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A gas scintillator detector for 2D dose profile monitoring in pencil beam scanning and pulsed beam proton radiotherapy treatments

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Abstract

In order to address dosimetry demands during proton therapy treatments utilizing pencil beam scanning and/or pulsed beam accelerators, we have developed a xenon-filled Gas Scintillation Detector (GSD) that can monitor delivered dose and two-dimensional beam centroid position pulse-by-pulse in real time, with high response linearity up to high instantaneous dose rates. We present design considerations for the GSD and results of beam tests carried out at operating proton therapy clinics. In addition to demonstrating spatial resolution with σ of a few hundred microns in each transverse dimension and relative dose precision better than 1% over large treatment areas, the test beam results also reveal the dependence of the GSD dose normalization on dose rate, beam energy, and gas impurities. The results demonstrate the promise of the GSD technology to provide an important addition to dosimetry approaches for next-generation ion beam therapy.

1. Introduction

Recent and ongoing improvements to the facilities for delivering proton and other ion beam radiotherapy are aimed at realizing the precision potential of this cancer treatment modality while greatly decreasing its cost. Among the most important of the technological upgrades are the introduction of Intensity-Modulated Proton Therapy (IMPT) via pencil beam scanning (PBS) treatments (Lomax *et al* 2001, Pedroni 2012) and the use of compact superconducting pulsed-beam accelerators (Peggs *et al* 2007, Matthews 2009), such as synchrocyclotrons. These and other improvements are fueling rapid growth – about 16% per annum worldwide (PTCOG 2016) – in the number of proton and ion beam therapy clinics. The present paper reports on instrumentation development that addresses new demands on radiation dosimetry imposed by these accelerator and treatment plan upgrades.

The PBS approach allows delivery of a tailored radiation dose closely conforming to a tumor volume of arbitrary shape, via two-dimensional lateral scans of a beam of narrow (typically < 1 cm) diameter at a series of fixed beam energies. The highest energy is chosen to position the Bragg peak in the energy deposition profile at the distal edge of the target tumor, while a succession of lower-energy scans is then used to fill in the dose, as required, at depths closer to the proximal edge of the tumor. Beam intensity and position can be adjusted at every step in the process, to facilitate true 3-D “painting” of the tumor volume, while sparing healthy tissue, including critical organs, in close proximity to the tumor. This approach not only

reduces the time, cost and toxicity of individual patient treatments, but furthermore improves their precision and the range of tumors to which proton therapy is well suited (Lomax 1999, Kooy and Grassberger 2015). But PBS also makes the treatment delivery reliant on proper functioning of many hardware and software components. It requires dosimetry capable of monitoring the dose delivered to every 3-D spot (voxel) in the treatment, in real time and preferably with sub-millimeter transverse spatial resolution. Such resolution, exceeding the capability of commercial strip ionization chambers, is obtainable with radiographic film or scintillating screens, but not for real-time dosimetry during patient treatment.

The use of compact superconducting pulsed-beam accelerators is reducing ion beam facility footprints and costs and improving ease of operation by allowing fully automated beam control (Matthews 2009). For example, the S250 superconducting synchrocyclotron (SCSC) system developed by Mevion Medical Systems (Mevion 2016) combines the traditionally separated accelerator and beam delivery gantry into a single cost-effective unit. Roughly half of the new ion beam radiotherapy facilities being developed worldwide will utilize SCSC technology from either Mevion or IBA (IBA 2016). The SCSC beam is delivered typically in pulses of several microsecond duration, at a repetition rate up to 1 kHz, giving a beam-on duty factor of 1% or less. Long-term efforts to develop other advanced acceleration technology (Peggs *et al* 2007, Flanz and Smith 2009), based on either a high-gradient dielectric wall accelerator (Caporaso *et al* 2008) or a laser-driven medical accelerator (Schwoerer *et al* 2006, Linz and Alonso 2007, Murakami *et al* 2009), would also produce pulsed beam with short pulses and low duty cycle.

We emphasize here the contrast between such pulsed-beam accelerators and more conventional ion beam therapy accelerators, such as cyclotrons, which may deliver the beam in radio-frequency *micropulses* whose time separation (typically nanoseconds, rather than milliseconds) is short in comparison to the characteristic time response of the physical processes used in a detector exposed to the beam. The detector then senses the beam from such conventional accelerators as being delivered *continuously*, with a macroscopic duty factor of essentially 100%. In contrast, the small duty factor of the new generation of pulsed-beam accelerators implies that the *instantaneous* beam current sensed by dosimeters (*i.e.*, averaged over their characteristic time response) during treatment can be up to tens of μA , two to three orders of magnitude larger than that with continuous beam accelerators. At the resulting high instantaneous dose delivery rates, the response of air ionization chambers conventionally used as treatment dosimeters becomes nonlinear, due to recombination of the produced ions (Almond 1984, Palmans *et al* 2006, Nariyama 2006). This effect makes it highly desirable to develop alternative real-time dosimeters that operate linearly up to much higher dose rates.

The first proton therapy treatment room combining an SCSC accelerator with PBS capabilities has very recently begun initial patient treatments in Nice, France (IBA 2016), and comparable clinics will be coming online over the next year or two (Mevion 2016). For dose monitoring during treatment, the Nice facility relies on air ionization chambers that will require significant recombination corrections at the high instantaneous dose rates envisioned. The imminent demands of this new class of treatment centers enhances the urgency for developing new, cost-effective dosimetry solutions that simultaneously provide

dose accuracy and linearity to high dose rates, as well as high spatial resolution attainable in sub-millisecond measurement intervals.

The desired performance parameters of such dosimeters are fixed by clinical procedures and demands. The device must accommodate beam scans covering the largest tumor areas to be treated with ion beam therapy, typically $\sim 30 \times 30 \text{ cm}^2$. Within this sensitive area, it must clearly distinguish beam displacement by typically several millimeters in moving from voxel to voxel in a pencil beam scan, favoring 2-D spatial resolution of 1 mm or better. It should be capable of measuring and archiving the dose delivered to *each voxel* with a relative precision of $\sim 1\text{--}2\%$ for the voxels with the highest doses. The time interval for delivery of that dose can vary from several μs with a pulsed-beam accelerator to several ms in a pencil beam discrete-spot scan executed with a continuous-beam accelerator. Intermediate between those extremes are continuous-beam fast raster scans planned for some new facilities (Noda 2012, Pedroni 2012), where the dosimeter should be able to track delivered dose in intervals of tens of μs , during which the beam moves by no more than 1-2 mm.

Dosimeter output to feed back to the beam control system should ideally be available on millisecond time scales, in order to influence subsequent steps in the treatment in case hardware or software problems yield voxel doses that deviate significantly from the treatment plan. For example, a signal indicating such a significant deviation might be used to pause the treatment prior to a repainting of the same energy layer that was planned for delivery during the same patient breathing cycle. Measurement capability should span a dynamic range $\sim 100:1$ in spot-to-spot dose variations, as may occur near the edges of the radiation field or even in central regions for lower energy layers, where the delivered dose builds on the proton energy deposition tail from higher-energy layers. When positioned upstream of the patient, the dosimeter must not introduce troublesome energy or angular spread to the pencil beams traversing it.

