Rheological regional properties of brain tissue studied under cyclic creep/recovery shear stresses

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Abstract. The rheological properties of brain tissue were studied by repeated creep-recovery shear tests under static conditions for different regions, Corpus callosum CC, Thalamus Th and Corona radiata CR. Non-linear viscoelastic model was also proposed to characterize the transient/steady states of shear creep results. From the creep-recovery data it was obvious that the brain tissues show high regional anisotropy. However, the both samples exhibit fluid viscoelastic properties in the first shear stress cycle of 100 Pa, while this behaviour evolutes to solid viscoelastic with cyclic effect.

1. Introduction

Traumatic brain injury (TBI) is considered as a major worldwide health problem. In developing countries accident rates in general and traumatic brain injury in particular are increasing as traffic increases besides other factors like industrialization, falls and ballistic trauma [1]. The importance of protecting the head from injury during impact and after, is gaining wider recognition, which implies a good knowledge of the mechanical behaviour of the structure to be protected and in particular the cerebral matter. Rheological phenomena may result in shortening of the durability of structural components. Obviously, it is not possible to study in experiments the influence of a violent shock on an in vivo human head. The researchers thus had recourse to the technique of modelling by the finite element method (FEM) of the human head to understand and to predict head injuries [2], [3] ... These FE models often contain a detailed geometrical description of the anatomical components but lack accurate descriptions of the mechanical behaviour of the brain tissue. As well, as the bio-fidelity of these objects depends intimately on parameters which characterise the modelled organic material making essential in this way its experimentation. In parallel, in vitro studies were realized in small proportion on the man [4-6] and mainly on the animals, mostly porcine brains [6-11], when the availability of mechanical data on in vivo tissues remains limited [4], [12-13]. An overview of previous studies on the mechanical properties of brain tissue is giving by Harpko et al. [10]. In these studies brain tissue can be described as viscoelastic material but with different results as in the shear modulus [9]. These considerable differences in results may be caused by variations in material tested, test conditions, testing protocols...

In current study, the inter-regional creep and cycling stresses effects on in vitro porcine brain tissue are studied. We will try to determinate a model of a brain shock response based on detailed material...
data carried out *in vitro* on three different regions testing under shear stress of 100 Pa. In fact, we started the test by short logarithm scale time at the first second to studies the transient state.

2. Materials and methods

2.1. Samples preparation
The samples used result from fresh porcine brains; were obtained from a local slaughterhouse. Slices from the corona radiata (CR) and corpus callosum (CC) substances from white matter, thalamus (Th) substance of 2 mm were cut. Porcine brain tissue from six-month-old pig brains was chosen as a substitute for human brains because of availability and the possibility to minimise the post-mortem time at testing [6]. To prevent dehydration and to slow down degradation of the tissue, the brains were placed in a physiological solution of Ringer-lactate at 6 °C immediately after acquisition and subsequently were tested within post mortem times ranging 5 hours after sacrifice. From the slices, cylindrically shaped samples were obtained from, using a cylindrical sharp tube with a diameter of 20 mm which was applied from the medial to the lateral side.

2.2. Creep/recovery test
Measurements were conducted using a controlled-stress rheometer (Carri-Med CSL100) in parallel plate configuration. The samples are subjected to angular shearing’s under constant stress $\sigma_0$ of 100 Pa for 30 s then it was left to recover for 30 s, during which the compliance $J$ (creep/recovery) values versus time are recorded. During the test, samples were covered by a moist chamber to prevent dehydration and tested at (20±0.1) °C. By keeping the same sample to reduce the effect of inter-sample variation, and then tested a second time following the same procedure eight times in order to study the load effects and to characterize the tolerance criteria. Between each cycle, the material was left to recover for up period of 60 s at zero shears. In order to check the sample adhesion, it was glued to the upper and lower plate of the rheometer with cyanoacrylate adhesive to prevent slippage during the shearing of the sample.

3. Results and Discussion

3.1. Creep/recovery measurements
In this study, creep-compliance tests were carried out in order to determine the parameters evolution of rheological behaviour model for different brain tissues regions and cyclic effect under static conditions. The viscoelastic properties of the cerebral matter were studied by imposing a constant shear stress in transient and steady state. The porcine brain samples taken from CR, CC and Th regions are tested under constant cyclic shear stresses of 100 Pa. Firstly, the stress was applied for CC sample during 30 s and the resulting compliance was measured taking logarithmic scale for the first second, then the N same stresses was reapplied each 2 min eight times. A compilation of the shear creep-recovery curves of this sample are presented below in figure 1. Then, from each first creep phase, inter-regional comparison between three samples: CC and CR sample from white and Th from gray matter is shown in figure 2. The creep evolution of the time deformation for each curve (see the first creep part of CC sample in figure 1 and 2) can be resuming in three quite distinct phases:

- **Instantaneous Elasticity (from O to A)** represented by instantaneous compliance $1/k_0$ with underdamped oscillations. The observed response can be influenced by the application of shear stress at short times [14] or other factors as, it is common for elastic samples to resonate with the applied actuator and transmit transient waves through the sample. These oscillations due to the important shear rate represent typically non-linear viscoelastic behaviour [15] were also observed in the study [16] of living tissue including a stress of 150 Pa; which the use of a nonlinear viscoelastic model showing that the model response did not closely represent the vibration of the experimental result as like Kelvin-Voigt generalized model. So in this work we used this unsteady state to deduce directly the viscoelastic parameters of the brain sample.
- **Primary creep region (from A to B)** this phase presents a time dependent where the shear strain rate decreases with time. This second region can be represented by Kelvin-Voigt body and determine the characteristic parameters [17].

