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

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Abstract: [N-Methyl-^{11}C](R)-1-(2-chlorophenyl)-N-(1-methylpropyl)-3-isoquinoline carboxamide [^{11}C]PK11195 is a widely used radiopharmaceutical for in vivo assessment of translocator protein 18 kDa (TSPO) activity using positron emission tomography. Here we present an interesting case of unusual distribution of [^{11}C]PK11195, that is a lack of uptake in tissues known for high expression of the TSPO.

Keywords: Translocator protein, PK11195, PET, carbon-11.

Positron emission tomography (PET) radiotracer [*N*-methyl-^{11}C](*R*)-1-(2-chlorophenyl)-*N*-(1-methylpropyl)-3-iso-quinolinecarboxamide ([^{11}C]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]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]PK11195 PET, the whole-body distribution and dosimetry of [^{11}C]PK11195 have not been studied until very recently [2, 5, 6]. Here, we report a case of atypical distribution of [^{11}C]PK11195.

The [^{11}C]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]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]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}).

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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]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]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]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]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 biodistri-bution of [^{11}C]PK11195 in one subject. The reason for this atypical distribution remains unknown, but a low TSPO density is suggested as an explanation.

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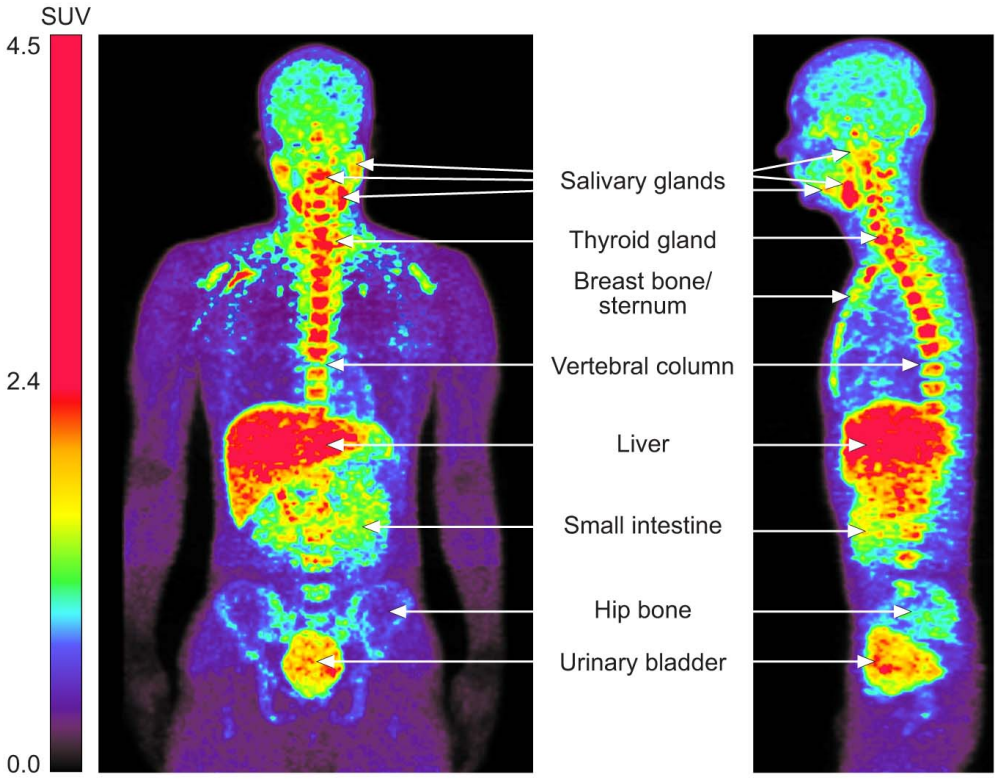

Fig. (1). PET scan of a healthy human subject with unexpected whole-body distribution of radioactivity after intravenous administration of [^{11}C]PK11195.

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