InSyTe FLECT/CT Application Note

Tumor imaging using a vascular imaging agent

Abstract

Optical imaging is an established approach for studying cancer in preclinical animal models. Near infrared fluorescence tomography is an emerging optical imaging modality that enables 3D visualization and deep tissue imaging capabilities. Commercially available fluorescent imaging probes further enable imaging of specific physiology that informs disease state and progression. This application note provides guidance regarding optimal usage of an off-the-shelf vascular imaging agent (AngioSense 750EX) paired with the InSyTe FLECT/CT fluorescence tomography imaging system to image a preclinical model of breast cancer.

Materials and Methods

Research Animal Use

All experiments were performed in accordance with the Institutional Animal Care and Use Committee at University of California, Irvine for in vivo experiments. No invasive or surgical procedures were used in these studies and all imaging activities were performed under appropriate anesthesia to minimize animal distress.

Animal Model

Female BALB/c mice (15g mass) were inoculated with 1×10^6 4T1 mouse mammary adenocarcinoma cells for tumor initiation. Cells were injected subcutaneously to form tumors on the hind quarter of each mouse. Tumors developed after 5-7 days post injection and imaging performed within 10 days of injection prior to sacrifice.

Fluorescent Imaging Agent

A non-targeted fluorescent agent, AngioSense 750EX (PerkinElmer, Waltham, MA), was used as a tumor probe, utilizing the increased and leaky tumor vasculature for accumulation in the tumor. The imaging agent doses were administered per the manufacturer recommendation in the product datasheets.

InSyTe FLECT/CT Imaging

Prior to imaging, depilation was performed over the tumor site. Mice were anesthetized by 1.5% isoflurane inhalation during imaging. Mice (n=3) were imaged using the InSyTe FLECT/CT for acquisition of 3D fluorescence tomography images. Imaging was performed at 24 hours post-injection to allow sufficient probe accumulation in the tumor, as recommended by the vascular imaging agent datasheets. Acquired data was then computationally reconstructed into 3D volumetric images.

Results

The objective of this study is to demonstrate that the InSyTe FLECT/CT, which provides 3D optical imaging capability with anatomic reference, can be used in conjunction with commercially available fluorescent imaging agents. Figure 1 is an overlay of fluorescence tomography data acquired at 24 hours post-injection of AngioSense 750EX onto the corresponding CT image for this mouse. Figure 2 has a reflectance geometry image of the acquired fluorescence tomography data at 24 hours post-injection,

showing the tumor and the mapped fluorescence in a 2D projection overlaid onto a 2D X-ray image (radiograph). The reflectance visualization modality enables researchers to directly visualize the raw acquired data without computational reconstruction-derived artifacts common in computed tomography approaches. The limitation of this technique is that it lacks the depth information and visualization in 3D enabled by tomographic imaging.

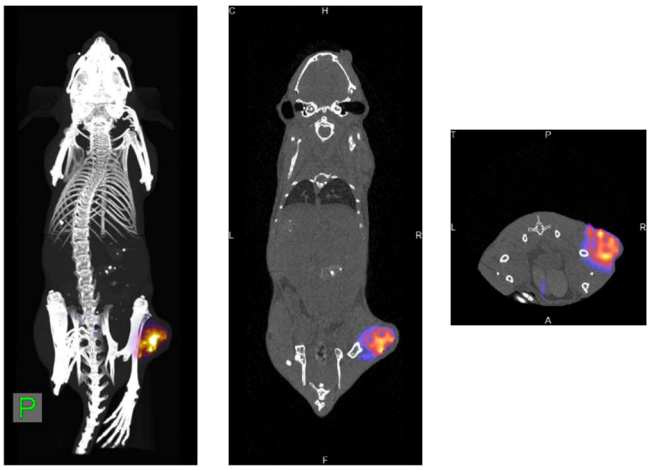

Figure 1: 3D fluorescence tomography images with co-registered CT images showing (left) maximum intensity projection, (center) coronal, and (right) transverse slices

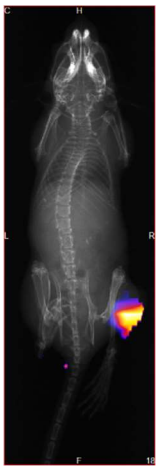

Figure 2: 2D reflectance fluorescence image projected onto 2D X-ray image

Conclusion

Imaging of preclinical models of cancer is an important method in oncology research. The use of a commercially available, near-infrared labeled vascular imaging agent as a tumor probe in conjunction with the InSyTe FLECT/CT enables researchers to visualize tumors in 3D and 2D reflectance modalities with an optical imaging system. Visualization in 3D provides the opportunity for further quantitative metrics, such as changes in tumor size and volume, therapeutic agent distribution and concentration, and other biological phenomena. Additionally, the 2D reflectance imaging capability of the InSyTe FLECT/CT serves as a complementary modality to allow researchers an alternative and fast method of imaging, especially for subcutaneous tumor models. In summary, this application note demonstrates the capability of using commercially available imaging agents with the InSyTe FLECT/CT system, enabling a powerful research method.