Technical Note: A prototype clinical proton radiography system
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Ethan A. DeJongh¹, Don F. DeJongh²*, Igor Polnyi¹, Victor Rykalin¹, Christina Sarosiek²+, George Coutrakon², Kirk L. Duffin³, Nicholas T. Karonis³⁴, Caesar E. Ordoñez³, Mark Pankuch⁵, James S. Welsh⁶⁷, John R. Winans³

¹ProtonVDA LLC, Naperville, IL 60563, USA
²Department of Physics, Northern Illinois University, DeKalb, IL 60115, USA
³Department of Computer Science, Northern Illinois University, DeKalb, IL 60115, USA
⁴Argonne National Laboratory, Data Science and Learning Division, Argonne, IL 60439, USA
⁵Northwestern Medicine Chicago Proton Center, Warrenville, IL 60555, USA
⁶Edward Hines Jr VA Medical Center, Radiation Oncology Service, Hines, IL 60141, USA
⁷Department of Radiation Oncology, Loyola University Stritch School of Medicine, Maywood, IL 60153, USA

*Denotes Senior Author
+Corresponding Author: csarosiek1@niu.edu, 1425 W Lincoln Hwy, DeKalb, IL 60115

ABSTRACT

Purpose: To demonstrate a proton imaging system based on well-established fast scintillator technology to achieve high performance with low cost and complexity, with the potential of a straightforward translation into clinical use.

Methods: The system tracks individual protons through one (X, Y) scintillating fiber tracker plane upstream and downstream of the object and into a 13 cm-thick scintillating block residual energy detector. The fibers in the tracker planes are multiplexed into silicon photomultipliers (SiPMs) to reduce the number of electronics channels. The light signal from the residual energy detector is collected by 16 photomultiplier tubes (PMTs). Only four signals from the PMTs are output from each event, which allows for fast signal readout. A robust calibration method of the PMT signal to residual energy has been developed to obtain accurate proton images. The development of patient-specific scan patterns using multiple input energies allows for an image to be produced with minimal excess dose delivered to the patient.

Results: The calibration of signals in the energy detector produces accurate residual range measurements limited by intrinsic range straggling. The use of patient-specific scan patterns using multiple input energies enables imaging with a compact range detector.

Conclusions: We have developed a prototype clinical proton radiography system for pretreatment imaging in proton radiation therapy. We have optimized the system for use with pencil beam scanning systems and have achieved a reduction of size and complexity compared to previous designs.

Key Words: proton imaging, proton radiography, calibration
1. INTRODUCTION:

ProtonVDA LLC has developed a prototype clinical proton radiography system for pretreatment patient setup and range verification in proton radiation therapy. Kohler first proposed proton radiography in 1968 as a high contrast imaging modality. Since then, researchers have shown that proton radiography can be used as a pretreatment quality assurance tool in proton therapy. In particular, it can be used as a proton range check to detect differences between the actual and the predicted proton range from anatomical changes and, in addition, to align the patients to the treatment beam. Recent studies have explored the potential of proton radiographs to reduce uncertainties due to patient-specific Hounsfield units to relative stopping powers conversion used with x-ray CT scans.

The detector system described in this technical note tracks single protons of known incident energy and direction from low-intensity pencil beams. Tracker planes measure the location of individual protons upstream and downstream of the object. The steering of the pencil beam scanning system determines the direction of the incoming proton. After traversing the object, the residual energy of the proton is measured in a scintillating block energy detector with a set of photomultiplier tubes (PMT). The difference in the incident and measured residual energy of each proton is converted to water equivalent path length (WEPL) through the object. The WEPL values are then binned into pixels at the isocenter plane, which is the plane normal to the beam located at a defined distance from the accelerator scanning magnets. The water equivalent thickness (WET) is calculated as the most likely WEPL value in each pixel and displayed as a grey-scale proton radiographic image. The image reconstruction methods used to produce a proton radiographic image from the WEPL data produced by this system are described in detail by Ordoñez et al.

