First macro-scale damage properties for Wharton's jelly membrane undergoing tensile loading using finite element analysis.

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Abstract

1. Introduction:

Over the last decades, a growing interest has been developed in using biologically derived tissues for regenerative medicine. Wharton's jelly (WJ) distinguishes itself due to its availability both from technical and ethical standpoints. Indeed, this mucous connective tissue present in the umbilical cord is a perinatal waste that offers a valuable source of biological material for wound dressing applications (1). The identification of its mechanical properties are, however, still required to both predict its behavior and integration as well as to guarantee easy handling during surgery. WJ exhibits a nonlinear viscous behavior that is indeed poorly described in the literature (2). Bilinear characterization approach has been often used to give insights into its stiffness, maximal stress and strain before failure (1, 3). A thorough understanding of this tissue behavior at both the macro and micro-scale is essential for developing innovative medical devices. While macro-scale characterization aids in designing

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materials that are user-friendly for surgeons, information at the micro-scale provides insights into cell interactions critical for mechanotransduction and tissue regeneration.

This work is focused on a macro-scale approach to address the gap in the literature regarding the WJ mechanical and damage properties. A hyperelastic behavior law (Ogden (1972)) was adapted to include damage response in WJ tensile behavior using the continuum damage mechanics (CDM) approach (4). Tensile test data combined with a uni-dimensional analytical approach give access to the first time to the WJ damage properties. These results are implemented as initial values in a three dimensional finite element method (FEM) on FEBio software enabling the visualization of failure locations in the WJ structure.

2. Materials and Methods

2.1 Samples

Umbilical cords were obtained from informed patients and in compliance with the usual legal ethical rules. The amniotic membrane and the blood vessels were removed from the umbilical cord to keep the remaining WJ. The latter was washed to remove the remaining blood using buffered saline solution (PBS) and freeze-dried, resulting in a devitalized WJ membrane.

2.2 Mechanical assessment

Rectangular-shaped samples (n= 6) were cut from WJ membranes with average dimensions 0.90 ± 0.20 x 4.40 ± 0.55 x 11.8 ± 0.44 mm3. The tensile tests were performed in close physiological conditions and consisted of a preload followed by several loading cycles up to 10% engineering strain and a last load up to failure with a displacement rate of 0.01 mm/s matching quasi-static conditions.

2.3 Data Processing

Analytical and FEM approaches were used for the material's parameters determination, the first approach giving the initial optimization conditions for the second. A third-order Ogden hyperelastic law was considered for material characterization due to its ability to represent nonlinearity (2). The assumption of incompressibility was made due to high water content inside the membrane and previous work done by Pennati (2001) (3) where Poisson's coefficient was about 0.47. Hence a bulk modulus parameter was fixed to enforce incompressibility, the latter determined using linear elastic modulus obtained from bilinear characterization. The Ogden behavior law was enhanced by CDM (4) with a damage variable expressed through a Weibull distribution with two parameters (α and μ both unitless) depending on a damage criterion expressed in terms of Green-Lagrange strain. The μ and α parameters gave respectively a strain threshold and the transition sharpness between the damaged and undamaged states. The optimization loop for both approaches was performed using Python scripts and the COBYLA method. This externalized loop has allowed the optimization over the FEM for load path up to failure.

3. Results and Discussion:

The following results are expressed through the mean and standard deviation. The experiments showed a nonlinear viscous behavior expressed by the WJ consistent with previous work (2). The rectangular shape of the samples and the stress concentration at their extremities made it challenging to induce failures in the central region. Over 6 samples only one failed in the central region. The maximum engineering stress and corresponding stretch were respectively about 595.39 ± 118.16 kPa and 1.43 ± 0.14. The analytical study allowed quick determination of material parameters while the FEM optimization process took from 10 hours up to one day per sample. Poisson's effect was visible in the simulation and the shear modulus obtained was about 150.14 ± 40.52 kPa in accordance with previous analytical works (2) providing confidence regarding the parameter's determination. The μ and α

parameters were respectively 0.56 ± 0.22 and 1204.41 ± 2842.64. The α parameter exhibits a strong standard deviation due to the variability regarding the more or less progressive failure propagation and points out the need of micro-structure investigations to decrease this uncertainty. The maximum damage which gives insight regarding the failure location is centered on the FEM geometry. This observation differs from the experimental and might be due to the idealized rectangular geometry used for the FEM simulations which can not be perfectly replicated experimentally. Indeed, samples may exhibit irregularities leading to stress concentration and failure in different locations.

4. Conclusion & Outlooks:

The macro-scale damage response was reproduced using both analytical and FEM approaches giving the very first results for such WJ's properties. The externalized optimization loop performed using Python script linked to FEBio has allowed the use of an inverse method over load paths up to failure. However, the hypothesis of incompressibility as well as the hydro-chemo-mechanical couplings within WJ derivatives pose significant challenges for regenerative medicine applications. These challenges are particularly relevant when considering water content to describe the observed viscous response. This aspect is currently being investigated through simulations and medical imaging.

5. References

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