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Instrumentation for High-Dose, High-Resolution Dosimetry for Microbeam Radiation Therapy using Samarium-Doped Fluoroaluminate and Fluorophosphate Glass Plates

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Abstract

We show that 1% Sm-doped fluoroaluminate (FA) glass plate and a suitably modified fluorescence confocal microscope provide an excellent radiation detection platform for high-dose measurements at high resolution down to the micron scale. We have used a custom-modified fluoroscopic confocal microscope apparatus to scan, separate, detect, and digitize the photoluminescence signals from Sm^{3+} and Sm^{2+} ions in both FA and fluorophosphates (FP) glasses within a selected focal depth of the microscope below the sample surface. The response (R) of Sm-doped FA and FP glass plates to incident x-ray radiation was studied in detail in which R was defined as the difference in the ratio of photoluminescence (PL) signals from Sm^{2+} and Sm^{3+} before and after irradiation. We report on a number of important issues related to the use of these Sm-doped FA and FP glass plates in microbeam radiation therapy (MRT) dosimetry: The dependence of the Sm^{3+} to Sm^{2+} conversion, and hence R on the dose rate over some four orders of magnitude; the energy dependence of R at a given dose rate for both FA and FP samples with various concentrations of Sm^{3+} doping; R vs dose behavior at different energies up to 2000 Gy_{air} and the derivation of the detector calibration curves; the stability of the Sm-doped plates after they have been exposed; the instrumental limits of the present measurement technique.

1. Introduction

There are currently a number of techniques for the measurement of radiation dose along with a variety of potential materials for use in dosimetry as reviewed, for example, in references [1,2,3,4,5,6,7]. Of particular interest is the dosimetry that would be required in the implementation of Microbeam Radiation Therapy (MRT), which is a promising synchrotron-based cancer treatment technique. MRT has been shown to have the potential to improve upon spatially broadbeam radiotherapy methods. The MRT technique is based on the noticeably different responses of tumors and healthy tissue after irradiation by multiple narrow and parallel planar beams of irradiation. In MRT, highly collimated x-rays pass through a multi-slit collimator (MSC), segmenting the incident x-ray radiation before it is delivered to a patient. It has been shown that healthy tissue adjacent to the narrow sections of irradiation helps with the repair of damaged tissues, whereas tumors do not show this ability, allowing for substantial doses to be delivered to a patient with minimal damage to healthy tissue. There have been many papers in the last ten to fifteen years that address various issues related to the use of MRT and its benefits in cancer treatment [8,9,10,11,12,13,14]. The technique requires a high incident x-ray energy and must be able to deliver large doses to a patient in a very short timescale in order to maintain the desirable tissue sparing effect associated with the technique.

The accurate measurement of these microbeams is essential for patient care and for treatment planning. The "peak" dose at the center of the microbeam and the "valley" dose between the adjacent microbeams can differ by hundreds of grays over a distance of several microns and incident x-ray energies of interest can vary from 50 – 250 keV. In order to satisfy the dosimetry requirements of MRT, a detector must be able to simultaneously measure both a peak and valley dose with a spatial resolution on the scale of microns, and must be able to do so over a large energy range and at high dose rates. Ultimately, a two-dimensional (2D) cross-sectional image of the dose distribution is required.

Multiple techniques for the measurement of these microbeams have been previously discussed, including Gafchromic films, MOSFET detectors, Si strip detectors, single crystal diamond detectors, polymer gels, fluorescent nuclear track detectors, etc.; see examples in references [15,16,17,18,19,20]. The technique must be able to measure doses from a few Grays to thousands of Grays and over various energy ranges. A major problem with many dosimetric materials is the saturation of the sensitivity at high dose or a limited dynamic range that is unable to simultaneously measure both the range from the valley dose (a few Grays) to the peak dose (thousands of grays); a known-problem that has been already discussed in the literature (e.g. [21]). A promising measurement method involves using the valence conversion of rare earth ions which, when embedded in a suitable material, can serve as a measurement of the delivered dose. Upon irradiation with various forms of excitation, such as x-rays, β and γ -irradiation, and photoexcitation, rare earths have shown the ability to change their valence state in various media [22,23,24,25,26]. Of particular interest among the rare earths is samarium, since the emission spectra of Sm^{3+} and Sm^{2+} ions are easily distinguishable and emit in the orange and red regions of the spectrum respectively, which are well suited for detection by photomultiplier tubes (PMTs).

The conversion process for Sm^{3+} to Sm^{2+} is strongly dependent on the host material. Previous work has shown that Sm-doped FP and FA glasses can be used as dosimetric detectors,

which have the capability of measuring both large doses and the peak-to-valley dose ratio (PVDR) at high resolution, both are important considerations in the future success of MRT. These Sm-doped glass plate dosimeters utilize the distinguishable photoluminescence (PL) signals from the conversion of Sm^{3+} to Sm^{2+} as a function of the dose delivered. These PL signals are then measured using a modified fluorescence confocal microscopy detection system that is tuned to the emission wavelengths of these ions. Using this method it has been shown that resolution on the order of microns can be achieved [27,28,29,30,31,32,33,34,35]. This work investigates one of the most important issues in the calibration of any detector for accurate dose measurement: the dependence of the response of the detector to the incident x-ray energy and the incident dose rate. We have examined the conversion of Sm^{3+} to Sm^{2+} of Sm-doped FA and FP glasses over a wide range of dose rates (four orders of magnitude) and energy values (35 to 130 keV) and how these Sm-doped plates can be calibrated so that they measure the correct incident dose.

In the present paper, we discuss the conversion of Sm^{3+} to Sm^{2+} in these materials and how the conversion process is affected by the dose rate and incident x-ray energy. An important factor in the success of MRT is the high incident dose rate which helps minimize any "smearing" of the microbeams that may occur from the patient's movement, or from micron level shifts resulting from vascular flow within the irradiated tissue. An additional important consideration is that of the incident x-ray energy; the energy must be high enough to penetrate deeply into patient tissue and ensure that sufficient dose is delivered to the desired region. Ideally, the response of a dosimeter should be independent of the incident x-ray energy as well as the incident dose rate. In practice, however, a dosimeter response needs to be calibrated when the energy range of the incident x-rays is large [36].

