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Preclinical Studying of Stable Fe-Citrate Effect on 68Ga-Citrate Tissue Distribution

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Abstract : Background and aims: 68Ga-citrate is one of prospective radiopharmaceutical for PET-imaging of inflammation and infection. 68Ga-citrate is 67Ga-citrate analogue using since 1970s for SPECT-imaging. There's known rebinding reaction occurs past Ga-citrate injection and gallium (similar iron Fe3+) binds with blood transferrin. Then radiolabeled protein complex is delivered to pathological foci (inflammation/infection sites). But excessive gallium bindings with transferrin are cause of slow blood clearance, long accumulation time in foci (24-72 h) and exception of application possibility of the short-lived gallium-68 (T½ = 68 min). Injection of additional chemical agents (e.g. Fe3+ compounds) competing with radioactive gallium to the blood transferrin joining (blocking of its metal binding capacity) is one of the ways to solve formulated problem. This phenomenon can be used for correction of 68Ga-citrate pharmacokinetics for increasing of the blood clearance and accumulation in foci. The aim of real studying is research of effect of stable Fe-citrate on 68Ga-citrate tissue distribution. Materials and methods: 68Ga-citrate without/with extra injection of stable Fe-citrate (III) was injected nonlinear mice with inflammation models (aseptic soft tissue inflammation, lung infection, osteomyelitis). PET/X-RAY Genisys4 (Sofie Bioscience, USA) was used for non-invasive PET imaging (for 30, 60, 120 min past injection 68Ga-citrate) with subsequent reconstruction of imaging and their analysis (value of clearance, distribution volume). Scanning time is 10 min. Results and conclusions: I. v. injection of stable Fe-citrate blocks the metal-binding capability of transferrin serum and allows decreasing gallium-68 radioactivity in blood significantly and increasing accumulation in inflammation (3-5 time). It allows receiving more informative PET-images of inflammation early (for 30-60 min after injection). Pharmacokinetic parameters prove it. Noted there is no statistically significant difference between 68Ga-citrate accumulation for different inflammation model because PET imaging is indication of pathological processes and is not their identification.

Keywords : 68Ga-citrate, Fe-citrate, PET imaging, mice, inflammation, infection
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