constant viscosity captures the essential features of brain tissue: nonlinearity, pre-conditioning, hysteresis, and tension-compression asymmetry. With stiffnesses and time constants of $\mu_\infty = 0.7$ kPa, $\mu_1 = 2.0$ kPa, and $\tau_1 = 9.7$ s in the gray matter cortex and $\mu_\infty = 0.3$ kPa, $\mu_1 = 0.9$ kPa and $\tau_1 = 14.9$ s in the white matter corona radiata combined with negative parameters α_∞ and α_1 , this five-parameter model naturally accounts for pre-conditioning and tissue softening. Increasing the number of viscoelastic modes improves the agreement between model and experiment, especially across the entire relaxation regime. Strikingly, two cycles of pre-conditioning decrease the gray matter stiffness by up to a factor three, while the white matter stiffness remains almost identical. These new insights allow us to better understand the rheology of different brain regions under mixed loading conditions. Our family of finite viscoelastic Ogden-type models for human brain tissue is simple to integrate into standard nonlinear finite element packages. Our simultaneous parameter identification of multiple loading modes can inform computational simulations under physiological conditions, especially at low to moderate strain rates. Understanding the rheology of the human brain will allow us to more accurately model the behavior of the brain during development and disease and predict outcomes of neurosurgical procedures.

Keywords: Human brain; Rheological testing; Finite viscoelasticity; Ogden model; Parameter identification

1. Introduction

The rheology of the human brain plays an important role in brain function and failure [1]. With the opportunity to develop personalized three-dimensional human head models [2], computational simulations are promising tools to predict mechanically mediated pathways of brain damage [3] and to improve neurosurgical procedures [4]. The quality of numerical predictions critically relies on accurate constitutive models and, equally importantly, on the thorough calibration of their model parameters [5]. Model calibration is extremely challenging since the rheology of materials like the brain strongly depends on the spatial and temporal scales of interest [6]. Variations in experimental protocols, loading modes, loading rates, and spatial resolution have generated contradictory results both

qualitatively and quantitatively [7]. Clearly, to develop an appropriate rheological model, it is essential to understand the loading-mode specific, time-dependent material response. Even for quasi-static loading rates, brain tissue exhibits a highly nonlinear, conditioning, hysteretic, and tension-compression asymmetric behavior [8–10]. While several studies have identified the linear viscoelastic material parameters of human brain tissue at small strains and under a single loading mode [11–15], time-dependent phenomena at finite strains and under arbitrary loading conditions remain less well characterized. So far, large strain viscoelastic constitutive models have only been calibrated for porcine brain under a single loading mode [16–18], but not for human brain under multiple loading modes. The objective of this study is therefore to establish a finite strain, nonlinear, viscoelastic constitutive model that captures the response of human brain tissue under various loading conditions. We performed simple shear, uncon-

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