Intraoperative visualization of the boundaries of tumors is currently very difficult, leading to incomplete excision, the need for further surgery, and increased likelihood of cancer recurrence. Our goal is to develop a novel portable imaging system for surgical guidance. The system uses two complementary imaging modalities and specialized imaging tracers to help cancer surgeons locate and visualize tumors or lymph nodes (i.e. surgical targets). Tracers are dual-labeled with radioisotopes and fluorophores.

**Gamma imaging** – useful for imaging deep surgical targets through thick tissue
- A unique, hand-held mobile gamma camera (MGC) that has adjustable sensitivity and spatial resolution is used
- Gamma ray emission from tracer isotope is detected by the MGC to form a 2-D image of the tracer distribution within the patient

**Visible and near infrared fluorescence (NIRf) imaging** – precisely co-registered video rate visible (normal color images of the patient’s surface) and NIRf (images of the tracer) images
- The NIRf signal can penetrate through several millimeters of tissue
- Surface targets are visualized with very high (sub-millimeter) spatial resolution
- Fused visible (anatomy) and NIRf (tracer distribution) images are updated at up to 30 frames per second

**Pilot human study of MGC:** Accurate staging of lymph nodes in melanoma patients is crucial because of the increased likelihood of metastasis for positive (malignant) nodes. The MGC of the IMIS has been evaluated in a pilot study of sentinel lymph node biopsy in 20 melanoma surgeries.

**Results:** The MGC detected all (4/4) positive (malignant) lymph nodes, including one that was missed by the current gold standard non-imaging gamma probe. There were cases in which the MGC was able to clarify probe findings, both to disprove presence of a distinct hot spot, and to demonstrate that a node was part of a nodal group normally not removed due to associated morbidity.

**Preclinical study using visible/NIRf video camera:** The visible/NIRf optical system has been used to image a mouse model of breast cancer. Mice bearing MCF-7 mammary pad tumors were injected with a novel breast tumor targeting fluorescent tracer (Dongfeng Pan, PhD.).

**Results:** A still frame taken from a fused visible/NIRf video is shown below, demonstrating depiction of four separate breast tumors. Below right, the excised tumors were imaged post-surgery and showed non-uniform distribution of the tracer within the tumors that was consistent with histopathological analysis of the distribution of necrotic tumor cells.

A standard three bar USAF 1951 target was used to evaluate the spatial resolution of the NIRf system. Target images were acquired at a working distance of 30 cm, typical of that expected to be used during surgery. The contrast transfer function plotted on the right demonstrates sub millimeter spatial resolution, more than sufficient for precise surgical guidance.

The IMIS NIRf visualization depth was evaluated using an intralipid based phantom emulating the optical scattering and attenuation properties of human tissue in the NIR region. The figure on the right shows the SNR of a 9.9 mm diameter simulated acrylic lesion filled with 20 µM ICG plotted versus lesion depth. The SNR is > 2 for lesion depths up to 8 mm.

The two components of the IMIS have been tested clinically and preclinically. The integrated IMIS will be tested later this year among melanoma surgical patients.

**Collaborators:** The MGC was developed in collaboration with Jefferson Lab and West Virginia University. Craig Slingluff, Joshua Judge, and Lynn Dengel are UVA surgical collaborators. Collaborators in the development of multi-modal imaging tracers include Dongfeng Pan, Kimberly Kelly, Jiang He, the Netherlands Cancer Institute in Amsterdam, and the Vrije Universiteit Brussel in Belgium.