[11C]PBR28 Macrophage Targeted Positron Emission Tomography–Computed Tomography in Rheumatoid Arthritis: Results of a Pilot Study

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Background: It is well established that early recognition and treatment of synovitis is integral to the prevention of permanent joint damage and co-morbidity in RA. PET is being increasingly recognized as a sensitive means of detecting and quantifying early synovitis. PET ligands to translocator protein (TSPO), a mitochondrial cholesterol transporter known to be upregulated on activated macrophages, are increasingly being demonstrated to have utility in detecting and quantifying synovitis. The TSPO PET tracer [11C]PK11195 has been demonstrated to detect subclinical synovitis in patients with RA. However, the second-generation TSPO PET tracer [11C]PBR28 has a higher affinity for TSPO and less signal:noise ratio, thus it may be a more sensitive and specific tracer for imaging synovitis. Binding of second-generation tracers is affected by a single nucleotide polymorphism (SNP), rs6971, with homozygotes binding tracers with low affinity. Our group has so far demonstrated rs6971 homozygote prevalence at 12% in the RA population, comparable to healthy populations. Here we present findings from a proof-of-principle pilot study using [11C]PBR28 to image synovitis in patients with RA.

Methods: Patients with RA affecting the knees or ankles were included, as well as healthy controls. Homozygotes for rs6971 were excluded. Patients underwent a US scan and clinical examination of the group of joints to be imaged with PET-CT. Semi-quantitative scores for synovitis on clinical examination and US were applied.

[11C]PBR28 was injected as an i.v. bolus at the start of a 90 min dynamic PET acquisition. PET data were reconstructed using filtered back-projection correcting for attenuation and scatter (based on a low-dose CT acquisition). Regions of interest (ROIs) were drawn on synovial tissue in the knee or ankle joints. Standard uptake values (SUVs) for all ROIs were calculated.

Results: To date, six PET-CT images have been acquired: four from patients with known RA and 2 from those without inflammatory arthritis. SUVs of [11C]PBR28 positively correlate with synovitis scoring on clinical and US assessment, with no significant uptake in healthy joints. Interestingly, elevated SUVs were observed in the knee joint of an RA patient with no

clinical or US evidence of inflammation, consistent with subclinical synovitis detected on subsequent MRI.

Conclusion: We demonstrate a significant increase in the uptake of [11C]PBR28 in inflamed joints, with significant positive correlation of SUVs with clinical and US assessments of synovitis. The potential of [11C]PBR28 to detect subclinical synovitis is demonstrated by the fact that elevated SUVs were seen in the knee joint of an RA patient without clinical or US evidence of synovitis. Further patients are required to confirm these initial findings. The impact of binding affinity due to the rs6971 SNP on [11C]PBR28 PET-CT of inflamed joints remains to be fully assessed.

Disclosure statement: The authors have declared no conflicts of interest