68Ga-NODAGA-RGD is a suitable substitute for (18)F-Galacto-RGD and can be produced with high specific activity in a cGMP/GRP compliant automated process.

Abstract:

(18)F-Galacto-cyclo(RGDfK) is a well investigated tracer for imaging of ™z3 expression in vivo, but suffers from the drawback of a time consuming multistep synthesis that can hardly be established under GMP conditions. In this study, we present a direct comparison of the pharmacokinetic properties of this tracer with (68)Ga-NODAGA-cyclo(RGDyK), in order to assess its potential as an alternative for (18)F-Galacto-cyclo(RGDfK). (68)Ga labeling of NODAGA-cyclo(RGDyK) was done in full automation using HEPES-buffered eluate of an SnO(2) based (68)Ga-generator. Using M21 (human melanoma) xenografted BALB/c nude mice, biodistribution studies and micro-PET scans were performed for both (18)F-Galacto-cyclo(RGDfK) and (68)Ga-NODAGA-cyclo(RGDyK), and for the latter, in vivo stability was assessed. IC(50) was determined in a displacement assay on M21 cells against (125)I-echistatin. (68)Ga-NODAGA-cyclo(RGDyK) was produced with high specific activity (routinely ca. 500 GBq/μmol) within 15 min. IC(50) values are similar for both substances. Tracer uptake was similar in ™z3 positive tumors (1.45%±0.11% ID/g and 1.35%±0.53% ID/g for (68)Ga-NODAGA-RGD and (18)F-Galacto-RGD, respectively) as well as for all other organs and tissues, with the exception of gall bladder and intestines, where
(18)F-Galacto-cyclo(RGDfK) uptake was significantly higher, which can be explained by the higher hydrophilicity of (68)Ga-NODAGA-cyclo(RGDyK) (logP=-4.0 vs. -3.2 for (18)F-Galacto-RGD). Only intact tracer was detected 30 min p.i. in organs and tumor; however, minor amounts of metabolites were found in the urine (6% of total urine activity). (68)Ga-labeling of NODAGA-RGD can be performed rapidly and efficiently within 15 min in a GMP compliant process. Similar preclinical results were obtained in comparison with (18)F-Galacto-RGD. Therefore, (68)Ga-NODAGA-cyclo(RGDyK) is a suitable replacement for (18)F-Galacto-cyclo(RGDfK).