3D dosimetry for proton therapy

S Beddar
Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA
E-mail: abeddar@mdanderson.org

Abstract
We have been developing novel 3-dimensional (3D) detector systems using organic plastic and liquid scintillators to measure and image the dose distribution from proton therapy beams in near-real time. Proof-of-concept and initial feasibility studies using a single charge-coupled device camera have already been conducted. Our recent studies focused on the characterization of scanning proton beams used for patient treatments using a 3D liquid scintillator-based detector system with a set of scientific-complementary metal-oxide-semiconductor (sCMOS) cameras. The basic concept consists of using a large volume of a solid or liquid scintillator to measure or image the dose distributions from proton beams in 3D. We recently developed a large liquid scintillator-based detector system consisting of a \(20 \times 20 \times 20\)-cm transparent acrylic tank filled with a water-equivalent, commercially available liquid scintillator that generates scintillation light when irradiated with protons. To track rapid spatial and dose variations in spot-scanned proton beams, we used 3 high-speed sCMOS cameras to image the scintillation light signals from 3 orthogonal projections in cine mode. Furthermore, we developed a new image acquisition approach that synchronized camera imaging times with dynamic pencil-beam deliveries to efficiently capture the dose and therefore enable accurate dosimetric calculations. This system was fully developed and characterized at the Proton Therapy Center at The University of Texas MD Anderson Cancer Center. We show that such systems can provide fast and accurate measurements of the range, lateral profile, and lateral position of scanning proton beams with excellent spatial resolution (0.21 mm). We also demonstrate that such detectors can rapidly measure proton beam characteristics and intensities at multiple energies, which makes them an ideal tool for scanned proton-beam systems, beam quality assurance studies, and verification of patient treatment delivery.

1. Introduction
While photons continue to be used for radiation therapy, the use of proton therapy has grown over the last few years. The steep dose gradient at the distal edge of the proton Bragg peak can be used to create treatment plans that accurately target tumors while minimizing dose exposure of healthy tissues. Spot-scanned or pencil-beam proton therapy is particularly attractive for delivering complex treatment plans because of its ability to precisely contour the tumor in 3 dimensions (3D) while avoiding critical organs and reducing the harmful neutron background [1]. Significant technological advances in proton beam delivery systems, however, have outpaced the development of clinical dosimeters, which play a vital role in safety and quality control for proton therapy. Ionization chambers are the prevailing gold-standard dosimeters. They are routinely used for quality assurance measurements of machines and treatment plans. However, ionization chambers provide single-point measurements that are time consuming, suffer from volume averaging effects, and are therefore poorly suited for mapping complex treatment plans. These problems can be partially overcome by using 2D configurations of ionization...
chambers, which have been used for mapping large-field dose variations and symmetry [2]. As alternatives to ionization chambers, Fricke and polymer gels have been studied for 3D chemical dosimetry [3], and commercially available 3D radiochromic gels have also been used for commissioning studies of small-field systems [4]. These dose-integrating dosimeters require long preparation times and are not reusable; therefore, they are not ideal for dynamic imaging applications, such as those of scanned proton-beam systems.

Organic scintillators, because of their water equivalency and energy independence, have been shown to be a good fit for precision dosimetry applications [5]. Early work with volumetric organic scintillators for 3D dosimetry highlighted several promising features, including high spatial resolution, good temporal resolution, and flexibility for applications involving photons, protons, and other heavy-ion particles [6,7]. These works focused on the development of a large-volume liquid scintillator (LS) coupled to optical cameras for 2D dosimetry of photons [8] and proton beams [6,7,9]. Organic scintillators, however, exhibit reduced light output at the Bragg peak due to their high ionization density. This phenomenon is called ionization quenching and is quantified as linear energy transfer for charged particles. We previously developed an ionization quenching correction for organic scintillators using the Birks equation [10]. In this work, we describe the design and development of a 3D detection system based upon an LS detector. We describe the detector design and evaluate its performance for proton-beam therapy.

