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Case Study

Analyzing the Biodistribution of Fibroblast Activation Protein Imaging Compound with Cryo-Fluorescence Tomography

Introduction

A presentation from the 2023 Annual Congress of the European Association of Nuclear Medicine (EANM) titled "Preclinical characterization of novel radiolabeled and fluorescent-labeled Fibroblast Activation Protein (FAP)-targeting ligands using gamma counting, SPECT imaging and Cryo-Fluorescence Tomography (CFT)" explored the development of FAP fluorescent agents to be used in conjunction with FAP PET for guided surgical resection.[1]

This research compared biodistribution in U-87 MG tumor-bearing mice by comparing a 1 μg dose of either a ZW800-1 fluorescent-labeled FAP compound (RXT-1341) and a 67Cu-labeled NOTA-conjugated FAP compound (RTX-1363S) of otherwise analogous structure. Three animals were imaged longitudinally using SPECT/CT at 1h and 24h post-administration. Additional animals were sacrificed at 1h or 24h post-administration for gamma counting or CFT imaging. Drug uptake was determined from regions of interest from SPECT and CFT images, including tumor, knee joint, liver, and kidney. The biodistribution of the ZW800-1 FAP compound from CFT was compared to the accepted SPECT and gamma counting (GC) methods.

Key findings from the study include:

1. Expert visual assessment concluded that there is comparable biodistribution between SPECT and CFT imaging methods and that no significant differences in macro tissue distribution were noted at either time point (Figure 1);

2. CFT imaging provided higher resolution, whole-body information than SPECT, yielding insights such as the local distribution of the ligand on the surface of the bone and heterogeneity of distribution within the tumor (Figure 2);

3. Analysis was performed, demonstrating the longitudinal intensity values relative to liver in tumor, knee joint, and kidney (Figure 3)

Figure 1.

