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PET and near-infrared fluorescence imaging of tumors using a single cRGD-based peptide

INTRODUCTION

Despite technological improvements, accurate intraoperative imaging of tumors remains difficult. Targeted near-infrared (NIR) fluorescence imaging has demonstrated to visualize tumors more accurately during surgery. A drawback of fluorescence is its limited penetration depth of approximately 8 mm. Hybrid tracers allowing both preoperative nuclear and intraoperative fluorescence imaging can be a solution. Preoperative targeted imaging can assist in surgical planning. Subsequently, the same tracer enhances intraoperative real-time detection of the target. cRGD peptide targets integrins associated with angiogenesis (e.g. αvβ3) and has been used successfully for nuclear and fluorescent imaging agents.

AIM: this study evaluates the hybrid tracer cRGD-DFO[89Zr]-ZW800F for PET and NIR fluorescence imaging in cancer mouse models

MATERIALS AND METHODS

First, cRGD-DFO-ZW800F was tested in vivo in mice with orthotopic colorectal (HT29-luc2; n=8) and pancreatic (BxPC3-luc2; n=3) cancer.
A dose of 10 nmol was injected intravenously. The dose was based on previous results with cRGD-ZW800-1. Imaging was performed using the Pearl and the prototype FLARE Imaging system at 4h and 24h post injection.

Second, since ZW800-1 was unstable, the stability of ZW800-1 Forte (ZW800F) after labeling DFO with 89Zr was assessed.

Third, cRGD-DFO[89Zr]-ZW800F (10 nmol, 3 MBq) was administered to mice (n=8) with orthotopic colorectal (HT29-luc2) cancer.
PET-CT was performed at 1h, 4h and 24h post injection.
Biodistribution was performed at 4h and 24h post injection mice were sacrificed and several tissues were excised to determine the percentage of the injected dose per gram (%ID/g).

RESULTS

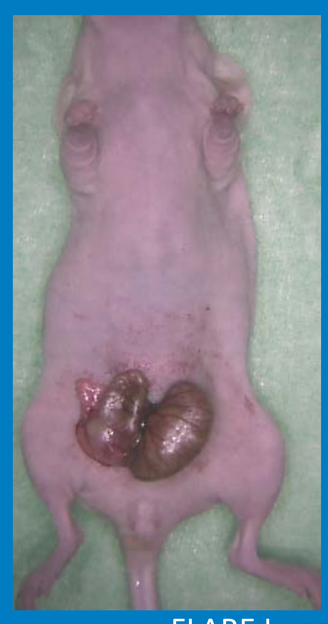
In vivo, tumor-to-background ratios using the Pearl for HT29-luc2 were 3.6±1.1 and 3.8±0.9 and for BxPC3-luc2 2.6±0.2 and 2.2±0.5 at 4 and 24h, respectively.

The fluorescence signal of cRGD-DFO-ZW800 (2.2 kDa; emission peak at 759 nm) remained stable after labeling with 89Zr. PET-CT at 4h allowed visualization of colorectal tumors of the mice injected with cRGD-DFO[89Zr]-ZW800F.

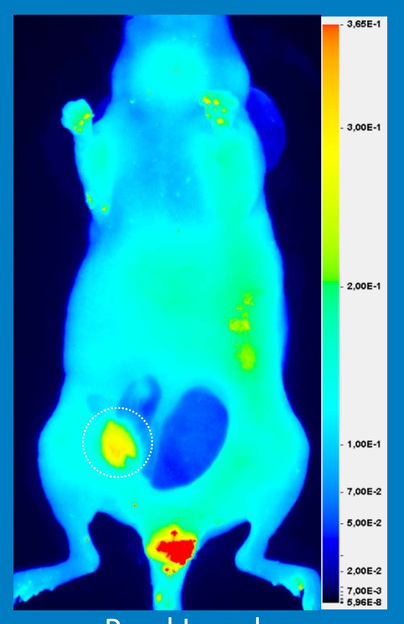
Biodistribution at 4h showed the highest uptake of the tracer in kidneys (16.8±8.6 %ID/) followed by urine, liver, colon content and tumor (0.9±0.1 %ID/g).

