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In vivo X-Ray excited optical luminescence from phosphor-doped aerogel and Sylgard 184 composites

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ABSTRACT

X-Ray excited optical luminescence (XEOL) is a new and noninvasive diagnostic technique suitable for in situ biochemical imaging and disease detection. The X-Ray excited optical luminescence of phosphor doping in crosslinked silica aerogel and Sylgard 184 hosts was investigated in this study. Composite silica aerogels and Sylgard 184 samples of 5%, 15%, and 50% concentrations by weight of La_2O_2S:Eu phosphor were prepared and inserted subcutaneously in a Sprague-Dawley rat and excited by X-Ray emission at 70 and 100 kV. A fiber optic bundle positioned within 5 mm of the sample collected the luminescence signal and conveyed it to a photomultiplier detector. The signal intensity scaled with dopant concentration. The time dependence of the predominantly red luminescence consisted of 60 cycle bursts of approximately 8 ms duration. The amplitude was modulated at about 10 Hz with a 60% depth. This indicates the time dependence of the X-Ray source. A simulation showed how to observe phosphor decay between individual burst pulses. The emission from the two types of composite samples was easily detected from the outside of the skin layer. Both Sylgard 184 and crosslinked silica aerogels are biocompatible and bio stable materials that could serve a variety of potential XEOL applications. These very strong signals imply potential for creating new *In-vivo* sensing applications and diagnostic tools.

1. Introduction

X-Ray Excited Optical Luminescence (XEOL) is a new noninvasive spectroscopic diagnostic method that uses X-Rays to excite optical luminescence from a phosphor material that is embedded within a biomedical host of interest. In recent years such techniques have been proposed as a promising photo-physical mechanism to exploit for imaging of biomedical implants and organs, among others (Chen et al., 2011; Osakada et al., 2014). Typically, the luminescence is measured externally to the biomedical host and the emission characteristics contain vital information about the host in which the luminescent target is situated (Chen et al., 2012).

The work of Chen et al. is an illustrative example (Chen et al., 2011). They fabricated a continuous phosphor layer on top of a linear array of silver strips where the strip width and spacing between strips was the same. As a small-spot X-Ray source moves across the sample, an external detector produces a periodic modulation, bright when only the phosphor is illuminated and dimmer when incident on the silver which partially attenuates the X-Ray source before exciting the phosphor layer underneath. As H_2O_2 that is present in the host dissolves the silver, the modulation depth decreases. This allows the presence of H_2O_2 to be sensed and quantified.

Carpenter et al. successfully demonstrated the ability to image Tb and Eu phosphors, both micro and nano-sized versions, in a gelatin phantom and small animal model (Carpenter et al., 2010, 2012). The differing wavelengths of the respective phosphor materials allowed for multiplexed contrast imaging. They also combined radio luminescent methodology as well as X-Ray excited luminescence.

Sylgard 184 (Dow Corning) is of the Polydimethylsiloxane (PDMS) family and is an optically clear and inert material used extensively for a wide variety of studies including optical, biomedical, and aerospace applications (Sabri et al., 2013a, 2012a, 2008). The versatile nature of this family of polymers allows for fine tuning of bulk and surface properties as needed for each study and application (Fontenot et al., 2016).

Another class of materials with a promising future as host material is aerogels (Leventis et al., 2002) which offers many attractive features relevant to this area of research. For aerospace, their low thermal conductivity and low density are of obvious value (Sabri et al., 2011). For biology and biomedicine, the tunable chemical, physical, and

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surface properties have great potential for *in vitro* and *in vivo* applications (Sabri et al., 2014, 2011, 2013b). For instance, as implants, they may serve as scaffolding for cell growth and confinement (Sabri et al., 2012b). The basis for what is reported here comes from our recently related work with incorporating phosphors into these materials. The authors (Sabri et al., 2014) showed that the phosphor powder when doped into Sylgard and crosslinked silica aerogels does not chemically alter it and the luminescence properties of the bare powder are preserved. The temperature dependence of the phosphor powder and doped Sylgard were the same. A subsequent effort examined optical luminescence from doped PDMS samples viewed through the dermis of a rat and excited by 405 nm light (Sabri et al., 2015). Red luminescence was readily detectible through the rat skin. The best results were for the instance where the excitation first excited the sample and then traversed the skin to an externally located detector. Next, coupons of Sylgard and aerogel with various phosphor powder concentrations were prepared and inserted underneath rat dermis. X-Ray images revealed that image contrast could be enhanced. X-Ray attenuation coefficients were obtained for 60 kV X-Rays (Allison et al., 2015). The present work reported here follows logically from these previous efforts. The primary concern here is to illustrate and quantify the visible luminescence signal levels generated by X-Rays and detectible through the rat dermis. This has not been done before for these materials. But also, in the course of the effort, additional X-Ray attenuation coefficient data for some of the Sylgard samples was acquired for 70 and 100 kV X-Rays thus supplementing the attenuation information at 60 kV in reference (Allison et al., 2015).

