Contribution ID: **193** Type: **Poster**

66Ga-labeling of DOTA-conjugated cyclic RGDfK dimer for αvβ3 integrin overexpression tumors

Monday 17 September 2012 17:30 (1h 30m)

Angiogenesis is an essential process in solid tumours growing beyond 2 to 3 mm3, since diffusion is no longer sufficient to supply the tissue with oxygen and nutrients. Integrins αvβ3 have been shown to play an important role in a series of pathological processes including angiogenesis and tumour cell metastasis. It has also been shown that peptides based on the Arg-Gly-Asp (RGD) sequence have a high affinity and selectivity for αvβ3 integrins. The aim of this research is to prepare and evaluate 66Ga-DOTA-Glu-[cyclo(Arg-Gly-Asp-D-Phe-Lys)]2 (66Ga-DOTA-E-[c(RGDfK)]2), as potential diagnosis agent for the early and specific detection of cancers overexpressing αvβ3, and evaluate its potential as possible agent for therapy. Gallium-66 was produced on a 11 MeV cyclotron via the 66Zn(p,n)66Ga reaction and radiochemical separation was performed by ion exchange chromatography using a AG 50W X-4 cation exchange column. For radiolabelling 30 µl of the peptide conjugated solution (400 ug/ml, H2O with 1% EtOH), 25 µl 1 M HEPES, pH 7.0 and 25 µl 0.25 M NH4OAc, an pH 5.5, were mixed with 66Ga stock solution (50 µl 0.1M HCl) and incubated for 20 min at 95℃. When needed, labelled peptides were purified by SPE on an Oasis HLB cartridge, product eluted with a small volume of 25% EtOH and diluted to <5% EtOH in PBS. In vivo studies were performed on a Focus 120 microPET System using C6 and U87MG xenografts in nude mice.

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Session Classification: Poster Session

Track Classification: Radiopharmaceutical chemistry, radiodiagnostics, radiotherapy, theragnostics