Design of a Range Calorimeter for Proton Beam Therapy Quality Assurance

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1 The Development of Cancerous Cells

Cancer is the term for diseases in which abnormal cells divide uncontrollably and invade nearby tissues [1]. In 2017, Cancer Research UK announced that approximately 367,000 new cancer cases are confirmed each year in the UK (a 13% increase since 1995), with approximately 164,000 deaths per year [2]. This rise in cases can be attributed to an increased average life expectancy in humans, with over one third of all UK cancer diagnoses made in patients over 75 [2]. Given this prevalence, the processes that lead to the development and division of cancerous cells is a heavily documented area of medicine.

Mitosis is the process by which cells divide, separating the duplicated DNA of the cell into two, newly formed nuclei. Cells spend the majority of their lives growing, replicating DNA and carrying out their specific biochemical functions within their host organism; a collection of processes referred to as interphase [3]. The mitotic phase of a cell forms only a small fraction of its overall life cycle, accounting for 10–20% of its lifetime. Genes within cells regulate this cell division mechanism, with proto-oncogenes stimulating the division itself, and tumour suppressor genes ensuring the division rate is controlled [4].

Accelerated cell division can result from the occurrence of errors in the proto-oncogenes as the cell divides. The ability to suppress cell division can be reduced when errors are introduced into the tumour suppressor genes. If errors were to occur in a healthy cell such that its functioning was no longer optimal for the body, the controlled death mechanism, known as apoptosis, would kick in [5]. The danger arises from these errors existing alongside errors within the apoptosis mechanism. With an accelerated growth and a failing ability to self-destruct, a cell is allowed to spend its entire lifetime dividing and transmitting these errors to surrounding cells — the basis of cancer.

Humans born after 1960 face the harsh reality that they have a 50% chance of receiving a cancer diagnosis at some stage in their lifetime [2]. With cancer having an undeniable impact on the global population, the treatment of the various forms of the disease remains at the forefront of medical research efforts.

2 Cancer Treatment

Cancer treatments are not limited to uses that aim to eradicate the cancer and cure the patient entirely (curative treatments). In some cases, a combination of treatments can be used to form part of their palliative and preventative care, which seek to relieve the symptoms of cancer and prevent its recurrence respectively.

Surgery: Surgery is the preferred method of treatment for cancer patients where the tumour is localised and accessible. Surgeons will remove the tumour and an additional area of healthy tissue surrounding it, referred to as a clear margin [6]. Surgery alone will not usually be a cure if the cancer has spread however, therefore surgical procedures are sometimes used in conjunction with other treatment methods.

Radiotherapy: Radiotherapy is the next best treatment option, with 60% of UK cancer patients receiving radiotherapy as part of their treatment plans [2]. Radiotherapy procedures can be internal treatments such as Brachytherapy, or more commonly, external beam therapy. External beam treatments are typically conventional X-ray radiotherapy, or more specialised particle therapy in a limited number of cases. Despite its wide usage, X-ray radiotherapy is well-known for the damage it causes in healthy cells beyond the tumour.

Chemotherapy: Despite causing some of cancer's notorious side-effects, chemotherapy is actually a less frequently used treatment, particularly in those diagnosed in the early stages of the disease [7]. Cytotoxic agents are used to damage the double helix structure of the exposed DNA as the cancer cells rapidly divide. Whilst effective, chemotherapy also damages healthy cells, particularly those that regenerate often. This includes hair follicles, cells in the gastro-intestinal lining and reproductive system, and bone marrow.

In 40% of cancer cases, radiotherapy is the most significant part of the treatment [8].

3 X-Ray Radiotherapy

In order to generate the radiation for X-ray radiotherapy, electrons are accelerated with a voltage in a linear accelerator (LINAC) until they reach the appropriate energy for treatment, with those not at the exact energy filtered out whilst travelling on a curved trajectory. The electrons are then fired at a metal target, typically tungsten, in order to generate X-rays. These X-rays are shaped by collimators in the treatment head of the machine in order to match the tumour volume. X-ray photons entering the body can damage cancerous cells, with a double strand break in the DNA helix structure being a goal of radiotherapy [9].

With absorbed dose defined as the absorbed energy in a volume over the mass of the volume, understanding how a photon deposits its energy in a medium is vital for X-ray radiotherapy. Photons lose their energy as they interact with the tissue of a patient via three main processes: Compton scattering, the photoelectric effect and pair production. Crucially, the deposited dose of radiation is high at small depths, approximately 1–4cm deep in the tissue (depending on the LINAC energy). This can be seen in Fig. 1., where the peak of the photon depth-dose curve is followed by an elongated tail of radiation deposition.

