Expected proton signal sizes in the PRaVDA Range Telescope for proton Computed Tomography

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ABSTRACT: Proton radiotherapy has demonstrated benefits in the treatment of certain cancers. Accurate measurements of the proton stopping powers in body tissues are required in order to fully optimise the delivery of such treatments. The PRaVDA Consortium is developing a novel, fully solid state device to measure these stopping powers. The PRaVDA Range Telescope (RT), uses a stack of 24 CMOS Active Pixel Sensors (APS) to measure the residual proton energy after the patient. We present here the ability of the CMOS sensors to detect changes in the signal sizes as the proton traverses the RT, compare the results with theory, and discuss the implications of these results on the reconstruction of proton tracks.

KEYWORDS: Proton Therapy; Instrumentation for hadron therapy; proton Computerized Tomography (pCT); CMOS Active Pixel Sensors.
1. Introduction

Proton radiotherapy uses external beams of high energy protons to treat cancer. Proposed by Robert Wilson in 1946 [1], the first patient was treated with proton radiotherapy at Berkeley Radiation Laboratory (California, US) in 1954 [2]. Patients were not treated with protons in a clinical environment until 1989 when the Clatterbridge Centre for Oncology (Wirral, UK) started treating ocular cancers with 62 MeV protons [3]. However, the popularity of proton radiotherapy around the world has increased in recent years with a rapid increase in centres, both in operation and in the planning stages [4].

When a high energy proton interacts within a material it will deposit a fraction of its energy. The amount of energy deposited per unit length is known as the proton stopping power. As a proton slows it interacts more often, and the stopping power increases. This leads to a run away effect where a proton deposits most of its energy towards the end of its range, a phenomenon known as the Bragg Peak (BP). The location of the BP can be set within a tumour volume by modifying the incident kinetic energy of the protons. There is no energy deposition after the BP which is particularly useful in radiotherapy with a target volume immediately adjacent to a critical organ as this minimises the dose to healthy tissue behind the tumour. Three pieces of information are required to ensure the BP occurs within the tumour volume: (1) the location and size of the tumour, (2) the stopping powers of the body tissues between the beam and the tumour, and (3) the location of the patient relative to the beam during treatment.

Conventionally, a patient will receive a CT scan to locate the tumour and identify surrounding healthy tissues. However, a CT scan is obtained using beams of x-rays which yield an image of
the electron density of a material, not its stopping power. It is possible to convert the images to
stopping powers with a generally accepted uncertainty on the final proton range of 3.5% [5]. A
detailed Monte Carlo study suggests the contribution to this from the conversion is 1.5–2% [6]. This
propagates as an uncertainty on the position of the BP and can lead to under treatment of
the target volume or overdosing the surrounding healthy tissue. This uncertainty could be signifi-
cantly reduced, and treatment planning improved, if the patient was imaged directly with protons
producing a proton CT (pCT).

In order to obtain a pCT image, every proton must be tracked and their residual energy mea-
sured to calculate the energy lost through the patient. The Proton Radiotherapy Verification and
Dosimetry Applications (PRaVDA) Consortium, funded by the Wellcome Trust, are developing
a proof of principle instrument which would allow a pCT to be obtained using a fully solid state
device. The PRaVDA device will use four banks of silicon tracking sensors, two before and two
after the patient, to measure the proton direction and calculate the angle of deflection through the
patient [7]. The residual energy of the proton will then be measured in a Range Telescope (RT)
which is a stack of large scale CMOS Active Pixel Sensors (APS). The residual energy of the pro-
ton can be measured by identifying the final layer in which the proton is detected and converting
this to a water equivalent path length. The RT will be highly segmented in the sensor plane and as
such will be able to track multiple particles simultaneously, reducing the time required to obtain a
pCT. The instrument is designed to track and measure protons at a rate of more than 1M/s, leading
to a total scan time in the order of minutes.