The measurement of the PL from Sm^{3+} and Sm^{2+} ions was implemented by using a fluorescence confocal microscope as mentioned above. We have also examined the dependence of the response (Sm^{3+} to Sm^{2+} conversion) of the Sm-doped glasses on the focal depth below the sample surface in the confocal microscope measurements as a function of x-ray energy. If the response of the dosimetric plate depends on the focal depth into the sample, this dependence needs to be included in the calibration characteristics.

The dependence of the Sm^{3+} to Sm^{2+} conversion on the amount of Sm doping in FA and FP glasses has been examined previously [29,34]. In this work we extend the previous study by examining the stability of the Sm-doped glasses shortly after they have been irradiated up to a period of 15 days. Most importantly, we examine the energy dependence of the Sm^{3+} to Sm^{2+} conversion for different amounts of Sm-doping at a given dose. The Sm-doped FA glass plates in this work are able to measure doses up to 2×10^3 Gy in air and the measurement is independent of the dose rate; an important factor in the use of this technique in MRT.

2. Sm^{3+} -Doped Fluoroaluminate and Fluorophosphate Glass Plates

Sm doped glasses were synthesized using a melt quenching technique previously described in detail elsewhere [27,28,29,30,31,32,33,34,35]. Starting materials were mixed in a glove box in a dry nitrogen atmosphere and loaded in a carbon crucible where the mixture was then melted in an RF furnace at 1000 °C for 120 minutes. The glass was then quenched on a temperature controlled plate at 380 °C for 8 hours in an argon atmosphere in order to relieve internal stress and prevent cracking. The composition for FA glass in molar percentage is 10.0MgF₂ – 35.0AlF₃ – 20.0CaF₂

– 10.0SrF₂ – (15 – x)YF₃ – 10.0BaF₂ – x SmF₃ and for FP glass is 10.0MgF₂ – (34.4 – x)AlF₃ – 30.4CaF₂ – 15.2SrF₂ – 10.0Sr(PO₃)₂ – x SmF₃ where x is the concentration of SmF₃, which can be varied from 0.1% to 10%. Following synthesis, the glass materials were polished and cut into approximately 2 mm by 3 mm rectangular pieces for subsequent experiments. A typical glass plate thickness was ~1.5 mm. All percentages quoted hereafter are in mol.%. Some 120 samples were prepared for all the measurements. The density of the samples were measured by using the Archimedes principle of change in the measured weight of the sample in a liquid of known density. The sample density was 3.74 g cm⁻³. The refractive index of the samples was approximately 1.5 over the PL wavelengths used in this work [37,38].

One of the FA glass samples (where $x = 0$ in the composition formula) was ion-implanted near the surface of the sample as described previously [35]. The ion-implantation generated a distribution of Sm²⁺ ions within a depth 1 μ m and a peak concentration located at a 0.60 μ m depth from the surface. The luminescence properties of these glasses have been already described [35]. The purpose of this Sm²⁺ ion-implanted sample is to provide a verification for the axial luminescence collection range in the confocal photoluminescence confocal microscope.

3. Single Energy and Polychromatic X-Ray Irradiation, Dose and Dose Rate Delivery

Polished and cut samples were taken to the Biomedical Imaging and Therapy (BMIT) 05ID-2 beamline at the Canadian Light Source (CLS, the Canadian synchrotron), for x-ray irradiations. Using the facilities at the BMIT beamline the incident x-ray energy is tuned using a bent Laue double-crystal monochromator, which allows for monochromatic incident high energy x-rays to be selected with a resolution ($\Delta E/E$) of 10⁻³. When performing the irradiations for dose rate and energy dependence experiments, the total dose delivered to each sample was kept constant at 200 Gy_{air} (Gy in air) as measured by an ionization chamber (model 31022, PTW-Freiburg). For dose rate measurements, the incident x-ray energy was kept constant at 50 keV, which is closest to the peak photon flux rate for the BMIT beamline and allows the maximum dose rate range to be delivered to a sample. It is important to emphasize that all dose rate measurements were done at one given energy and the total dose was kept constant. Likewise, for the samples irradiated while investigating the energy dependence experiments, the incident dose rate was kept constant at 175 mGy/s, which is the quoted dose value in air at the surface of the sample i.e. entrance dose in air. The incident x-ray energy was selected using a monochromator where the x-ray energy range was between 35 keV and 130 keV. The energy range is similar to that recently used in an MRT optimization study [39]. In order to modify the delivered dose rate to each sample, the wiggler magnetic field was modified between 2 and 3.9 T and additional aluminum filters were placed in the beam path to reduce the dose rate without modifying the x-ray energy. In the case of all samples, a 1 mm aluminum filter was present in the beam. Irradiation of collimated microbeams on Sm-doped glass plates were performed using a tungsten multislit collimator (MSC) with a slit width of 50 μ m where the slits are separated by 400 μ m (center-to-center distance). The collimator was manufactured by Usinage et Nouvelles Technologies, Morbier, France. Samples were irradiated in the dark and wrapped in aluminum foil until readout experiments were performed using a modified fluorescence confocal microscope described below.

X-ray irradiation experiments involving PL spectra and signal stability were completed using a FAXITRON x-ray cabinet with a tungsten anode operating at 110 kVp at an approximate

dose rate of 40 Gy/min in air. This dose value represents the dose delivered in air at the surface of the sample, and not within the sample itself. The FAXITRON x-ray source is polychromatic with a mean energy of 49.3 keV taken from fluence simulations given at the Siemens website [40]. The exposure rate was measured by an ionization chamber (Keithley 35050). PL spectra of irradiated samples were measured using an ASEQ fiber input mini-spectrometer with spectral resolution better than 1 nm. The excitation source used was a 405 nm laser diode.