The detector system is designed to minimize the size and complexity of the hardware such that it can easily be integrated into proton therapy treatment rooms. The use of pencil beam scanning allows for the use of a single upstream tracker plane and a reduction of the delivered dose delivered as described in Sections 2.1, 2.3, and 3.2. A calibration procedure to obtain WEPL from PMT signals has been developed, which allows for fast signal readout and minimal electronics, as described in Section 2.2.

2. METHODS AND MATERIALS:

2.1 Tracker planes

The proton radiography system includes one set of (X, Y) tracker planes in front of the object and one set after the object. The sensitive area of the tracker planes is 38.4 x 38.4 cm². Each X and Y tracker plane uses two layers of tightly packed 1 mm² scintillating fibers, offset by one half fiber width, as illustrated in Figure 1a. The fibers are grouped into 12 bunches of 32 fiber pairs, where pairs of fibers in each bunch with the same numerical label are connected to a single silicon photomultiplier (SiPM), as illustrated in Figure 1b. A single detected hit could have occurred in any of 12 X-locations and Y-locations, respectively, and the actual (X, Y) position of the hit is determined based on the intended direction of the pencil beam as defined by an accelerator plan for the time of the proton hit. This design allows for a reduction of the number of light sensors and electronics channels by a factor of 12 relative to other designs.
Figure 1. a) Cross-section of an x or y tracker plane consisting of 2 layers of scintillating fibers each 1 x 1 mm$^2$ by 40 cm active length. The tracker planes consist of 12 bunches of 32 fiber pairs per bunch. Fiber pairs in each bunch with the same numerical label are attached to a single Silicon photomultiplier (SiPM). b) Top view of four adjacent fiber bunches. One fiber pair from each bunch is read out through a common SiPM. So, each SiPM reads out 12 fiber pairs regularly spaced across the plane.

2.2 The energy detector and calibration to WEPL

The energy detector contains a compact 13 cm-thick scintillator block and 16 photomultiplier tubes (PMTs). The scintillating block has a sensitive thickness of 10 cm, and the radiographic image is acquired from several proton scans using different energies in different regions of the object. The use of several energies ensures that all protons pass entirely through the object and have a residual water-equivalent range of less than 10 cm. For example, the variations in WET in the pediatric head phantom used in this project (Computerized Imaging Reference Systems, Inc., model HN-719) require a minimum of three energies for a complete anterior-posterior (AP) proton radiograph. Scintillating photons are collected into a 4 x 4 grid of PMTs. The scintillator sides not covered by the PMTs are painted black to absorb photons, and the PMTs collect only direct photons that have not scattered off the walls. This approach minimizes the collection time of photons.