In this paper we report on the development and initial beam tests of a novel Gas Scintillation Detector (GSD) designed as a dosimeter to deliver the above performance characteristics in a cost-effective package (Cameron *et al* 2015). We describe the design of a prototype GSD and the setup for beam tests in Sec. 2. In Sec. 3 we present data from tests using pencil beam scans, showing how and with what precision 2-D beam centroid position and dose are extracted from the signals emerging from the readout electronics. In Sec. 3 we also report on the dependence of the GSD dose measurement on dose rate, as varied with both continuous and pulsed-beam accelerators, as well as on the GSD dose normalization against air ionization chambers as a function of beam energy and of contaminant levels in the scintillating gas. In Sec. 4, we describe planned improvements for clinical versions of the GSD, with conclusions summarized in Sec. 5.

2. Methods

2.1 Design considerations

A dose measurement method with the most promise to overcome the non-linearity of the standard ion chamber at high dose delivery rates utilizes the direct measurement of scintillation light emitted in a gas filled chamber (Coutrakon *et al* 1991) by the de-excitation

of gas molecules on nanosecond-level time scales. By detecting the fast scintillation light directly, one bypasses problems associated with ion-ion recombination, which occurs over much longer time scales. For the GSD we have chosen xenon as the scintillating gas, due to its high scintillation light yield and negligible self-absorption of the resulting photons (Policarpo 1981, Serra *et al* 2014). The primary scintillation photons, in the vacuum ultraviolet (VUV) range peaked at a wavelength near 175 nm, result from the decay of the diatomic (dimer) states, $\text{Xe}_2^* \rightarrow 2\text{Xe} + \text{photon}$. These excited gas molecules are generated by electromagnetic excitation of xenon atoms by passing protons, followed by xenon atom-atom interactions, processes that account for about 20% of the energy loss of the proton (Policarpo 1981). The lifetime of the excited dimer states is 110 ns (Policarpo 1981, Baldwin 1981).

Ionization of xenon atoms is sometimes followed by electron-ion recombination and the generation of more excited dimers. The resulting *recombination luminescence* contribution to the VUV scintillation light occurs after a typical electron thermalization delay time $\approx 2 \mu\text{s}$ in xenon gas at atmospheric pressure (Takahashi *et al* 1982), and then exhibits both fast (sub-microsecond) and slow (characteristic decay time of tens of μs) components (Mimura *et al* 2010). This recombination contribution has been partially suppressed in a number of previous experiments by application of a drift electric field to remove the electrons to a separate detector region reserved for an ionization measurement, with that separated ionization measurement sometimes carried out by accelerating the electrons to stimulate *secondary* xenon scintillation (e.g., see Serra *et al* 2014). In addition, recent searches for rare particle physics processes have used high-pressure xenon gas or liquid xenon to enhance the overall photon yield. However, for in-beam dosimetry use the prompt scintillation yield is ample at atmospheric Xe pressure and the ionization signal is unnecessary, removing the need for an electric field. Under these conditions recombination luminescence is expected, on the basis of previous work (Mimura *et al* 2010), to contribute much less than half of the total VUV scintillation yield. The total yield of prompt scintillation photons, including recombination luminescence, is proportional to the radiation dose delivered to the xenon gas.

When the fast xenon scintillation light is collected in multiple photodetectors, the GSD also provides position measurement capability. The predominant sensitivity to the 2-D location at which dose is delivered arises simply from the differential solid angle for collecting scintillation photons produced at an off-center site in oppositely situated photodetectors. This sensitivity is optimized by minimizing reflections of the scintillation photons from chamber walls, again in contrast to standard gas scintillator design for nuclear and particle physics experiments. In the absence of reflections and light attenuation and scattering in the gas, the position sensitivity can be easily estimated. For photodetectors of area A positioned to the left and right at equal distances R from the detector center, scintillation photons produced along the line between the two at a displacement x from the center toward the left photo-detector will be collected with a left-right asymmetry

$$a_x \equiv \frac{N_L - N_R}{N_L + N_R} \cong \frac{A(R-x)^{-2} - A(R+x)^{-2}}{A(R-x)^{-2} + A(R+x)^{-2}} \xrightarrow{x \ll R} \frac{2x}{R}, \quad (1)$$

where N_L and N_R denote, respectively, the number of photons detected in the left and right photodetectors.

For position sensitivity in two dimensions, a minimum of three photodetectors is required. As seen in Fig. 1, the prototype GSD we have fabricated and tested is outfitted with six photomultiplier tubes (PMTs), arranged symmetrically at 60° intervals around the azimuthal edge of a cylindrical chamber. The geometrical arrangement used provides three pairs of diametrically opposed PMTs, from whose asymmetries we deduce non-orthogonal coordinates we label x , u and v . The u and v information can be combined to extract the vertical coordinate y at which the scintillation photons were generated, as well as an alternative measure of x . Thus, the use of six PMTs rather than the minimal three provides, in addition to symmetry and excellent 2-D position resolution, redundancy in case one of the PMTs or its readout electronics should develop a problem during measurements.

The PMTs used were model 9107QB from ET Enterprises (Adit 2016), compact tubes with an active photocathode area of 2.5 cm diameter, 11 dynodes and a fused silica window to provide sensitivity down to 160 nm. The typical quantum efficiency of the PMTs at the peak of the xenon scintillation spectrum is $\sim 25\%$. Each tube viewed the gas volume through a 1.6-mm thick fused silica optical and vacuum window. Bias was applied to each PMT, and its output anode signal was processed, through a tapered resistive-chain voltage divider base (ET model C637B) designed to handle anode currents up to 100 μA without introducing significant gain sag.

To the extent that the linear relationship seen in Eq. (1) between measured asymmetry and coordinate is observed to be valid in the vicinity of the GSD center, the asymmetries are sensitive to the *beam centroid* coordinates at which the scintillation light is produced, and not to the size or shape of the pencil beam intensity profile over which they are averaged. The insensitivity to size and shape extends also to any electron-ion recombination region surrounding the pencil beam path. The beam size and shape are relevant to treatment planning and are generally measured during beam commissioning and subjected to daily or weekly quality assurance measurements, made with different dosimeters, at operating proton therapy clinics. If it were desired to monitor these beam characteristics as well during patient treatments, then the GSD (and commercial ion chambers, as well) would have to be complemented by a true 2-D imaging dosimeter, *e.g.*, using Gas Electron Multiplier technology (Nichiporov *et al* 2016).

The delivered dose is extracted from the *sum of measured yields* in the six PMTs. The summed solid angle of the six PMTs is relatively insensitive to position near the detector center, but increases as the beam approaches one or another of the PMTs. A correction for this increase can be based on the beam centroid position extracted from the measured PMT asymmetries. In order to maintain the desired dose measurement precision, the magnitude of this non-uniformity correction should be limited, favoring a geometry in which the PMTs are kept at a significant distance from the outer extents of anticipated beam scans. The optimal choice of the chamber radius R thus results from a tradeoff between position sensitivity (favoring small R , as seen in Eq. (1)) and dose measurement precision (favoring large R).

The prototype GSD in Fig. 1 was designed to test detector performance characteristics over a beam impingement area $\approx 15 \times 15 \text{ cm}^2$. Over this or even larger beam areas, the entrance and exit windows containing the gas volume must be made from low-outgassing materials strong enough to withstand gas cell evacuation, but thin enough to minimize energy loss and multiple scattering of the passing beam. For the prototype, we have favored mechanical robustness of windows that can withstand a pressure difference of 1 atm, by using 6061 aluminum of 0.16 cm thickness over a radius of 10 cm. The PMTs are mounted around a circle of radius $R = 17.9 \text{ cm}$, producing asymmetries that change, according to Eq. (1), by 1.12%/mm of beam spot displacement. Modifications to the GSD geometry and window design that would be needed in clinical applications, depending on the beam optics and location and space restrictions of the dosimeter, are discussed briefly in Sec. 4.

