Recent developments at the University of Pennsylvania’s Roberts Proton Therapy Center

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Abstract. The Roberts Proton Therapy Center treated its first patient on Australia Day 2010 with a double scattered proton beam. In 2012 the first patient was treated with pencil beam scanning and by that time patients were being treated in five treatment rooms. By March 2013 we were treating with pencil beam scanning (PBS) in three treatment rooms and double scattering in the other two. We currently treat about 100 patients per day in 4 treatment rooms, while one of our double scattering beam nozzles is being replaced with PBS. We treat 15 to 20 pediatric patients per day, many under general anesthetic. We treat a wide variety of indications in adult patients and all patients are registered on some form of clinical research protocol. We were the first proton center to have an operational CBCT system (September 2014) and Small Animal Radiation Research Platform (SARRP) on one of the beam lines which can be used for both x-ray and proton irradiations to support our radiobiology research program. Areas of physics related research described here include prompt gamma range monitoring, proto-acoustic range verification and the development of micromegas detectors for range verification through proton radiography and CT.

1. Introduction
Recent developments at the Roberts Proton Therapy Center (RPTC) include innovations in clinical application, medical physics and radiobiology research. The RPTC is fully integrated into the Department of Radiation Oncology and incorporates an Ion Beam Applications Proteus Plus system (IBA SA, Louvain-la-Neuve, Belgium), with four gantry rooms and one fixed beam room. When the purchase agreement was signed in June 2006, there was no commercially available pencil beam scanning (PBS) system for proton therapy. PBS was included as a research and development project within the contract. To mitigate the risk associated with PBS uncertainty, all four gantry rooms were supplied with double scattering (DS) and uniform scanning (US) and only two were provided with additional PBS capability. The fixed beam room has a PBS only beam line. This resulted in a very complex multi-modality facility, however, opting for this complex system proved to be a good choice because delays in deployment of PBS did not delay full clinical operation in all rooms.

Once PBS was operational in three rooms it became clear that this was the modality of choice for most patients because of the superior dose distributions achievable. Therefore, the facility operated with three PBS and two DS treatment rooms, until a DS room closed down for upgrade to PBS in late 2016. This room resumed clinical treatments in March of 2018. Eventually planned upgrade of the remaining DS room will create a PBS only facility. This continual upgrade philosophy also saw the use of the first gantry mounted proton cone beam computed tomography (CBCT) unit in September 2014; three PBS gantries are equipped with this technology.
2. Clinical Operation

Table 1 shows the total number of patients (adult and pediatric), categorized by treatment site, treated at the RPTC, since January 2010 and projected through until the end of the 2018 financial year which starts on July 1st, 2017 and ends on June 30th, 2018. Note the decrease in the percentage of urological (prostate) cases treated from 35% in FY2011 to 17% in FY2018. Also notable is the significant increase in the numbers GI, head and neck and thoracic cases treated, starting around FY2013, as the number of available PBS rooms increased by adding two PBS gantry rooms, which allowed for greater flexibility in treatment planning and improved dose distributions.

| Disease Site       | Financial Year | Total |
|--------------------|----------------|-------|
|                    | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
| Breast             | 1    | 0    | 6    | 13   | 30   | 44   | 28   | 31   | 153  |
| Endocrine          | 13   | 21   | 17   | 26   | 27   | 25   | 22   | 14   | 165  |
| Gastro-intestinal  | 14   | 48   | 93   | 136  | 117  | 116  | 120  | 86   | 730  |
| Gynecology         | 3    | 4    | 6    | 16   | 14   | 10   | 3    | 9    | 65   |
| Head & Neck        | 10   | 16   | 33   | 66   | 75   | 97   | 95   | 96   | 488  |
| Hematology         | 4    | 17   | 23   | 51   | 50   | 48   | 60   | 58   | 311  |
| Metastatic         | 3    | 2    | 11   | 9    | 16   | 18   | 32   | 24   | 115  |
| Missing            | 13   | 21   | 46   | 5    | 2    | 1    | 4    | 14   | 106  |
| Musculoskeletal    | 29   | 33   | 37   | 56   | 65   | 56   | 56   | 57   | 389  |
| Neurological       | 56   | 76   | 112  | 132  | 119  | 149  | 164  | 165  | 973  |
| Other              | 1    | 4    | 2    | 5    | 3    | 3    | 3    | 3    | 24   |
| Skin               | 0    | 0    | 2    | 2    | 6    | 7    | 4    | 7    | 28   |
| Thoracic           | 13   | 57   | 67   | 103  | 122  | 142  | 114  | 127  | 745  |
| Urology            | 105  | 178  | 161  | 156  | 117  | 111  | 129  | 111  | 1068 |
| Total              | 265  | 477  | 614  | 772  | 763  | 827  | 832  | 964  | 5359 |

The above totals include pediatric cases for which the annual treatment numbers are as follows;

| Pediatric cases | 55 | 96 | 119 | 134 | 141 | 162 | 139 | 163 | 1009 |

3. Research Developments

3.1. Range verification

There are a number of projects addressing the issue of range uncertainty; these include prompt gamma emission studies, protoacoustics and proton radiography.