In this paper, we demonstrate the ability of large scale CMOS APSs to measure the signal size
of the protons as they travel through the RT and compare the results with theoretical models. In the
final reconstruction this additional information would allow us to interpolate between layers and
reduce the range uncertainty in the proton range. The paper is structured as following: An overview
of the CMOS used for this study is given in Section 2, the experiments are outlined in Section 3,
and the clustering algorithm to identify protons is explained in Section 4. Results are presented in
Section 5 and further discussed in Section 6. Finally, our conclusions are stated in Section 7.

2. The DynAMITe Sensor

For this study the protons were detected using the Dynamic range Adjustable for Medical Imaging
Technology (DynAMITe) sensor [8]. DynAMITe is a radiation hard CMOS APS [9] constructed
in a 0.18 µm CMOS process with a total active area of 12.8×12.8 cm² developed by the MI-3 Plus
consortium. The pixel array consists of two imagers, the Pixel (P) camera with 100 µm pixel pitch
and the Sub-Pixel (SP) camera with 50 µm pixel pitch, superimposed on top of each other. The
epitaxial layer of the sensor is 12 µm thick on a silicon substrate yielding a total wafer thickness
of 725 µm.

When a charged particle interacts with the sensitive region of DynAMITe it deposits energy
via ionisation, the free electrons are then collected via diffusion at a photodiode. The signal size is
expressed in term of Digital Number (DN) and previous studies have show a gain within the sensor
of 50 e⁻/DN [8].

The work presented here utilised the low noise, higher spatial resolution SP camera. A rolling
shutter is used to sequentially read out each row of the sensor. A read out rate of approximately
1400 frames/s was achieved by coupling the rolling shutter with the ability to read out a small region of interest within the sensor (in this study the central 10 rows). The high frame rate was required to record each individual proton within the beam.

3. Experiments

Two experimental locations were used to collect the data for this paper. The MC40 cyclotron at the University of Birmingham was used for proton energies below 36 MeV and the iThemba LABS cyclotron allowed protons with energy up to 191 MeV to be studied. Both experiments relied upon having a very low proton fluence to ensure that there was minimal pile-up in the sensor and allowed us to study individual protons.

3.1 University of Birmingham Cyclotron

The proton source at the University of Birmingham is a Scanditronix MC40 cyclotron. The cyclotron is capable of producing beams of protons with a wide range of energies (3-38 MeV) with an energy spread (defined as the FWHM of the energy distribution) of 0.1 MeV. The cyclotron can deliver proton currents ranging from pA to µA. The protons are deflected into a large vault where experimental equipment can be housed. It is possible to achieve a beam of 50 mm diameter in this vault by defocusing the proton beam using quadrupole magnets located approximately 3 m from the end of the vacuum beampipe nozzle.

A BP was reconstructed to precisely determine the energy of the proton beam. The charge collected over a 20 s period by a Markus Chamber \[10\] was recorded with various thicknesses of Perspex before the chamber. The proton current before the Perspex was measured using a PTW 7862 Ionization Chamber \[11\] located 1 cm from the nozzle and allowed fluctuations in the beam current to be accounted for. The ratio of charge in the Markus Chamber to the Ionization Chamber as a function of depth in Perspex is shown in Figure \[1\]. Superimposed on top of the BP measurements in Figure \[1\] is a simulated BP from the bhamBeamline simulation developed using the Geant4 toolkit \[12\]. The agreement between data and simulation is maximised with a beam energy at source of 36.3±0.2 MeV.

| Energy [MeV] | 35.3 | 27.3 | 9.4 | 8.4 | 7.8 | 5.9 |

The sensor was initially aligned by acquiring data with a high current (nA rather than pA) beam, and full frame readout of the sensor. The 10 rows which corresponded to the beam spot centre were then selected to allow fast read out for the remainder of the experiment. A current of 10 pA as measured in the ionisation chamber, corresponding to a proton current 0.06 pA, was then incident upon a DynAMITe sensor. The energy of the proton beam was degraded using Perspex

\[1\] A validated Monte Carlo simulation of the Birmingham Cyclotron beam line
Figure 1. Bragg Peak of the 36 MeV proton beam, the BP measurements are shown as black crosses where the length on the cross corresponds to the experimental error, the simulated BP is the dashed black line and the red line is the simulated proton energy at various depths through the PMMA.

to allow the signal sizes within the sensor to be evaluated both in the plateau region and the peak of the BP. The Perspex degraders used are listed in Table 1 alongside the expected proton energy (also shown in Figure 1) at the sensor surface, extracted from a simulation with initial parameters matching those given above.

