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Publication date:
2015

Document Version
Early version, also known as pre-print

Link to publication from Aalborg University

Citation for published version (APA):
Modeling PET tracer uptake kinetics in inflammation and infection imaging using a porcine osteomyelitis model – preliminary results

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Introduction
Bone marrow infection (osteomyelitis) is a severe condition that can result in degradation of the affected bone and disability, as well as systemic infection originating from the osteomyelitic foci. Osteomyelitis is often hard to treat with antibiotics, and surgery is frequently needed.

The present study investigates PET scanning (Positron Emission Tomography) of pigs with experimental osteomyelitis, modeling the human condition, and permitting testing of new diagnostic tracers. PET uses short-lived radioactive tracers to reveal physiological and pathological events in the living body.

Using dynamic (rather than static) PET scans allows kinetic analysis of the results. This can reveal details of the uptake process, thereby giving more information on the advantages and disadvantages of the studied tracers.

Kineti c modeling
To study the uptake and release of the tracers, kinetic modeling was performed. Volumes-of-interest (VOIs) were drawn on lesion sites in the right limb. To compare with non-infected sites, similar VOIs were drawn at the same anatomical position in the non-infected left limb. In this preliminary analysis, all considered volumes were spheres of approximately the same size as the lesions as seen on the CT scans.

For a given VOI, the mean PET signal (Bq/mL) over time was analyzed as follows:

Water flows freely with the blood plasma, and its initial uptake will be a measure of blood flow in the tissue. More precisely, the kinetics of the 18O-water was analyzed with the compartment model shown in Figure 2a. The Kr uptake rate constant was taken as measure of blood flow.

The possible infection/inflammation tracers were analyzed with the compartment model shown in Figure 2b. This model has a second tissue compartment allowing modeling of irreversible tracer uptake. To test if uptake was indeed irreversible, a Patlak plot was made for the time-dependent signal. If uptake is irreversible then the Patlak plot will become a straight line with positive slope. The slope of the Patlak plot will be the “irreversible uptake rate” (Kf rate), describing the irreversible uptake.

Briefly, the Patlak plot assumes that after some time, blood and the “irreversible” compartment are in equilibrium. The rate Kd describes the irreversible uptake from this combined blood/irreversible compartment, see Figure 2c. For further explanation, see Jødal (2015).

The plasma measurements for 13C-methionine and 11C-PK11195 were metabolite-corrected, while the other tracers did not show significant metabolization.

Results
One osteomyelitis lesion in the femoral head/neck of the first pig, and one in the metatarsus II bone of the fourth pig was studied.

Water: For both lesions, the kinetic modeling showed blood flow to be similar in the infected and non-infected side. Infected (right) and non-infected (left) sides are comparable to Table II.

Possible infection/inflammation tracers: In both lesions, all four tracers showed linear uptake and no irreversible uptake. An example of a Patlak plot is shown in Figure 3. The ratio between the right (infected) and left (non-infected) side was highest for FDG and lowest for PK11195. Infected (right) and non-infected (left) sides are compared in Table II.

PK11195 showed similar values of the plasma input curve. Other researchers have found this tracer to be sticking to tubing, which could give erroneously low values in the plasma curve initially while making later values unreliable.

Discussion and outlook
Inflammation and infection usually results in increased blood flow, at least in the acute state, and it is therefore surprising that these two lesions had water uptake (blood flow) at the same level as the corresponding non-infected positions in the opposite leg. Further analysis of these and other lesions are to be made to see if this finding is general for osteomyelitic lesions, which could be a part of the inability of systemic antibiotic therapy.

Of the possible infection/inflammation tracers, FDG uptake was found to have the highest uptake ratio relative to the non-infected side. A high ratio can, if it is distinctive when non-infectious, indicate infection, although uptake in other tissue (e.g. muscle uptake) should also be taken into account before the Patlak plot did not show high ratio in any of the two lesions, and furthermore showed strange results giving suspicion of sticking to tubing, which makes the tracer hardier to work with.

The series of pig scans continues, but without PK11195 as a tracer. Knowledge of which tracers are taken up by osteomyelitic lesions can hopefully lead to improved scanning of patients with suspicion of osteomyelitic infections.

References

www.turkpetcentre.net/analyse/analys_mod_patlak_interpretation.html