2. Materials and methods

2.1. LS detector design

The 3D detector consisted of a LS-filled tank (20 × 20 × 20 cm) constructed of acrylic. The transparent tank surfaces facing the cameras allowed the scintillation signal to be captured by cameras, while the opaque surfaces minimized the influence of ambient light on measurements. Optiphase HiSafe3 (PerkinElmer, Waltham, MA) was the choice of LS (0.986 g/cm³) and doubled as a phantom and an active element for measuring the radiation field without perturbation. The reference coordinate system was oriented as shown in figure 1.a. As illustrated in the figure, camera $X$ was positioned such that it pointed directly into the front surface of the tank perpendicular to the proton beam direction (the $z$-axis). Two mirrors located on the top and one side of the tank redirected the scintillation light to cameras $Y$ and $Z$, respectively, for generating additional beam perspectives (Figures 1.a and 1.b). Cross-hair markers imprinted on the tank surfaces allowed geometric calibrations to correct for optical artifacts such as light refraction, lens perspective, lens distortion, and rotational/translational shifts between the camera and the tank [9]. The tank and cameras were securely mounted on an optical breadboard to make the system portable and robust.

2.2. Optical system design

Three Zyla 5.5 scientific-complementary metal-oxide-semiconductor cameras (Andor Technology Ltd., Belfast, UK) were used for imaging. The camera sensors were equipped with 2560 × 2160 pixels, with an individual pixel size of 6.5 µm. A 16-bit analog-to-digital converter digitized the light signal. The cameras were capable of sustaining a full-frame transfer rate of 30 frames per second (fps) using a USB3.0 data transfer interface. Smaller regions of interest, such as the 1100 × 1100-pixel region of interest selected for this study, further increased the imaging rate (96 fps), resulting in better time resolution (10.33 ms) for the 3D detector. The cameras were fitted with 20.5-mm fixed-focal-length objective lenses (Schneider Optics, Van Nuys, CA). The lens selection was based on calculations of depth of field [7] and field of view. With a 750-mm working distance and f/8 aperture setting, a 20-cm focal depth situated around the center of the tank was obtained.

All the experiments were conducted using spot-scanned proton beams at the Proton Therapy Center at The University of Texas MD Anderson Cancer Center at Houston.
Figure 1. (a) Schematic of the 3D detector consisting of a liquid scintillator-filled tank, mirrors, and 3 sCMOS cameras. Two mirrors placed at 45° angle to the top and right tank surfaces redirected the scintillation light to cameras Y and Z, respectively. (b) Integrated light projections of a spot-scanned proton beam captured by the detector.

2.3. Techniques to synchronize camera acquisitions with proton beam deliveries

To capture the complete dose delivered to the detector, camera imaging cycles must be coordinated with dynamic proton-beam delivery intervals. However, the beam delivery system at our institution does not produce a compatible signal that can be used to directly trigger cameras. We therefore developed an Arduino microcontroller-based camera-triggering technique that used a combination of signals obtained from the beam delivery system to acquire images only during the duration of the beam delivery. These synchronization techniques offered the flexibility to either capture all the pencil-beam spots with identical energies in a single camera frame (the "spill-based" synchronization technique) or to capture individual beam-spots (the "spot-based" synchronization technique).

The spill-based camera synchronization technique used synchrotron-generated radiofrequency extraction START and STOP signals to trigger and terminate camera cycles (Figure 2) [11]. While the synchrotron produced proton energies ranging from 72.5 MeV to 221.8 MeV, each energy was delivered in a different "spill" of protons, and each spill could contain more than a single spot. This imaging approach combined all spots with identical energies into a single spill, which could last up to 4.4 s, in a camera frame. A 2.1-s inter-spill duration allowed the camera sufficient time to read and digitize the collected signal and be ready for the next spill. This synchronized imaging approach captured all the delivered spots and used significantly fewer camera frames (# frames = # spills).

The spot-based camera synchronization technique used an additional signal in the form of dose monitor (DM) pulses to allow imaging of individual proton beam spots (Figure 2). The DM pulses provided a count of the number of spots delivered by the treatment plan. A Schmitt trigger was used to eliminate the noise on the DM pulses before the microcontroller unit counted them. The microcontroller used an interrupt mode to monitor the DM pulse deliveries every 1 ms and thereby check the status of the spot delivery. The DM pulse readout by the microcontroller indicated active spot delivery, and the absence of DM pulses indicated completion of the spot delivery. At the end of spot delivery, the microcontroller sent a trigger signal to the camera to terminate the current frame and initiate a new frame. Using this method, the number of spots delivered by the synchrotron could be reliably counted and imaged.
3. Results/Discussion

