Development and characterization of optical readout well-type glass gas electron multiplier for dose imaging in clinical carbon beams

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ABSTRACT

The use of carbon ion beams in cancer therapy (also known as hadron therapy) is steadily growing worldwide; therefore, the demand for more efficient dosimetry systems is also increasing because daily quality assurance (QA) measurements of hadron radiotherapy is one of the most complex and time consuming tasks. The aim of this study is to develop a two-dimensional dosimetry system that offers high spatial resolution, a large field of view, quick data response, and a linear dose–response relationship.

We demonstrate the dose imaging performance of a novel digital dose imager using carbon ion beams for hadron therapy. The dose imager is based on a newly-developed gaseous detector, a well-type glass gas electron multiplier. The imager is successfully operated in a hadron therapy facility with clinical intensity beams for radiotherapy. It features a high spatial resolution of less than 1 mm and an almost linear dose–response relationship with no saturation and very low linear-energy-transfer dependence. Experimental results show that the dose imager has the potential to improve dosimetry accuracy for daily QA.

1. Introduction

Radiotherapy using carbon beams is an effective treatment for various cancer types. There has been continuous increase in the demand for carbon-ion beam treatment worldwide [1]. Generally, radiotherapy systems based on accelerators consist of a number of complex equipment that are fully used for treatments. To provide high quality treatment, all the equipment used for radiotherapy must be stable and accurate. Therefore, there is a strong emphasis on quality assurance (QA), to provide effective treatment and prevent accidental irradiation. To guarantee treatment quality, the American Association of Physicist in Medicine (AAPM) have reported on the necessity of QA for all devices [2]. The report includes descriptions of QA items and evaluation methods, as well the frequency of conducting QAs. In other words, daily QA measurements are necessary for every hadron radiotherapy treatment [3,4]. Ionization chambers (ICs) are primarily used for the QA measurements owing to their accurate linear dose–response relationship. However, conventional ICs are not position-sensitive, and two-dimensional (2D) measurements for QA require point-by-point scanning, which is a limitation in terms of throughput. Moreover, array-type ionization chambers have recently been used [5], which cover a large field of view and are position sensitive; these characteristics overcome the challenges posed by conventional ICs. However, their position resolution is only approximately 5 mm, and a higher spatial resolution is necessary for complex treatment plan measurements.

Various solid-state detectors have been developed for this purpose,
such as solid scintillator detectors [6–8], thermoluminescence dosimeters [9], radiochromic films [10], and semiconductor detectors. However, there is room for further improvement in the linearity of these detectors’ responses owing to their linear energy transfer (LET) dependence caused by the quenching effect; i.e., they lose linearity in a high-LET region, such as the Bragg peak in a hadron beam.

As mentioned above, an IC (the most fundamental gaseous detector) is known to have a good linear dose–response relationship for hadron beams, and a very low LET-dependence. Moreover, one of its most attractive features for practical use is its radiation-hardness against heavy ion beams [11]. These features are also expected to be present in gaseous detectors such as gas electron multipliers (GEMs) [12,13]. Furthermore, in GEM devices, gas scintillation has good proportionality with primary ionization, and the 2-D distributions of gas scintillation can be easily obtained using optical readout [14]. The linearity of gaseous detectors can be further improved for high LET ion beams such as a carbon beam [15–18]. However, a slight quenching effect was observed at the Bragg peak region in these studies. This is because conventional GEMs require cascading to achieve sufficient gas gain. Therefore, the gaps between these GEMs cause primary scintillation, which is not negligible for carbon beam dosimetry, and the detector loses its linearity owing to the ionization that occurs outside of the region of interest (ROI). In addition, while high-resolution 2D dose imaging can be performed using a micro-pattern gas detector (MPGD), such as a GEM, its use is limited to experimental situations (reduced beam intensity) owing to charging up effects and the risk of discharges in the MPGD.

In this study, we focused on minimizing the factors that degrade peak-to-plateau ratio in high LET carbon beam measurement, and developed a robust 2D digital dose-imager for the treatment QA of hadron therapy using a glass GEM. The dose imaging system is based on our previous work: an X-ray imager developed by combining a glass GEM, dark box, mirror, optical lens, and cooled charged-coupled device (CCD) camera [19,20]. We have made a fundamental improvement to the detector design for hadron therapy application, focusing on improving the linearity of the response to the high-LET carbon beam. The dose imaging system was tested and characterized in a hadron therapy facility (Heavy Ion Medical Accelerator in Chiba, HIMAC) [21] with clinical intensity, demonstrating its performance.