In order to minimize reflections of the scintillation light, all inner surfaces of the aluminum cover plates and the cylindrical aluminum chamber have been subjected to the Deep Space Black™ coating process provided by N-Science Corporation (N-Science 2016). With this coating, total hemispherical reflectance of xenon scintillation photons should be held below 1%.

The prototype GSD's aluminum chamber encloses a gas thickness of 5 cm and a xenon volume of 4.6 liters, filled to atmospheric pressure, corresponding to an energy loss of 70 keV for 200 MeV protons traversing the gas. A single such proton produces $\sim 10^3$ primary scintillation photons (e.g., see Table 1 in Serra *et al* 2014), of which ~ 1 on average will be detected in one of the six PMTs. A single clinical beam pulse containing typically $\sim 10^7$ such protons will then produce a hefty signal in all the PMTs.

The yield of scintillation photons from clinically interesting proton beams is far too high to read out the PMT signals using individual pulse processing. Rather, one requires fast integrating electronics to digitize the cumulative charge delivered to each PMT's anode over intervals that are comparable to or smaller than the time required for individual spot irradiations in a pencil beam scan. The resulting charge asymmetries between opposite PMTs must be determined for a single spot to a precision of 1% or better to attain the desired spatial resolution. In the prototype GSD, the anode signal outputs from each pair of oppositely situated PMTs are fed to dual-channel I200 integrators produced by Pyramid Technical Consultants (PTC 2016). These units are designed to integrate currents in the range from 0.1 pA to 100 μA over time intervals that can be adjusted down to 20 μs . The digitized integrator outputs are transferred at rates up to 10 Mbps over optical fiber to a PTC A500 Loop Controller, and thence over Ethernet to the control computer. For the beam tests reported in this paper, computer control and processing of the data were handled with the PTC Diagnostic Software package (PTC 2016).

2.2 Setup for Beam Tests

No clinical treatment rooms that combine pulsed beam accelerators and PBS capabilities were yet available for testing the prototype GSD on the schedule of interest. Hence, we have tested some aspects of detector performance with pencil beam scans and continuous beam at the Northwestern Medicine Chicago Proton Center in Warrenville, Illinois and others with pulsed, double-scattered beam at the S. Lee Kling Proton Therapy Center at Barnes Jewish

Hospital in St. Louis, Missouri. For both sets of tests, the prototype GSD was positioned at the treatment isocenter outside the beam gantry. In addition, a pre-prototype version of the GSD (described further below) was exposed to higher instantaneous beam fluxes than were available at either of the above facilities, during tests utilizing a pulsed pencil (but not scanned) beam at the Proton Dose Test Facility of the Indiana University Cyclotron in 2013. Planned tests of the prototype GSD at the latter facility had to be canceled when the facility operations were terminated in December 2014. The conditions for the various tests are summarized in Table 1 and described in more detail in the following subsections.

2.2.1 Chicago Proton Center tests—Tests at the Chicago Proton Center utilized a simple beam scan that delivered nominally equal doses, typically 0.5 monitor units (MU, see Mayles *et al.* 2007) to 169 spots in succession, with 1.0 cm spacing between spots to span a square pattern covering the range from -6.0 to $+6.0$ cm around the treatment isocenter both horizontally and vertically. The spacing of spots in this test pattern was coarser than in typical PBS patient treatments, but provided more-than-sufficient data for detailed calibration of the beam position and dose reconstruction with the GSD. Each full scan was normally completed in less than one second. Scans were executed with proton beams of energy 225, 150 and 98 MeV. The beam currents measured at the IBA cyclotron output ranged from 300 down to 20 nA, thus spanning a 15:1 range in dose rate. GSD dose measurements were calibrated against simultaneous measurements made with the primary clinic air ionization chamber. As a secondary dose monitor in one of the Chicago Proton Center runs, we mounted a small Markus chamber (PTW 2016) directly behind the GSD and aligned with its center. Beam centroid positions extracted from the PMT asymmetries measured with the GSD were calibrated against the target spot positions in the programmed beam scan.

As there was no access to a control signal from the IBA cyclotron that would indicate imminent beam delivery, the GSD readout electronics were gated instead with a signal derived from a 0.64-cm thick plastic trigger scintillator mounted in-beam behind the GSD. Each pencil beam scan was preceded by a low-dose irradiation of a single pilot spot used by the IBA control software to correct subsequent spots for any mis-steering of the beam. The pilot spot irradiation occurred anywhere from 0.7 to 1.7 seconds before the start of the 169-spot scan. Pilot spot signals in the trigger scintillator were then used to gate the GSD readout electronics on for a total interval of typically 1.8 seconds, allowing observation and characterization of background currents for roughly a half-second before and after each pencil beam scan. This total interval was subdivided into integration cycles, each of duration between 10.0 and 25.0 ms, depending on the beam energy and beam current. At the end of each such cycle the integrator ADCs were reset and stabilized, a process that took 53 μ s. Each such integration cycle typically spanned two or three spots in the beam scan, and was further subdivided into 40-60 subsample periods, with the ADC values reported, but not zeroed, at the end of each subsample. This approach allowed us to measure the buildup of PMT charge every 250-500 μ s during irradiation of each individual spot in the scan.

The PMT high voltages were adjusted to match approximately the six integrated PMT charges when the beam was near the GSD central axis, while avoiding integrator ADC saturation during any of the integration periods. This required bias voltages ~ 400 V,

corresponding to PMT gain factors ~ 100 . Typical PMT anode currents when the GSD was exposed to beam at the higher beam currents used were then $\sim 1 \mu\text{A}$. With the choice of 1000 pF for the integrator capacitors, the ADCs would then saturate after ~ 10 ms exposure to beam. The integration periods, even in the midst of the beam scan, included beam-off intervals when the beam was steered from one spot to the next, so that the duration of beam exposure was always shorter than the integration period.

Many features of the beam scans and of the raw data provided by the GSD readout electronics can be discerned in Fig. 2, where the integrator output from each PMT is shown as a function of time during a portion of one pencil beam scan at a beam energy of 150 MeV. The three figure frames correspond to the three integrator modules, from which the PMT charge ratios are sensitive, respectively, to coordinates x , u and v . Each point in the figure represents the output from one integrator channel at 250 μs subsample intervals. Succeeding points lie on a steep slope when the beam is on, and are constant when the beam is off. The charge from each channel is reset to zero at the end of each 10 ms integration period. The full 0.2-second extent of Fig. 2 covers 39 of the total 169 spots in the beam scan, encompassing the 13-step vertical scan at each of three horizontal locations: $x = +2$, $+1$ and 0 cm with respect to the midpoint of the scan area. For this particular scan, it took roughly 2 ms to deliver the 0.5 MU dose to each spot, 3 ms to steer the beam from one spot to the next in the same scan line, and 15 ms to steer the beam from the bottom of one vertical scan line to the top of the next at a displaced horizontal position.

In the upper frame of Fig. 2, the ratio of Left (blue points) to Right (orange points) PMT charges is nearly constant during each vertical scan, but changes significantly with horizontal location, from approximately 1.0 at $x=0$ cm to 1.3 at $x=1$ cm and 1.7 at $x=2$ cm. The corresponding ratios in the lower two frames change significantly with both horizontal and vertical beam location, as expected for the u and v coordinates. The PMT charge ratios within each frame thus exhibit the strong position sensitivity of the GSD, while the sum of the six PMT charges accumulated in each spot, from which the dose is to be reconstructed, is nearly constant throughout this portion of the beam scan.

