

## A POSSIBLE NEW MOLECULE FOR DIAGNOSIS AND FOLLOW UP OF BLADDER CANCER: THE RADIOLABELED POLYMER $^{99m}\text{Tc}$ -PEI-MP

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**Introduction:** The polymer PEI-MP (polyethyleneimine, functionalised with methylphosphonate groups) was initially synthesized for palliative therapy of bone metastases after convenient radiolabelling. However, in biodistribution studies performed with this polymer radiolabelled with different radionuclides, was obvious a higher uptake by the bladder wall, that might demonstrate a certain selectivity to bladder cells, and so, to bladder cancer cells. The aim of this study was to evaluate the efficacy of PEI-MP radiolabeled with  $^{99m}\text{Tc}$  for imaging diagnosis and follow up of bladder cancer.

**Material and Methods:** Because PEI-MP should act as a carrier with high selectivity to bladder cancer cells and not to induce any harm, it was analysed the cytotoxicity in bladder carcinoma cell line (CRL-1472) using the MTT test and flow cytometry. The radiochemical purity of  $^{99m}\text{Tc}$ -PEI-MP was achieved using ascending microchromatography. Then, cellular uptake studies were performed using  $^{99m}\text{Tc}$ -PEI-MP and  $\text{Na}^{99m}\text{TcO}_4$  as control. Cell samples were collected during four hours, centrifuged to separate supernatant and pellet. Subsequently, the

radioactivity of each portion was counted to determine percentage of uptake. The *in vivo* studies were performed using four groups of Balb/c nu/nu mice: two normal groups injected with  $\text{Na}^{99\text{m}}\text{TcO}_4$  and  $^{99\text{m}}\text{Tc}$ -PEI-MP and two with bladder carcinoma xenotransplants injected with the same complexes. Radiopharmaceuticals were administered by an intravenous injection in the tail vein (22-37MBq), with the animal anesthetized and previously placed on a gamma camera detector. Subsequently, were acquired dynamic and static images for 2 and 4 hours, and mice were euthanized and organ samples where weighted and counted in a well-counter to obtain percentage injected activity per gram of organ (%ID/g).

**Results:** The MTT assay and flow cytometry tests showed that PEI-MP is not cytotoxic. The radiochemical purity of  $^{99\text{m}}\text{Tc}$ -PEI-MP was  $\geq 85\%$ . The uptake studies demonstrated that the uptake was higher for  $^{99\text{m}}\text{Tc}$ -PEI-MP in relation to their control. Biodistribution with  $^{99\text{m}}\text{Tc}$ -PEI-MP showed that the excretion of this complex occurs primarily through the renal system. The tumour/muscle ratio was superior to 1,2.

**Conclusions:**  $^{99\text{m}}\text{Tc}$ -PEI-MP seems to be optimal for diagnosis and follow up.

**Keywords:** PEI-MP, Bladder cancer, Noninvasive diagnosis.

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