4. Optical Measurement Technique: Modified Fluorescence Confocal Microscope

Response values for samples irradiated were measured using a custom confocal fluorescence microscopy readout system, which has been described in some detail previously [28,29,32,33,34]. Figure 1 shows a schematic of the confocal microscopy apparatus. The apparatus was a modified commercial confocal microscope (MultiProbe 2001 TM CLSM, Molecular Dynamics). The excitation beam at 473 nm (blue) was generated by a diode-pumped solid-state (DPSS) laser, whose beam is reflected by a 570 nm dichroic mirror (DM) towards an objective lens that focuses the laser at a selected focal depth within the sample. The intensity of the blue excitation laser beam in readout during confocal scanning was 0.5 μ W. Upon excitation, Sm^{3+} and Sm^{2+} ions emit distinct and separable PL signals which are collected from the objective lens and guided towards a set of photomultiplier tubes (PMT). These signals are focused using an achromatic lens onto a pinhole and the resulting beam is then directed towards a 650 nm dichroic mirror which separates the Sm^{3+} and Sm^{2+} signals towards two separate PMTs fronted with a 600 nm band-pass filter (BPF) and a 660 nm long-pass filter (LPF), respectively. Figure 2 shows the spectral characteristics of the excitation and the two photomultiplier tubes with filters. The Sm^{3+} and Sm^{2+} signals are measured simultaneously and PL signals are digitized for calculation of the response of the Sm-doped glass plate.

The use of the confocal readout system requires the objective lens to be suitably placed below the sample so that the focal point in the sample that determines the volume of collection is well defined. This process is achieved by using a filter to block the 473 nm emission from the DPSS laser and allow the pump laser diode emission ($\lambda = 808$ nm) from the blue laser to pass through a filter. The reflection of this 808 nm beam from the sample surface is then recorded by changing the objective lens height from the sample surface, until a maximum reflection from the surface is registered. Once the location of the sample surface is known, the actual depth of the focal point inside the sample from the surface can be easily determined through straightforward optics. A movement of the objective by a distance D corresponds to the movement of the focal point in the sample by d where $d = D/n$, where n is the refractive index of the sample, as shown in Figure 3 (a). The motion D is measured and converted to d in plots where the PL measurements were recorded as a function of distance from the sample.

It is important to identify the laser excitation volume and the volume from which the PL signals are collected in the confocal microscope set-up in Figure 1. As shown in Figure 3 (b), the 470 nm excitation volume includes the cone-volume above the focal point up to the sample surface and the cone-volume below the focal point. The volume responsible for the PL signals however is different in the vertical (z) and lateral (x, y) directions. The vertical range Δz of signal collection, the *vertical resolution*, for an infinitely small pinhole would also be diffraction limited. In the present case, to obtain the best signal-to-noise ratio over a very large dynamic range (from 5 –

2000 Gy), the highest pinhole size was selected (200 μm) so the vertical range Δz was much larger than the diffraction limited value and is determined experimentally as described below.

Figure 4 shows the PMT1 signal obtained from the Sm^{2+} -ion implanted FA glass as a function of distance d below the surface. The signal peak is roughly at 1 μm and the PMT1 signal decays and is half at about $d \approx 21 \mu\text{m}$. The full width at half maximum (FWHM) vertical range Δz for PL signal collection is therefore about 42 μm . This vertical range Δz represents approximately the vertical resolution of the confocal microscope used and, in the current application, it is significantly larger than typical confocal applications where Δz would be a few microns; the present measurement uses a large pinhole to capture PL signals with acceptable S/N ratio at the low dose range. The significance of the results in Figure 4 is that if we place the focal point at $d = 20 \mu\text{m}$, then the vertical region from the surface to a depth of about 40 μm will primarily contribute to the PL signal, that is, we can exclude the spurious PL signals from the regions below and laterally further than Δx (the width of the focal point). Figure 5 shows the Sm^{3+} signal from PMT2 as a function of d . As expected this signal increases with d as the PL capture range is moved more into the sample. As will be shown below in the results section, the response of the Sm-doped plate to x-ray exposure remains constant up to about $d \approx 20 \mu\text{m}$, which is the d chosen in this work. There is one more distinct advantage to using a confocal microscope to probe only the depth Δz from the surface, which is roughly 40 μm . Over this distance, the radiation induced photodarkening is negligible, where this had to be considered in examining the PL from the whole sample with a thickness of a few millimeters as shown in reference [32], and included in the dosimetric response.

5. Lateral Resolution in Optical Measurements and the Spatial Microbeam Profile

In the lateral direction, the resolution defined as Δx in Figure 3 (b), is determined by diffraction effects and depends on the lens objective characteristics (numerical aperture, NA) and the wavelength of interest, λ , through the relationship $\Delta x \approx 0.61\lambda/\text{NA}$ [41]. For $\lambda \approx 700 \text{ nm}$ and $\text{NA} = 0.75$ for the objective lens used, $\Delta x \approx 0.5 \mu\text{m}$. Figure 6 demonstrates the high image resolving power of the current system by displaying the XY scanned PL from a 4 μm fluorescent microsphere, obtained from MultiSpeckTM Multispectral Fluorescence Microscopy Standard, Molecular Probes.

The measurements in Figure 6 were independently verified by imaging the same slide on a commercial two-photon microscope (Prairie Technology Ultima IV). The lateral resolution of the microscope was calibrated with a stage micrometer 2mm/0.01mm with overall accuracy 0.0015mm (S20, Pyser Optics).

The resolution capability of the microscope was also examined by scanning a 1951 USAF resolution plate collected through the reflection of the incident laser on the target surface through the 20 $\times$ objective lens. The image from the latter scan is shown in Figure 7, and shows group 6 and 7 of the resolution plate where the smallest line widths are 4.38 μm and 2.19 μm , respectively. They can be easily resolved.