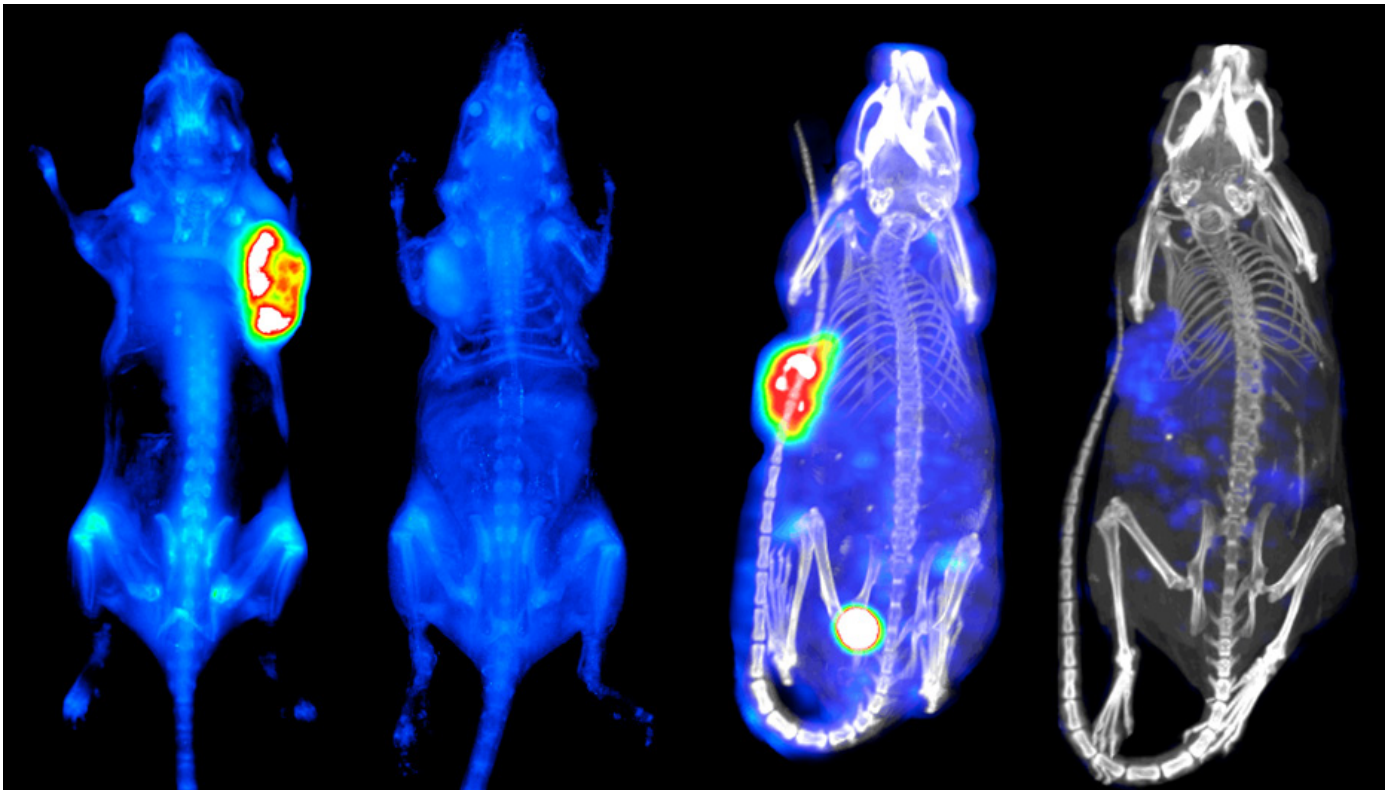

Figure 1: MIP images of (left-to-right) CFT at 1h, CFT at 24h, SPECT/CT at 1h, and SPECT/CT at 24h. All images are shown on a scale of 0-8, normalized to liver.

Figure 2.

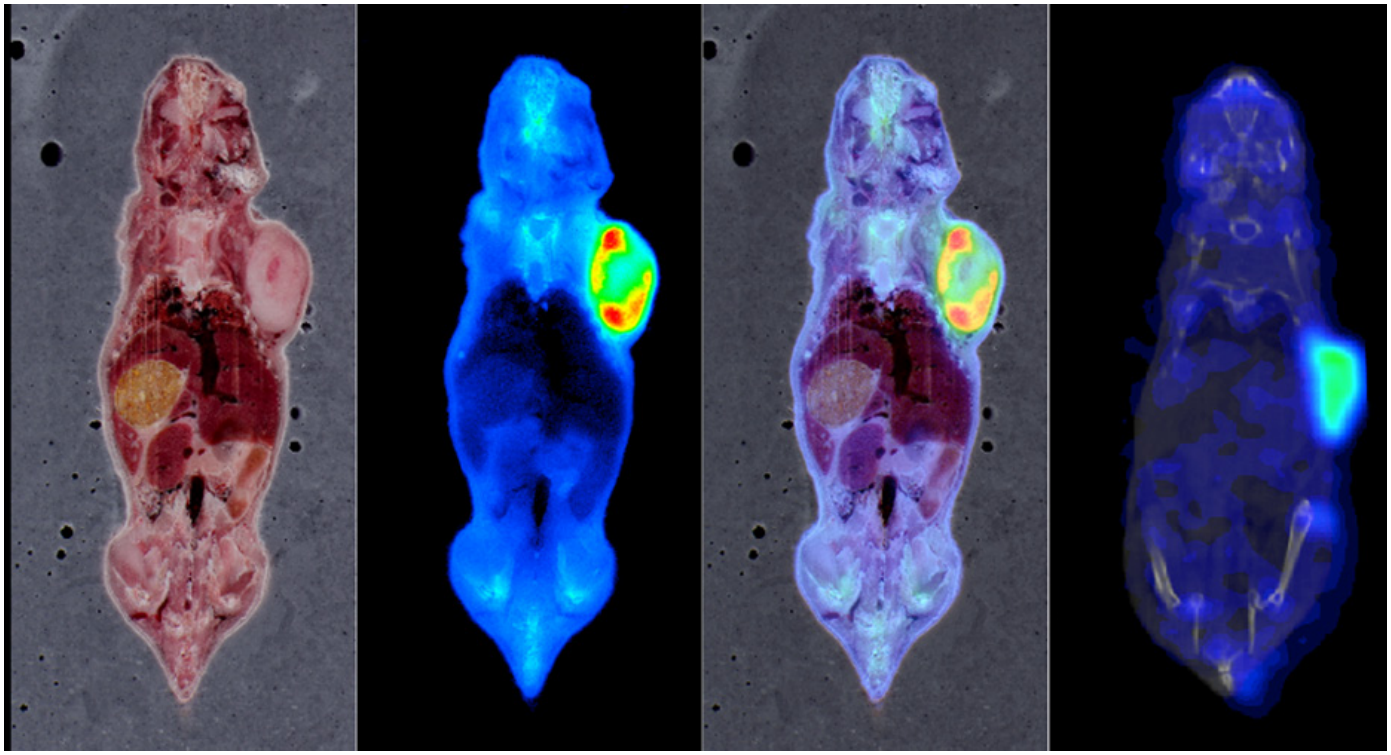

Figure 2: (left-to-right) Anatomical White-light, fluorescence, and overlaid image of a representative CFT slice. Representative SPECT/CT slice. All images are from 1h post-administration.

Figure 3.