- **Secondary Creep region (from B to C)** it’s a linear phase where the brain sample moves in only viscous flow. Generally the deformation of this phase is irreversible.

![Figure 1. Creep-recovery curves of the CC sample response under eight cyclic shear stresses $\sigma_0$ at 100 Pa level in real time.](image)

![Figure 2. Comparative curves of the different region samples: each creep phase consists of instantaneous elastic (OA), retarded elastic (AB) and viscous (BC) deformation.](image)

Once the stress is removed we can see a partial recovery of the deformation indicates the non-linearity of the material behaviour. The sample was destructed and the irrecoverable deformation (represented by $J_v$ in figure 1) can be considered as memory effect. The rest has been dissipated in viscous flow (approximately 50 % of deformation at the first cycle), that confirmed the finding of [17]. The overall pattern of rest white matter curves was similar with total decrease of values: the difference between successive cycles is decayed exponentially, and eventually disappears at the sixth stress for CC sample (as reported in figure 1), due to the straightening of axons fibres. It is distinct from the other central nervous system regions, in that it has longitudinal arrangement of axonal fibers, rather than a more random distribution [18]. It is seen in many others studies that the mechanical properties of the corpus callosum substance is remarkably different from an author to another [7], [10-11], [17]. These differences can be due to many experimental conditions of the tests as the type of the sample cut tested region which presents a high structural anisotropy. The CC substance presented high strong force and become more elastic with cyclic number could be a consequence of the orientation of the axonal fibers. Inter-regional comparison between the creep curves of both samples shearing at 100 Pa, as showing in figure 2 indicated a few difference between CC and CR from white matter and the Th from gray matter properties in shear. These curves showed that the Th region is stiffer than CR region than CC region in shear at this stress level, which coincides with previous comparisons regional studies [11], [19].

3.2. **Creep test mathematical model**
In order to studies the evolution of the rheological behaviour of brain tissue under constant stress; we are interested first to model its response in transient then in steady state. Typically at short time we can observe damped oscillations, which after the deformation take a certain asymptotic variation. The most common mechanical equivalents of rheological behavior are the Maxwell and Kelvin models. Burgers model [20] or $i^{th}$ order generalized Kelvin-Voigt which is a Kelvin and a Maxwell model placed in series can be used to analyze the creep data in steady-state. This model ensures a good description of the polymeric and the biological general observed behaviours [5], [21-22]. But this
standard model presents insufficiencies when we want to characterise the details of the transient which are not correctly fitted. For this reason we associate to the first term of the Kelvin Voigt model an underdamped function. The creep curves of cerebral tissue present a viscoelastic liquid behaviour for a value of the imposed constant shear stress $\sigma_0$ of 100 Pa, which can model by:

$$J(t) = \frac{1}{k_0} (1 - \frac{1}{\sqrt{1 - \xi^2}} e^{-\omega_0 \xi t} \cos(\omega_0 \sqrt{(1 - \xi^2)} t - \varphi)) + \frac{1}{k_1} (1 - e^{-t/\eta_1}) + \frac{1}{k_2} (1 - e^{-t/\eta_2}) + t/\eta_{\infty}$$ (1)

Where $1/k_0, 1/k_i$ are the instantaneous and the retarded creep compliances. $\eta_i, \eta_\infty$ are the dynamic and the Newtonian viscosities. $\xi, \omega_0, \varphi$ are respectively : the damping factor, the natural frequency and the oscillator phase.

The theoretical model $J(t)$ proposed is perfectly adapted to represent the experimental creep curves for all creep stages of each sample, as seen in the figure 3 for Th sample sheared under a constant stress of 100 Pa during 30 s. By adapting for each cycle the parameters values evolution are studied with more detail in other paper submitted to publish.

![Creep model curve of the first cycle experiments results of Th sample sheared under a constant stress of 100 Pa during 30 s](image)

Creep compliance value is mainly associated with softness. The increase of the stress level risk damaging the cerebral matter, over a certain stress value. The degradations result in the loss of elasticity or dissipated flow under 100 Pa stress level as shows it the first incomplete recovery curve (see figure 1). By applying N steps of a same constant shear stress for 30 s on the brain sample, where each step change the internal structure of the brain tissue and transform the mechanical proprieties.

4. Conclusion

The present paper outlines around a mechanical characterization of three different regions in the brain from white and gray matter, which are the corpus callosum, corona radiata and thalamus. These regions present a distinct structures and mechanical properties. The results obtained from the creep tests in shearing were performed to determine the evolution of viscoelastic behaviour under static conditions. A constant shear stress of 100 Pa was applied on the CC, CR and Th samples for 30 seconds and the resulting creep compliance $J$ was measured. This creep tests proved that the three substances have reversible part due to their elasticity besides an irreversible part due to the viscous properties with differences between their properties in creep. From those results we can showed that the Th region is stiffer than CR region than CC region in shear at this stress level. The stiffness effect of CC samples which present a high structural anisotropy, can explain by crosslinked of the brain fibers with cyclic shearing and the significant liquid loss part, which give a rigid matter. The elasticity parameters in transient, as in steady state can be determined with novel theoretical compliance model. Finally we can easily characters the behaviour of the brain matter under shear stress with a classical creep/recovery tests. The repeated solicitation of the shear stress reveals a memory phenomenon which transforms the behaviour of the brain tissue.
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