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BLADDER COLLAGEN MODULATION AFTER PARTIAL BLADDER OUTLET OBSTRUCTION COMPARING THE RABBIT AND THE RAT MODELS.

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 compare to our previous model in rabbits.

Study design, materials and methods
Twenty young female white Wistar rats between 200g to 300g were divided into two groups: control and six-week obstructed, each composed of ten rats. The control group was initially underwent to a sham operation. The six-week obstructed rats 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 22G (0.7mm) needle besides it. Six weeks later these animals were sacrificed and the bladders removed. All bladders were fixed in 10% formaldehyde. Serial sections of 5 µm were obtained from paraffin embedded material and stained with Masson and Picrosirius red. Then, results were compared with our previous model developed in rabbits, which had the same time of obstruction. Additionally, we performed immunochemistry to confirm the remodeling between types I and IIII collagen.

Results
Mean thickness of the bladder wall differed statistically significant between control and six-week groups ($p < 0.001$). Control bladders presented with thin grouped detrusor muscle cells (DMC) without interstitial fibrosis and six-week group bladders presented with thick grouped DMC hypertrophy and a smooth subserous fibrosis. These results corroborates with our findings in the previous model. Type I collagen concentration decreased not significantly after obstruction time between the groups (3.80% x 3.44%, respectively; $p = 0.57$) and type III collagen presented a significant increase in the six-week obstructed group (4.00% x 6.14%, respectively; $p < 0.05$) (Figures 1 and 2). This found was different from what we presented in rabbit model, where type I collagen concentration decreased significantly after obstruction time between the two groups (5.07% x 3.43%; $p < 0.05$) and type III collagen presented a significant increase in the six-week group (2.01% x 4.49%; $p < 0.001$). Immunochemistry performed in the rat model confirmed a non significant decrease of type I collagen and a significant increase of type III collagen from the sham group to the six-week obstructed group ($p < 0.05$).

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. Both models are concordant in these founds, with a modest difference regarding type I collagen alteration.

Concluding message
We reproduced in this study the bladder wall hypertrophy in two similar experimental models and demonstrated the interesting progressively time dependent collagen remodelling that could be one cause, at least, of bladder dysfunction.

Figure 1. Sham group: Picrosirius red stained analysis of collagen demonstrating an evident prevalence of type I collagen (red stained).

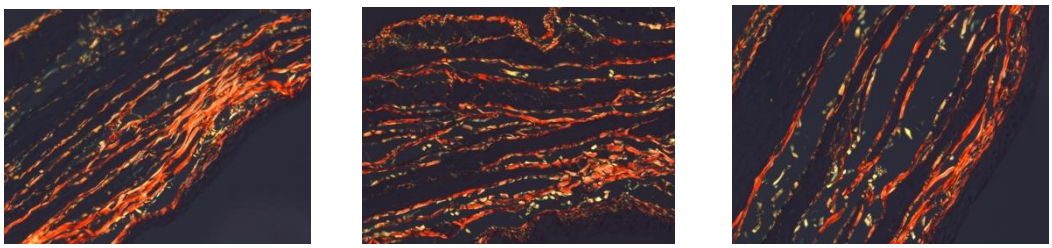
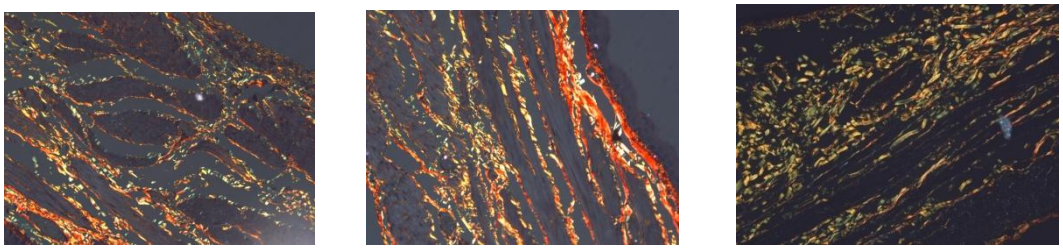


Figure 2. Six-week obstructed group: Picrosirius red stained analysis of collagen demonstrating an evident prevalence of type III collagen (yellow and green stained).



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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
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