2. Methods

2.1. Detector design

The detector consists of a gas-filled chamber and an optical camera mounted in a dark box (Fig. 1a). The chamber containing the glass GEM (Radiment Lab, Inc., Japan) is filled with scintillation gas (Ar/CF₄ (90:10)). The glass GEM is fabricated on a 600 μm thick glass with a 190 μm diameter hole, placed in a 280 μm pitch. Copper electrodes are formed on both sides of the glass substrate. There are more than 100,000 holes in the glass GEM, and each hole works as a gas scintillation proportional counter. In our previous study, we acquired high-resolution X-ray, neutron, and proton images based on this gas scintillation technique [19,20]. However, these developments were primarily focused on high-resolution imaging, and not on dose imaging. Therefore, the detector for dose distribution measurements may be improved. In this study, we made a fundamental improvement to the detector design for hadron therapy use, mainly focusing on improving the linearity of the measurement response of high-LET ion beams. Fig. 1b shows a diagrammatic sketch of the cross-section view of the well-type glass GEM detector with optical readout. The specifications of the conventional imager and the improved optical readout glass GEM detector are listed in Table 1, and the details of the modifications are explained in Fig. 2. Because the induction gap causes an additional unwanted gas scintillation outside of the ROI in conventional GEM geometry (Fig. 2, left), the improved detector has a single glass GEM mounted directly on top of the anode electrode forming a well-type detector [22], which lacks an induction gap to achieve the required linearity (Fig. 2 right). The hadron beam entrance is formed with a Cu-coated 2 mm thick glass epoxy board, which is implemented as the cathode. Compared with thin-film cathodes, this cathode provides a flatter surface and achieves a more uniform response. Particles interact at the 1.5 mm thick drift gap, which is the ROI for the measurement. The gas-filled chamber is attached to a dark box containing a mirror and an optical camera. Hadron beams enter through the entrance window of the chamber and ionize the gas. When the hadron beam enters the detector and ionizes the gas molecules in the ROI, the electrons drift to the glass GEM and are multiplied by a strong electric field in the holes. This process is called an electron avalanche, and during this avalanche process, gas scintillation is caused by the de-excitation of Ar/CF₄ molecules. The dose distribution can be easily detected by observing this gas scintillation distribution from the bottom of the chamber through a transparent window. The mirror in the dark box prevents the camera from being irradiated with hadron beams. Unlike our X-ray imager, a silver-coated metal mirror is used instead of a conventional glass mirror to minimize Cerenkov light emission caused by delta-rays (which increases noise and degrades linearity) [23]. For the same reason, transparent indium-tin oxide (ITO)-coated film is used as the anode electrode instead of ITO-coated glass.

2.2. Experimental setup

We tested our glass-GEM-based dose imaging detector using clinical intensity carbon beams, and its dose-imaging performances are tested. The dose image was acquired using a ±3% uniform 150 mm± (±1% uniformity for 100 mm±) 290 MeV/u carbon beam derived at the biology beamline in HIMAC [24]. The beam intensity was the same as that used in radiotherapy (2 × 10¹⁰ (particles / second)), and the image was obtained over a 30 s exposure time. The detector, represented in Fig. 3, comprised a 280 × 280 × 30 mm³ gas chamber that was continuously flushed (50 mL/min) with an Ar/CF₄ 90/10 vol% gas mixture at 1 atm for 10 h. Inside the chamber, a single glass GEM was mounted directly on top of the anode electrode forming the well-type detector. The first measurements of the Well-type glass GEM were performed with the drift field voltage, and the voltage applied to the glass GEM was set to 500 and 1120 V. The voltage applied for the second measurements were 400 and 1150 V for the drift field and glass GEM, respectively. These conditions guaranteed stable detector operation for the clinical beam intensity. The spatial response of the GEM detector was investigated by placing a patient collimator in front of the detector. The spatial resolution of the glass GEM detector was estimated from the image profiles at the edge of the collimator.

For the dose imaging capability study, a mono-peak beam and spread out Bragg peak (SOBP) beam with a modulation extent of 60 mm in depth were used. Depth-dose profiles were measured with both the
conventional and improved glass GEM detectors, and the results were compared with measurements acquired using a reference IC (PTW 34045, Advanced Markus Electron Chamber, Germany). Calibrated Polymethyl methacrylate (PMMA) slabs were used as a beam range shifter to perform water equivalent depth-profile measurements; the schematic of their geometry is shown in Fig. 3.