In addition to measurements with pure xenon at atmospheric pressure, measurements were made for several beam scans executed at the end of one running period at the Chicago Proton Center with the stepwise calibrated addition of small amounts of dry air, to assess how GSD yields were affected by gas contamination.

2.2.2 S. Lee Kling Proton Center tests—A run at the S. Lee Kling Proton Therapy Center was used to test prototype GSD performance with a pulsed-beam accelerator (Mevion S250 superconducting synchrocyclotron). Beam pulses with a typical duration of 3 μs were delivered every 2.0 ms, at time-averaged dose rates from 64 to 320 MU/minute. This facility utilizes a double-scattering system and a range modulator wheel to produce clinical beams with a spread-out Bragg peak and large lateral extent. Our measurements were made with a configuration that provided a spread-out beam energy range from 216 to 226 MeV (equivalent range in water from 30 to 32 cm) and a lateral field size of 14 cm diameter, collimated before the GSD with either 4×4 or $10 \times 10 \text{ cm}^2$ square brass apertures. The small ($\approx 0.15\%$) duty factor resulted in *instantaneous* PMT anode currents as much as 70

times higher than those to which the GSD was exposed during the Chicago Center runs. However, due to the large beam area, the *localized* instantaneous beam flux (nA/cm^2), to which conceivable non-linearities in xenon scintillation light yield might be sensitive, was always considerably smaller than sampled in the Chicago runs.

The physical setup of the GSD was similar to that described above for the earlier Chicago Center runs. But we used a different triggering approach to accommodate the very different time structure of the beam. The GSD integrators were gated on for a single integration period of $176\text{ }\mu\text{s}$ duration surrounding each beam pulse, using a logic signal derived from the ion source trigger signal for the Mevion accelerator. Each integration period was subdivided into 8 subsamples of $22\text{ }\mu\text{s}$, allowing us to measure PMT charges from background currents for a few subsamples immediately before and immediately after arrival of the beam pulse. The PMT anode currents deduced from the charges recorded on successive subsamples are illustrated in Fig. 3. The volume of data recorded was limited by gating the integrator off during the bulk of the 2 ms period separating successive beam pulses.

From data such as that in Fig. 3, we conclude that the scintillation light yield from the GSD is always confined within a single $22\text{ }\mu\text{s}$ interval containing beam arrival. We see no evidence of appreciable recombination luminescence contribution to the light yield, whose slow component would have resulted in measurable PMT current in the subsample(s) immediately following beam arrival. Also note from Fig. 3 that, in contrast to the results for the same two PMTs in the lower frame of Fig. 2, the ratio of charges for the two PMTs remains constant from pulse to pulse, even as the beam intensity varies typically by $\pm 20\%$, because the beam centroid position does not change.

2.2.3 Light pulser tests of prototype GSD PMTs—As a follow-up to the beam tests described in the preceding subsections, we also performed bench tests of several of the prototype GSD PMTs, illuminating them with a pulsed blue LED whose output light yield could be varied over a wide range. The LED was mounted on the prototype GSD in place of one of the six PMTs, so that it could illuminate three of the opposing PMTs. The light intensity on the PMT directly opposite the LED was about twice as high as that at the PMTs displaced by 60° . The LED was pulsed with a time structure similar to that of the proton beam at the S. Lee Kling Center, namely, $4\text{ }\mu\text{s}$ long pulses delivered at 500 Hz. The same pulser also provided the trigger pulse used to gate the integrators, using the same characteristic times as during the S. Lee Kling Center beam tests: $176\text{ }\mu\text{s}$ integration periods, each divided into 8 subsamples of $22\text{ }\mu\text{s}$ duration. The integrated charges per LED pulse were recorded for PMTs receiving different light intensity over a wide range of LED driving amplitudes. These measurements allowed us to study the linearity of PMT response to input light intensity, as reflected in the relative variation of the different PMT anode currents.

2.2.4 Pre-prototype GSD tests—The other test data reported here were acquired with a pre-prototype gas scintillation detector illustrated in Fig. 4. This was a much smaller area detector of 9.5 cm thickness, containing xenon gas at 1 atm pressure, with light collected in two PMTs. This pre-prototype was exposed to 205 MeV proton beam from the Indiana University Cyclotron, with a time structure of $20\text{ }\mu\text{s}$ width beam pulses delivered at 500 Hz frequency. Taking the 1% duty factor into account, instantaneous beam currents up to 220

nA were used. Radiographic film measurements showed the beam lateral profile to be of Gaussian shape with $\sigma \approx 5$ mm, so that beam fluxes impinging on the GSD reached 200 nA/cm², a value higher than that sampled in any of the prototype GSD tests described above.

The pre-prototype response was measured over a wide range of beam currents and compared to the response of a two-plane air-filled parallel-plate ionization chamber open to the ambient atmosphere, which was swapped in for the pre-prototype at the same location. For both the pre-prototype's PMTs and the ionization chamber, output charge was processed with gated integrator cards, a VME-based data acquisition system and custom LabView software different from the Pyramid Technical Consultants system used for the current prototype. The beam current for each measurement was measured on a beam stop just before and just after each pre-prototype or ionization chamber exposure, and was monitored continuously during each measurement by a secondary electron emission monitor.

2.3 Data analysis procedures

Before beam centroid positions and delivered dose are extracted from the prototype GSD data for each spot in a pencil beam scan, two small corrections are applied to the raw integrated PMT charges. The first is subtraction of background that arises primarily from two sources: DC offset currents of typically a few nA and 60 Hz noise from AC power. The subtraction relies on background repetition patterns determined from integrated charges measured immediately before and after each beam scan. After the subtraction, any residual background remains below 1% of the PMT charges accumulated for individual irradiation spots during the beam scans, as verified by the reproducibility of integrated charge from subsample to subsample during periods when the beam is being steered between spots. Additional evidence that the background was not affected by the beam being on was obtained during the Chicago Proton Center tests carried out with reduced beam intensity. The longer spot irradiation times in those runs allowed us to verify that the PMT currents extracted from the integrated charges, following the normal background subtraction procedure, remained quantitatively constant from subsample to subsample after an initial short beam current buildup period during each spot irradiation.

The second small correction accounts for charge that may have been lost during integrator ADC resets that happen to occur during a spot irradiation. As seen in Fig. 5, integration subsamples affected by an ADC reset at the start of the period are easily identified by positive spikes in the PMT currents extracted from two successive subsample integrator outputs. These spikes correspond to the periodic abrupt reductions in integrated negative charge seen in Fig. 2, where one such ADC reset is explicitly labeled. The correction is generally made under the assumption that the PMT currents are constant in time during any intermediate subsample (*i.e.*, neither the first nor last subsample for a given spot irradiation). Then, the lost fraction of subsample charge is given by the ratio of the ADC reset and settling time (53 μ s) to the affected subsample duration (53 μ s plus the subsample period 250 μ s for the Chicago Proton Center runs). When the ADC reset occurs at the start of the *last* subsample for a given spot irradiation (as, for example, at 0.694 s in Fig. 5), we replace the subsample duration by the inferred *beam-on* time during the affected subsample, which is in turn deduced assuming that while beam was on the true PMT current was unchanged

from the preceding subsample. No correction is made when the ADC reset occurs at the start of the *first* subsample for a spot irradiation (as at 0.734 s in Fig. 5), when an integrated charge less than 80% of the charge increment recorded for the subsequent subsample indicates that beam turned on only after the ADC reset. The maximum lost charge is 20% during any single subsample and the observed variation of PMT current among subsamples unaffected by an ADC reset indicates that the correction should be accurate to about 5% of the lost charge. These corrections thus reduce any reset error to a level below about 0.2% for an individual spot, which typically spans about 5 subsamples.

