Purpose: Radio Luminescence Imaging is being investigated for its potential to provide biological feedback during radiation treatment. We are investigating the use of biologically-targeted phosphor nanoparticles to enable high-resolution molecular imaging with standard therapeutic systems. This work demonstrates the ability of this technique to image multiple molecular markers in a small-animal model. We investigate their potential in resolving markers pertinent to treatment monitoring.

Method and Materials: Images were acquired with a custom-built imaging system incorporating a Princeton Instruments Pro-EM camera CCD with 512x512 pixels) and a 50mm lens. Tb- and Eu-doped BaYF4 nanoparticles of linearly varying amounts (0mg/ml:10mg/ml; 2.5mg/ml:7.5 mg/ml; 7.5mg/ml:2.5mg/ml; and 10mg/ml:0mg/ml) were mixed into cuvettes and imaged under irradiation with an 80keV X-ray source (Pantak Therapax). BaYF4 nanoparticles were also placed in the right foreleg and right and left flanks of a nude mouse. In another experiment, phosphor nanoparticles were placed in a cylindrical plug-shaped phantom and irradiated with a 9MeV electron beam produced by a Varian Trilogy linear accelerator. All images were processed with custom spectral unmixing software, which enabled the visualization of each phosphor.

Results: Concentrations less than 0.1mg/ml were resolved. Spectral unmixing showed excellent separation of the phosphor nanoparticles ($r = -0.98$), demonstrating the multiplexing ability of the technique. In addition, phosphor concentrations showed excellent linearity ($R>0.99$), with excellent separation of the phosphor nanoparticles. Images of the phosphor nanoparticles implanted in the fore and hindquarters demonstrated the ability to spectrally separate in small-animal model.

Conclusion: The ability of radio luminescent imaging was demonstrated in phantom and small-animal models, for both X-rays and electron beams. Enabling simultaneous imaging of multiple molecular imaging markers is possible in Radiation Therapy applications. This technique has potential for introducing the monitoring of biological markers during treatment.

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