The scanning speed of the confocal microscope system is largely dependent on the desired resolution and field of view. The system uses a galvo mirror to achieve a rectangular raster scanning method, where the image is scanned left to right in the x -direction and then is moved

down to the next line in the y -direction where the process is repeated. Using the $20\times$ objective lens gives an approximate field of view (FOV) of 0.75×0.75 mm. A typical scan setting using the $20\times$ objective lens collects an image with approximately 500×500 pixels, although higher resolutions can be achieved (2500×2500 pixels). The reason for selecting a lower resolution is due to the relatively long PL decay lifetimes of the Sm^{3+} and Sm^{2+} ions, due to so called "forbidden" $4f \rightarrow 4f$ transitions that are characteristic of samarium ions, which are between 4 and 10 ms [35]. Signal collection requires a dwell time at each pixel that is larger than the PL lifetime decays of the Sm ions, and so each pixel is excited for 20 ms before moving to the adjacent pixel. The Time it takes to scan a field of view along x is $500 \text{ pixels} \times 0.02 \text{ s}$ or 5.3 s. The scan of the whole field of view (500×500 pixels) is then 5000 s or about 1.4 h. At the highest achievable resolution ($(2500 \times 2500 \text{ pixels})$) this time approximately is 34.7 h. This measurement time could be reduced significantly by scanning only the region of interest within the FOV or creating a more efficient scanning method. Further, samarium doped oxyfluoride glass ceramics have been shown to be capable of high resolution microbeam dosimetry, and exhibit parity-allowed $5d \rightarrow 4f$ transitions which have PL decay lifetimes on the order of nanoseconds [28], cutting the read-out time from hours to minutes.

A spatial profile of a microbeam as recorded on a Sm^{3+} -doped FA glass plate under x-ray irradiation at the Canadian Light Source is shown in Figure 8. The image on the left is a 2D image of a single irradiated microbeam on a 1% Sm-doped FA glass slide where the incident beam was put through a MSC. The incident x-ray energy was selected to be 50 keV and the total dose delivered was measured as $200 \text{ Gy}_{\text{air}}$ before passing through the collimator. The collimator has a series of $50 \mu\text{m}$ slits which are separated by a distance of $400 \mu\text{m}$, center to center. The circles in the plot on the right of Figure 8 are the experimental points from the confocal lateral scan whereas the solid curve is a Monte Carlo simulation of the beam through the collimator [42,43,44]. The measured profile agrees very well with simulations and highlights the high resolution that can be obtained with these Sm-doped glasses in a fluorescence confocal microscope readout. This work only considered the systematic calibration of the system for dose measurement and does not report XY scans of PL images for studying the beam shape at different energies; this will be reported in the future.

6. X-Ray Response Calibration Curves and Equations

The change of valence from Sm^{3+} to Sm^{2+} upon x-ray irradiation can be used as measure of the x-ray dose delivered. Previous work with Sm-doped FA and FP glasses examined the conversion of Sm^{3+} to Sm^{2+} over a wide range of doses and demonstrated the reusability of bulk doped samples by reversing the valence change from Sm^{2+} to Sm^{3+} after extended UV exposure or annealing above the glass transition temperature [27,28,29,30,31,32,33,34,35]. The glass transition temperatures for FA and FP glasses were measured to be 440°C and 462°C , respectively. The Sm^{3+} ions act as electron trapping centers in order to become Sm^{2+} . It appears as though the conversion process is controlled by hole trapping, since, once the glass samples have reached saturation (no further conversion to Sm^{2+}), the presence of Sm^{3+} ions can still be observed. Additionally, increasing the overall doping concentration of Sm^{3+} ions does not lead to a greater number of valence conversions to Sm^{2+} . Figure 9 shows the distinct and separable PL spectra and primary atomic excitation levels of Sm^{3+} and Sm^{2+} in 1% Sm doped FA glass before and after

irradiation. The response R , as opposed to responsivity (which is response per unit input into the sensor) of a Sm-doped glass plate detector is defined as,

$$\text{Response} \equiv \frac{I_{\text{PMT}(2+)} }{I_{\text{PMT}(3+)}^{\text{Irradiated}}} - \frac{I_{\text{PMT}(2+)} }{I_{\text{PMT}(3+)}^{\text{Non-irradiated}}} \quad (1)$$

where $I_{\text{PMT}(2+)}$ and $I_{\text{PMT}(3+)}$ are the measured signal intensities from the two photomultiplier tubes which measure the emissions from Sm^{2+} and Sm^{3+} through a 660 nm long-pass filter ($I_{\text{PMT}(2+)}$) and a 660 nm band-pass filter ($I_{\text{PMT}(3+)}$), respectively as shown in Figure 2. It is possible to formulate a more rigorous definition for the conversion and hence the response by examining the whole PL spectra before and after irradiation and deriving the weighting coefficients needed to combine the individual PL(Sm^{3+}) and PL(Sm^{2+}) to generate the overall spectrum from the irradiated sample as demonstrated in [32]. This approach was not used here due to the computational times involved in finding the weighting factors as well as the distinct advantage of implementing the definition above in the hardware i.e. by using two separate PMTs with filters to capture the Sm^{3+} and Sm^{2+} emission bands. During readout there is some unavoidable bleaching of the Sm^{2+} as the result of the excitation source, thus the calculated response of the sample is taken as the average response within the 0.5 second period following the opening of the shutter.

Previous works have shown that varying the concentration of Sm dopants within the bulk sample leads to differing conversion rates of the Sm ions, most notably, the lower the concentration, the larger the number of ions converted from Sm^{3+} to Sm^{2+} and thus greater the response of the material [28,34]. It has also been shown that the host glass material plays a role in the dynamic range of the dosimeter; prior work has shown that both FA and FP glasses have exhibited a dynamic range of 1 Gy_{air} to 10 kGy_{air} [34]. For the purposes of this research, we have investigated multiple Sm dopant concentrations embedded in two hosts, FA and FP, to study the effect of the dose rate and energy of x-rays on the conversion from Sm^{3+} to Sm^{2+} . It is also instructive to note that while FA and FP glass materials have been shown to be excellent host materials for the valance conversion of Sm-ions, photodarkening is present within the glasses after large doses have been deposited. This is particularly strong in FP glasses, which causes the transmittance to drop in the same region of wavelengths as the emission of Sm^{3+} [32]. There is a very small change in the transmission at 600 nm with x-ray irradiation in FA glasses, so the photodarkening of FA glasses was ignored. Error bars are determined by measuring the standard deviation of the response across a two dimensional uniformly irradiated glass plate. A total of 120,531 data points (response values) were measured and the standard deviation was found to be 4.57%. The latter represent the error in the response value.