### 2.3. Data acquisition and analysis

Dose images were acquired using a cooled CCD camera (Bitran BUS2LN, Japan). To consider the camera offset, a dark background image was obtained without the beam, using the same exposure time as in the beam measurements; it was then subtracted from the images obtained using the beam. The images were processed offline to correct for the background and remove extremely hot pixels using the function called “remove outliers (Parameters: Radius = 2.0, Threshold = 50)” provided by open-source software (ImageJ, National Institutes of Health, Bethesda MD, USA). Then, the images were analyzed using the ImageJ software to determine the light yield by averaging the pixel values over a glass GEM effective area for all measurements. For the measurement of a depth–dose profile, data (averaged pixel values) were obtained to increase the water-equivalent PMMA thicknesses up to 170 mm, starting without a range shifter (0 mm). Here, the peak-to-plateau ratio is

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**Table 1**

Specifications of the conventional glass GEM-based X-ray imager and well-type glass GEM for dose imaging.

<table>
<thead>
<tr>
<th>Component</th>
<th>Previous study [20]</th>
<th>This study</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray imager</td>
<td></td>
<td>Dose imager</td>
</tr>
<tr>
<td>Gas Multiplier</td>
<td>100 × 100 mm glass GEM with 2 mm induction gap</td>
<td>100 × 100 mm well-type glass GEM</td>
</tr>
<tr>
<td>Gas</td>
<td>Ar/CF₄ (90:10)</td>
<td>Ar/CF₄ (90:10)</td>
</tr>
<tr>
<td>Anode</td>
<td>ITO coated glass</td>
<td>ITO coated film</td>
</tr>
<tr>
<td>Cathode</td>
<td>Al-coated 25 μm thick polyimide foil</td>
<td>2 mm thick glass epoxy board, 50 μm thick Cu-coated</td>
</tr>
<tr>
<td>Camera</td>
<td>Hamamatsu ORCA-Flash 4.0 16 bit</td>
<td>Bitran BUS2LN (16 bit 4 M pixels)</td>
</tr>
<tr>
<td>Lens</td>
<td>Nikon NIKKOR 85 mm F1.4</td>
<td>Nikon NIKKOR 50 mm f/1.2</td>
</tr>
<tr>
<td>Mirror</td>
<td>Glass mirror</td>
<td>Silver coated metal mirror (ALMECO V96-100)</td>
</tr>
</tbody>
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**Fig. 1b.** Schematic of the well-type glass GEM detector with optical readout.

**Fig. 2.** Schematic diagram of the optical readout glass GEM detector. (Left) Conventional scintillating glass GEM detector. Scintillation caused in areas other than the ROI became a limitation for the dose imaging application. (a) Primary gas scintillation caused in the gas volume filled in the induction gap. (b) Cerenkov light generated in the optical glass window. (c) Cerenkov light generated in the glass mirror. (Right) Improved design for hadron therapy use. The induction gap is removed to avoid primary scintillation by the well-type glass GEM. Second, a glass optical window is replaced with conductive film directly attached to the glass GEM, which is implemented as an anode and optical window. Third, the conventional glass mirror is replaced by a steel mirror, which emits no Cerenkov light.
defined as the ratio of the value measured at the Bragg peak depth to that measured at a depth of 0 mm, i.e., the plateau of the depth-dose profile.

3. Experimental results

3.1. Imaging

The results of hadron beam imaging using a glass GEM detector are shown in Fig. 4. This demonstrates the carbon ion beam imaging performance of the dose imager without a range shifter. Fig. 4a is a photograph of a patient collimator that was actually used in previous treatment, and the image obtained using this collimator is shown in Fig. 4b. The spatial resolution of the detector was quantitatively evaluated using the edge profile of the collimated image. The image of the 100 × 100 mm sensitive area of the glass GEM detector consists of 1038 × 1038 pixels, i.e., each pixel has a size of 0.072 × 0.072 mm. The edge profiles were analyzed using the same error function method used in [20], resulting in a σ of 5.5 pixels. Therefore, the spatial resolution can be calculated as 0.39 mm (σ), which is equivalent to a full width at half maximum (FWHM) of 0.93 mm, thereby achieving the targeted sub-millimeter spatial resolution lateral direction. (Fig. 4c).

3.2. Dose measurement

A linear dose–response relationship is another requirement for dose imaging detectors. Depth-dose distributions were measured using a PMMA phantom (range shifter) of variable thickness. One of the most important components required to achieve a linear response over the entire dynamic range is to switch off the anti-blooming function of the camera [25]. Sixteen-bit.tif images were analyzed using ImageJ, and the average pixel value of the images at each depth was converted to depth–dose profiles. Figs. 5a, b, and 6 display the depth-dose profiles measured using the glass GEM detectors and the reference IC, respectively.

