# Polyethyleneiminomethyl phosphonic acid (PEI-MP) radiolabeled with technetium-99m as a potential new radiopharmaceutical for diagnosis of bladder cancer

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**Introduction:** The polymer PEI-MP (polyethyleneiminomethyl phosphonic acid) might be labelled with $^{99m}$Tc. It was initially synthesized for palliative therapy of bone metastases after convenient radiolabelling, however in biodistribution studies performed with different PEI-MP/radionuclides, was obvious that the bladder wall was a target organ [1-3], demonstrating a certain selectivity to bladder cells, and so, to bladder cancer cells. The aim of this study was to evaluate the efficacy of $^{99m}$Tc-PEI-MP for diagnosis of bladder carcinoma, evaluating in vitro and in vivo the biokinetics and biodistribution of $^{99m}$Tc-PEI-MP.

**Material and Methods:** The radiochemical purity of $^{99m}$Tc-PEI-MP was achieved using ascending microchromatography (ITLC-SG/acetone and W3MM/citrate1M). In order to determine the hydrophilicity or lipophilicity of $^{99m}$Tc-PEI-MP, it was determined the partition coefficient, after radiolabelling. Cellular uptake and retention studies were performed using the LigandTracer instrument after add $^{99m}$Tc-PEI-MP or Na$^{99m}$TcO$_4$ (control) to the culture medium of a petri dish with the cells. Subsequently, the radioactivity uptake and retained by cells was determined over time. The in vivo studies were performed using 4 groups of balb/c nu/nu mice: 2 normal injected with Na$^{99m}$TcO$_4$ (control) and $^{99m}$Tc-PEI-MP and 2 with bladder carcinoma xenotransplants injected with the same complexes. After injection, were acquired dynamic and static images for 2 and 4h. For biodistribution proposes, mice were euthanized after the static images and organ samples where weighted and

counted in a well-counter to obtain percentage injected activity per gram of organ (%ID/g).

**Results:** The radiochemical purity of $^{99m}$Tc-PEI-MP was ≥90%. The *n*-octanol/water partition coefficient was negative during time, demonstrating that $^{99m}$Tc-PEI-MP is a hydrophilic complex. The in vitro uptake and retention studies demonstrated that the uptake was higher for $^{99m}$Tc-PEI-MP in relation to their control and that the retention is stable and high. The biodistribution with $^{99m}$Tc-PEI-MP showed that the excretion of these complexes occurs primarily through the renal system. Tumour/muscle ratio for $^{99m}$Tc-PEI-MP was >1. Tumour/bladder, tumour/bone, tumour/liver and tumour/lungs ratios were always <0.5.

**Conclusions:** $^{99m}$Tc-PEI-MP seems to be optimal for diagnosis of bladder cancer and its metastasis. The results demonstrated that $^{99m}$Tc-PEI-MP is a hydrophilic complex and therefore water soluble, being expected that in vivo the excretion occurred by the renal system. These results were confirmed by in vivo imaging and ex vivo biodistribution studies. The uptake by the tumour was always superior to 1, and therefore it could be an advantage in determine the level of invasion to the muscle involving the bladder and to support the surgery. The uptake by the bone, liver and lungs was high comparing with the tumour uptake, and therefore in case of distant metastases the mass would appear as a cold lesion. **References:** [1] Dormehl IC *et al*: Biodistribution and pharmacokinetics of variously sized molecular radiolabelled polyethyleneiminomethyl phosphonic acid as a selective bone seeker for therapy in the normal primate model. *Arzneimittel-Forschung* 2001,51(3):258-263; [2] Botelho MF *et al*: Dosimetric evaluation of the polyphosphonate; PEI-MP labelled with 117mSn, 186Re and 99mTc as potential diagnosis/therapeutic bone agents. *European journal of nuclear medicine and molecular imaging* 2006,33:S309.

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