The response values after irradiating 1% Sm doped FA and FP glasses over a dose rate range that covers roughly four orders of magnitude were measured. Figure 10 shows that there is no evidence of a dose rate dependence from the lowest (0.7 mGy_{air}/s) to the highest (5 Gy_{air}/s) dose rates available at the BMIT beamline at the CLS using monochromatic energy x-rays. It is possible to achieve higher dose rates by using a polychromatic beam, but the goal of this experiment was to show whether there is any dependence at all on the dose rate at a given energy. In all samples, the incident x-ray energy was selected to be 50 keV and the overall dose delivered was chosen as 200 Gy_{air} as measured by a high dose ionization chamber. The choice of 50 keV x-ray energy was based on peak photon flux rates at the CLS and, of course, the need to relate the present work to

previous experiments at the CLS where 50 keV was used. The results from Figure 10 clearly show that the response R is independent of the dose rate in both of the host glass materials. This is a distinct advantage since the dose calibration curve for relating the response to the actual dose does not need to be modified for different dose rates, i.e. the calibration curve can be used under all dose rates.

The x-ray energy dependence of the response was measured for both Sm-doped glasses, FA and FP, as shown in Figure 11 from 35 to 130 keV. For all irradiated glasses in Figure 11 the dose rate was kept constant at 0.175 Gy_{air}/s and the total dose delivered was maintained at 200 Gy_{air}. Notice that there is a strong dependence on the x-ray energy as the Sm-dopant concentration is decreased from 5% to 0.2% in FA glass. 5% Sm doped FA glass shows not only a much smaller response but also a much weaker energy dependence, while the 1% Sm doped FA glass exhibits a large response and a stronger x-ray energy dependence than that for 5% Sm. 1% Sm doped FP glass has a smaller response and a weak energy dependence.

Figure 12 compares the dose response curve for 1% Sm-doped FA glass with energies ranging from 40 – 120 keV. Each point on the graph corresponds to an individual piece of sample, meaning that the total dose is not an accumulative dose. Put differently, using a new sample for each dose (exposure) avoids using a single sample in multiple irradiations. These results indicate that, for a wide range of energies, the dose delivered can be measured from a range of 5 Gy to 2000 Gy, which covers the dose range for most MRT applications. The response (R) vs Dose (D) measurements have been plotted on a log-log scale in Figure 12. Although the initial rise is linear, as the dose becomes larger, the linearity is lost. The simplest assumption would be a first order kinetic equation for the rate of conversion under a limited supply, which implies an exponential rise towards saturation i.e.

$$R = R_o [1 - \exp(-D / D_o)] \quad (1)$$

where R_o and D_o are the constants. The best fit parameters of Equation to the data in Figure 12 are shown in Table 1. It can be seen that Equation (1) provides a good fit to the data over the whole dose range and energy range. Under low doses, $R = (R_o/D_o)D$ i.e. R is linearly proportional to the incident dose. The ratio R_o/D_o represent the slope of the initial linear rise in R vs D and hence the initial sensitivity of the detector glass. The inset in Figure 12 shows R_o/D_o vs. x-ray energy E and it can be seen that R_o/D_o decreases with the photon energy, which accounts for the lower dose-sensitivity at higher energies. As a point of interest, a parabolic fit was also tried in which $R = aD - bD^2$, where the second term causes the fall of R below the linear behavior as D increases. While the parabolic equation also has two constants as Equation (1), the fit to the parabolic equation was found to be worse. A power law fit of the form $R = AD^m$ (where A and m are constant) yields R^2 coefficients that are worse than both the exponential and the parabolic forms. The curves in Figure 12 serve as the calibration curves for the 1% Sm³⁺-doped FA glasses at different x-ray energies. We can also speculate on the saturation behavior by noting that the dose needed to reach 90% saturation $D_{90} = 2.3D_o$ which, from Table 1, is 2,335 Gy at 120 keV.

For all the previous figures in this work, the total focal depth from the sample surface (d) has been set to 20 μ m as discussed in Section 2. However, by changing the incident energy, this can also play an important factor in the response of the Sm-doped glass material as a function of

both the incident x-ray energy and the selected confocal depth. Prior published work involving Sm-doped FA glasses irradiated at the CLS had used an energy of 50 keV and a focal depth of 20 μm to measure the response values [28,34]. Figure 13 compares the focal depth against the response values for two x-ray energies, 40 keV and 120 keV, and shows that response can be shown to be constant as the focal depth increases up to a certain depth, depending on the incident x-ray energy, then the response decreases. Increasing the focal depth beyond 40 μm and attenuation of the emitted light within the host glass begins to affect the collection of light as well as the decrease in the Sm^{2+} concentration. These results indicate that over such a large energy range as is investigated in this paper, the energy dependence can influence the response values and requires careful attention during calibration.

As part of the work in this paper, multiple concentrations of Sm-dopants have been investigated towards characterizing the energy and dose rate dependence of FA and FP glass samples. Figure 10 and Figure 11 show that the host glass material (FA vs FP) and smaller concentrations of Sm-dopants in the host glass (0.2 to 5 % Sm) give rise to a larger conversion of Sm^{3+} to Sm^{2+} under the same irradiation conditions. An important consideration in these materials is the overall stability of the sample, that is, the response of the sample should not change between the time of irradiation and readout. Figure 14 shows the change in the response R of various Sm-doped glass plates as a function of time right after irradiation up to 15 days. As can be seen from Figure 14, the Sm-dopant concentration plays an important role in the stability of the samples. The spontaneous reconversion from Sm^{2+} to Sm^{3+} appears to be related to the availability of hole traps, since 1% Sm-doped FA glass appears to be very stable after irradiation, whereas the response of 0.2% Sm-doped FA glass appears to decrease noticeably immediately after irradiation. Regardless of concentration, it appears that the response values of all samples appear to be stable after 24 hours following the cessation of irradiation. The above result indicate that 1% Sm-doping is the most suitable concentration for dosimetric purposes due to the stability of the irradiated signal and the capability of detecting response values over a wide range of incident x-ray energies. While 0.2% Sm is more sensitive (Figure 11), its stability is worse than 1% Sm (Figure 14).

