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Ex-vivo Bio-distribution Studies of a Potential Lung Perfusion Agent

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Abstract : After the development of a potential surrogate of MAA, and its successful application for the diagnosis of pulmonary embolism in artificially embolized rats' lungs, this microparticulate system were radiolabelled with gallium-68 to synthesize 68Ga-SBMP with high radiochemical purity >99%. As a prerequisite step of clinical trials, 68Ga- labelled starch based microparticles (SBMP) were analysed for their in-vivo behavior in small animals. The purpose of the presented work includes the ex-vivo biodistribution studies of 68Ga-SBMP in order to assess the activity uptake in target organs with respect to time, excretion pathways of the radiopharmaceutical, %ID/g in major organs, T/NT ratios, in-vivo stability of the radiotracer and subsequently the microparticles in the target organs. Radiolabelling of starch based microparticles was performed by incubating it with 68Ga generator eluate (430±26 MBq) at room temperature and pressure without using any harsh reaction condition. For Ex-vivo biodistribution studies healthy White Wistar rats weighing between 345-460 g were injected intravenously 68Ga-SBMP 20±8 MBq, containing about 2,00,000-6,00,000 SBMP particles in a volume of 700µL. The rats were euthanized at predefined time intervals (5min, 30min, 60min and 120min) and their organ parts were cut, washed, and put in the pre-weighed tubes and measured for radioactivity counts through automatic Gamma counter. The 68Ga-SBMP produced >99% RCP just after 10-20 min incubation through a simple and robust procedure. Biodistribution of 68Ga-SBMP showed that initially just after 5 min post injection major uptake was observed in the lungs following by blood, heart, liver, kidneys, bladder, urine, spleen, stomach, small intestine, colon, skin and skeleton, thymus and at last the smallest activity was found in brain. Radioactivity counts stayed stable in lungs with gradual decrease with the passage of time, and after 2h post injection, almost half of the activity were seen in lungs. This is a sufficient time to perform PET/CT lungs scanning in humans while activity in the liver, spleen, gut and urinary system decreased with time. The results showed that urinary system is the excretion pathways instead of hepatobiliary excretion. There was a high value of T/NT ratios which suggest fine tune images for PET/CT lung perfusion studies henceforth further pre-clinical studies and then clinical trials should be planned in order to utilize this potential lung perfusion agent.

Keywords : starch based microparticles, gallium-68, biodistribution, target organs, excretion pathways
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