

## **BIAXIAL PASSIVE MECHANICAL PROPERTIES OF DIABETIC BLADDER WALL**

### Hypothesis / aims of study

The prevalence of diabetes in the United States is continuing to increase and diabetic cystopathy was showed to occur in 25% to 87% diabetic patients<sup>1,2</sup>. Previous study showed diabetic cystopathy was induced by diabetic neuropathy and/or diuresis that lead to the alternations in bladder compliance, function and tissue components<sup>3</sup>. To understand the impact of these changes at tissue and organ levels and how they relate to functional changes, we hereby apply biaxial biomechanical testing in the diabetic bladders and quantify the time-course changes in the biaxial mechanical properties of diabetic bladders.

### Study design, materials and methods

Diabetes was induced in adult female Sprague-Dawley rats by a single intraperitoneal injection (65mg/kg body weight) of Streptozotocin. Chronic diuresis was induced by feeding 5% sucrose in water. Whole bladders were harvested at 2-week, 4-week and 8-week post-treatment. Mechanical properties of 10 mm square tissues obtained from the bladder body were tested using planar biaxial testing at room temperature in the modified Krebs's solution. Loads were monitored along both orthogonal axes by two load cells during testing. Stresses along the longitudinal and circumferential axes were determined in the Lagrange sense (measured force/unloaded cross-sectional area). An initial equibiaxial stress protocol was performed to mechanically precondition the tissue specimen. The maximal 100kPa stress was applied in the circumferential and longitudinal (base-apex) directions, and resulting axial strains were measured.

### Results

The bladders exhibited a non-linear stress-strain relationship, mechanical anisotropy and asymmetric mechanical coupling. Both axes showed rapidly increasing stresses at higher stretches. Under maximal equi-biaxial stress, the stretch in the circumferential axis was greater than that in the longitudinal axis. The maximal stretch in the circumferential axis and areal strain continued increased in both treated rats over the 4-week period. In 8-week diabetic rats, the maximal stretch in the circumferential axis showed a further increase compared with 4-week diabetic rats ( $1.42 \pm 0.09$  versus  $1.31 \pm 0.05$ ,  $p=0.02$ ). The maximal stretch in the circumferential axis was similar in 4-week and 8-week diuretic rats ( $1.32 \pm 0.06$  versus  $1.32 \pm 0.10$ ,  $p=0.96$ ). In 8-week diabetic rats, the areal strain showed a further increase compared with 4-week diabetic rats ( $0.64 \pm 0.11$  versus  $0.46 \pm 0.09$ ,  $p=0.01$ ). However, the areal strain was similar in 4-week and 8-week diuretic rats ( $0.47 \pm 0.12$  versus  $0.48 \pm 0.12$ ,  $p=0.98$ ).

### Interpretation of results

Both diabetes and diuresis altered the mechanical properties of bladder wall over the 8-week period. Up to 4-week time period, both diabetes and diuresis had similar impact on the changes of the mechanical properties. "Early" changes of mechanical properties in diabetes may be due to functional adaptation to bladder overdistension and/or an increase bladder work induced by diuresis. Further changes of mechanical properties in 8-week diabetic bladder wall may be induced by other diabetic effects, such as diabetic neuropathy, diabetic myopathy or changes of the extracellular matrix.

### Concluding message

We suggested that the "early" changes (up to 4-week treated) of mechanical properties were mainly induced by diuresis and the "late" changes (8-week treated) were induced by other diabetic effects. These data may be used in computational simulations of the bladder to predict the effects of diabetes and further treatment.

References

1. The continuing epidemics of obesity and diabetes in the United States. JAMA 2001; 286: 1195-1200
2. Diabetic cystopathy: epidemiology and related disorders. Ann Intern Med 1980; 92: 318-321.
3. Diabetes and diuretic-induced alterations in function of rat urinary bladder. Diabetes 1988; 37: 949-955.

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