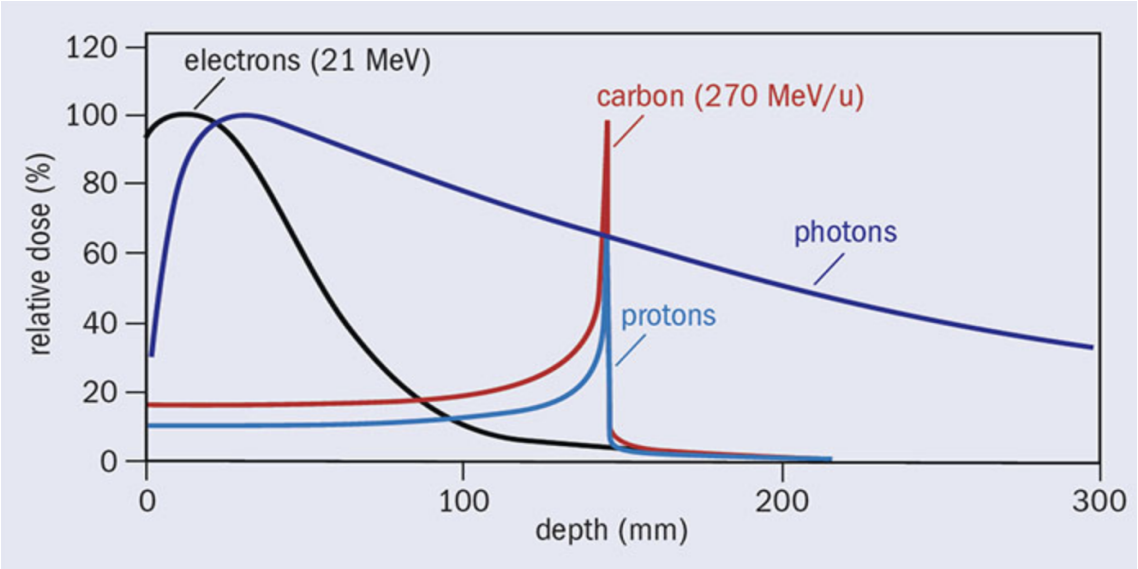

Figure 1: Depth-dose curves for a variety of radiotherapy treatments. A gradual decrease in depth beyond the peak energy loss can be seen for photons, whilst a sharp peak in energy loss occurs at the end of the path for protons and ions — the Bragg peak. Source: [10]

In order to maximise the dose deposited at the site of the tumour, patients are often treated with X-ray beams from a number of directions, and in some cases, a 360 degree

sweep.

When exposing significant portions of the body to radiation, it is important to consider the organs at risk during the treatment planning, as well as the age of the patient. In specific cases like these, it can be beneficial to consider alternative radiotherapy treatments, where dose deposition is highly localised, and damage before and after the tumour is significantly reduced. Such results can be achieved with particle therapy, most commonly, proton therapy.

4 Proton Therapy and the Bragg Peak

The depth-dose curve of protons sits in stark contrast to that of X-ray photons, evident in Fig. 1. Proton therapy exploits the fact that the proton deposits most of its energy at the end of its path – a sharp spike known as the Bragg peak. With (ideally) no dose deposited beyond the Bragg peak, protons are an attractive candidate for this specialised radiotherapy.

As of September 2020, there are 90 Particle therapy centres worldwide, with the majority providing proton therapy and some larger centres utilising carbon ions for ion therapy [11]. The first UK proton therapy centre, the Clatterbridge Cancer Centre, started treatment in 1989, but is limited to the treatment of ocular tumours due to a low maximum beam energy of 62MeV[11]. A huge milestone for Proton Therapy in the UK was the development of the Christie Proton Therapy Centre in Manchester, which started treating patients in 2018 [11]. This is the first UK high-energy proton therapy centre provided on the NHS. There are currently two more centres under construction in the UK, another forming part of the private Rutherford Health Centre network, and a second NHS facility at University College London Hospital (UCLH) [11].

To utilise protons for cancer treatment, the narrow depth range of the Bragg peak must be expanded to cover the tumour volume. By varying the energy of the incident proton beam and superimposing the Bragg peaks upon variations, a "spread-out Bragg peak" (SOBP) is produced, as shown in Fig. 2. This technique is referred to as pencil beam scanning and provides the appropriate beam modulation required to create an SOBP. The ability to precisely control the depth of the Bragg peak contributes to the rationale of proton beam therapy.

Heavier ions like carbon also have a Bragg peak, also providing a dose-distribution appropriate for radiotherapy. The Bragg peak in heavy-ion therapy is more pronounced than for proton therapy due to the heavier mass of the particles. Elastic Coulomb scattering is also reduced as a result of this higher mass, and so a sharper Bragg peak, and therefore treatment field, can be obtained with heavy ions. However, the clinical gain of heavy ions in particle therapy is slightly counteracted by the small dose deposited beyond the tumour; a result of nuclear fragmentation of the ions.

