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► **To cite this version:**

Roman Allais, Antoine Capart, Anabela da Silva, Olivier Boiron. Opto-mechanical characterisation of intervertebral disc phantoms. 48th Congress of the Society of Biomechanics, Oct 2023, Grenoble, France. hal-04295598

HAL Id: hal-04295598

<https://hal.science/hal-04295598>

Submitted on 22 Nov 2023

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Opto-mechanical characterisation of intervertebral disc phantoms

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1. Introduction

Degeneration of the intervertebral discs (IVD) is a natural process that appears as early as twenty years of age and does not present any particular clinical symptoms. It is only after a period of several years to several decades, when pain appears, that a diagnosis can be made using usually magnetic resonance imaging. The severity of the disease is commonly assessed by grading schemes relying on contrast imaging analysis and one of the clinical goals in recent years is to better objectify the diagnosis through quantitative imaging. In this context, photoacoustics (PA) is a promising approach as it allows a non invasive spectroscopic probing of soft tissues to retrieve physiological markers of degeneration such as porosity or collagen concentration. A previous work by Metwally, *et al*, 2019 on lumbar porcine discs showed the potential of PA for such a goal. Hence, in this preliminary study we aim to create and characterise hydrogels which mimic the optical, mechanical and acoustic properties of an IVD to assess the possibility to use photoacoustics for disc degeneration estimation.

Briefly, photoacoustics can be seen as a two-step process. First, a medium is hit by a laser pulse and then an acoustic wave is created as a result of the optical energy absorbed. From the measured acoustic signal which probed the medium, the goal is first to retrieve the initial acoustic pressure and subsequently the optical parameters through inverse problems resolutions. Finally, the chromophores concentrations of the medium that we target, water and collagen, can be deduced from the optical properties. The optical part is governed by the radiative transfer equation (Eq.1) which models the light propagation in the medium. This equation on the specific intensity (L in $\text{W.m}^{-2}.\text{sr}^{-1}$) is parametrised by the light speed c , a phase function p describing the optical scattering anisotropy of the medium and two coefficients μ_a and μ_s defining respectively the optical absorption and scattering of the medium. For soft tissues, this rather computationally expensive equation is often reduced to a diffusion equation (Eq.2) under the ‘light diffusion approximation’, which holds for IVD. This

equation on the fluence (ϕ in W.m^{-2}) is parametrised by μ_a and $\mu_s' \approx 0.1\mu_s$. A thorough derivation of these equations and their assumptions can be found in Arridge, 1999. Hence, knowing the values of these two parameters is required to optically characterise a medium.

$$\frac{1}{c} \frac{\partial L}{\partial t} + \nabla L \cdot s = -(\mu_a + \mu_s)L + \mu_s \int_{4\pi} p(s, s') L(r, s', t) ds' + S \quad (\text{Eq.1})$$

$$\frac{1}{c} \frac{\partial \phi(r, t)}{\partial t} - \nabla \cdot (D(r) \nabla \phi(r, t)) + \mu_a(r) \phi(r, t) = S(r) \quad (\text{Eq.2})$$

$$\text{With } D(r) = \frac{1}{3(\mu_a(r) + \mu_s'(r))}$$

2. Methods

2.1 Phantoms preparation

With the end goal of mimicking an IVD, we used agarose hydrogels with TiO_2 powder. We hypothesised that the mechanical response of our samples would be driven by the agarose concentration while the optical response would be mostly tuned by the TiO_2 concentration. The agarose concentration ranges from 0.25 to 2 % w/w and the TiO_2 ranges from 0.1 to 0.5mg/mL. Briefly, a mix of agarose and TiO_2 was mixed in ddH₂O and heated under magnetic stirring. Finally, the solution was poured in cylindrical moulds and stored at 4°C for gelation. As for now, only one sample was made for each combination of agarose and TiO_2 concentration, resulting in 12 hydrogels to characterise.

2.2 Optical characterisation

Under the light diffusion approximation, the optical coefficients μ_a and μ_s' can be experimentally estimated using the integral reflectance and an empirical model as defined by Gobin, *et al*, 1999. Thus, with this approach we could find the relationships between the optical properties of our samples and the components’ concentrations and, on the other hand, by varying the wavelength of the light source from 590 to 815nm by step of 25nm, characterize the absorption spectrum of our samples.

2.3 Mechanical characterisation

The hydrogels were punched to create 32mm-large and 20mm-tall cylindrical samples on which we performed an unconfined stress relaxation compression at the room temperature using a custom-built test bench. Then, we modelled the hydrogels by a Mooney-Rivlin law with two parameters (C_{10} and C_{01}) and two viscoelastic branches following a Maxwell-generalised model. The inverse problem was solved using Levenberg-Marquardt algorithm and the built-in optimisation module of *COMSOL Multiphysics 5.5*. To ease the optimisation, the problem was solved in two steps: we first found the best values of the Mooney-Rivlin parameters and one viscoelastic branch and then we ran a second optimisation using these values to find the best parameters for the second viscoelastic branch.