We report here for the first time, X-Ray excited optical luminescence results for two new host materials, (1) crosslinked silica aerogel, and (2) Sylgard 184, for several phosphor loading levels. Aerogel and Sylgard 184 composite samples containing 5%, 15%, and 50% wt La_2O_2S:Eu were prepared and placed subcutaneously in a Sprague Dawley rat and excited to luminesce using a commercial X-Ray system. The phosphor used for this study, La_2O_2S: Eu, is a well-known X-Ray scintillator and is similar to other XEOL phosphors used in published studies. The emission by the $^{3+}$Eu activator consists of many spectral lines in the range of 400–700 nm. These have spectroscopic designations ^5D_i where i=0, 1 or 2.

One of the motivations concerns exploring the possibility of XEOL-based in-vivo thermometry. The subject phosphor here can be used to measure temperature with a high degree of precision (Allison and Gillies, 1997). For more background, recent resources that survey luminescent materials for thermometry including relevant spectroscopy, signal, and error analysis are Brübach et al. (2013) regarding thermographic phosphors and Brites et al. (2016) which reviews a wide range of luminescent lanthanide materials. In addition there are other potential ways that XEOL may be exploited that attract interest. For example, Rogalskim (2016) developed a means for determining micron-scale displacement from XEOL-generated spectra. They mention possible applications such as sensing strain on orthopedic implants and tendon/ligament tears.

2. Materials and methods

2.1. Synthesis and preparation of samples

Crosslinked silica aerogel and Sylgard 184 composite samples with phosphor powder concentrations of 5, 15, and 50 wt% were prepared as described in detail previously by the authors (Allison et al., 2015). Phosphor powder lanthanum oxysulfide La_2O_2S: Eu, 0.1 mol% (Phosphor Technology SKL63, lot 15010) was combined with the pre-polymer and crosslinker of Sylgard 184 (Dow Corning, Midland, MI) prior to the curing stage of the two-part elastomer and outgassed and cured, as described previously (Allison et al., 2015). Similarly, using the sol-gel technique described elsewhere in detail (Allison et al., 2015), crosslinked silica aerogels containing La_2O_2S:Eu of different concentration levels was synthesized and dried by means of the supercritical drying technique. Both types of samples were prepared in 4 cmx4cm custom designed aluminum molds and cut to the desired geometry after final curing and drying steps were completed. Images of the samples are shown in Fig. 1 (Allison et al., 2015).

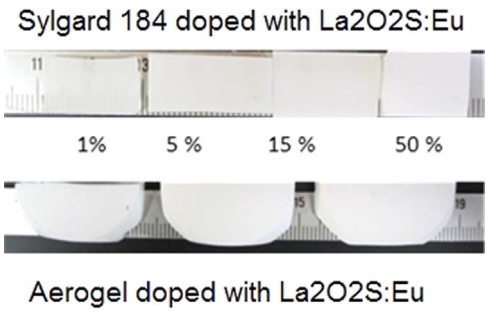

Fig. 1. Photographs of La2O2S:Eu-doped Sylgard (top) and aerogel (bottom).

2.2. Implant insertion

The surgical procedure described here was performed on a single male Sprague-Dawley rat weighing 350 g described in detail previously (Leventis et al., 2002). Samples were inserted subcutaneously into the incision pocket created in the back of the rat, while situated on the X-Ray imaging table of a DuoView X-Ray imaging system (Revo Squared, GA). The samples were in full contact with the skin and were immobilized without the use of any sutures, adhesives, or staples. This study was approved by the Animal Care and Use Committee at the University of Memphis.

2.3. Excitation and luminescence detection

Image clarity was assessed for several different configurations of the DuoView X-Ray's parameters. Imaging was performed using impulses from 0.8 to 5 s duration at 25 mA cathode current and 70 kV or 100 kV settings. Fig. 2 illustrates the test setup used for this study. To observe luminescence occurring from the composite Sylgard 184 and aerogel samples, the fiber-optic probe was placed approximately 2 mm above and to the side of the surface of the skin at the site of the incision. Control images were taken using only the probe and the specimen table to isolate any interference created by the X-Ray beam in the fiber optic probe and no signal was observed.

The fiber optic probe consisting of a 3-meter long fiber bundle of about 78 each 200 μm diameter optical fibers collected the XEOL. The collection area was approximately 2 mm^2. The bundle delivered the

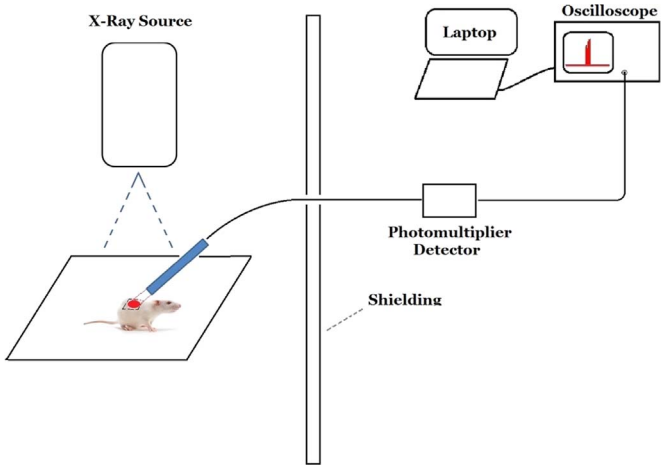

Fig. 2. Test Setup for X-Ray Excited Optical Luminescence.