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Characterisation of a Fluorescent Dye Library using a Dual-Labelled PSMA-617-based Tracer

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Introduction: In the field of dual-labelled tracers and fluorescence-guided surgery (FGS), ICG and IRDye800CW have been established as the most commonly used dyes. However, fluorescent dyes have continued to evolve. In order to investigate the suitability of such new dyes for potential clinical application, a library of dyes was conjugated to a PSMA-617-based tracer (DP). The aim was to identify a candidate with the most promising pharmacokinetic and optical properties to improve precise real-time feedback during surgery. **Materials and Methods:** Pharmacokinetic behaviour was assessed in BALB/c nu/nu mice bearing LNCaPPSMA+ xenografts by μ PET/MRI at 1h and 2h after injection of 0.5 nmol (2.8 kDa - 3.2 kDa) of the ^{68}Ga -labelled hybrid molecules. Fluorescence was determined *ex vivo* as well as organ distribution 2 h p.i.. **Results:** *In vivo* studies revealed different pharmacokinetic profiles depending on the conjugated dye. Two candidates showed rapid clearance 1 h p.i. with high tumour uptake 2 h p.i.: DP-09 (9.14 %ID/g tumour, 26.27 %ID/g kidney) and DP-15 (7.67 %ID/g tumour, 7.68 %ID/g kidney). In contrast, DP-24 showed a slower clearance at 1 h p.i., but three times higher tumour accumulation compared to the others (22.94 %ID/g tumour, 61.97 %ID/g kidney). **Conclusion:** The three candidates identified were shown to have a promising pharmacokinetic profile after conjugation with the fluorescent dyes, making them suitable for further investigation. With improved photostability and higher quantum yields compared to ICG and IRDye800CW, the selected candidates may lead to an advantage in FGS.

Preferred type of presentation

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