3. Results and discussion

Our first results suggest that optical scattering is mostly driven by the TiO_2 concentration (C_{TiO_2}): μ_s' increases linearly with C_{TiO_2} and decreases with the wavelength (λ) between 590 and 815nm (Fig.1.A). Moreover, for C_{TiO_2} above 0.5mg/mL, TiO_2 appears to marginally impact the absorption spectrum (Fig.1.B); hence, the optical absorption can be tuned with the agarose concentration while the scattering is driven by the TiO_2 . Assuming the IVD as a biphasic medium made up of water and collagen and knowing the porosity, one can compute typical values of μ_a and μ_s' for IVD at different levels of degeneration. Using the reference values of Sekar, *et al*, 2017, our hydrogels show optical scattering similar to IVD but the optical absorption appears too strong (Fig.1.A, B, D). This could be due to experimental limitations: the approach relying on the integral reflectance could be inaccurate for weakly absorbing samples; a validation experiment using integrating-spheres is planned.

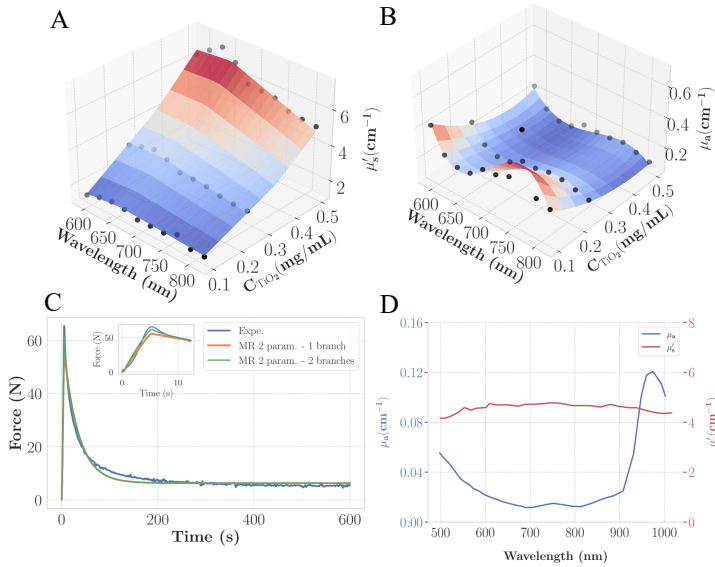


Figure 1: (A) μ_s' and μ_a (B) as a function of λ and C_{TiO_2} for a 1% agarose hydrogel. The black dots display the experimental data. (C) Example of model fitting to the stress relaxation data. (D) Typical IVD μ_a and μ_s' values based on the water and collagen measurements of Sekar, *et al*, 2017.

As for the mechanical problem, our models fit well the experimental relaxation curves (average RMSE<0.65N). Adding a second viscoelastic branch considerably improves the short-term fit (Fig.1.C). Notably, it decreases the maximal error by up to 50%. The average values of the Mooney-Rivlin and first viscoelastic branch parameters are reported in Table 1. Our results are in good agreement with the literature; similar trend are reported for hydrogels whose agarose concentration ranges from 3 to 5%

(Wang, *et al*, 2021). In their hydrogels, Wang and colleagues reported values of 28.4kPa for C_{10} and -20.8kPa for C_{01} with a trend to increase with agarose concentration. However, these values fall short when compared to the one taken by Schmidt, *et al* (2007) in their numerical model of an IVD in which they use $C_{10} = 180\text{kPa}$ and $C_{01} = 45\text{kPa}$ for the annulus fibrosus.

	C_{10} (kPa)	C_{01} (kPa)	β (-)	τ (s)
Agar. 0.5%	3.9 ± 0.4	-2.8 ± 0.4	2.7 ± 0.7	121.7 ± 31.5
Agar. 1%	13.7 ± 3.4	-9.5 ± 2.4	3.0 ± 0.9	123.6 ± 16.7
Agar. 2%	11.8 ± 1.6	-6.1 ± 1.3	10.3 ± 2.2	29.3 ± 3.5

Table 1: Values of the Mooney-Rivlin and first viscoelastic branch parameters (mean \pm std)

4. Conclusions

Our first results are promising as we now have baseline values for both mechanical and optical parameters. Acquisition and numerical simulations of photoacoustic signals are ongoing. Meanwhile, future work will consist in adapting the components to better model an IVD. To improve the optical absorption we plan to add collagen while we project to use chondroitin sulfate or crosslinking to better tune the mechanical response of our hydrogels.

Acknowledgements

This work is supported by the *Emplois Jeunes Doctorants 2021* grant of the Région Provence Alpes Côte d'Azur.

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Keywords: Intervertebral disc; Photoacoustics; Soft tissue; Hydrogel; Characterisation

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