Biodistribution at 24h showed the highest uptake of the tracer in kidneys (8.6±1.0 %ID/g at 24h) followed by liver and tumor (0.8±0.2 %ID/g). Comparing 4h and 24h, the %ID/g strongly decreased in urine (-93%), colon content (-82%), blood (-70%), and kidneys (-48%), while it only mildly decreased in liver (-20%) and tumor (-14%).

NIR fluorescence imaging at 4h

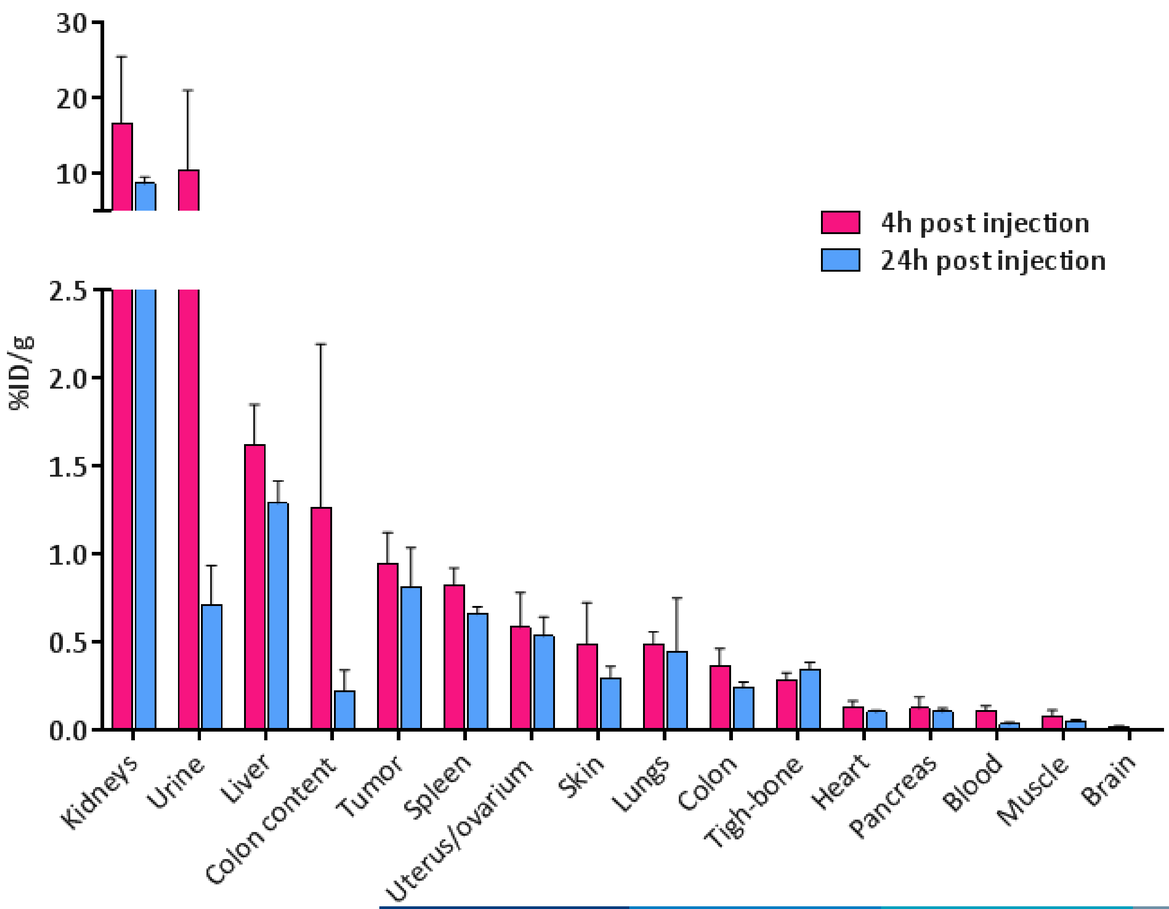


FLARE Imaging System



Pearl Impulse

Biodistribution of 10 nmol cRGD-DFO[^{89}Zr]-ZW800 (3 MBq)



CONCLUSION

This study shows the feasibility of PET and fluorescence imaging of tumors with a single injection of cRGD-DFO[89Zr]-ZW800F.

This multimodal tracer can overcome inherent drawbacks of NIR fluorescence imaging.

cRGD-DFO[89Zr]-ZW800F allows translation of preoperative imaging to the intraoperative situation.

PET-CT at 4h post injection