[^{18}F]FS-DPA: Synthesis and evaluation in a rat stroke model.

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Recently, an ultrafast ^{18}F/^{19}F isotopic exchange based on sulfur (VI) fluoride exchange (SuFEx) has been described.[1] In the present work, the novel SuFEx radiolabeling was used to prepare a ^{18}F-labeled fluorosulfurylated DPA-714 (**1**) analogue ([^{18}F]FS-DPA ([^{18}F]**2**)). DPA-714 is a selective agonist at the translocator protein 18 kDa (TSPO), a biomarker with relevance for different neurodegenerative and psychiatric diseases, stroke and brain tumors.[2-4] The corresponding radioligand [^{18}F]DPA-714 is widely used in preclinical and clinical TSPO PET studies. Consequently, the suitability of [^{18}F]FS-DPA for imaging of neuroinflammation was evaluated in a transient stroke rat model using [^{18}F]DPA-714 as a reference TSPO-specific PET tracer using µPET.

2 (15 µg) was ^{18}F-labeled in MeCN at 40 °C for 3 min. The resulting crude radiotracer was purified by solid phase extraction affording [^{18}F]**2** in the ready-for-application form in 42±3% activity yield within 25 min. 3 adult Sprague Dawley rats underwent occlusion of the anterior cerebral artery (ACA). T2-weighted MRI was performed after 24 h to visualize the edema in the ACA territory, demarcating the area of subsequent neuroinflammation. After 4 weeks, rats were measured with the TSPO [^{18}F]**1** (0-30 min p.i.) and with [^{18}F]**2** (0-120 min p.i.) using µPET (Siemens Focus 220, **Fig 1**). Both tracers reliably visualized neuroinflammation in the ACA territory. Maximum uptake was SUV_{bw} 257 ± 43 for [^{18}F]DPA-714 and SUV_{bw} 412 ± 82 for [^{18}F]FS-DPA, 0-30 min p.a. After 2 h, SUV_{bw} of [^{18}F]FS-DPA was still 260 ± 53. Signal-to-noise ratio (SNR) was 3.6 ± 1.3 for [^{18}F]DPA-714, and 3.1 ± 0.5 for [^{18}F]FS-DPA (0-30 min p.i.). SNR of [^{18}F]FS-DPA increased over time and amounted to 3.8 ± 0.7 (90-120 min p.i.). Both [^{18}F]DPA-714 and [^{18}F]FS-DPA underwent fair defluorination with a bone SUV_{bw} of 229 ± 25 (90-120 min) for [^{18}F]FS-DPA.

[^{18}F]FS-DPA is a promising candidate for high-quality visualization of neuroinflammation. Easy accessibility and a very fast and simple preparation ([^{18}F]**2**: 25 min *vs.* [^{18}F]**1** 45 min[5]) combined with excellent preclinical imaging properties justify further preclinical and, possibly, clinical studies with this tracer.

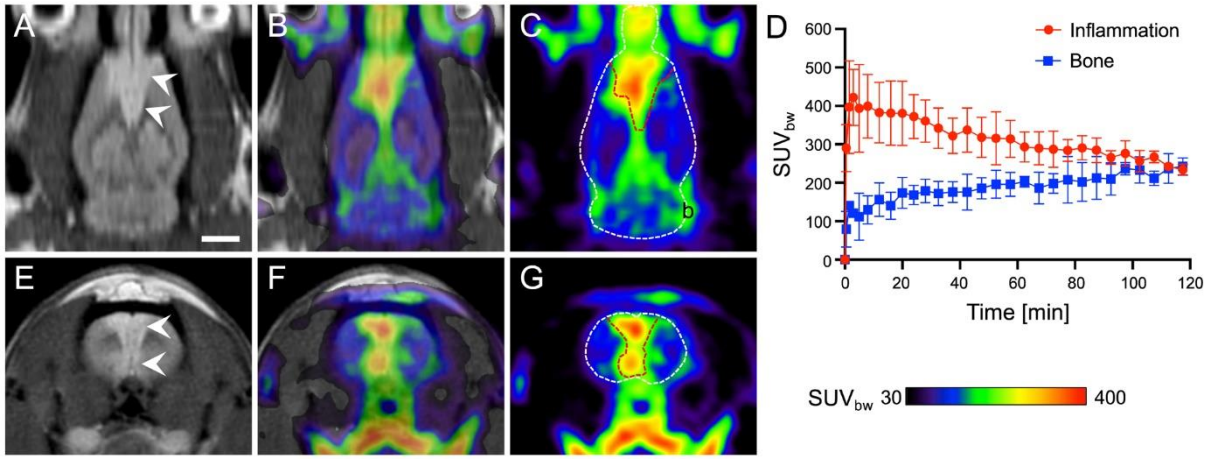

Figure 1. *In vivo* evaluation of [^{18}F]FS-DPA ([^{18}F]**2**) in a rat stroke model (n=3). Shown are individual summed images (30–60 min p.i.) of one rat with corresponding MRI (T2) in horizontal (**A**–**C**) and transverse (**E**–**G**) orientation. MRI (T2) at 24 h post-stroke showed edema in the ACA territory (arrowheads in A+E). PET images (C+G) were taken 31 days after stroke, the former edema is indicated by a red outline. The time-activity curve (**D**) showed a slow washout of [^{18}F]FS-DPA from the inflammatory area, and a steadily increasing bone uptake.

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[2] B. Zinnhardt, *et al.*, *Eur. J. Nucl. Med. Mol. Imaging* **2021**, DOI 10.1007/s00259-021-05276-5.

[3] E. L. Werry, F. M. Bright, M. Kassiou, in *Neurodegener. Dis. Biomarkers. Neuromethods, Vol 173* (Eds.: P. V. Peplow, B. Martinez, T.A. Gennarelli), Humana Press, New York, NY, **2022**, pp. 407–427.

[4] L. J. De Picker, B. C. M. Haarman, *Eur. J. Nucl. Med. Mol. Imaging* **2021**, DOI 10.1007/s00259-021-05308-0.