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Poster Session 1

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A comparative study to analyse the potential of 99mTc-PEI-MP for diagnosis and 188Re-PEI-MP for therapy of bladder carcinoma and osteosarcoma

Sara Ferreira[1,3], Mafalda Laranjo[1,2], Ana M. Abrantes[1,2], Ana F. Brito[1,2], Luís Metello[4], Jan Zeevart[5], Werner Louw[5], Irene Dormehl[6], **Maria F. Botelho**[1,2], *[1]Biophysics Unit, IBILI, Faculty of Medicine, University of Coimbra, Coimbra, Portugal; [2]CIMAGO, Faculty of Medicine, University of Coimbra, Coimbra, Portugal; [3]School of Sciences, University of Minho, Braga, Portugal; [4]Nuclear Medicine Course, High Institute of Allied Health Technologies of Porto's Polytechnic Institute, Porto, Portugal; [5]Radiochemistry Department, NECSA, Pretoria, South Africa; [6]Department of Internal Medicine, University of Pretoria, Pretoria, South Africa. Contact e-mail: filomena@ibili.uc.pt*

Introduction: The water-soluble polymer PEI-MP (polyethyleneimine, functionalised with methylphosphonate groups) that might be labeled with 188Re (emits high energy β- particles) and 99mTc presents a strong potential for metabolic radiotherapy and diagnosis, respectively. The aim of this study was to evaluate in vivo the potential of 188Re-PEI-MP as therapeutic agent and 99mTc-PEI-MP as diagnostic agent for bladder carcinoma and osteosarcoma. Material and methods: Cytotoxicity of PEI-MP was investigated in bladder carcinoma cell line (CRL-1472) using the MTT test for different concentrations of PEI-MP (1 μM to 1000 μM) and incubation times (24h, 48h, 72h and 96h). Radiochemical purity of 99mTc-PEI-MP and 188Re-PEI-MP was achieved using ascending microchromatography. For the in vivo studies eight groups of Balb/c nu/nu mice were used: four normal groups injected with Na99mTcO4 (n=10), 99mTc-PEI-MP (n=10), Na188ReO4 (n=18) and 188Re-PEI-MP (n=17), respectively; two with bladder carcinoma xenotransplants injected with Na188ReO4 (n=8) and 188Re-PEI-MP (n=12), respectively; two with osteosarcoma xenotransplants injected with Na188ReO4 (n=17) and 188Re-PEI-MP (n=19) respectively. When the tumors reached the appropriate volume, radiopharmaceuticals 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 min (20 frames, 30 seconds). Static images (2 min) were performed with a 256x256 matrix, where each of the six 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 were weighted and counted in a well-counter to

obtain percentage injected activity per gram of organ (%ID/g). Results and discussion: The MTT assay showed that PEI-MP is not cytotoxic. The radiochemical purity of 188Re-PEI-MP and 99mTc-PEI-MP was higher than 85%. Biodistribution results, with Na188ReO4 and Na99mTcO4, showed a higher uptake by the thyroid, bladder and stomach, following a normal biodistribution. The biodistribution with 188Re-PEI-MP and 99mTc-PEI-MP showed that the excretion of these complexes occurs primarily through the renal system, with a small fraction being eliminated by the hepatobiliary system. In mice with osteosarcoma tumor/muscle ratio was greater than 1.0, and for mice with bladder carcinoma the tumor/muscle ratio was greater than 1.5. Conclusions: The 188Re-PEI-MP seems to be promising in the treatment of both types of cancer, but with a greater potential for bladder cancer, given its biodistribution and tumor/muscle ratio. Following the same biodistribution as 188Re-PEI-MP, 99mTc-PEI-MP seems to be optimal for diagnosis and follow up of both types of cancer.

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