Human Subject with Unexpected Biodistribution of $^{[11]}$C$\text{PK11195}$

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Abstract: [N-Methyl-$^{11}$C](R)-1-(2-chlorophenyl)-N-(1-methylpropyl)-3-isoquinolinecarboxamide ($^{[11]}$C$\text{PK11195}$ is a high-affinity ligand for the 18 kDa translocator protein (TSPO), previously known as the peripheral benzodiazepine receptor (PBR). According to the available gene array datasets, the highest expression of TSPO is seen in the lungs and heart [1, 2]. At the cellular level, TSPO is expressed in monocyte/macrophage lineage cells and, within the central nervous system, in activated microglia, i.e. the brain-resident macrophages. Accordingly, $^{[11]}$C$\text{PK11195}$ has been used for in vivo visualization of TSPO and, thereby, the microglial activation in inflammatory brain diseases, such as, multiple sclerosis and amyotrophic lateral sclerosis [3, 4]. Despite the widespread use of $^{[11]}$C$\text{PK11195}$ PET, the whole-body distribution and dosimetry of $^{[11]}$C$\text{PK11195}$ have not been studied until very recently [2, 5]. Here, we report a case of atypical distribution of $^{[11]}$C$\text{PK11195}$.

The $^{[11]}$C$\text{PK11195}$ was prepared as described earlier [2]. The radiochemical purity was 99.9%, and specific radioactivity was 32.8 MBq/nmol at the time of injection, as determined by radio-HPLC. Whole-body $^{[11]}$C$\text{PK11195}$ PET imaging was performed on a healthy volunteer (male, age 23 years, height 180 cm, weight 76 kg) using an Advance PET scanner (General Electric Medical Systems, Milwaukee, WI, USA) operated in 2D mode. Imaging was performed with the subject in the supine position and arms alongside the body. The subject was intravenously injected with 704 MBq of $^{[11]}$C$\text{PK11195}$, and the whole-body PET scanning proceeded from the head to the pelvic floor, excluding legs. Six bed positions were required for this measurement, with a 5-min acquisition time for each position. The acquired data were iteratively reconstructed, with attenuation correction, using ordered subset expectation maximization algorithm. Regions of interest were drawn on the areas of certain organs and urinary bladder, followed by the calculation of the standardised uptake values (SUV mean).

Whole-body PET images revealed an atypical biodistribution of radioactivity with enhanced uptake in the excretory and metabolic pathways (Fig. 1). Liver (SUV mean 1.94), vertebral column (SUV mean 1.77), salivary glands (SUV mean 1.67), thyroid gland, urinary bladder (SUV mean 1.49), hip bone, breast bone and small intestine (SUV mean 1.06) are clearly visible (arrows). However, the radioactivity uptake is very low in heart (SUV mean 0.78), lungs (SUV mean 0.26) and kidneys, which normally have high densities of TSPO [1, 2].

It has been previously reported by our team [2, 5] and others [6, 7] that radioactivity after intravenous injection of $^{[11]}$C$\text{PK11195}$ is generally distributed in urinary bladder, adrenal gland, liver, salivary glands, heart, kidneys, and vertebral column. Poor radiochemical and chemical quality, or very low specific radioactivity could potentially be responsible for the atypical biodistribution of any radiotracer. However, in this case, both the radiochemical purity and the specific radioactivity were in line with our previous $^{[11]}$C$\text{PK11195}$ studies (n=19 subjects), with values >99% and 35±9 MBq/nmol, respectively [2, 5], and thus, they cannot explain the unexpected biodistribution findings. Furthermore, the subject had no significant prior medical history and was not on any medication at the time of the whole-body PET scan. Previously, however, Brown et al. have reported a similar unexpected distribution with another TSPO tracer, $^{[11]}$C$\text{PBR28}$ [8]. In their study, one subject had decreased radioactivity uptake in organs with known high TSPO densities, i.e., brain, lungs, heart, spleen, and kidneys. Concordant with our finding with $^{[11]}$C$\text{PK11195}$, the heart, spleen, lungs, and kidneys could not be identified visually in this subject. The biodistribution was similar to that in a monkey with pre-blockade of receptors by means of high doses of nonradioactive PK11195.

In conclusion, in a larger study on a total of 19 human subjects, we observed unexpected whole-body biodistribution of $^{[11]}$C$\text{PK11195}$ in one subject. The reason for this atypical distribution remains unknown, but a low TSPO density is suggested as an explanation.
**REFERENCES**


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