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Upper urinary tract urothelial tumours targeted with biodegradable drug-eluting stents

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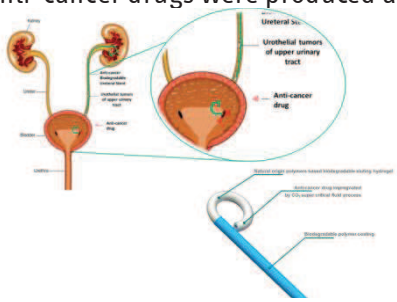
INTRODUCTION & OBJECTIVES: Biodegradable ureteral stents developed have proven to be an interesting alternative to conventional stents. Additionally, they could be applied as exceptional drug eluting stents, specially for urothelial tumours of upper urinary tract. In this case the conventional method of drug administration is via drug instillation. This has several drawbacks, such as high concentration dosage, increased side effects, short residence time and poor bioavailability. To avoid these problems, biodegradable ureteral stents impregnated by supercritical fluid CO_2 (SCF) with four anti-cancer drugs were produced and their performance evaluated.



MATERIAL & METHODS: The preparation of biodegradable stents was tested with four different formulations. The suitable concentration of gelatin and alginate and crosslinking agent was optimizedand bismuth was added to confer radiopaque properties to the stent. The preliminary in vivo validation studies of the biodegradable stents was conducted in female domestic pigs at the University of Minho, Braga, after formal approval by the institution's review board and in accordance with its internal ethical protocol for animal experiments. In which concerns drug eluting stents, paclitaxel, epirubicin, doxorubicin and gemcitabine were impregnated and the release kinetics in artificial urine solution (AUS) was followed for 9 days by UV spectroscopy in a microplate reader. The anti-tumoral effect of the developed stents in cancer cell line (T24) and HUVEC primary cells, used as control, was evaluated.

RESULTS: The in vivo validation of this second-generation of ureteral stents performed was herein demonstrated. Biodegradable ureteral stents were placed in the ureters of a female pig, following the normal surgical procedure. The animals remained asymptomatic, with normal urine flow. The in vitro release study in AUS of the stents impregnated showed a higher release in the first 72h for the four anti-cancer drugs impregnated and after this time a plateau was achieved and the stent degraded after 9 days. The direct and indirect contact of the anti-cancer biodegradable stents with the T24 and HUVEC cell lines confirm the anti-tumour effect of the stents impregnated with the four anti-cancer drugs, reducing around 75% of the viability of the T24 cells after 72h and no killing effect in the HUVEC cells.

CONCLUSIONS: The use of biodegradable ureteral stents in urology clinical practice not only reduces the stent-related symptoms but also open new treatment therapy's, like in urothelial tumours of upper urinary tract. We have herein demonstrated its clinical validation an in vivo model. And we have also shown the killing efficacy of the anti-cancer drug eluting biodegradable stents in vitro for the T24 cancer cells, with no toxicity observed in the control, non-cancer cells.