We conducted several studies using spill-based camera synchronization technique to analyze and quantify the performance of the 3D LS-based detector. The results are described in detail by Darne et al. (2017) [11]. Here, we briefly summarize the highlights of this detector. The detector had submillimeter imaging resolution (0.21 mm) for all 3 cameras and was found to be useful for generating complete light distribution profiles for the proton beams, which is especially useful around the high-gradient Bragg peak region. The synchrotron delivered pencil beams within a typical duration of 1 to 10 ms. A temporal resolution of 10.33 ms for the cameras was therefore critical for real-time imaging of dynamically delivered proton spots. Amongst other features, the detector demonstrated good stability (1%) over a period of 3 weeks, a linear signal-to-noise ratio ranging from 20 dB at 5 mGy to 85 dB at 10.6 Gy, and an excellent measurement linearity response (99.6%) over a 3-orders-of-magnitude change in the scintillation light intensity. The utility of the detector to support near-real-time measurements of proton ranges was also evaluated over all 94 synchrotron-generated beam energies. The average range measurement accuracy across all the beam energies was found to be 0.07 ± 0.03 mm [11]. The range measurement uncertainty for doses below 1 cGy was found to be ±0.36 mm, indicating good precision for low dose measurements. The detector was able to rapidly calculate the beam ranges for all 94 energies in a clinically feasible time frame (< 10 min). The detector was also able to determine the size of each pencil spot from the full-width-half-maximum of the lateral beam profiles. Finally, the detector used proton beam perspectives collected from all 3 cameras to facilitate 3D location of the beam position within the detector with an average accuracy of 1 mm.

For an actual treatment plan, each energy layer can comprise a large number of individual spots delivered at different locations. If all these proton spots were combined into a single frame, the image analysis would become overly complicated. To overcome this problem, we developed the spot-based synchronization technique. The ability to isolate and analyze individual beam profiles within a treatment plan in 3D would help to detect errors. Furthermore, we found that the spot-based synchronization
technique was able to capture the complete dose delivered by the beams, which could be lost with non-triggered image acquisitions because of unsynchronized imaging and the presence of camera deadtime. In addition, we found signal-to-noise ratio dependence such that low-intensity unsynchronized imaging pixels could lose as much as 10% ± 0.4% mean signal intensity compared to triggered acquisitions. Thus, synchronization prevented signal loss and improved the ability of the detector to measure dose in 3D. It also simplified image analysis and reduced the size of the generated imaging data sets.

We previously conducted a simulation study to demonstrate a 3D reconstruction of scintillation light emission using limited camera projections [12]. Our future work will involve imaging a patient treatment plan using a spot-based triggering technique with the developed maximum a posteriori algorithm for 3D reconstruction of the scintillation light. This light will be converted into precise dose by using an improved energy density by secondary electrons model for the ionization quenching correction [13]. In the future, we will apply this model to all 94 beam energies for accurate 3D dosimetry.

4. Conclusion
This study showed that an LS-based detector can be used for fast (10.33 ms), high-resolution (0.21 mm), accurate (< 0.2 mm) range prediction and precise mapping of dose distributions in real time. The camera-triggering schemes provided additional flexibility in collecting the pencil beams to simplify the image analysis. The proposed system, therefore, has the potential to enable efficient, high-resolution 3D quality assurance studies of clinical proton beams.

5. Acknowledgements
We would like to thank Chinmay Darne, Fahed Alsanea, Daniel Robertson, and Narayan Sahoo for their contributions to this project. We would also like to acknowledge Amy Ninetto from the Department of Scientific Publications at UT MD Anderson Cancer Center. The research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under Award Number R01CA182450.

6. References
[1] Xu XG et al 2008 Phys. Med. Biol. 53 R193
[2] Poppe B et al 2006 Med. Phys. 33 1005
[3] Lepage M and Jordan K 2010 J. Phys.: Conf. Ser. 250 012055
[4] Kevin J 2010 J. Phys.: Conf. Ser. 250 012043
[5] Beddar AS et al 1992 Phys. Med. Biol. 37 1883
[6] Beddar S et al 2009 Med. Phys. 36 1736
[7] Archambault L et al 2012 Med. Phys. 39 1239
[8] Ponisch F et al 2009 Med. Phys. 36 1478
[9] Hui CK et al 2015 Biomed. Phys. Eng. Express 1 025204
[10] Robertson D et al 2014 Phys. Med. Biol. 59 23
[11] Darne CD et al 2017 Phys. Med. Biol. 62 5652
[12] Hui C et al 2014 Phys. Med. Biol. 59 4477
[13] Alsanea F and Beddar S 2017 J. Phys.: Conf. Ser. 847 012022