A NEW APPROACH FOR MODELING AND ANALYZING THE VISCOELASTIC BEHAVIOR OF BLADDER WALL TISSUE

[1] Jiro Nagatomi, [2,3]Michael B. Chancellor, and [1,3]Michael S. Sacks
[1]Department of Bioengineering, [2]Department of Urology, [3]McGowan Institute for Regenerative Medicine
University of Pittsburgh, Pittsburgh PA 15261; email: msacks@pitt.edu

INTRODUCTION

Previously our laboratory demonstrated using biaxial stress relaxation tests that the viscoelastic behavior of rat bladder wall is dependent on the health state (normal vs. neurogenic) as well as on the initial stress level [1]. Although these mechanical testing results were fitted relatively well to a reduced relaxation function (RRF: part of the Fung QLV theory [2]) we observed time-dependent residuals between the model prediction and the experimental data [1] Since the bladder is composed largely of smooth muscle with varying amounts of collagen and elastin in the extracellular matrix, we hypothesized that modeling of the bladder wall would require multiple RRFs specific for each component.

The present study, thus, proposes a new modeling approach to predict the stress relaxation response of the bladder wall. Furthermore, an experimental method has been established to test the stress relaxation behavior of the decellularized bladder extracellular matrix in order to determine the contribution of the matrix on viscoelasticity of the bladder wall tissue.

METHODS

New Approach for Viscoelastic Modeling of Bladder Tissue

In an attempt to dissociate the contributions of the extracellular matrix and the smooth muscle components of the bladder wall tissue, the following form of the reduced relaxation function, RRF, was suggested.

$$G_{total}(t) = (1 - e^{-\beta\sigma}) \cdot G_{ECM}(t) + e^{-\beta\sigma} \cdot G_{sm}(t) \qquad (1)$$

In this formulation, the total RRF consists of two independent RRF's for the ECM and for smooth muscle, bound by an exponential recruitment function that is dependent on the initial stress level, σ, under the assumption that the higher the stress, the more ECM is loaded and contributes toward the overall stress relaxation response of the tissue.

According to the Fung QLV model, the RRF is formulated with a continuous relaxation spectrum. In the present study, based on the literature reports on the stress relaxation behavior of smooth muscle [3], we assumed that the smooth muscle component of the bladder tissue would follow this spectrum. For the extracellular matrix of the bladder, however, based on our previous results we assumed that the relaxation spectrum could not be described with a constant. Therefore, as a first attempt, we suggested that the following dual Gaussian form of the relaxation spectrum for the bladder ECM.

Decellularization of Bladder Tissue Specimen and Biaxial Stress Relaxation Tests

Whole bladders were harvested from female Sprague-Dawley rats and were placed immediately in tris-buffered saline (TBS) at 4 °C for up to 48 hours. The bladders were then treated in a series of detergent solutions to decellularize using a method adapted from the literature [4].

Equi-biaxial stress relaxation tests were performed using a custom-made biaxial testing device [5] in modified Kreb's solution at 37 °C for up to 3 hours according to the established protocol [1]. Briefly, an equi-biaxial quasi-static testing run with 12 loading-unloading cycles was performed to precondition the tissue (at either 25 or 100 kPa) and to determine the strain levels necessary for the subsequent equi-biaxial stress relaxation run. Next, the specimen was loaded to the strain-levels representative of 25 or 100 kPa stress in both axes in 50-millisecond ramping time and was held at these strain levels to relax for the following 10,000 seconds (2 hours 47 minutes).

RESULTS AND DISCUSSION

Decellularized bladder specimens were used in biaxial stress relaxation tests to determine the contribution of the extracellular matrix to the viscoelastic behavior of the bladder wall tissue. The results of stress relaxation tests provided evidence that compared to intact bladder tissue, the decellularized bladder tissue relax less over the testing period of 10,000 seconds. Based on these findings, the RRF for the extracellular matrix, G_{ECM}, was determined.

Finally, the stress relaxation data for normal rat bladder tissue were fitted successfully ($r^2 > 0.99$) with our new viscoelastic model, which produced smaller residuals compared to the conventional QLV (data not shown).

CONCLUSIONS

The present study demonstrated for the first time that stress relaxation response of the bladder tissue can be divided into the contributions of the extracellular matrix and smooth muscle components. Further experimental validation and detailed analyses of the structure of the ECM will allow development of this model into a structure-based viscoelastic model of the bladder.

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