Upgrading a multimodal SPECT-PET-Optical-CT for integrated fluorescence tomography

Felix Gremse[1,2], Stephan Blazis[3], Ruud Ramakers[3,4], Sofia Koustoulidou[3], Chao Wu[3], Yutaro Takahashi[3], Fabian Kiessling[1], Staf van Cauter[3, 4], Freek Beekman[3, 4]

1) Experimental Molecular Imaging, Aachen, Germany
2) Gremse-IT GmbH, Aachen, Germany
3) MILabs B.V., Utrecht, The Netherlands
4) Section Biomedical Imaging, RST, TU-Delft

Introduction

Fluorescence tomography (FLT) determines the three-dimensional fluorescence distribution in laboratory mice. Longitudinal imaging allows determination of the biodistribution, i.e. the elimination and retention of fluorescence-labelled drugs or drug delivery systems. The combination with an external anatomical modality such as µCT is beneficial for reconstruction and image analysis [1]. While fusion with molecular imaging modalities such as PET and SPECT may provide additional readouts from the same animal, the shuttling between devices and postprocessing required for co-registration makes this workflow impractical for applied research under high-throughput and routine conditions. Hence, our aim was to upgrade an existing SPECT-PET-Optical-CT with an integrated FLT to enable multimodal and longitudinal SPECT-PET-FLT-CT imaging, suitable for sophisticated applied molecular imaging research.

Material and Methods

SPECT-PET-Optical-CT

Figure 1: Left: A commercially available integrated SPECT-PET-Optical-CT (MILabs B.V., Utrecht, The Netherlands) was upgraded with a continuous wave near-infrared laser diode (730 nm).
Right: A partially transparent mouse holder with integrated anesthesia and heating system, built-in marker holes for robust fusion, compatible with SPECT and PET, was designed and produced using 3D-printing.

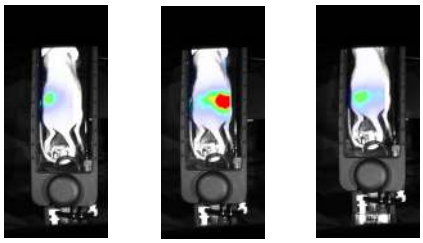


Figure 2: Phantoms and anesthetized mice were scanned after rectal insertion of a pipette tip filled with µCT contrast agent and fluorescence [1]. Mice were scanned again after i.v. injection of µCT contrast and OsteoSense 750 EX. 24h later, mice received i.v. injection of SPECT (Tc-99m-MDP) and PET (18F-FDG) tracers and were scanned in all four modalities.

Imaging

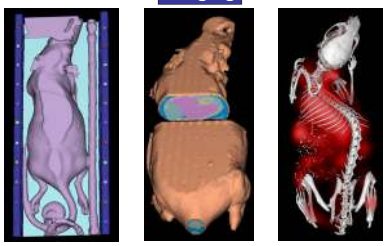


Figure 3: Automated mouse-bed segmentation and marker detection was used for an accurate geometric model for ray casting of CCD pixels onto the mouse surface for reconstruction. Heterogeneous scattering and absorption maps were derived [2] and used for GPU-accelerated iterative reconstruction of the 3D fluorescence distribution [3].

Results

Phantom results

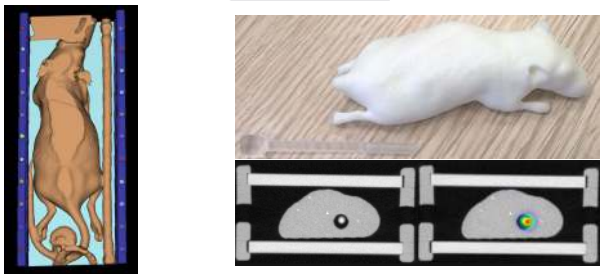


Figure 4: Left: CT-FLT and SPECT-PET-FLT-CT scans were acquired successfully, and all marker holes were automatically detected resulting in accurate and automated image fusion.
Right: A 3D-printed mouse phantom with fluorescence insertion was used for testing and the FLT reconstruction showed proper signal alignment.

In vivo results

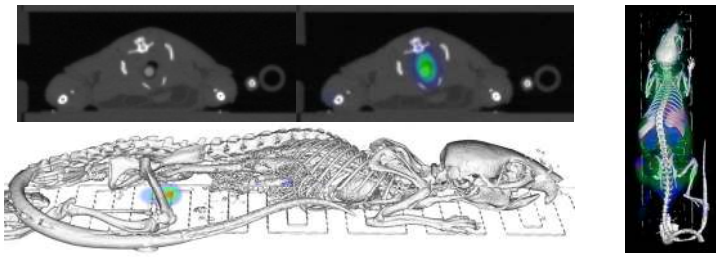
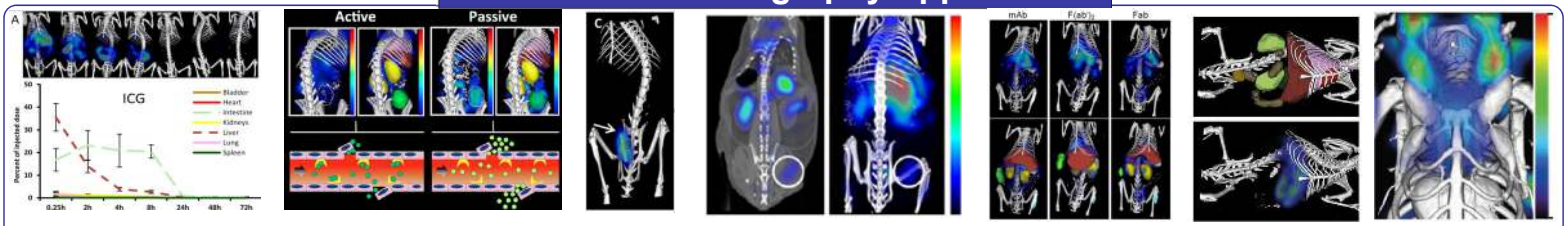


Figure 5: Left: The fused FLT-CT data showed localization of the fluorescence at the rectal inclusion and the FLT-CT scan shortly after OsteoSense injection showed strong signal in the urinary bladder, as expected. µCT data showed early signal in blood vessels and then accumulation in liver and spleen. The thin copper wires of the heating system caused only marginal µCT artefacts.
Right: The fused SPECT-PET-FLT-CT data showed FDG and MDP accumulation at expected locations, e.g. heart and joints, respectively, while OsteoSense accumulated in bones and joints.

Fluorescence Tomography Applications



Al Rawashdeh et al 2017
Theranostics
Biodistribution kinetics

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Active/passive targeting

Rosenhain 2017
JBP
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JNM
PET-MRI validation

Ergen et al 2017
Biomaterials
Liver cell targeting

Schober et al 2014
Nature Medicine
Vascular inflammation

Data acquired with separate CT and FMT

Discussion

The upgraded SPECT-PET-FLT-CT enables multimodal imaging of mice in four modalities in a single imaging session, delivering spatially resolved molecular information in three modalities together with anatomical µCT information essential for quantitative analysis. All four modalities can be used for longitudinal imaging providing information for advanced image analysis using kinetic modelling.

References

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Acknowledgements

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