Rare Earth Nanoparticle Imaging and Optical Phantom Fabrication for Surgical Guidance

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INTRODUCTION

When surgeons attempt resection, it is often difficult to adequately locate their subject. In the case of tumor resection, for example, a surgeon might have access to a camera-captured hypodermic image of the tumor's emissions without possessing a reference point to the patient's skin. Live feed imaging systems, displayed on an external monitor, aide in the process, but require surgeons to constantly shift their gaze between monitor and patient. To overcome this, our next step was to rig a projector system, displaying a processed image of the tumor's emissions upon the patient's tissue.

Rare Earth (RE) Nanoparticles are used as contrast agents, making their way to the object of interest after injection into the patient. An overhead camera with the appropriate highpass filter picks up the nanoparticle's emissions. Imaging processing programs designed in LabView are used to adjust brightness and contrast, and threshold the image to outline areas of high RE concentration.

It is also needed to establish standardized subjects to compare multiple surgical guidance systems, setups, and image processing styles. These phantoms, objects used to measure image techniques, often have absorbance and reflective properties similar to that of human tissue. These phantoms can be made with nanoparticles of different concentrations placed at different depths or within different substances such as silicon or gelatin.

CONTRAST AGENTS

Indocyanine Green (ICG), an FDA-approved dye absorbing at short wave infrared (SWIR) wavelengths, has been used for tissue and organ perfusion diagnostics. Rare Earths, contrastingly, operate with absorption spectrums at higher IR wavelengths. The longer wavelengths cause less light scattering, resulting in deeper penetration into the subject tissue.

The phantoms detailed in this paper make use of both pure RE Nanoparticles and RE Albumin Nanocomposites (ReANC). Albumin, a water-soluble family of globular proteins, is used to coat RE nanoparticles, thus increasing biocompatibility and allowing for in vivo testing. ReANCs have been administered as IV injections into the tail vein of mice. These particles migrate to tumors by the Enhanced Permeability and Retention Effect (EPR) as well as to organs, notably the spleen and liver. Additional biomarkers, only activated upon tumors, can be added to differentiate tumors from these organs.

PHANTOMS

METHODS

Two phantom types were created using two different 3D-printed molds designed in Solidworks (See Figure 1).

Phantom A tests for varying concentration and depth. The mold contains step-like platforms within a thin-walled box. The box contains 12 cylindrical holes (depth 2mm, radius 5mm, volume 0.157ml) arranged in a 4x3 grid, with 4 holes at each depth below the surface of the box (1mm, 3mm, 5mm). At each depth, 3 holes contain Erbium ReANCs of different concentrations (5x, 2.5x, 1.25x). The fourth hole acts as a control. Two molds were printed: one to be filled with silicone and TiO_2 , the other with gelatin.

While gelatin's properties are more reactive of human tissue's water content than silicone, it is much less long-lasting. Gelatin's properties change over time as its hardens, leaving silicone as the default substance used for phantoms.

Phantom B compares multiple nanoparticle types. The 3D-printed mold contains 4 cylindrical holes (depth 5mm, radius 7.5mm, volume 0.884ml) containing Erbium, Holmium, and Thulium nanoparticles, along with a TiO_2 control. Desired concentrations of inclusions: 625 μg/ml.