7. Discussion and Critique

Previous work with Sm-doped FA and FP glasses examined the conversion of Sm^{3+} to Sm^{2+} over large dose ranges and how these samples could be shown to be reusable through the process of UV exposure or thermal annealing around the glass transition temperature by reconverting the Sm^{2+} ions back to their original Sm^{3+} state, demonstrating their usefulness as a dosimetric detector for MRT. Overall it has been shown that after long periods of irradiation, photodarkening is present in both FA and FP glass samples, although the changes in absorbance for FA glasses are primarily in the UV region, whereas FP glasses can become so dark that they may become of little use for high-dose dosimetry. These results confirm the findings of this research, which show that when 1% Sm-dopant FA and FP samples are exposed to identical irradiation conditions, the response values are higher for FA glasses than FP as shown in Figure 10, Figure 11 and Figure 14. Overall, the properties of FP glasses are better understood than those of FA glasses, which makes them useful for research purposes. FP glasses have evidence of phosphorous-oxygen hole and electron centers (POHC and POEC) which have been well studied [27], while the hole traps within FA glasses are tentatively associated with fluorine complexes and oxygen contamination [45,46,47,48]. The conversion of Sm^{3+} to Sm^{2+} is controlled by a hole trapping process, which is

clearly evident when we compare the overall response values of FA glass samples in which the Sm-dopant concentration has been varied, as in Figure 10 and Figure 14. These indicate that the increase in the number of total electron acceptors, Sm^{3+} ions, does not lead to a higher conversion, i.e. response. This result is somewhat non-intuitive, but is apparent when comparing the response values of 0.2% and 5% Sm doped FA glasses in Figure 10 and Figure 14, which have a marked difference in response values to the same irradiation conditions. While lower concentrations lead to larger a conversion from Sm^{3+} to Sm^{2+} , there is a trade off in the stability of the sample. Figure 14 indicates that 1% Sm-doped FA is a stable sample that does not change after irradiation while still showing strong conversion, and is an ideal candidate for MRT dosimetry purposes.

The dose rate and energy dependence of dosimeters is an important consideration. MRT relies on adjacent healthy tissue aiding in the repair of tissue damaged from radiation. The success of MRT requires minimal movement of the patient in order to prevent "smearing" of the microbeams which would cause a decrease in the PVDR. MRT uses dose rates up to thousands of Gy/s, so the response of the detector should not change as the incident dose rate is altered. Figure 10 indicates that there is no evidence of a dose rate dependence resulting from the irradiation of the samples, which is an important discovery in this work. It appears that the conversion from Sm^{3+} to Sm^{2+} and the hole trapping process is not influenced by the flux of incident x-rays.

The dependence of the response on the incident dose is shown in Figure 12 at different photon energies. It is important to emphasize that each point represents a different sample so that the dose is not accumulated dose. Using a single sample and then carrying out measurements from one dose to the next would not necessarily represent the true response vs. dose characteristics because in the latter case the dose would be a "cumulative dose". The dependence of the response on the x-ray energy can be understood from the dependence of the actual energy deposited as the photon energy increases. Although the incident dose in air is the same for all the exposures (1 kGy in air) in Figure 11, the deposited energy in the FA glass decreases with photon energy because the photoelectric effect's cross section falls more rapidly with energy than the linear attenuation coefficient; around 40 keV, they are approximately the same. Consider the change in the response in Figure 11 from 40 keV to 130 keV. The photon fluence Φ_{ph} in the two cases are different. We can calculate Φ_{ph} from the Boone equation [49],

$$\Phi_{\text{ph}} = \frac{1}{a + b\sqrt{E \ln E} + \frac{c}{E^2}} \quad [\text{photons mm}^{-2} \text{ mR}^{-1}] \quad (2)$$

here E is the photon energy in keV, and $a = -5.0233 \times 10^{-6}$, $b = 1.8106 \times 10^{-7}$, $c = 0.0088387$. 1 kGy in air is equivalent to 114 kR so that Equation (2) at 40 keV gives $\Phi_{\text{ph}} = 2.41 \times 10^{15}$ photons cm^{-2} , and at 120 keV it gives $\Phi_{\text{ph}} = 2.24 \times 10^{15}$ photons cm^{-2} , a small difference of about 7%. The change in the fluence along with the large reduction in the energy absorption coefficient μ_{en} can provide a qualitative explanation of the energy dependence in Figure 11 and Figure 12. The attenuated photon fluence within Δz is $\mu \Phi_{\text{ph}} \Delta z$ where μ is the linear attenuation coefficient. The total energy deposited, $\Delta E_{\text{deposited}}$, into a volume within Δz from the surface per unit area (cm^{-2}) would be,

$$\Delta E_{\text{deposited}} = (\mu_{\text{en}} / \mu)(E \times 10^3 \times 1.602 \times 10^{-19})(\Phi_{\text{ph}} \mu \Delta z) \quad [\text{J cm}^{-2}] \quad (3)$$

in which the photon energy E is kept in keV. Using the photon fluence from Equation (2) and the appropriate values for μ_{en} for the FA glass, within 20 μm , the deposited energy at 1 kGy is 183 J cm^{-2} at 40 keV. It is smaller at 130 keV with values of 18 J cm^{-2} for the photoelectron effect and 41.3 J cm^{-2} for incoherent scattering, a total energy deposition of 59 J cm^{-2} , a decrease by a factor of 3 from 40 to 130 keV at the same dose level. One can immediately see that the difference can qualitatively explain the reduction in the response with increasing photon energy. The deposited energy would change the concentration of structural defects created and hence the concentration of hole traps needed for the Sm^{3+} to Sm^{2+} conversion as previously discussed [27,28,29,30,31,32,33,34]. While the experimental results can be explained qualitatively from fundamental physical arguments, a detailed kinetic model would be needed that has multiple rate equations to predict the exact dependence, which is beyond the scope of this paper.