The residual range of each proton is measured and converted to WEPL using the following method. The 16 PMTs on the backend of the energy detector measure the light output generated by the protons that passed through the object. The light output depends on the residual energy and the position of the proton with respect to the energy detector. By combining the 16 PMT signals, only four PMT readout variables, named E, U, V, and C, are acquired to reduce the amount of electronics required and to minimize the data volume output. The E signal is the total sum of all 16 PMT signals. The U and V signals are weighted sums of the PMT signals along diagonals of the 4 x 4 array, as shown in Figures 2a and 2b. The C signal is a weighted sum of the PMT signals based on the two concentric squares in the 4 x 4 array, as shown in Figure 2c. For most positions, the E signal increases approximately linearly with the residual range of the proton but with a position-dependent slope, as shown in Figure 3b. The position of the proton entering the energy detector is known from the tracker planes. Therefore, the E signal alone gives an accurate measure of the residual range for most protons entering the detector. However, some positions have non-linear slopes in the E signal at large residual ranges, and many protons will undergo multiple Coulomb scattering throughout the energy detector, confounding the linear E-signal dependence. For these cases, the U, V, and C signals provide additional information to improve the residual range accuracy. The determination of the residual range from these signals is described in the following paragraphs.
A calibration procedure was developed to convert the energy detector signals E, U, V, and C to residual proton range. Protons are delivered to a 30 x 40 cm$^2$ field at 44 different residual ranges. We rely on the range calibration of the energy selection system at NMCPC used for proton treatment and solid water blocks of well-known thicknesses to precisely set the residual range of the calibration protons. Approximately 100 protons are delivered to each of the 5.2 million spots spaced 1 mm apart in the transverse direction and 0.25 mm in depth. The E, U, V, and C signals for each proton are measured and the average E, U, V, and C signals for each spot (denoted as $\bar{E}$, $\bar{U}$, $\bar{V}$, $\bar{C}$, respectively) is calculated. From these data, the EUVC covariance matrix $K_{EUVC}$ is calculated and collected into a 3D calibration grid of (X, Y, Residual Range). The covariance matrix for each spot is defined as
\[
K_{EUVC} = \begin{bmatrix}
\text{cov}(EE) & \text{cov}(EU) & \text{cov}(VE) & \text{cov}(EC) \\
\text{cov}(UE) & \text{cov}(UU) & \text{cov}(UV) & \text{cov}(UC) \\
\text{cov}(VE) & \text{cov}(VV) & \text{cov}(VC) \\
\text{cov}(CE) & \text{cov}(CU) & \text{cov}(CV) & \text{cov}(CC)
\end{bmatrix},
\]

where \( \text{cov}(AB) \) is the covariance between two variables \( A \) and \( B \).

For each proton in an imaging scan, the \((X, Y)\) position is known from the downstream tracker plane, and the E, U, V, and C signals are calculated from the energy detector signals. From the E, U, V, and C values of the protons and the locations in the calibration grid that correspond to the measured position of the protons derived from the downstream tracker, a \( \chi^2 \) is calculated using

\[
\chi^2 = \Delta^T K_{EUVC}^{-1} \Delta
\]

and

\[
\Delta = \begin{bmatrix}
E - \bar{E} \\
U - \bar{U} \\
V - \bar{V} \\
C - \bar{C}
\end{bmatrix}
\]

The three lowest \( \chi^2 \) values versus range are fitted with a parabolic function, and the residual range of the proton is the location of the minimum of the fit. The proton WEPL is calculated as the difference between the water-equivalent range of the incident proton and the residual range of the proton measured by the energy detector.

### 2.3 Patient-specific scan pattern

For proton radiography, the useful data comes only from protons that pass entirely through the object and stop in the energy detector. The Bragg peak of the protons is deposited in the energy detector, and the dose delivered to the patient is part of the entrance region of the proton depth-dose curve. Due to the compact nature of the residual energy detector, energy modulation is required to ensure protons pass through the object and have a residual water-equivalent range of less than 10 cm at every \((X, Y)\) location. In clinical practice, dose-minimization is achieved by developing a patient-specific scan pattern. A previously acquired x-ray CT image of the patient can be used as the basis to determine what beam energy should be used for which \((X, Y)\) position. The Hounsfield units are converted to proton relative stopping power, and a digitally reconstructed WET image is created. This image is then used to determine the set of energies for the proton radiography scan as a function of \((X, Y)\) positions. The goal of this method is to maximize the number of imaging protons that stop in the energy detector and minimize the Bragg peaks stopping inside of the patient. In clinical use, this will minimize the imaging dose to the patient.

### 3. RESULTS

### 3.1 Calibration Accuracy

A proton radiograph of a block of solid water with known WET of 6.1 cm was taken to determine the accuracy of the calibration procedure. About 12 million protons with an energy of 128 MeV were
uniformly scanned across a 30 x 40 cm² field size. The resultant radiograph is shown in Figure 4a. The WEPL of each proton in the image is displayed in a histogram in Figure 4b. The mean ± rms WEPL of individual protons was calculated to be 6.124 ± 0.262 cm. Approximately 100 protons were binned into 1 mm² pixels, and the mean ± rms WET of all pixels in the radiograph was calculated to be 6.126 ± 0.024 cm, as shown in the histogram in Figure 4c.

