Automated synthesis and PET evaluation of both enantiomers of [18F]FMISO - DTU Orbit
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Introduction: [18F]FMISO, the widely used positron emission tomography (PET) hypoxia tracer, is a chiral compound clinically used as a racemic mixture. The purpose of this study was to synthesize the individual (R)- and the (S)-enantiomers of [18F]FMISO and compare their PET imaging characteristics.

Methods: The radiosynthesis of enantiopure (R)- and (S)-[18F]FMISO was based on Co(salen) (N,N’-bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediaminocobalt)-mediated opening of enantiopure epoxides with [18F]HF. The uptake and clearance of the individual [18F]FMISO antipodes were investigated using micro-PET/CT imaging performed on mice bearing FaDu tumors. Image-derived biodistribution was obtained from micro-PET/CT scans performed at 1 and 3 hours post injection (p.i.). In addition, the uptake patterns of each enantiomer were observed using two-hour dynamic micro-PET/CT scans and the time-activity curves from different organs were compared.

Results: The individual (R)- and (S)-[18F]FMISO enantiomers were synthesized in one step with high enantiomeric excess (ee) > 99% and radiochemical purity > 97% using custom-made automation module. The dynamic micro-PET/CT scanning revealed a faster initial uptake of the (R)-[18F]FMISO enantiomer in tumor and muscle tissues, however the difference became progressively smaller with time. The tumor-to-muscle (T/M) and tumor-to-liver (T/L) ratios remained nearly identical for the (R)- and (S)-forms at all time points. The micro-PET/CT imaging at 1 and 3 hours p.i. did not show any significant enantioselective tissue uptake.

Conclusions: Although the (R)-enantiomer of [18F]FMISO demonstrated a somewhat faster initial tumor and muscle uptake no significant enantioselective tissue uptake was observed at later time points. The T/M- and T/L- ratios for the (R)- and (S)-forms were the same within the experimental error at all times. Therefore, the use of enantiopure [18F]FMISO is unlikely to present any practical clinical benefit for PET imaging.

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