3.2 iThemba LABS Proton Source

The iThemba LABS has a clinical proton beam used to treat patients with head and neck cancers. At the isocentre the beam has a maximum range of 240 mm in water (corresponding to 191 MeV). The range of the beam can be degraded down to 30 mm (55 MeV) using two Graphite wedges, inserted into the beam upstream of the final collimator. The main cyclotron at iThemba is fed by a smaller cyclotron which contains the ion source. For this work we used ion source 2 as it allowed proton currents, measured on a Faraday Cup prior to the beam nozzle, down to 0.01nA compared to the typical currents of 100 nA from ion source 1, the clinical ion source.

Two DynAMiTe sensors were stacked together with 5 mm of Aluminium between the sensors and their readout clocks synchronised. A high current (few nA) beam was passed through the stack of sensors to allow the sensors to be aligned. The 10 rows that corresponded to the centre of the beam spot in each sensor were selected independently as to read out the same protons in both sensors. The beam current was then reduced to 200 pA and multiple frames captured from both sensors. The use of two sensors allowed the energy deposition to be studied for protons of 55 MeV in the first sensor and 41.5 MeV in the sensor behind the Aluminium simultaneously.

The energy loss through 5 mm Aluminium was evaluated via a Geant4 simulation using realistic input beam param-
4. Clustering Algorithm

Every frame collected by the sensor was stored as an image file containing the pixel value for all pixels which were read out. The proton signals were identified and noise suppressed within these frames using a double threshold technique. The clustering algorithm was developed using libraries from Scientific Python (SciPy) [13].

A high threshold, $T_1$, of 19 DN$^3$ was applied across the whole sensor and pixels below this value were assigned a value of 0 DN. The images were scanned for regions where multiple pixels with non zero values shared a common edge and these pixels were clustered together. The pixel in each cluster with the largest DN was identified as the cluster seed. A low threshold, corresponding to half the initial threshold, $T_2$, was applied to the eight neighbouring pixels around the cluster seed and the pixels which passed $T_2$ were added to the cluster seed. The sum of the signal in all of the pixels of the new cluster (cluster value) was then found, alongside the number of pixels in the cluster (cluster size). The use of the lower threshold allowed for the collection of charge which may have diffused into neighbouring pixels whilst the random noise signals were suppressed by the higher threshold.

5. Results

The clustering algorithm, outlined in Section 4, was applied to the data, leading to the distributions of cluster value as shown in Figure 2. The error bars on the data represent the statistical uncertainty due to the low proton currents. The energy deposition of high energy particles through thin layers follows a Landau distribution [14]. As the ratio between the particle energy and the thickness of the layer decreases the deposition becomes more Gaussian in shape. The higher energy data, taken at iThemba, was fitted with a Landau distribution and the lower energy data with a Gaussian as can be seen in Figure 2. The signal size was taken to be the Most Probable Value (MPV) of the Landau fits, and the mean of the Gaussian distributions. Cluster values below 100 DN were excluded from the Landau fits as these clusters are associated with secondary particles, originating from interactions with the collimators, hitting the sensor. If $T_1$ was raised from 19 DN to 30 DN, whilst keeping $T_2$ at 10 DN, these clusters are removed from the 55 MeV data (not shown in the Figure). However, the fit results are unchanged and a value for $T_1$ of 19 DN was used for consistency.