After the above corrections have been applied, the PMT charge is extracted for each spot in the scan by summing the integrator output over all subsamples where the PMT anode currents exceed the very low residual background level (see Fig. 5). The spot charges Q_i are then combined to extract the following asymmetries and summed yield:

$$\begin{aligned} a_x &\equiv [c_L Q_L - c_R Q_R] / [c_L Q_L + c_R Q_R]; \\ a_u &\equiv [c_{LU} Q_{LU} - c_{RD} Q_{RD}] / [c_{LU} Q_{LU} + c_{RD} Q_{RD}]; \\ a_v &\equiv [c_{RU} Q_{RU} - c_{LD} Q_{LD}] / [c_{RU} Q_{RU} + c_{LD} Q_{LD}]; \\ a'_x &\equiv a_u - a_v; a'_y \equiv (a_u + a_v) / \sqrt{3}; \\ Y &\equiv c_L Q_L + c_R Q_R + c_{LU} Q_{LU} + c_{RD} Q_{RD} + c_{RU} Q_{RU} + c_{LD} Q_{LD}. \quad (2) \end{aligned}$$

In Eq. (2), the subscripts L, R, LU, RD, RU and LD refer, respectively, to the PMT orientations left, right, left up, right down, right up and left down, as viewed by the beam. The six c_i are position-independent weight factors near unity applied to correct for possible mismatches among the PMTs in gain, quantum efficiency, VUV photon transmission probability, integrator calibration, etc. They are adjusted to place the central spot in the beam scan at asymmetry values $a_x \approx a'_y \approx 0$ and to balance the contributions of each PMT to the summed yield Y near the center of the GSD. The effective horizontal and vertical asymmetries a'_x and a'_y are deduced from the measured a_u and a_v under the assumption that the axis for vertical beam displacements deviates by 30° from the GSD diameters joining left up to right down, and right up to left down PMTs. Comparison of a_x and a'_x provides a real-time cross-check on the stability of all PMT gains.

3. Results

3.1 Pencil beam scan data

Figure 6 shows the results for the measured PMT asymmetries a'_y vs. a_x for a typical pencil beam scan. In frame (a), the 169 spots in the beam scan result in a simple pattern of clearly discernible spots in this two-dimensional PMT asymmetry space. One of the goals of the GSD design is to reveal possible mis-steering of spots, which may result in over- and under-dosages, in real time by looking for deviations from the characteristic pattern shown in frame (a). The discernible tilt of the pattern in Fig. 6(a) toward lower a'_y as a_x increases suggests that a_u and a_v should, in fact, have been given unequal weighting in extracting a'_y . The curvature of the pattern near the edges of the beam scan reflects a two-dimensional dependence of the PMT asymmetries on beam centroid position as the beam spot moves far

away from the GSD central axis. Both of these effects are easily corrected by combining a_x and $a_{y'}$ to derive two “linearized” effective asymmetries, whose relationship more closely reflects the square pattern of the beam scan, as seen in Fig. 6(b):

$$\begin{aligned} a_x^{lin} &= a_x \left(1 + 0.2a_{y'}^2 + 0.035a_x a_{y'} \right); \\ a_{y'}^{lin} &= a_{y'} \left(1 + 0.04a_x + 0.4a_x^2 \right) + 0.087a_x + 0.049a_x^2 - 0.027. \end{aligned} \quad (3)$$

The linearization represented in Eq. (3) and Fig. 6(b) is a convenient, though not strictly necessary, aspect of the data analysis that gives derived asymmetries bearing simple, basically cubic, relationships with beam horizontal and vertical position (see Fig. 7). Near the center of the scan, the linear term dominates, with slopes that are quantitatively consistent with the simple estimate of 1.1%/mm change in asymmetry deduced from Eq. (1) for our prototype GSD radius.

Using the best-fit cubic relations in Fig. 7 to reconstruct beam centroid positions from the measured PMT asymmetries generally reproduces the target coordinates of the beam scan within about 1 mm. The remaining deviations still exhibit small systematic trends as a function of position within the scan, which are optimally corrected by extending the expressions in Fig. 7 with polynomial terms up to 5th-order in the measured asymmetries a_x , a_u and a_v . In all, we are able to reproduce the beam centroid coordinates for the 169 scan points with an rms deviation ≈ 0.2 mm using 23 (for x) or 25 (for y) adjustable polynomial coefficients, as seen in the fit residuals in Fig. 8.

The results in Fig. 8 have been averaged over three distinct 225-MeV beam scans, in an attempt to reduce contributions to the rms deviations that arise from actual beam position fluctuations within any single scan. Indeed, we observe small scan-to-scan systematic deviations from the best-fit position reconstruction algorithm, which we attribute to beam targeting errors typically of order 0.2-0.3 mm, convoluted with the intrinsic GSD spatial resolution ≈ 0.2 mm. Beyond these small targeting errors, we observed several mm mis-steering errors for $< 0.1\%$ of all spots.

The spatial resolution inferred from the measurements with lower-energy (98 and 150 MeV) proton beams at the Chicago Proton Center is also consistent with 0.2 mm. That resolution is maintained despite larger pencil beam diameters at the lower energies because the GSD is sensitive to beam centroid position, and not to beam spot size or shape. Given the observed asymmetry sensitivity $\approx 1.1\%/mm$, this resolution implies that the PMT asymmetries can be measured for a single spot in a pencil beam scan with a standard deviation uncertainty $\approx 0.2\%$, dominated in this analysis by uncertainties in the background subtraction from integrated PMT charges. For runs taken with much lower-intensity beams, the signal-to-background ratio decreases substantially and the spatial resolution correspondingly deteriorates, still remaining well under 1 mm, and thereby satisfying our design goal even at the lowest beam currents studied.

The GSD dose measurement for each spot in a scan is derived from the weighted sum Y of PMT integrated charges (see Eq. (2)), and is calibrated against the corresponding charge

measurement (Q_{IC}) recorded by the clinic's primary ionization chamber. The ratio Y/Q_{IC} is plotted as a function of 2-D beam target coordinates for a typical 225-MeV scan in Fig. 9(a). We see there that the PMT sum is relatively flat near the GSD center and increases slowly and quadratically as the beam moves toward the PMT circle, where the summed solid angle for scintillation photon collection increases. The quadratic dependence is revealed clearly in Fig. 9(b), where we plot the weighted average PMT charge (Y divided by the sum of the weighting factors c_i in Eq. (2)) summed over scan points within a square subset of the beam scan, and divided by the sum of Q_{IC} values for the same subset of scan points. As the summing square grows from 2 to 12 cm on a side (encompassing the full beam scan in the latter case), the plotted dose normalization ratio increases quadratically by about 7.5%.

