B-5

Dual Labeling as a Tool for Cross-Validating the Imaging Properties of a Hybrid Somatostatin Analog

Servando Hernandez Vargas[1]; Sukhen C. Ghosh[1]; Julie Voss[1]; Jo Simien[1]; Ali Azhdarinia[1]

[1]McGovern Medical School, Institute of Molecular Medicine

BACKGROUND: Combining radioactive and fluorescent contrast enables quantitative analysis of intraoperative imaging agents. We selected the somatostatin receptor-2 (SSTR2) targeted agent, 68Ga-DOTA-TOC, as a model for a dual-labeled analog, and used a multimodality chelator (MMC) to overcome steric effects of dye labeling on receptor binding. Here, we investigated the tumor targeting properties of a hybrid somatostatin in vivo.

METHODS: Nude mice implanted subcutaneously with SSTR2-overexpressing HCT116 cells (HCT116-SSTR2) were used for in vivo evaluation of tumor targeting. Near-infrared fluorescence (NIRF) imaging and ex vivo biodistribution were conducted at early (3h, 68Ga) and delayed (24 h, 67Ga) time points to determine tracer pharmacokinetics. Excised tissues underwent NIRF imaging to qualitatively assess tracer biodistribution and gamma counting to obtain the corresponding quantitative values. Histological analysis was performed on tumor and non-tumor cryosections.

RESULTS: At 3 h post-injection, optical/nuclear imaging demonstrated that 68Ga-MMC(IR800)-TOC tumor uptake could be well-visualized by both modalities along with prominent kidney signal. 68Ga-biodistribution data was in agreement, showing %ID/g values of 3.8±0.8 (tumor) and 46.1±4.2 (kidneys) (n=4), in addition to notable background signal. Ex vivo optical imaging findings at 3 h were similar to the 68Ga-biodistribution data and showed early tumor

accumulation with high renal clearance. Delayed NIRF imaging (24 h) allowed the reduction of background fluorescence, resulting in significantly increased contrast for key sites of NET formation, as well as a 33% increase in tumor-to-muscle ratio. Interestingly, contrast ratios determined by NIRF were nearly identical to those obtained from the 67Ga-biodistribution data. Imaging of tissue sections further supported in vivo and ex vivo data and revealed the highest fluorescent signal in tumors with low uptake in non-tumor sites.

CONCLUSION: The MMC scaffold is effective for developing a dual-labeled octreotide analog. For the fluorescent DOTA-TOC analog, a delayed optical imaging time point (24 h) provides an optimal tumor-to-tissue contrast.