The measured signal size as a function of proton energy can be seen in Figure 3. The error bars on the data increase as the proton energy decreases due to a combined effect of a reduced fluence through the Perspex and a spreading in the beam energy due to range straggling. The signal sizes in Figure 3 are compared with the theoretical proton stopping powers in silicon as tabulated by SRIM [15], NIST [16] and a modified version of the TestEm0 example code released with Geant4. The stopping powers are expressed in terms of the Linear Energy Transfer (LET) in units of keV/µm. The change in observed signal size is in excellent agreement with the theoretical values for the LET. This demonstrates the ability of the CMOS sensor to fully collect the charge deposited by a proton across a range of energies.

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3 A threshold of 19 DN corresponds to approximately 3.5 times the noise in a sensor which was shielded from light and yielded a noise rate of just 2 hits/frame across the whole sensor during the Birmingham experiments.
Figure 2. Cluster values obtained when applying the clustering algorithm to the data for various proton energies. The 55.0 MeV and 41.5 MeV data was taken at the iThemba LABS, energies below this were obtained at the University of Birmingham. The lines of best fit to data are also displayed.

6. Discussion

Previous studies have demonstrated the identification of, and the tracking of single protons through two layers of CMOS [17]. Extrapolating this to track protons through a simple binary readout RT, i.e. a proton either leaves a signal in a layer or not, the range of the proton can be inferred from the final layer with an observed signal. As suggested here [18] the addition of analogue readout in
The charge is collected in a small volume within the CMOS wafer and back-thinning the bulk has a minimal effect on the performance of the CMOS [22]. This would reduce the WET of a
single layer and require additional layers of CMOS or thicker Perspex to fully contain an equivalent energy protons. Additional layers would increase the cost of the instrument but also improve the resolution, therefore, back-thinning of the CMOS is a viable option for an extension to the current project once proof of principle has been demonstrated.

The LET spectrum extracted from Geant4 demonstrates the power of Monte Carlo software to predict the behaviour of the RT and this has allowed a full scale detector simulation to be developed with confidence in the results. This will allow algorithms to be developed which incorporate the additional signal data into the final proton track reconstruction. The testing of such algorithms to evaluate the effect on the uncertainty requires additional sensors and will be addressed in future work.

The cross section for inelastic nuclear interactions in silicon is higher than in organic scintillators due to the increased atomic number. Should a proton undergo an inelastic nuclear interaction the range of the proton would be mis-reconstructed and the pC image will be degraded. There are two scenarios where this could happen in the PRaVDA RT: (1) the proton undergoes an inelastic interaction within the sensitive region of a layer or (2) the proton undergoes an inelastic interaction in the insensitive region such as the bulk silicon. As a nuclear interaction will lead to a significantly increased signal in the sensor the first scenario can easily be handled by applying cuts on the maximum allowed signal size. The second scenario will be accounted for using an iterative approach. The RT will allow energy measurements to be made in highly segmented spatial dimensions. Within each spatial region the range of the protons will vary due to range straggling but events with a significantly different range when accounting for straggling can be removed.

It is clear that both scintillator slabs and layers of solid state detectors are suitable technologies for a range telescope. The precise 3-dimensional tracking of the path of each individual proton until it stops, however, is a feature of only the latter and is a unique approach to the pCT problem. The spatial discrimination inherent in our proposed RT design has the potential to breakdown the concepts of separate tracking and energy measuring instruments and although our initial prototype retains this distinction, with thinned substrates it need not. Also, with sufficient radiation-hardness, a RT could also be used as a proton-integrating detector and image the treatment beam for QA at high beam currents. These points demonstrates the unique possibilities of our design and the development of a solid state RT is worth examining further.

7. Conclusion

We have demonstrated the ability of a CMOS device to measure the signal size of individual protons at a range of energies corresponding to those within the PRaVDA RT. The ability to measure a signal of varying size within the sensors of the RT will allow the proton range to be interpolated between layers and thus reduce the uncertainty on the range of the protons. This will allow multiple protons to be accurately reconstructed simultaneously and reduce the time to obtain a pCT to acceptable levels for a clinical device.

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