188Re-PEI-MP as a potential agent for metabolic radiotherapy

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Abstract: Introduction: 188Re is a promising radionuclide for metabolic therapy because of the emission of high energy beta-particles. The development of water-soluble bone-seeking polymers such as PEI-MP (polyethyleneimine, functionalised with methylphosphonate-groups) that might be labeled with 188Re are recent approaches, with a strong potential for bone cancer treatment. The aim of this study was to evaluate the efficacy of 188Re-PEI-MP, as
therapeutic agent for osteosarcoma, through in vitro and in vivo models.
Material and Methods: Radiochemical purity of 188Re-PEI-MP was achieved using microchromatography. In vitro studies were performed in human osteosarcoma cell-line (MNNG-HOS). Uptake studies were performed using the complex 188Re-PEI-MP and Na188ReO4 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. In vivo studies were performed using four groups of Balb/c nu/nu mice: two normal groups were injected with Na188ReO4 (n=18) and 188Re-PEI-MP (n=17) respectively; two with osteosarcoma xenotransplants were injected with Na188ReO4 (n=17) and 188Re-PEI-MP (n=19) respectively. When tumor reached the appropriate volume, Na188ReO4 and 188Re-PEI-MP were administered by an intravenous injection in the tail vein (22-37MBq), with the animal anesthetized and previously placed on the gamma camera detector. Immediately, a dynamic acquisition followed, with a 128x128 matrix for 10 minutes (20 frames, 30 seconds). Static images (2 minutes) were performed with a 256x256 matrix, where each of the four groups was divided into two groups, of which one was imaged at 120 minutes, and the other at 240 minutes. For biodistribution proposes, mice were euthanized 2 and 4 hours after injection and organ samples where weighted and counted in a well-counter to obtain percentage injected activity per gram of
organ (%ID/g).
Results: In vitro results demonstrated that the uptake was higher for 188Re-PEI-MP (12.2%) than for Na188ReO4
(0.2%), remaining constant over time. Biodistribution results, with Na188ReO4, showed a higher uptake by the thyroid, bladder and stomach, while with 188Re-PEI-

MP the target organ was consistently the bladder, with little uptake in bone tissue and tumour (tumour/muscle ratio>1). The excretion of both tracers was mainly renal with a small fraction of the complex through hepatobilliary system.

Conclusions: 188Re-PEI-MP seems to be an agent for metabolic therapy of bone cancer. However, as the in vivo
results suggest that the bladder could be another target organ, preliminary in vitro results in human bladder cancer
cell-line (CTRL1472) showed a tumour/muscle ratio greater than 1.5.

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