With maximum dose deposition confined to such a localised region, it is vital to know exactly where the Bragg peak lies, with minimal uncertainty. Such precision motivates the need for regular procedures within proton therapy centres that ensure commissioning standards and patient safety remain uncompromised. This is achieved by carrying out regular quality assurance (QA).

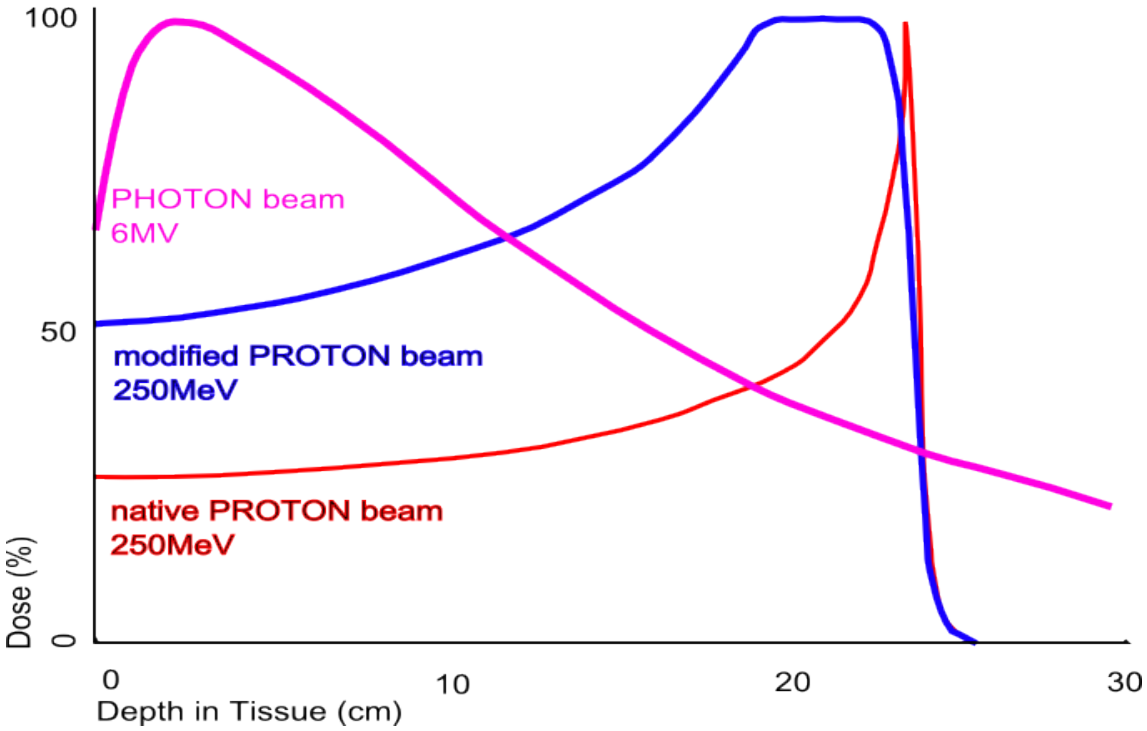

Figure 2: The SOBP is obtained by modifications of the native proton beam. Superpositions of Bragg peaks at various proton energies result in a flat-top peak that conforms to the shape of the tumour. Source: [10]

5 Quality Assurance in Proton Therapy

Quality assurance (QA) comprises all measures that ensure a system functions as it did during acceptance and commissioning.

5.1 Current Quality Assurance Procedures

Water is the simplest proxy for human tissue, and so is often used in proton therapy QA. For proton range QA, the majority of PBT facilities utilise water phantoms, which are thin radiation detectors submerged in water tanks. An example device is the PTW Peakfinder, which is a closed water column containing a large diameter ionisation chamber for scanning depth. Despite the high-resolution depth-dose measurements at any gantry angle, the measurement time remains a significant pitfall to these devices, with daily QA procedures taking approximately one hour.

The duration of beam range measurements can be reduced with the use of multi-layer ionisation chambers (MLIC), two of which have been made commercially available by IBA Dosimetry: IBA Zebra and IBA Giraffe. With each consisting of 180 stacked ionisation chambers, held together by aluminium degrader plates, the Zebra and Giraffe can be used for small and large field measurements respectively.

A 2013 investigation with the Zebra [12] found the measurement time to be 20 times less than those for water phantoms, however the setup time was only 3 times less — suggesting setup complexity is still an issue with these MLICs. Furthermore, the use of aluminium degrader plates adds to the complexity of WET measurements, with scattering effects on the PDD curve shape.

It is evident that there is a gap in the market for a QA detector that is able to take fast and accurate WET measurements and with reduced setup complexity. By simplifying the procedure, the number of personnel able to perform QA increases and the total time decreases.