Corrections for the geometric variations seen in Fig. 9 are again best made via 5th-order polynomials in the measured PMT asymmetries a_x , a_u and a_v , in addition to one overall dose normalization factor against Q_{IC} . Figure 10 shows the frequency distribution for a typical scan of the resulting percentage difference between the spot-by-spot GSD dose reconstruction after these corrections and the ion chamber dose measurement. The observed rms deviations range from 0.7% to 1.0% over many scans, and include the convolution of both GSD and ion chamber measurement uncertainties. These results verify that the GSD is, indeed, capable of meeting our design goal for dose measurement precision, as well as for spatial resolution.

3.2 Dependence of GSD dose measurements on dose rate

One of the primary goals for the GSD is to provide dose measurements that remain linear with actual delivered dose up to the high instantaneous dose rates characteristic of pulsed beam delivery. There are two independent sources of conceivable non-linearity. The more troublesome source, arising from physical processes intrinsic to light production in the scintillating gas, would be sensitive to the localized instantaneous intensity of the incident beam. In order to search for non-linearity of this type, we carried out measurements for the prototype GSD with pencil beam scans covering a range of 15:1 in dose rate with the continuous proton beams at the Chicago Proton Center. We accessed even higher instantaneous beam intensities with the pre-prototype GSD in tests with the pulsed pencil (but not scanned) proton beams at the Indiana University Cyclotron.

The second source, associated with possible saturation in PMT and integrating electronics performance at high photocathode and anode currents, is less serious because performance limits can be ameliorated by adjusting PMT voltages, redesigning PMT bases or choosing PMTs with different photocathode materials, if necessary. We explored limits on PMT and electronics linearity by exposing the prototype GSD to the very short pulses and large beam areas provided by the S. Lee Kling Proton Therapy Center. These measurements were supplemented by bench tests utilizing a pulsed LED to illuminate some of the PMTs on the prototype GSD.

The pencil beam scan results for GSD dose normalization factor as a function of dose rate are plotted in Fig. 11(a). The dose rate for each point represents the mean value over the 169 spots in a scan of the peak ion chamber current recorded during each spot. From lowest to highest dose rates, the scans were executed with beam currents of 20, 40, 65, 100, 150, 201,

250 and 300 nA, all measured at the output of the IBA cyclotron. In order to perform scans at the lowest and highest beam currents, some IBA treatment delivery controls had to be overridden, so that it is not guaranteed that the beam current reaching the GSD was given by a constant fraction of the beam current extracted from the cyclotron. There is no indication of any appreciable variation in pencil beam *profile* as the beam current was changed: the beam horizontal and vertical widths reported by the clinic's ion chambers were stable within a few percent throughout the measurements. An ion chamber current of 0.4 μA in Fig. 11(a) corresponds to delivery of a 0.5 MU spot dose in 2.0 ms. The GSD dose normalization factors in Fig. 11(a) correspond to the ratio of weighted mean PMT charge to ion chamber charge resulting from the best-fit correction of geometric dependences represented in Fig. 10. These are very similar, but not identical, to the central values seen in Fig. 9(b).

The results in Fig. 11(a) show that the GSD dose measurement remains as linear as the ion chamber measurement within 1% up to a dose rate of about 300 MU/s, but thereafter rises by about 2% by 400 MU/s. This small increase at the highest beam currents occurs where we might expect the ion chamber response to show first signs of recombination-induced saturation. That interpretation is supported by Fig. 11(b), where the ion chamber current appears to fall slightly below a linear relationship with beam current out of the cyclotron at the two highest dose rates measured. The interpretation is further supported by the results shown in Fig. 12 for an air ionization chamber and for the pre-prototype GSD in the measurements made at the Indiana University Cyclotron with 1% duty factor pulsed pencil beams.

The results in Fig. 12 demonstrate that saturation induced by ion-ion recombination sets in for the air ionization chamber at instantaneous beam intensities above about 130 nA/cm², while the pre-prototype GSD response remains linear within 1% up to the highest intensities studied. (Note that beam currents in Fig. 12 were measured at the pre-prototype location, while those in Fig. 11(b) were measured at the output of the Chicago Proton Center's cyclotron.) Instantaneous beam intensities anticipated during pencil beam scans with short-pulse proton accelerators may exceed 1 $\mu\text{A}/\text{cm}^2$, given duty factors as small as 0.1%. While the response of air ionization chambers will be highly non-linear at that level, the encouraging results for the GSD point to the need for further tests utilizing beams from the new and upcoming treatment rooms that combine pulsed-beam accelerators with pencil beam scanning (IBA 2016, Mevion 2016). The absence of appreciable recombination luminescence contributions to the GSD light yield, indicated by the results in Fig. 3, provides additional encouragement that the prompt xenon scintillation response will remain linear up to the relevant localized beam intensities.

There are limits on the linearity of PMT response, as we have explored during the runs at the S. Lee Kling Proton Therapy Center. For the runs taken with a $4 \times 4 \text{ cm}^2$ aperture, the instantaneous PMT anode currents during beam pulses remained below 15 μA , and the GSD response remained linear as a function of dose rate and exhibited no anomalies. Without changing high voltage applied to the PMTs, we observed instantaneous PMT anode currents of typically 70 μA when we exposed the GSD with a $10 \times 10 \text{ cm}^2$ aperture. At the latter level, two of the six PMTs showed clear signs of gain saturation and abnormal time-dependence of their signal ratios to the other PMTs. The affected gains seemed to recover

when there was a gap between successive beam pulses of 6 ms or more, but not when the gap was the more normal 2 ms.

In subsequent bench tests illuminating several of the GSD PMTs with a pulsed blue LED mocking up the beam time structure at the S. Lee Kling Center (few μ s wide pulses at 500 Hz), we explored the PMT behavior at high input light intensity systematically, by varying the LED amplitude in small steps. We found that such PMT non-linearity typically sets in, with significant output pulse shape distortion, at anode currents around 40 μ A. Such anode currents are still well within the range where the ET9107QB PMTs should be stable against space charge limitations near the end of the dynode chain. However, the photocathode current density exceeded the 7.5 nA/cm² limit beyond which alkali cathodes, such as that in the ET9107QB (Adit 2016), have been observed to experience radial voltage drops associated with photocathode bleaching (Knappe *et al.* 2012). This performance limit indicates that PMTs with different photocathode materials may be better suited for use with the highest envisioned instantaneous beam currents. In addition, PMT voltages should be adjusted in clinical uses to avoid reaching excessive anode currents, which are not needed to attain excellent signal-to-background ratios when the instantaneous dose rate is high.

3.3 Dependence of GSD dose measurements on beam energy and gas contamination

It is also important to understand how the GSD dose measurement normalization depends on beam energy and on possible impurities in the xenon gas. These aspects were tested during pencil beam scan runs at the Chicago Proton Center. Figure 13 plots the extracted GSD dose normalization factor for three beam scans carried out, in succession, at 98, 150 and 225 MeV. The normalization factor against an air ionization chamber is seen to decrease by about 7% for a 100 MeV reduction in beam energy, with roughly one-third of the reduction resulting from the known difference between xenon and air in the energy dependence of proton stopping power. The remainder of the effect might arise from energy dependence in the number of scintillation photons produced per keV of energy deposit in xenon (e.g., see Table 1 in Serra *et al* 2014), but there are no precise measurements in the literature of xenon scintillation yield vs. incident energy. Data for the number of ion pairs produced per MeV deposited in air are more precise (Jones *et al* 2007), but still cannot rule out a few percent change with incident proton energy.

