

## BLADDER COLLAGEN MODULATION AFTER PARTIAL BLADDER OUTLET OBSTRUCTION IN RABBITS

### Hypothesis / aims of study

Partial bladder outlet obstruction (PBOO) induces an increase in bladder mass, smooth muscle content and collagen deposition, sometimes generating bladder dysfunction represented by impaired contractility and compliance. We conduct this study aiming to provoke a representative model of outlet obstruction and to investigate the temporal pattern of morphological and histological changes of the bladder wall.

### Study design, materials and methods

Fifteen young white New Zealand male rabbits were divided into two groups: control, with six rabbits and six-week obstructed, with the other nine. The six controls were initially sacrificed and their bladders removed for analysis. The nine six-week obstructed rabbits initially underwent a partial outlet obstruction surgery under general anesthesia. After the urethra was dissected a 5-zero nylon suture was passed and tied loosely around the urethra with an 8 Fr catheter. Six weeks later these animals were sacrificed and the bladders removed. All bladders were fixed in 10% formaldehyde. Serial sections of 5  $\mu$ m were obtained from paraffin embedded material and stained with Masson and Picrosirius red.

### Results

Six animals from the obstructed group died before to complete six weeks of obstruction and then they were considered the intermediate group. Mean thickness of the bladder wall differed statistically significant between control, intermediate and six-week groups (4 nm x 14 nm x 29 nm, respectively;  $p < 0.001$ ) (Figure 1). Control bladders presented with thin grouped detrusor muscle cells (DMC) without interstitial fibrosis; intermediate group bladders were characterized by an intense DMC hypertrophy with a large amount of myofibroblasts and a great subserous fibrosis; and six-week group bladders presented with thick grouped DMC hypertrophy and a smooth subserous fibrosis. Type I collagen concentration decreased significantly after obstruction time between the three groups (5.07% x 2.45% x 3.43%, respectively;  $p < 0.05$ ) and type III collagen presented a significant increase in the six-week group (2.01% x 2.20% x 4.49%, respectively;  $p < 0.001$ ) (Figure 2).

### Interpretation of results

Partial bladder outlet obstruction actually induces a bladder wall hypertrophy, clinically represented as a progressive increased bladder mass. It also provokes a collagen remodeling during all obstruction period decreasing type I collagen content, which was substituted by a progressively increased type III collagen interstitial deposition. This reorganization of the connective tissue with scarring likely is due to the bladder dysfunction after PBOO.

### Concluding message

We reproduced in this study the bladder wall hypertrophy and demonstrated the interesting progressively time dependent collagen remodelling that could be one cause, at last, of bladder dysfunction.

### References x

Figure 1. Bladder wall thickness (nm) in the three groups: A – control group; B – intermediate group; C – six-week group.

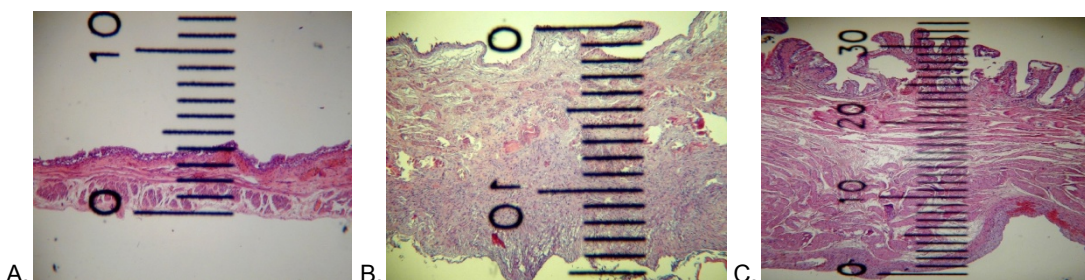
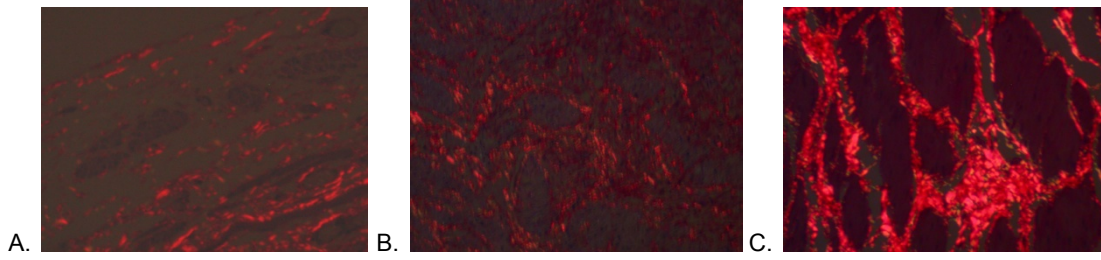


Figure 2. Picrosirius red stained analysis of collagen demonstrating an evident increase in its amount between the three groups: A – control group; B – intermediate group; C – six-week group.



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**ANIMAL SUBJECTS:** This study followed the guidelines for care and use of laboratory animals and was approved by Ethic Comitee of the University of Sao Paulo School Medicine