3.1.1. Prompt gamma emission. When protons lose energy in passing through the patient a portion of that energy is loss in elastic and inelastic nuclear interactions [1]. The inelastic interactions can leave the target nuclei (typically 12C, 14N and 16O) in an excited state as shown in figure 1 or can produce new isotopes. The excited states de-excite through emitting gamma rays which generally have very short half-life (typically in the µs-ps range). The induced isotopes may also have short half-lives but many have longer ones of several minutes or more. This project has been in collaboration with IBA a prototype IBA prompt gamma system has been clinically tested.

The prototype uses a gamma camera with a knife-edge collimator to detect the gamma signal emitted along the path of the proton beam during PBS therapy. The distal edge of the individual pencil beam Bragg peaks may be detected. In a clinical trial the measured Bragg peak positions in a patient were compared with simulated Bragg peak profiles from the treatment planning system. The clinical subject was a brain patient treated with three fields; a lateral, an oblique and a vertex field. Prompt gamma emission imaging was performed on 6 of the 30 treatments over a 14 day period. The measured average range shifts for the lateral, oblique and vertex fields were -0.8±1.3 mm, 1.7±0.7 mm
and -0.4±0.9 mm, respectively [2]. Typically, the position of the Bragg peak may be determined with an accuracy of 2mm.

3.1.2 Protoacoustics. An alternative and novel approach to range verification is to detect the acoustic pressure wave generated when protons slow down and stop. The first experimental measurements of this phenomenon by Sulak et al in 1979 [3], but recently there has been renewed interest in the technique, which has stimulated research at the RPTC. The principle relies on using multiple detectors to determine the “time-of-flight” of the pressure wave from its origin (proton path and Bragg peak) to the detector. This knowledge combined with the known velocity of sound in the phantom medium ($c$) is used to determine the position of the Bragg peak as illustrated schematically in figure 2.

One problem is obtaining a sufficiently short proton pulse to provide adequate signal for detection. Calculations show that to efficiently generate protoacoustic signal the proton pulse width should ideally be less than 10µs. Synchrotrons and linear accelerators may satisfy this requirement but it is problematical for isochronous cyclotrons without modification, although synchrocyclotrons with their pulsed output produce pulses in this range. Another problem will be the need for accurate knowledge of the acoustic properties of the different tissues of the body; simulations addressing this issue have been published by [4].

3.1.3. Proton radiography. Micromegas detectors have been developed in collaboration with the University Physics and Astronomy Department [5]. These detectors can have multiple applications but most recently they have been applied to proton radiography. Pixelated detectors have been built and spatial resolutions of 0.3 mm has been demonstrated measuring the position of step functions in a
phantom at image doses of 2 cGy. Water equivalent thickness (WET) can be measured with an accuracy of 60 µm. At 0.2 cGy image dose the resolution degrades to 0.9 mm. A multilayer device can be used to determine residual WET and reconstruct a proton radiograph. Initial measurements have been made using a single layer Micromegas detector and varying the incident beam energy.

Figure 3. A proton image of a head phantom obtained by varying the beam energy and detecting the WET using a single layer Micromegas detector. The proton radiograph (on the left) is compared to a DRR generated from a CT image of the head phantom. These early results demonstrate the feasibility of using the Micromegas technology in this application.

3.2. **SARRP for radiobiology research**
A dedicated research room at the end of the clinical beam line has recently been commissioned. This room is equipped with two research beam lines. A small animal radiation research platform (SARRP), incorporating x-ray imaging and x-ray beam delivery, has been installed at the end of one beam line enabling the image guide irradiation of small animals with the proton beam.

4. **Conclusions**
Some of the more significant medical physics research projects currently undertaken at the University of Pennsylvania’s Roberts Proton Therapy Center have been briefly described. It represents a small fraction of the wide variety of clinical, medical physics and radiobiology research performed at this institution using the proton beam.

5. **References**
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