A complete multiple modality workflow for assessing drug biodistribution and efficacy in a breast cancer xenografts

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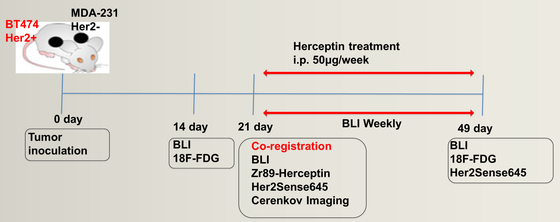
1 PerkinElmer's G8 PET/CT scanner expedites Go/No-go decisions

Positron-Emission Tomography (PET) is a non-invasive translational imaging tool that provides quantitative 3D imaging. PET can rapidly and reliably provide visualization of drug efficacy in preclinical animal models. Long-lived isotopes, like Zirconium-89 (3.3 days), are appropriate for tracking antibodies in vivo and can be imaged with PET to determine the PK/PD. The aim of this study was to develop and validate a preclinical imaging workflow to assess biodistribution, targeting and therapeutic potential of 89Zr-labeled antibody.

2 In Vivo Experimental Design



Day 0: Luciferase-expressing BT474 (HER2+) and MDA-MB-231 (HER2-) breast cancer cells were orthotopically implanted into athymic nude mice.

Day 14: 18F-FDG PET scan to assess the initial glycolytic potential of the tumors prior to treatment.

Day 21: 89Zr-labeled-Trastuzumab (35 μCi per mouse i.v.) prior to herceptin treatment (cold trastuzumab injected i.p. at 50μg twice/week for 4 weeks) to assess compound PK/PD.

Day 49: Optical imaging and an 18F-FDG PET scan.

3 Proposed Workflow

89Zr labeling of Herceptin

Standard radiochemical techniques were used to label Herceptin with 89Zr for in vivo tracking using PET imaging.

PET, Optical and micro CT In Vivo Imaging

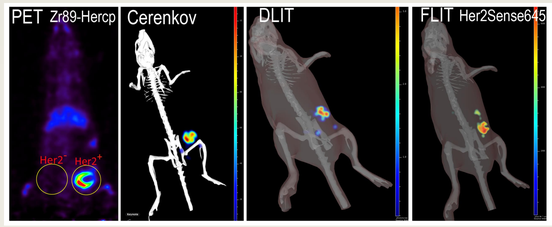
The IVIS Spectrum was used for optical imaging. Bioluminescence imaging to detect Luc-expressing tumor cells was performed, while a fluorescent imaging agent was used to provide tumor biology information.

The G8 PET/CT scanner was used to image tumor metabolism using 18-F FDG, and 89Zr labeled antibody distribution in serial PET scanning sessions.

Ex vivo verification

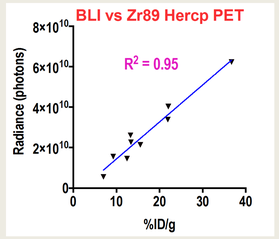
The Wizard^2 Gamma Counter for Ex Vivo Biodistribution Analysis

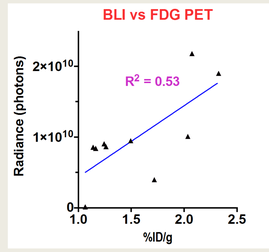
4 Experimental Results



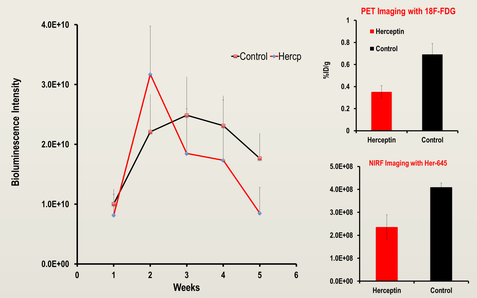
Day 21 PET scan shows rapid and specific accumulation of the Herceptin agent in the HER2+ tumor

Quantitative correlation of multiple imaging modalities





Therapeutic Efficacy

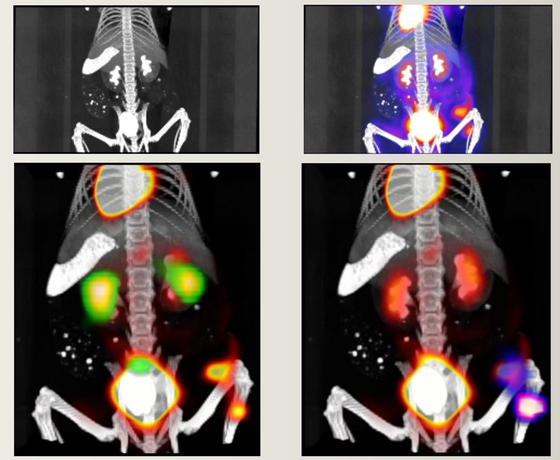


Top: Quantitative correlation between Bioluminescence and PET and using 89Zr-labeled Herceptin and 18F-FDG.

Bottom: Bioluminescence imaging was used to longitudinally monitor drug efficacy in this breast cancer model. PET and Fluorescence imaging also informed on effects of drug treatment.

5 Multiple Modality Image Fusion

A multi-step post imaging procedure was developed to fuse data from multiple modalities, allowing the researcher a visual interpretation of the imaging data, combining multiple modalities to inform on various processes in disease progression and treatment response.



Top Left: Contrast-enhanced CT, Top Right: PET/CT

Bottom Left: Combined PET, CT, FLIT, Bottom Right: Combined PET, CT, DLIT BLI

6 Value Proposition

PerkinElmer offers a suite of preclinical in vivo imaging systems for longitudinal, non-invasive imaging. Paired with reagent and radiometric detection solutions, PerkinElmer provides a complete multiple modality imaging workflow to deliver rapid Go/No-Go decisions in early drug discovery research.