Bioresorbable ureteral stent translation for *in vivo* model

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Statement of Purpose: A urinary stent is a thin tube, which is inserted in the ureter to prevent or treat the obstruction of urine flow from the kidney. Currently, nearly 100% of the people who have an urological stent are likely to develop a bacterial infection within 30 days, which increases morbidity threefold. Silicone, latex, PVC and polyurethanes are the most widely used materials for the preparation of stents. Nonetheless, severe clinical complications may result from the use of these materials such as, fracture, encrustation and infection. In some of the cases, the ureteral stents are temporary and it is often required a second surgery to remove the stent. These problems were the motivation to design new bioresorbable urological stents based on natural polymers, which present biocompatibility, anti-bacterial properties and can be tailor-made into a custom suitable stent. In this work with the objective to go beyond lab-bench it is important to evaluate the ability to implant the designed stent without major changes in current surgical procedures. In this sense we performed a first *in vivo* test, using a female pig model. The main objective of this first phase was to evaluate the *in vivo* performance of ureteral stents developed.

Methods: Polymeric solutions were prepared as described in a previous work[1]. Water uptake and polymer degradation studies were executed using an artificial urine immersion solution. The ability to avoid bacterial adhesion and the creation of a biofilm was evaluated according to describe *Khandwekar and Doble*[2]. Cytotoxicity and cell adhesion studies were also executed with a L929 cell line according ISO10993[3]. A female pig (*Sus scrofa domesticus)* with 25-30 kg weight were used in the *in vivo* study. Before insertion the degradable ureteral stents developed was hydrated in simulate body fluid for 3 minutes. A 0.035-inch diameter Aquatrack® Hydrophilic Nitinol Guidewire was inserted in the ureter, followed by a ureteral stent before cystoscope removal. A degradable stent was inserted over the guide wire. A pusher was used to insert the stent into the urinary system. The guide wire was then removed, leaving only the stent.
It was tested the normal procedure of insertion of urethral stent under general anesthesia under endotracheal intubation and mechanical intubation. The specimens were subjected to rigid cystoscopy with bilateral ureteral catheterization using biodegradable catheters.

Results: The developed ureteral stents characterization *in vitro* presented high water uptake ability but are able to maintain their shape and integrity. The degradation timeframe can be tuned from 14 days, to longer periods. In vitro assessment of possible encrustation, i.e. the deposition of Mg and/or Ca salts, was also evaluated by SEM-EDS and no encrustation was observed up to 28 days. The ability to avoid bacterial adhesion and the creation of a biofilm was evaluated with *S. aureus bacterias (gram positive), Escherichia coli and klebsiella (gram negative)* and we obtained results comparable with commercially available stents (Biosoft duo, Porgés, Coloplast). Cytotoxicity and cell adhesion studies were also executed to compare the developed materials with a commercial stent. The described ureteral stents, when in contact with a physiological medium, become hydrogels, exhibiting biocompatible and non-cytotoxic characteristics. The presence of a high equilibrium water content, provides soft, lubricious, and flexible characteristics to the devices, similar to natural tissue.

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Figure 1. a) imagen do stent b) imagem do porco for a c) imagem por endoscópio

The *in vivo* performance of biodegradable ureteral stent developed demonstrated similar properties in terms of commercial available with the same procedure for ureteral stent insertion. The biodegradable ureteral stent slipped perfectly into the cystoscopy and the hydrophilic guidewire into the bladder through the urethra. The ureteral stent developed remains intact throughout the procedure and is not fragmented and proved easy removal if necessary. Unfortunately the full insertion of ureteral stent in the ureter was not achieved due to higher hydration of the stent and therefore loss of mechanical performance of the biodegradable ureteral stent. The obtained results demonstrate the feasibility to develop a new bioresorbable ureteral stent.

Conclusions: From the experimental performed we concluded that the surgical procedure performed daily in clinical practice does not need further chances with our developed degradable ureteral stent. The ureteral stent could be inaltered through the urethra and the bladder nonetheless the placed in the ureter was not as successful as expected. Future work includes the optimization of the mechanical properties of the stent in order to pass the ureteral orifices and settle in the ureter.

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