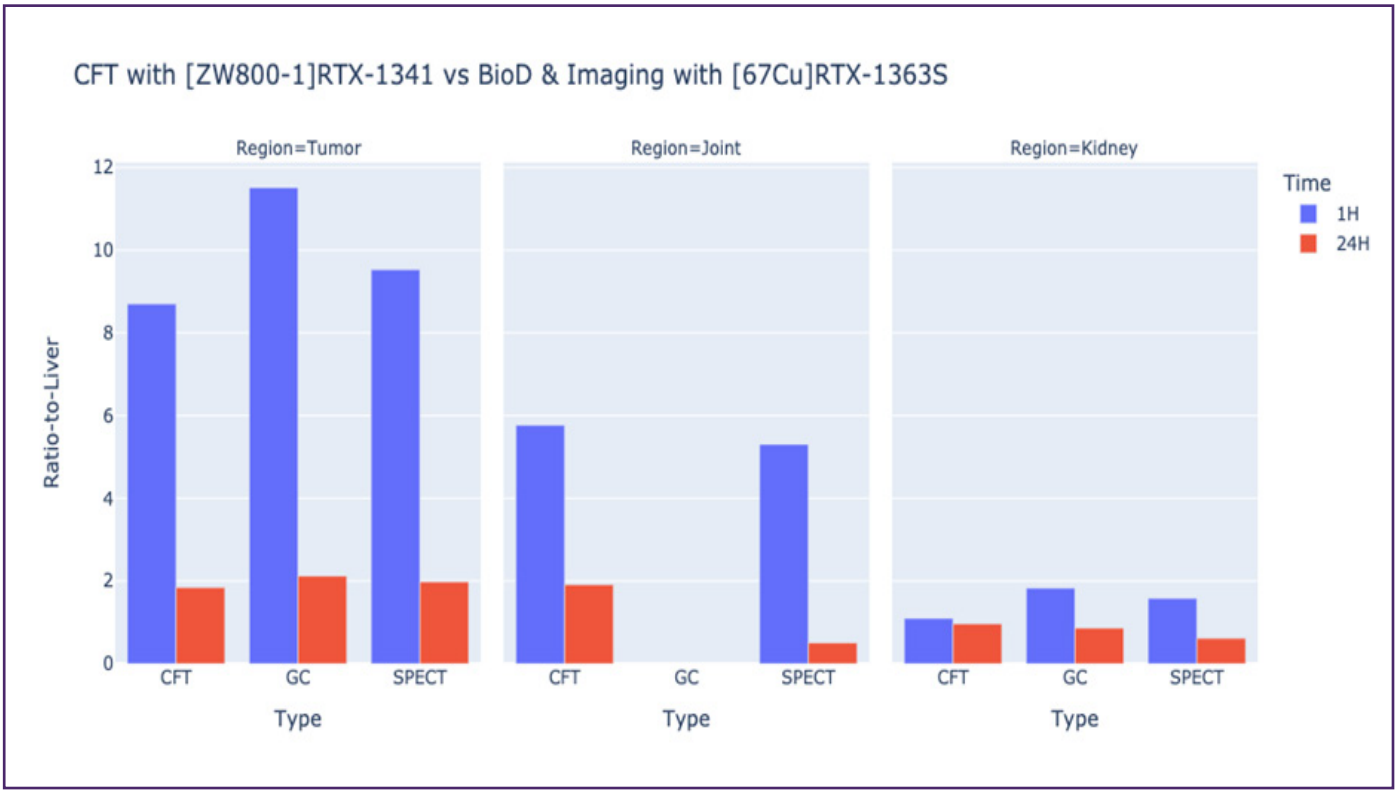

Figure 3: Analysis of CFT, gamma counting, and SPECT data for tumor, knee joint, and kidney. Data are shown at 1h and 24h. All data are normalized to mean liver signal.

Conclusions & Discussion

This study demonstrates that evaluating drug biodistribution by CFT yielded results comparable to gold-standard techniques such as SPECT and gamma counting. Like SPECT, CFT provides high sensitivity whole-body imaging, leading to similar conclusions between the two methods. CFT on the other hand boasts even greater resolution when compared to SPECT and operates via fluorescence imaging, eliminating the need for radioactive reporters. It is also important to note that physiochemically similar characteristics between ZW800-1 and Cu-N3O2 may have contributed to similarities in tissue biodistribution, further emphasizing that for certain ligands systems CFT can complement radiolabeled techniques for compound screening.

CFT in comprehensive biodistribution analysis provided insights into drug discovery and delivery, thereby contributing to advancements in preclinical research and therapeutic strategies. The versatility of CFT in applications, including oncology & immunotherapy, gene & cell therapy, and neurology, emphasizes the need for further research and development in advanced imaging modalities. The continued exploration of CFT and its integration into preclinical studies holds potential for paving the way for improvements in therapeutic interventions and drug delivery systems.

Reference 1. Hesterman, Novicki, White, Stokes, Cordova, Toddes, Silva, Burke, Domarkas, Wright, Archibald, Yost, Heimann, DiMagno, Hillier, Patel, Orcutt, Amor, Tully, Babich, Hoppin. EANM 2023. Preclinical characterization of novel radiolabeled and fluorescent-labeled Fibroblast Activation Protein (FAP)-targeting ligands using gamma counting, SPECT imaging and Cryo-Fluorescence Tomography (CFT).