The effects of xenon impurities were studied by introducing controlled leaks of dry air into the otherwise sealed GSD chamber. The contaminant level was gauged at each step of this process by measuring the GSD pressure increase in comparison with the initial xenon base pressure. One or two 169-spot pencil beam scans were carried out with 225 MeV proton beam at each step of this process, with results presented in Fig. 14. Frame (a) reveals that the detected GSD light yield decreases essentially following a Gaussian curve as the contaminant level increases, reaching a factor of 2 reduction for 1.5% contaminant. Frame (b) reveals that the position sensitivity of the PMT asymmetry measurement correspondingly *increases* quadratically with increasing contaminant fraction. The latter effect and at least part of the light yield reduction can be understood to arise from VUV light attenuation in the oxygen component of the contaminant dry air.

When there is appreciable attenuation of the scintillation photons in the chamber gas, the differential attenuation from an off-center site on paths toward opposite PMTs reinforces the geometric solid angle difference. In particular, if the attenuation length ℓ_{att} is long in comparison to the beam displacement x from the center, then Eq. (1) is modified to:

$$a_x \cong \frac{A(R-x)^{-2} \exp[-(R-x)/\ell_{att}] - A(R+x)^{-2} \exp[-(R+x)/\ell_{att}]}{A(R-x)^{-2} \exp[-(R-x)/\ell_{att}] + A(R+x)^{-2} \exp[-(R+x)/\ell_{att}]} \xrightarrow{x \ll R, x \ll \ell_{att}} x \left[\frac{2}{R} + \frac{1}{\ell_{att}} \right]. \quad (4)$$

The attenuation length for 170 nm photons in pure O₂ gas at room temperature and atmospheric pressure is ~ 1 mm (Watanabe *et al* 1953), so even a fraction of a percent O₂ contamination is capable of causing a significant increase in the position sensitivity and decrease in the collected light yield.

Using the approximation of Eq. (4) and noting that $2/R = 1.12\%/mm$, the results in Fig. 14(b) suggest that the average attenuation length for xenon scintillation photons decreases from more than 5 m in the absence of contaminant to about 50 cm by the time the contaminant fraction has grown to 2.7%. The loss of light yield in frame (a), however, is considerably greater than could be accounted for solely by an attenuation length of 50 cm. The results thus suggest an additional significant suppression of xenon VUV scintillation by the contaminant air, *e.g.*, by enhancing collisional de-excitation of the dimer once it is formed. The source of the apparent *quadratic* dependence of attenuation length and of scintillation suppression on contaminant pressure, suggested by the results in Fig. 14, is not yet understood.

The bottom line is that it should be straightforward for a sealed chamber with xenon at atmospheric pressure to keep contaminant levels well below 0.5%, where their effects on GSD performance appear negligible.

4. Discussion

A January 2013 international Workshop on Ion Beam Therapy, co-sponsored by the U.S. Department of Energy, the National Institutes of Health and the National Cancer Institute, assessed the desirable technical goals and needed R&D for accelerator, beam delivery and dosimetry performance at future clinics. The summary report from that workshop (Pistenmaa *et al* 2013) states the following, among numerous other requirements: “A spot size less than 5 mm FWHM at isocenter should be achievable for all ion species at all energies. ... Position accuracy pulse-to-pulse should be within ± 0.2 mm and should be monitored during beam delivery.”

The challenging goal of achieving this desired position precision on a pulse-by-pulse basis in an in-beam dosimeter with fast readout electronics (as opposed, say, to CCD readout), and at reasonable cost, has been one of the driving motivations in the developments reported in

this paper. The results presented in Sec. 3 indicate that the GSD is capable of meeting this goal, with a very modest number of electronic readout channels, when the GSD is located at the treatment isocenter. In clinical practice, the GSD would be mounted in a beam gantry nozzle at about half the distance from the final steering magnets to the isocenter. The 2D position resolution then required to monitor beam position at the isocenter to ± 0.2 mm depends on the beam delivery optics. For example, the recently installed rapid-scanning gantry 2 at the Paul Scherrer Institute in Villigen, Switzerland features point-to-parallel beam transport through the nozzle (Pedroni 2012), for which a 0.2 mm displacement of the beam at the isocenter corresponds to a 0.2 mm displacement at the nozzle dosimeters. For alternative beam transport designs, the GSD resolution of ± 0.2 mm might provide ± 0.4 mm precision at the isocenter.

Most regulatory agencies require that ion beam therapy clinics utilize two independent devices for real-time dose monitoring. Since air ionization chambers are the current industry standard, the GSD would most likely serve as a secondary dosimeter, complementing the ionization chamber with greatly improved position resolution, more linear response at high dose rates, and quite different sensitivities to changes in beam characteristics or environmental conditions. Such a two-dosimeter setup would facilitate *in situ* calibrations of the GSD dose measurement against the ion chamber as a function of beam energy and time.

The experience to date suggests a number of technical improvements over the tested prototype GSD that would benefit any clinical adoption:

- The use of much thinner (~ 100 μm) blackened foil entry and exit windows to reduce beam energy straggling and multiple scattering along the path to the patient. This requires adding removable cover plates to form entry and exit vestibules that can be evacuated and filled simultaneously with the chamber volume, in order to maintain safe pressure differences across the large-area thin windows. Once the detector is filled with gas, a small plastic balloon system attached within the gas line external to the GSD could be used to match any change in atmospheric pressure without introducing bowing of the thin windows.
- The addition of one or two optical ports around the GSD periphery to accommodate external pulsed UV or VUV light sources for bench-testing and calibration of the GSD.
- Modifications to the geometry of the GSD-photodetector assembly as needed to allow its mounting within the exit nozzle region of specific pencil beam delivery gantries, and to accommodate the actual beam optics associated with specific gantries.
- Use of alternative photodetectors, possibly other PMT models or more compact large-area avalanche photodiodes (LAAPDs), designed to handle higher incident VUV light intensities without gain reductions. The physical compactness of LAAPDs may also be useful in fitting the GSD in confined spaces without sacrificing dose measurement uniformity.

- Improved readout software to provide real-time 3-D display of the dose buildup vs. time and position during a pencil beam treatment, and readout electronics to facilitate rapid feedback signals to the beam control system.

5. Conclusions

The prototype test results reported here demonstrate that a xenon-filled Gas Scintillation Detector is uniquely well suited for real-time monitoring and archiving of dose delivered spot-by-spot (or pulse-by-pulse) in pencil beam scans carried out at proton therapy clinics utilizing continuous or pulsed-beam accelerators. The GSD can measure delivered dose to a relative precision better than 1% as a function of time (down to increments as short as 20 μ s) and of 2-D position (with spatial resolution $\sim$ 200 μ m) at which the dose is delivered. Furthermore, the GSD response appears to vary linearly within 1% with delivered dose over the entire range of dose rates studied to date. The rapid GSD response provides the potential for real-time feedback to catch treatment delivery problems and correct the subsequent dose delivery during a beam scan. The small number of readout electronics channels keeps the GSD cost-effective.

While the prototype tests demonstrate the potential of this technology to address clinical needs, considerable further operating experience in clinical environments, especially for treatments that combine pencil beam scans with short beam pulses, will be needed to assess the long-term reproducibility of GSD performance.

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Figure 1.
The prototype Gas Scintillation Detector mounted at the pencil beam delivery gantry isocenter at the Northwestern Medicine Chicago Proton Center.

Figure 2.

The integrated PMT charges recorded for the 6 GSD photomultipliers during a portion of a 150 MeV pencil beam scan at the Chicago Proton Center, encompassing vertical scan lines at horizontal locations of +2, +1 and 0 cm. Each vertical scan line irradiates spots from +6 to -6 cm in 1 cm steps. For this scan, the integrals were recorded every 0.25 ms and the ADC was reset every 10.0 ms. The three frames show results for pairs of diametrically opposite photomultipliers, illustrating the rapid change in their ratios as the beam moves from spot to spot.