**Figure 4**: a) Proton radiograph of a 6.1 cm thick block of solid water using 128 MeV protons. b) Histogram showing measured WEPL values and rms deviation for individual protons. c) Histogram showing the distribution of reconstructed average WET values per pixel.

### 3.2 Imaging Dose

A simulation was performed with TOPAS® version 3.1 to compare the dose deposited in the pediatric head phantom with a full-field uniform scan spot pattern and a patient-specific scan pattern. The simulation included three energies (180 MeV, 140 MeV, and 100 MeV) and a total imaging field size of 20 cm x 20 cm. Each pencil beam spot included 2,500 simulated protons, and the spots were spaced 0.5 cm apart, resulting in about 100 protons per 1 mm² pixel. The dose deposited in a selected axial slice of the phantom using the two different scan techniques is compared in Figure 5. Figure 5a shows the dose deposition from the full-field uniform scan. Many of the protons from the lower two energies stop in the patient. The data from these protons are not used in the image reconstruction and, therefore, are wasted dose to the patient. By using patient-specific scan patterns, such as in Figure 5b, the dose is reduced by a factor of eight in some regions, and the majority of the dose delivered is deposited by protons that are used in the image reconstruction.
4. DISCUSSION

The proton radiography system described in this technical note has a minimal amount of electronics, is low-weight, and compact, making it straightforward to translate the system into clinical use. The system is designed to operate with proton intensities up to 10 MHz. A 20 x 20 cm² field size with 100 protons per 1 mm² pixels can be delivered in less than one second. The system provides a fast and efficient method of pretreatment range verification and alignment procedures.

The use of only a single tracker plane upstream and downstream of the detector, as compared to two planes in initial designs, provides considerable volume savings; however, it removes the ability to measure incident and exit angles used during image reconstruction. With the use of scanned pencil beams, the incident angle can be calculated from the knowledge of the source-to-isocenter distance and the actual position of the pencil beam in the isocenter plane. There is, however, a reduction in spatial resolution due to multiple Coulomb scattering in the object, which randomizes the exit angle of the protons. Having a direct measurement of the proton angle would reduce the uncertainty of the path of the proton and increase spatial resolution. On the other hand, detection of range errors, may not require such a high degree of spatial resolution, justifying this cost-saving design.

The use of a compact monolithic residual energy detector further reduces the weight and size of the system. By using pencil beams and patient-specific scan patterns, the dose delivered to the patient is minimized to micro-Gy levels. Adjusting the energy according to object thickness reduces the nuclear interactions, which are eliminated during the data preprocessing step, thus reducing unnecessary imaging dose to the patient. On the other hand, the use of lower-energy protons will result in more extensive multiple Coulomb scattering and a further reduction of spatial resolution. As described previously, the use of an image reconstruction method for proton radiography that employs a most likely path algorithm where the exit angle is unknown can partially compensate for this loss of spatial resolution. Simulations comparing the use of one downstream tracker plane to two downstream tracker planes indicate the...
uncertainty of the path estimation is typically 0.3 mm larger for the single plane case. Future work will study the impact of this error on the final image.

5. CONCLUSION

We have described a proton radiography detector that can be translated into clinical use. It has been developed to be implemented on beamlines using low-intensity pencil beam scanning such that the same proton delivery system is used for pretreatment imaging, patient setup verification and subsequent treatment. A calibration procedure was developed for fast conversion of energy signals to water equivalent pathlength with a minimum amount of electronics. The use of the pencil beam scanning system for imaging allows for further reduction of the energy detector while allowing for optimizing the imaging dose.

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CONFLICT OF INTEREST STATEMENT
The authors have intellectual property rights to the innovations described in this paper. James S. Welsh has served as a medical advisor to ProTom International. Don F. DeJongh and Victor Rykalin are co-owners of ProtonVDA LLC.