For the mono-peak measurements (Fig. 5a and 5b), the output (image brightness) in the plateau region (water equivalent depth = 0) was plotted as 1.0, and the relative output at each depth was then plotted. Fig. 5a shows the entire depth profile (Bragg curve), and Fig. 5b shows a detailed view near the Bragg peak. By analyzing these measurements, the peak-to-plateau ratios were 4.48, 4.50, and 4.51 for the measurements with the IC and measurements 1 and 2 with the improved design glass GEM, respectively. As explained in the previous section, the detector has been modified to eliminate Cherenkov light contamination, which significantly improves the accuracy of the measurements and the peak-to-plateau ratio compared with the conventional design (peak-to-plateau ratio 2.78). Fig. 6 shows the depth–dose profiles obtained using a 60 mm SOBP beam; the values were normalized with the value at the same depth (117 mm).

4. Discussion

The optical readout gas detector has been previously investigated for the dose imaging of heavy ions. In this detector, the carbon-ion beam does not directly cause the photo emission of the gas. Instead, energy is transferred to the gas medium through the ionization of the gas, as in an IC. Therefore, it does not provide the quenching effect that is found in other solid scintillation detectors. Since there is a linear correspondence between the ionization and scintillation yield of the glass GEM, the dose distribution can be easily and quickly obtained through an image focusing on the surface of the well-type glass GEM using an optical camera. Additionally, the detector can be operated at clinical beam intensities without charging up effects in the GEM holes owing to the relatively low volume resistance of the insulating material [26]. This study is the first to measure a Bragg peak of a carbon beam peak-to-plateau ratio of more than 4 has been measured so sharply, with a spatial resolution of less than 1 mm. Owing to the single well-type GEM structure developed in this study, there is an absence of contamination in the induction gap and of Cherenkov emissions from the glass material. On the other hand, the primary scintillation in drift space can be counted as a signal coming from the ROI, and it will not degrade the measurement. Additionally, the glass substrate used in the glass GEM may cause Cherenkov light; however, because the glass GEM is sandwiched with copper electrodes (which is not transparent), and the holes are cylindrical, it can be considered that the Cherenkov light that reaches the camera is negligible and will not degrade the measurement. However,
Fig. 4. a) Photograph of a 30 mm thick brass collimator made for an actual hadron therapy treatment. b) Dose distribution image obtained with optical readout well-type glass GEM detector, which has a $100 \times 100$ mm effective area. The image was acquired within 30 s of integrating with a clinical intensity ($290$ MeV/u) carbon beam transmitted through a patient treatment collimator. c) Fitted result of an edge using the error function method.
the observed difference in the response of the fragmentation region (greater than 150 mm depth) should be investigated in the future. In Fig. 5, it can be observed that the glass GEM detector provides an underestimated response compared with the IC. Additionally, as shown in Fig. 6, the SOBP measurement exhibited non-negligible differences in the entrance region (depth 0 to 80 mm) from the IC. We assume that the disagreement is due to the difference in the stopping power of the fragmentation particles between air and Ar/CF$_4$. Therefore, the response of well-type glass GEM is relatively low compared with IC in the depth range of 90 to 140 mm, where the percentage of fragmentation particle increases. Future work will focus on improving the response of the fragmentation region and the SOBP by mixing Ar/CF$_4$ with a lighter gas to achieve an electron density close to that of air.

5. Conclusion

This work presents the design and first evaluation of a low LET-dependence dose imager based on optical readout from a well-type glass GEM for hadron therapy. We identified that the linearity degradation observed in GEMs was caused by the induction gap for GEMs and Cherenkov light from glass materials. These factors were carefully minimized, and the shape of the Bragg peak at 290 MeV/u was essentially identical to that of the peak measured with an IC. Our dose imager was successfully operated using a clinical intensity carbon beam, and the peak-plateau ratio increased to 4.50–4.51 at depth-dose profiles of the monopeak. Our dose imager exhibited excellent agreement with the reference IC, with a less than 1% difference in the peak-to-plateau ratio. Moreover, it provides higher spatial resolution than the conventional ICs, and enables the visualization of the dose distribution with submillimeter resolution (FWHM) in lateral direction. Thus, the dose imager showed a significant possibility in improving dosimetry accuracy for daily QA. Finally, because it is not appropriate to bring gas cylinders to the treatment site, a sealed gas operation is strongly required. However, in this study, the outgassing from the organic material used inside the gas chamber prevented the sealed operation of the detector. Realizing sealed operation by removing outgassing materials from the chamber and taking advantage of the use the glass GEM, which is entirely an inorganic material, remains for future work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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