Figure 3.

Anode currents for each integration subsample for two of the GSD PMTs during one small portion of a run at the S. Lee Kling Proton Therapy Center, taken with a nominal time-averaged dose rate of 256 MU/minute and a $4 \times 4 \text{ cm}^2$ aperture. Each current measurement is deduced from the difference between two successive ADC charge readouts, divided by the time interval separating them: either the 22 μs width of the subsample period or, for the positive spikes reflecting ADC resets, 75 μs including the 53 μs ADC resetting and stabilization interval. The negative spikes reflect beam arrival during the 4th of each set of 8 subsamples. The “missing” beam pulses near the left edge of the plot correspond to undesired positions on the rotating modulator wheel for the beam configuration used. Such empty pulses were used to measure small DC offset background currents that have been subtracted from the results in the figure. The horizontal axis represents integrator on time, ignoring the 1.77 ms off period between successive beam pulses. The plot spans 54 ms in real time.

Figure 4.

Drawing of the pre-prototype GSD exposed to pulsed pencil proton beams at the Indiana University Cyclotron, showing: the 9.5 cm thick xenon gas volume (1); the 38 μm thick stainless steel entry and exit windows (2); the vacuum-tight stainless steel housing (3); the fused silica optical windows (4); and the ET9107QB PMTs (5).

Figure 5.

The output currents Q/t for left and right GSD PMTs, extracted from the finite charge and time differences between adjacent subsamples in Fig. 2 and displayed as a function of time during a portion of the 150 MeV beam scan. One can clearly see the 13 spots in the vertical scan executed at $x = +1$ cm, and the beam current buildup during the 2 milliseconds of each spot irradiation. The sharpness of the trailing edge for each spot manifests the promptness of the collected scintillation light. The regular positive spikes correspond to ADC resets ($Q > 0$) in the integrating electronics, one of which is labeled in the charge recording of Fig. 2.

Figure 6.

(a) Vertical vs. horizontal PMT asymmetries (Eq. (2)) for a typical 169-spot pencil beam scan at the Chicago Proton Center. (b) Linearized vertical vs. horizontal PMT asymmetries extracted for the scan of frame (a) by a polynomial combination of a'_y and a_x (Eq. (3)).

Figure 7.

Plots of the (a) horizontal and (b) vertical pencil beam scan target coordinates vs. the corresponding measured, linearized PMT asymmetry for a typical scan. All 169 spots are included in each frame, but the 13 spots at the same target x or y value strongly overlap in linearized asymmetry values. The solid curves are best cubic fits to the data in each case, as described by the inset equations.

Figure 8.

Frequency distributions of deviations between (a) horizontal and (b) vertical beam centroid positions reconstructed from the measured PMT asymmetries and targeted beam coordinates in 225-MeV pencil beam scans. The asymmetries have been averaged over three distinct, but nominally identical, scans to reduce contributions from beam targeting fluctuations. The rms deviations over more than 140 degrees of freedom (scan points minus adjustable fit parameters) in each frame reflect an intrinsic GSD spatial resolution $\sigma \approx 0.2$ mm.

Figure 9.

Dependence of the weighted sum Y of PMT charges from the GSD on beam centroid position. (a) The ratio to ionization chamber charge Y/Q_{IC} plotted vs. horizontal and vertical position for the 169 spots in a 225-MeV pencil beam scan. Within the vertical scale range from 10 to 20, each unit interval is represented by a different shade of the plotted points. (b) The ratio of weighted average individual PMT charge ($Y/\Sigma c_i$) to average ion chamber charge, plotted vs. the side length of the square over which the beam scan data were averaged. The results are furthermore averaged over 225-MeV scans executed over a wide range of dose rates. The dashed blue curve illustrates the quadratic dependence of the GSD dose normalization on the beam scan dimensions.

Figure 10.

The frequency distribution of percentage deviations between spot-by-spot dose measurements reconstructed from the summed PMT yields and from the Chicago Proton Center primary air ionization chamber (IC), for a 225-MeV pencil beam scan. The rms deviations seen for many scans carried out under a variety of conditions range from 0.7% to 1.0%, and incorporate both GSD and IC dose measurement fluctuations.

Figure 11.

(a) The GSD dose normalization factors relating weighted mean PMT charge to ion chamber charge as a function of instantaneous dose rate for a variety of pencil beam scans carried out with 225 MeV continuous proton beam cyclotron output currents ranging from 20 to 300 nA at the Chicago Proton Center. The measurements are plotted with $\pm 0.5\%$ error bars reflecting their rms deviation about their mean value. The dashed line represents the average of the points below 300 MU/second. (b) The mean ion chamber currents used to measure dose rate in (a) plotted against the beam current out of the cyclotron for these runs, and compared to a linear extrapolation from the lower dose rates.

Figure 12.

Linearity tests of (a) an air ionization chamber and (b) a pre-prototype xenon gas scintillator detector, both utilizing 1% duty factor pulsed pencil proton beams over a wide range of beam currents, carried out at the Indiana University Cyclotron facility. The time-averaged beam current is indicated on the lower horizontal axis and the instantaneous current during beam pulses on the upper axis in both frames. Recombination-induced saturation of the ion chamber response in (a) sets in above 130 nA instantaneous current, while the xenon scintillation detector exhibits linear performance up to the highest beam currents studied, for two different values of the high voltage applied to the PMTs.

Figure 13.

The GSD dose normalization factor against the IBA air ionization chamber extracted from pencil beam scans at three different proton energies at the Chicago Proton Center, before (solid curve) and after (dashed curve) correction for the known difference between xenon and air in the energy dependence of the proton stopping power.

Figure 14.

Effects of dry air contaminant addition to the xenon on GSD (a) dose normalization and (b) horizontal position sensitivity. Frame (a) plots the ratio Y/Q_{IC} of weighted sum PMT charge to ion chamber charge, while (b) plots the slope near the center of the scan of linearized PMT asymmetry a_x^{lin} vs. beam spot target horizontal position x . In each frame, the results are plotted vs. the percentage partial pressure of the added air. The curves represent (a) Gaussian and (b) quadratic fits to the data.

Table 1

Conditions for GSD tests

Detector tested	Test Site	Nature of source	Beam energy (MeV)	Beam Duty Factor	Beam spot area (cm ²)	Instantaneous dose rates or beam currents	Performance details tested
Prototype (Fig. 1)	Chicago Proton Center	Clinical continuous pencil proton beams	98–225	≈100%	~0.2–0.8	25–400 MU/s	Spatial resolution; dose measurement precision & dependence on energy and gas contamination; linearity with dose rate
Prototype (Fig. 1)	S. Lee Kling Proton Therapy Center	Clinical pulsed, double-scattered proton beams	216–226	≈0.15%	16–100	360–2500 MU/s	Short current integration periods; promptness of signal; PMT performance at high light yield
Pre-prototype (Fig. 4)	Indiana University Cyclotron	R&D pulsed pencil proton beam	205	≈1.0%	~1.0	10–220 nA	Linearity of signal output with instantaneous beam flux
Prototype (Fig. 1)	Phenix Medical head-quarters	Pulsed blue LED	N/A	≈0.2%	N/A	N/A	PMT linearity at high instantaneous photocathode currents