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SPECT Imaging of Bacterial Infection Using 111-Indium Labeled Molecular Probes

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Purpose: Most molecular probes for infection imaging are unable to differentiate between inflammation and bacterial colonization. Zinc-dipicaloamine (Zn-DPA) ligands have high affinity for anionic cell membranes and fluorescent versions are known to selectively target bacterial cells over the nearly uncharged membrane surfaces of healthy mammalian cells. This study investigates SPECT imaging of gram-positive Streptococcus Pyrogenes (S. Pyrogenes) infection in mice using three novel Zn-DPA probes labeled with 111-In. Methods: Three Zn-DPA complexes were prepared and labeled with 111-In. Complex radiochemical purity was determined using reverse-phase HPLC. Direct tissue biodistribution studies were performed on CD-1 mice with an S. Pyrogenes leg infection 1 hour and 24 hours after dosing with probes (7 μg, 20 μCi). Whole body SPECT/CT imaging of CD-1 mice with a leg infection was obtained 0.8, 3.5 and 20 hours after intravenous probe injection (150 μg, 450 μCi). Results: All three Zn-DPA probes were complexed with radiopurities > 90%. Biodistribution studies revealed higher accumulation of probe in the infected leg than the blood and all organs other than the liver and intestines. High selectivity for the infected target leg (T) over the contralateral nontarget leg (NT) was reflected by T/NT ratios up to six. Whole-animal SPECT/CT imaging studies showed that intravenous dosing of Zn-DPA complex enabled detection of localized S. Pyrogenes infection with T/NT ratios up to four. Organ distribution varied greatly with probe structure suggesting that these probes have tunable properties for in vivo targeting optimization. Conclusions: Zn-DPA complexs are effective nuclear probes for detecting bacterial infection in living animals. With further development, these probes have potential utility as infection imaging agents within living patients.

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