6 Project Outline

6.1 The Quality Assurance Range Calorimeter (QuARC)

The UCL Proton Beam Therapy group is constructing a prototype for a new detector to be used in range QA. This detector, titled the Quality Assurance Range Calorimeter (QuARC), aims to permit WET measurements of proton range with a single beam. It also seeks to provide a compact enough solution so that the detector can be mounted directly onto the beam nozzle.

The QuARC is a plastic scintillator-based calorimeter focusing on the measurement of particle pencil beam ranges [13]. Scintillating materials fluoresce in response to charged particles or high-energy photons depositing their energy in the material. 49 2—3mm thick plastic scintillator sheets make up the scintillator stack, which is directly coupled to a CMOS sensor, as seen in Fig. 3. This sensor can take a maximum of 21 full resolution images with a total acquisition time of 840ms.

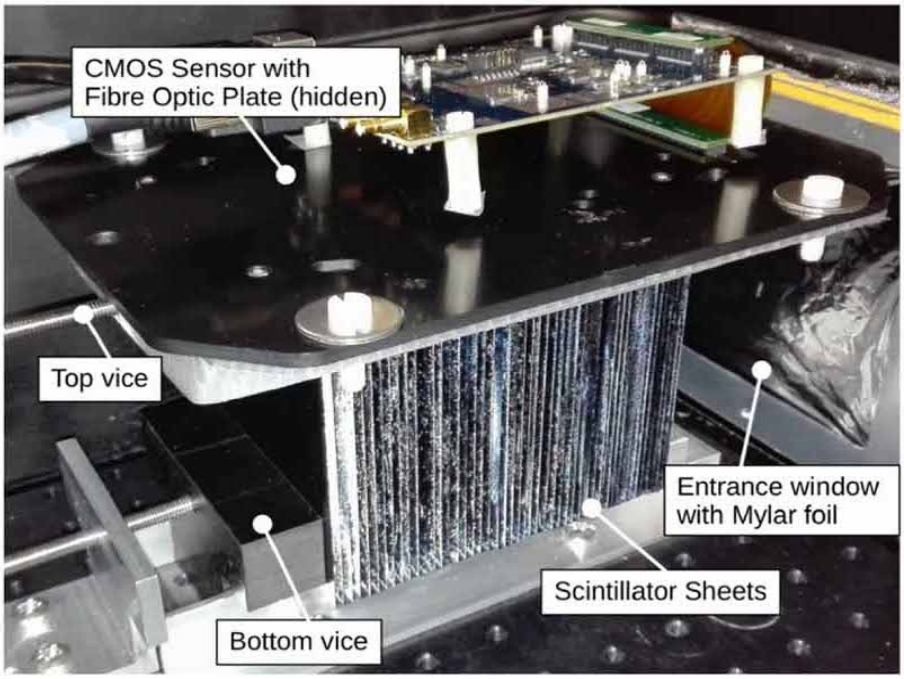

Figure 3: The Prototype range calorimeter with the scintillator stack coupled to a CMOS sensor. The beam direction is perpendicular to the cross-section of the sheets.

The success of the prototype at this stage is evident in recent experimental runs [13], where the proton range was measured with an accuracy of 400μm or better. The detector has demonstrated robust performance against small beam position and size variations, as well as radiation hardness tests.

The UCL PBT group has just begun to upgrade the readout system, due to its fragility when handled and limitations when moving forward with detector modularity. The readout

system is now photodiode based, with each scintillator sheet coupling to a photodiode, allowing the direct measurement of light output in each sheet and the omittance of complex image analysis. An FPGA configures an analogue to digital converter, connected to the photodiodes, and subsequently sends data to a PC.

6.2 Project Goals

October: Literature review. Researching the rationale for PBT and the medical applications of particle accelerators in preparation for the write-up.

November – December: Obtain an understanding of the current detector prototype and readout system. Analysis should be performed for current experimental runs to understand the signal for different operational conditions (including integration time and photodiode model). Understanding of, and practice with the Bragg curve fitting. Improvements for the current C++/ROOT code can be explored.

January – February: A Graphical User Interface (GUI) is to be developed to display the data acquisition process in real time. The core features of the GUI should be live Bragg peak displays, the ability to save experimental runs and commence proton range reconstruction. The possibility of using the GUI to analyse individual photodiode outputs could be explored.

As previously established, it is vital to ensure the complexity of the QA process is reduced, in order to maximise personnel able to perform quality assurance. Reducing the intricacy of QA will allow an increase of patient throughput in particle therapy centres and a web-based GUI will allow user control for all professionals on the local area network. For a more compact solution, a Raspberry Pi can host the display.

March: Culmination of all project work into the form of a final report and presentation.

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