Ideally the detector medium should be tissue equivalent so that the measured deposited dose is similar to dose in tissues. Tissue equivalent detectors, such as diamond detectors [18,50] are obviously very attractive in dosimetry. Unfortunately, Sm-valance conversion in glasses has only been seen in a few selected systems such as fluoroaluminate and fluorophosphate glasses, which are not tissue equivalent. Nonetheless, there is still much research interest in finding host material which are closer to being tissue equivalent.

The response of a dosimeter is generally a function of the radiation beam quality and the beam energy. For MRT purposes there is currently not a mutually agreed ideal energy for treatment purposes. Ideally, a dosimeter should not have a strong energy dependence. In practice however, when measuring an incident x-ray energy range that varies over hundreds of kiloelectronvolts, the response of a dosimeter will require calibration. The energy range can differ widely depending on the application and the target, from small animal experiments, to the eventual treatment of human patients. What is of primary importance is the incident x-ray energy range is sufficient to penetrate deep into the desired region of the tissue, the maximization of dose rate, the PVDR, and increasing the energy in order to reduce the overall dose that is deposited near the exterior of the subject, thus minimizing surface dose. Figure 12 indicates that a wide range of doses can be detected by 1% Sm-doped FA glass at multiple energies and is a suitable candidate for MRT purposes. Figure 13 indicates that at high doses (1 kGy) and lower energies such as 40 keV, the response R is shown to be constant within the first 20 μm of the Sm-doped FA glass samples, whereas for higher energies this does not play a significant role. The overall findings of this research illustrate that Sm-doped FA glasses, in comparison with Sm-doped FP glasses, are excellent candidates for high-dose and high-resolution applications for MRT dosimetry purposes and the optimum doping level points to 1% Sm.

8. Conclusions

Sm-doped Fluoroaluminate and fluorophosphates glasses have been examined for the purposes of high-dose measurements in microbeam radiation therapy (MRT) dosimetry. These samples utilize the valance conversion of Sm^{3+} ions to Sm^{2+} after irradiation as a measurement of the dose delivered. These two ions yield distinct and separable PL signals that can be detected using a fluorescence (PL) confocal microscopy system designed to separate and detect the emission wavelengths of these two ions. These Sm-doped glass detector plates were then characterized for high-dose dosimetry by investigating the detector response (defined in terms of the relative

intensities of the Sm^{2+} and Sm^{3+} PL signals) as a function of the incident x-ray energy (using monochromatic x-rays at the Canadian synchrotron) as well as the dose rate and the total dose incident on the detector (up to 2000 Gy in air). Each irradiation and subsequent measurements used a new but identical sample to avoid effects arising from accumulated dose.

It was found that the response of the irradiated glass plates did not show any dependence on the dose rate from $7 \times 10^{-3} \text{ Gy}_{\text{air}}/\text{s}$ to $5 \text{ Gy}_{\text{air}}/\text{s}$ at 50 keV (monoenergetic x-rays). Numerous samples were irradiated with doses up to $2 \times 10^3 \text{ Gy}_{\text{air}}$ and it was shown that the detector glass plates can be suitably calibrated over the large dose range accessed in this work, following an exponential behavior of the form $R = R_o[1 - \exp(-D / D_o)]$ from 40 – 120 keV. The constants R_o and D_o depend on the x-ray energy and are listed in Table 1. They are independent of the dose rate. Under low doses, the response vs. dose behavior was linear but falls below linearity at high doses.

The dependence of the response on the focal depth d of the objective lens from the surface of the sample was also investigated. The optimum depth d was determined to be 15–20 μm . This choice of d was in good agreement with the vertical range determined by using a surface Sm^{2+} -ion implanted FA glass plate. The choice of d also minimized the photodarkening effect, which had to be included in analysis in works [32] that did not use an optical microscope and the signals had to cross the whole sample thickness of several millimeters. The lateral resolution of the optical readout technique for measuring the response of Sm-doped FA glass plates was determined to be under 1 μm . The readout technique was demonstrated to be capable of determining the microbeam profile at 50 keV at the CLS.

Various glass sample compositions were irradiated in order to select the most suitable candidate for Sm-valence dosimetry. It was demonstrated that increasing the total number of Sm-dopants leads to a smaller Sm^{3+} to Sm^{2+} conversion, while lower concentrations lead to a spontaneous reconversion of Sm^{2+} to Sm^{3+} within hours after irradiation, which is not desirable. Further, photodarkening, which has a stronger presence in FP glasses, leads to complications in the readout method as a result of the change of absorbance in the same region as the emitted Sm^{3+} signals. The consideration of these factors lead to the choice of 1% Sm-doped FA as probably the most suitable Sm-doped glass. Overall, 1% Sm-doped FA glass has shown excellent conversion of Sm^{3+} to Sm^{2+} over a wide range of doses and energies and has shown no evidence of any dose rate dependence.

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7. Figures and Tables

Figure 1 An illustration of the confocal microscopy set up used in measuring Sm-doped glass plates. The excitation source is a 473 nm diode-pumped solid-state (DPSS) laser, which has an adjustable focal depth within the glass samples and an intensity that can be modified through the use of neutral density filters (ND). Emission from Sm³⁺ and Sm²⁺ ions are filtered through dichroic mirrors (DM), and then collected simultaneously by two separate photomultiplier tubes tuned to the Sm³⁺ and Sm²⁺ wavelengths through the use of band-pass (BPF) and long-pass filters (LPF). The detection ranges of these PMTs are given in Figure 2. The available objective are 10×/0.3NA (Meopta) and 20×/0.75NA (Nikon) and the available pinhole sizes are 200, 100, and 50 μm.

