Exploring the Intervertebral Disc Creep through Mathematical Modeling. An *in vitro* study.

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Disclosures: -

INTRODUCTION: The intervertebral disc (IVD) is a complex biological structure due to its biphasic character and its viscoelastic properties. Acting as a shock absorber, the IVD ensures together with the other spinal structures that high loads are supported and that the spine remains stable, mobile and flexible. This results in complicated relationships between external loads, the mechanobiology of the disc and its homeostasis [1]. However, although the viscoelastic properties of the IVD are often discussed in the literature, even today it is still not fully understood [2]. Since the viscoelastic properties of soft tissue have been mathematically analyzed extensively, modeling the creep behavior of the intervertebral disc is a valuable and promising approach to gain new insights into the biomechanical behavior of the IVD: Analyzing the time-dependent deformation (creep) of the IVD will provide important tools to investigate how prolonged loading can affect the nutrient transport, i.e., hydration and water transport, cell viability, matrix synthesis and the mechanosensitive activity of the disc. This study aims to evaluate different mechanical constitutive models to describe the viscoelastic characteristics intermediate between solid and fluid of the IVD. Therefore, a mathematical model can be useful to fully understand the relationship between the macroscopic and cellular level. Specifically, the long-term goal will be to identify a connection between the loading rate and the disc hydration state, as well as to further comprehend the whole mechanism behind disc degeneration and aging [3]. Hence, an *in vitro* study was performed on human cadaver specimens, with the aim to assess if the classical rheological models and Nutting's power law were able to guarantee a good modelling and fitting of the IVD creep behavior.

METHODS: Eight lumbar segments (L4-5) from fresh-frozen human spines with an average age of 48 years (range: 38-58) were used. For this study, specimens with bone defects or a degree of disc degeneration greater than 1 were excluded. The specimens were stored at -20 °C and thawed at 4 °C for 16 h before the experiment. After preparing and embedding in PMMA, the specimens were fixed in a universal spine tester [4] and loaded at pure unconstrained moments in bending and extension to assess the absolute neutral position. Next, the specimens were driven to the neutral position, enabling only the vertical translation measured by an inductive linear displacement sensor connected to the spine tester. A creep test was then performed by applying an axial compression load of 500 N for 15 minutes. Reduction in height of the intervertebral disc was considered and evaluated using the different rheological models and Nutting law to identify which constitutive model better fit the original data (Fig. 1) (Wolfram Mathematica v13. Software). A correlation analysis was performed to evaluate any relationships between the model parameters and the maximum value reached by the height disc reduction (DHR) (RStudio Software).

RESULTS SECTION: The creep curves were obtained for each specimen. An immediate reduction of the intervertebral disc height from the initial values resulted (mean values 0.94 mm). After 15 minutes, the disc height decreased by an average of 1.14 mm (min: 0.91 mm and max: 1.44 mm). From the data fitting, it was found that the Maxwell and Kelvin-Voigt models were not able to fit the data; meanwhile the most optimal models appear to be SLS1, SLS2 and Nutting's power law (Fig. 2). The calculation of the correlation matrices resulted in significant Pearson values (r) below the significance level ($p < 0.05$). Specifically, the most important findings are the linear regression identified between stiffness and the maximum value of the DHR for the SLS1 model ($r = -0.93$, with $R^2 = 0.84$) and for the SLS2 ($r = -0.93$, with $R^2 = 0.97$).

DISCUSSION: Creep curves were modeled through rheological models and Nutting's power law. It is immediately clear that there is no linear link between the reduction in disk height and the time through which the phenomenon occurs (Fig.2). SLS1 and SLS2 can capture the trend of data although missing the upward ramp of the curve. The Nutting's law seems to be the best fitting, as it not only fits the creep curve, but, also, its formulation considers the intermediate viscoelastic behavior of IVD between solid and fluid. However, the fitting is not always successful and sometimes cannot take some regions of data. This means that maybe a biphasic model that considers the dual solid and fluid nature of the disc should be formulated, also considering the direct link between the external loads and the mechanobiology of the IVD. The limitations of this study are the creep time duration, the lack of the histological study of the IVD tissue to assess the water content after the testing and that this mathematical model refers only to the mechanical response at the macroscopic level. Further studies will involve longer creep durations including recovery time and histological studies to try to identify this mathematical relationship in the mechanical response of IVD at the macroscopic and cellular levels.

SIGNIFICANCE: This *in-vitro* study provides insight on how necessary it is to find a new mathematical model for the long-term creep behavior of the IVD able to describe the mathematical and mechanical link between the macroscopic and cellular level. Hence, this could be an important step to try to describe the connection shown between the effect of loading rate and hydration of the intervertebral disc during its compression response.

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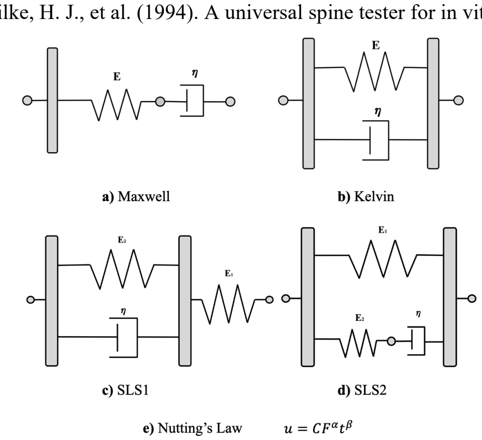

***Figure 1**. **a)** Maxwell's model: a spring in series with a dashpot; **b)** Kelvin-Voigt's model: a spring in parallel with a dashpot; **c)** First Standard Linear Solid model (SLS1 model): a Kelvin-Voigt model in series with a spring; **d)** Second Standard Linear Solid model (SLS2 model): a Maxwell's model in parallel with a spring; **e)** Nutting Law*

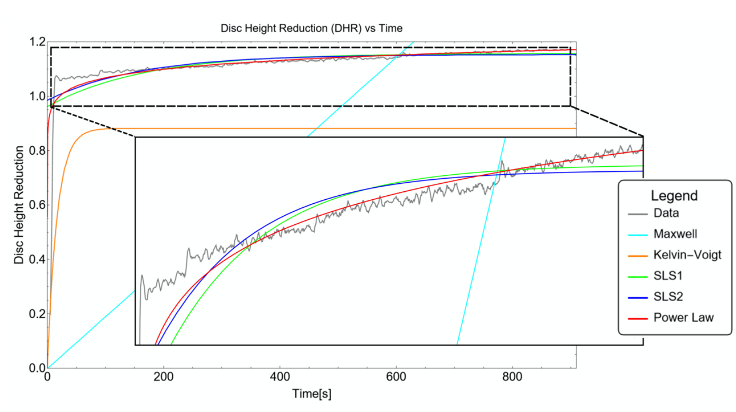

***Figure 2.** Fitting of creep curve (gray curve) with Maxwell model (cyan curve), Kelvin-Voigt model (orange curve), SLS1 model (green curve), SLS2 curve (blue curve) and Power law (red curve). Enlargement in the black box to better visualize the fitting curve.*