

Free Session

Biomaterial synthesis and characterisation

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Design of fibre-reinforced biomaterials based on novel hydrogels to mimic the vocal folds properties

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Introduction: The human vocal folds possess a specific multi-layered structure (*epithelium, lamina propria* and *muscle vocalis*) giving them extraordinary vibro-mechanical properties (<50Hz to >1500Hz) and unique abilities to endure large cycles deformations (10-50% stretching).¹ However, the comprehension of their vibro-mechanical properties is still largely unknown. A potential way to study these properties would be to mimic way the fibrillar and elastomeric structure of the vocal folds. In this respect, a novel tailorable elasto-mimetic hydrogel (mix of poly-lysine dendrimers (DGL) and polyethylene glycol (PEG-NHS)) that we developed could be interesting.² Its association with polycaprolactone nanofibers (PCLn) could provide composites of mechanical and vibrational properties close to the native tissue. Thus, the aims of this work were characterize the human vocal folds collagen and elastin organization and try to reproduce it through the design and mechanical evaluation of different nanofibres/hydrogels composites (nFHC) varying in hydrogel elasticity and nanofibrillar thickness, orientations or compositions.

Experimental methods: The histological organization of human vocal folds was evaluated with biphotonic microscopy (Zeiss LSM 780), using second harmony generation for collagen fibers (ex. 900nm, em. 450nm) and autofluorescence for elastin (ex. 760nm, em. 500nm) (Fig.1a). The iso- and anisotropic PCLn ($\varnothing=805\text{nm}$) were prepared using a jet-spraying method (Fig.1c).³ Hydrogels of different mechanical properties were obtained by mixing DGL and PEG-NHS aqueous solutions of various concentrations. The different nFHC were prepared *in situ* by percolation of hydrogel solutions through the PCLn. Finally, the mechanical properties for these materials were evaluated using tensile test (BOSE EF3200multitest).

Image:

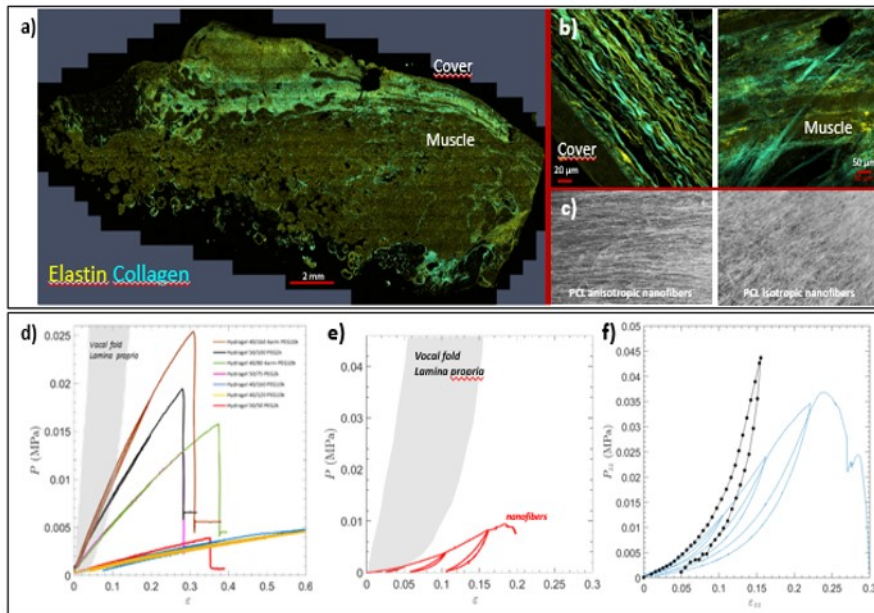


Fig.1. a) Representative view of a human vocal fold cross section showing the overall localization of collagen and elastin, b) their specific orientation in the cover and the muscle area and, c) the synthetic PCL nanofibers mimicking the anisotropic and isotropic fibrillar component. Mechanical properties (stress-strain) of d) the different synthetic hydrogels, e) a representative example of PCL nanofibers and, f) the resulting synthetic composite (blue line) compared to a human vocal fold (black line) in tension along the antero-posterior direction.

Results and discussions: The analyses of human vocal fold by biphoto microscopy revealed a specific organization of collagen and elastin fibers in the *lamina propria* area (fibers intertwined and mostly aligned). Also, were observed anisotropic zones of varying content of collagen or elastin. Conversely, only isotropic collagen bundles were observed in the muscle area (Fig. 1b).

Hydrogels consisting of different molecular ratios of DGL/PEG, different PEG_{MW} (2k, 10k or 40k) and different PEG geometry (star or linear) were synthesized. Increasing the PEG/DGL ratio resulted in an increased Young's modulus (from 10 to 75kPa in PEG2k at 5% strain) (Fig. 1d), while the increase of PEG_{MW} resulted in improvements in the hydrogel elongation at break (from 35% to <90%). Of high interest, all hydrogel types exhibited an almost pure elastic behavior without apparent hysteresis. Contrarily, tensile tests on the PCLn clearly indicated a lack of elastic properties and a plastic deformation, culminating to an elongation at break of about (20%) (Fig. 1e). nFHC could readily be obtained under different conformations (iso/anisotropic fibres homogeneously dispersed within hydrogel or as separate compartments or arranged in multiple layers). Strikingly, tensile test of homogeneous composites exhibited typical PCLn characteristics (resistance to elongation) while acquiring the hydrogel elastic properties. This composite-acquired property are close to the behavior of the human vocal fold of a 79 years old man,⁴ indicating the potential of our approach (Fig. 1f).

Conclusions: Through the design of nFHC, it was possible to provide simple, efficient and highly versatile tools to mimic the structure and mechanical properties of the vocal folds, in view of modeling and better understanding their unique mecano-biological properties. Current work focuses on studying the relative effects of nanofibers and hydrogel properties and conformations in the composite, to further improve mechanical mimicry.

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Disclosure of Interest: None Declared

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