Figure 2 Upper figure shows the excitation spectrum centered at 473 nm. The middle figures show the PL spectra from Sm^{3+} and Sm^{2+} ions. The lower figure shows the spectral response of the two photomultiplier tubes with their respective filters; long-pass for PMT1 and band-pass for PMT2. The detection ranges are 595 – 615 nm (FWHM) for PMT2 (Sm^{3+}) and 660 – 720 nm (FWHM) for PMT1 (Sm^{2+}).

Figure 3 (a) Schematic illustration of the motion of the objective lens and the movement of the focal point inside the sample. The objective lens moves by D and the focal point by d and the two are related through the refractive index. (b) The 470 nm excitation volume inside the sample defined by the objective lens is shown as shaded in darker blue. The luminescence signals within the width of the focal point and the vertical range Δz are measured.

Figure 4 The PL(Sm²⁺) signal from ion-implanted Sm²⁺ ions within 1 μm from the surface of a FA glass plate. Ion implantation peak is at 0.60 μm as shown in the insert [35]. The solid line is the best Gaussian curve fit with a half width at half maximum that is 21 μm

Figure 5 The PL signal vs distance from the sample surface. The blue dots represent Sm^{3+} values measured in 1% bulk Sm-doped FA glass and the red line is calculated from the fitted Gaussian signal from an ion implanted sample where Sm^{2+} ions reside within a depth of 600 nm, as shown in Figure 4, integrated from 10 μm outside the glass surface to 60 μm within the sample.

Figure 6 (left) An image of 4 μm fluorescent microsphere which was acquired using the confocal fluorescence microscopy readout system used in this work with the 20× objective. (center) the measured 1D profile of the 2D imaged microsphere from confocal fluorescence microscopy. (right) 4 μm fluorescent microspheres as measured by a 2-photon confocal microscope.

Figure 7 Image of a 1951 USAF resolution plate collected through the reflection of the incident laser on the target surface through a 20× objective lens. This image shows group 6 and 7 of the resolution plate where the smallest line widths are 4.38 μm and 2.19 μm, respectively.

Figure 8 (left) 2D image of a single irradiated microbeam on a 1% Sm-doped FA glass slide performed at the CLS. The incident x-ray energy was selected to be 50 keV and the total dose delivered was 200 Gy_{air} prior to passing through the collimator. The collimator has a slit width of 50 μm and the peaks are separated by a distance of 400 μm , center to center. (right) Plotted 1D profile of shown 2D image. The red circles indicate measured values of the microbeam profile and the blue lines indicate the modeled beamshape through Monte Carlo simulations [43] with the MCNP [42] radiation transport computer code of monochromatic 50 keV x-rays incident on 1% Sm-doped FA glass. These measured profiles agree well with simulations and the energy dependence on the microbeam shape will be discussed in greater detail in an upcoming paper.

Figure 9 PL spectra of 1% Sm doped FA glass before and after irradiation using a FAXITRON x-ray cabinet. The emission spectra of Sm^{3+} and Sm^{2+} are shown. The sample has been irradiated with an approximate dose of 1500 Gy_{air} . The left photo is the unexposed sample under UV excitation. The right photo is a sample that has been exposed a large dose. The image of red luminescence from the exposed glass was taken using a filter that suppressed wavelengths below 660 nm.

Figure 10 Response values (Ratio of $PL(Sm^{2+})/PL(Sm^{3+})$) of 1% Sm doped FA and FP glasses as a function of delivered dose rate to the sample. All samples were irradiated with a total dose of 200 Gy in air as measured by an ionization chamber with incident x-ray energy of 50 keV.

Figure 11 Response values (Ratio of $PL(Sm^{2+})/PL(Sm^{3+})$) of Sm doped FA and FP glasses. All samples were irradiated with a dose of 200 Gy in air as measured by an ionization chamber and the dose rate was set to be 175mGy/s. For all dopant concentrations and host glass materials, the response values decrease as a function of energy with the range of 35 to 130 keV. As the dopant concentration is increased the overall conversion of Sm^{3+} to Sm^{2+} decreases.

Figure 12 Response values (Ratio of PL(Sm²⁺)/PL(Sm³⁺)) of 1% Sm doped FA glass at multiple energies from 5 – 2000 Gy. Exponential fits are shown in Table 1. Each dot represents an individual piece of glass sample, that is, the dose shown is not cumulative. Equation for fitted line in the insert where R_0/D_0 vs. E is plotted is $(R_0/D_0) = (0.01043 \pm 0.001) - (7.5 \times 10^{-5} \pm 1.18 \times 10^{-5})E$.

Figure 13 Response of irradiated 1% Sm FA glasses as the focal depth of the incident laser in the fluorescent confocal microscopy (shown in Figure 1) is modified at two different energies, 40 keV and 120 keV. The total dose delivered to each sample is 1 kGy using a monochromatic x-ray energy synchrotron source. As the incident x-ray energy is increased the conversion of Sm^{3+} ions to Sm^{2+} is constant within a larger volume in the glass material. The vertical axis is the same for both.

Figure 14 Stability of varying Sm-dopant concentrations and host glass materials over time. All samples have been irradiated with an approximate dose of 500 Gy using a FAXITRON x-ray cabinet. Each data point represents an individual sample. It appears as though lower Sm-dopant concentrations are less stable after irradiation, although all samples appear to be stable after approximately 1 day.

Table 1 The best fits of $R = R_o[1 - \exp(-D/D_o)]$ to the experimental data in Figure 12. R^2 is the so-called R -squared goodness of fit or the coefficient of determination.

Energy (keV)	R_o	D_o (Gy)	R^2 Exponential fit
120	1.94 ± 0.22	1014 ± 156	0.9902
100	2.19 ± 0.27	789 ± 142	0.9723
80	2.62 ± 0.32	773 ± 128	0.9752
60	2.33 ± 0.18	359 ± 41.3	0.9840
40	3.20 ± 0.25	423 ± 43.8	0.9860

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