Proton Radiography for Clinical Applications

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Abstract

Proton imaging is not yet applied as a clinical routine, although its advantages have been demonstrated. In the context of quality assurance in proton therapy, proton images can be used to verify the correct positioning of the patient and to control the range of protons. Proton computed tomography (pCT) is a 3D imaging method appropriate for planning and verification of proton radiation treatments, because it allows to evaluate the distributions of proton stopping power within the tissues and can be directly utilized when the patient is in the actual treatment position. The aim of the PRoton IMAging experiment, supported by INFN, and the PRIN 2006 project, supported by MIUR, is to realize a proton computed radiography (pCR) prototype for reconstruction of proton images from a single projection in order to validate the technique with pre-clinical studies and, eventually, to conceive the configuration of a complete pCT system. A preliminary experiment performed at the 250 MeV proton synchrotron of Loma Linda University Medical Center (LLUMC) allowed acquisition of experimental data before the completion of PRIMA project's prototype. In this paper, the results of the LLUMC experiment are reported and the reconstruction of proton images of two phantoms are discussed.

Introduction

Proton radiation therapy is a high-precision form of cancer therapy, and may be considered as the most promising improvement since the introduction of photon and electron radiation therapy. There
has been a steadily increasing interest in proton therapy over the past 10 years. Proton beams can achieve highly localized dose distributions, which should result in higher probabilities for local tumour control and disease-free survival and lower probabilities for normal tissue damage for many different tumour sites. In radiation therapy, the more precise a treatment the more important is its technical quality. Therefore, to fully harness the power of proton radiation therapy, accurate and precise methods of dose calculation, proton range prediction, and verification of the patient position at the time of treatment are mandatory.

Several techniques have been proposed for proton planning and verification like those based on in-beam PET, prompt photons [1,2,3] and proton computed tomography; this paper is focused on the last technique.

At present, proton treatment centres utilize X-ray radiography or cone-beam CT to verify the position of the patient, and dose calculations rely on the patient morphology and electron densities obtained by X-ray CT. The CT Hounsfield numbers are then converted to proton stopping power relative to water using a calibration curve. This conversion can lead to errors in the calculation of proton range in patients of approximately of 5%[4]. For this reason, the advantage of using protons can be reduced in many clinical situations.

A proton imaging device can improve the accuracy in proton radiation therapy treatment planning and in the alignment of the patient with the proton beam, since it can provide images with exactly the same geometrical conditions encountered during the treatment. The idea to use protons for imaging was investigated at the end of the 1960s [5,6], but was abandoned due to the development of X-ray CT and the limiting factors in the quality of the proton images, mostly the inferior spatial resolution. The poor spatial resolution, compared to X-ray images, is due to multiple scattering of protons in the patient, which makes reconstruction along straight lines inaccurate. Moreover, uncertainties in stopping power or electron density arise from energy loss straggling due to the momentum spread of the beam entering the patient, and from proton range straggling in the patient. However, proton-by-proton track reconstruction techniques based on the most likely path concept
promise to improve the spatial resolution of pCR and pCT images. In addition, the measurement of the energy of each proton provides the best possible density resolution.

The first step to develop a pCT device is to construct a proton computed radiography (pCR) apparatus, capable to measure a single projection. The full tomography apparatus requires the rotation of the pCR device and suitable reconstruction algorithms.

Unlike images based on photon detection, proton radiographic images contain information on the range of protons passing through the patient. The energy loss is characterized by the proton stopping powers, which depend on the properties of the traversed materials. Their precise knowledge is essential for radiotherapy treatment planning. Therefore proton radiographs can be used for imaging purposes and treatment verification.

In literature, two different pCR approaches based on single particle tracking can be found. The group at Paul Scherrer Institute (PSI, Villigen, CH) proposed an apparatus made of two scintillating fiber hodoscopes, used to measure the entrance and exit coordinates, and a range telescope consisting of a stack of scintillator tiles [7],[8] to determine the residual range. The "Fondazione TERA" (Novara, I), instead, is developing a similar system with gas electron multipliers as tracking detector [9].

The pCT apparatus originally proposed by the groups at the Santa Cruz Institute of Particle Physics (SCIPP, USA) and Loma Linda University Medical Center (LLUMC, USA), consists of a tracker made of silicon microstrip detectors used to measure the entrance and exit proton coordinates and angles [10],[11]. In addition, a CsI calorimeter provides an independent measurement of proton residual energy [12]. After initial experiments with existing detector hardware, a pCT prototype for imaging head-size objects is now being developed in a collaboration between several U.S. institutions, including SCIPP, LLUMC, Northern Illinois University (NIU), and the Centre of Medical Radiation Physics (CMRP) at the University of Wollongong, Australia [13].

The PRIMA collaboration, (INFN, University of Florence and University of Catania) is developing a pCR prototype based on single proton tracking and calorimetric energy measurement, capable of
acquiring proton events at a 1MHz rate. Similar to the design suggested by SCIPP and LLUMC, this device consists of a silicon microstrip tracker and a calorimeter to detect the residual energy [14]. The development of data analysis and reconstruction algorithms has been initiated by using data coming from previous experiments. In particular, the data from a SCIPP-supported beam test at LLUMC have been considered [15]. The proton images of two phantoms obtained during this beam test are presented and discussed in detail in this paper.

**Materials and methods**

The beam test was performed at one of LLUMC’s proton synchrotron research beam lines with 200 MeV protons. The protons had a negligible energy spread (< 0.2 MeV) and were tracked with silicon strip detectors (SSDs) developed for the 1997 GLAST beam test [16]. A single CsI crystal calorimeter provided residual energy measurements and a trigger for the Si detector system readout. Two silicon detector planes were used as entrance and exit telescopes upstream and downstream the phantom, respectively. Because a single SSD can only record the position of a particle in one dimension, each plane was equipped with two single strip detectors (192 strips), rotated by 90°, in order to get x and y positions of single protons. A single detector module (4.5x×4.5×0.05 cm³) comprised 192 microstrips with a pitch of 236µm obtained by implanting p-type strips in an n-doped bulk. The calorimeter had the size 6.35×6.35×18.5 cm³, with a cross section larger than the silicon modules.

Fig. 1 shows a sketch of the pCR setup used in this beam test. Different configurations were tested with this setup, always keeping two tracking planes at the entrance and at the exit of the phantoms in order to get the position and direction of single protons before and after passing through the phantom object. Here we report the data acquired using two special phantoms designed for density and spatial resolution studies, which were embedded within a stack for homogeneous PMMA slabs,
each measuring 10×5.5×1.25 cm³.

The first phantom was custom-made and suitable for high-contrast spatial resolution studies. It consisted of a PMMA slab with 7 circular cavities with different diameters and thicknesses. In particular, the largest cavity consisted of a 10 mm diameter hole drilled at the centre of the slab. In addition, there were two smaller cavities, 6.25 mm diameter and 6.25 mm deep (half the thickness of a single slab), and four holes of 1mm diameter in each corner of the slab (see Fig. 2, left). An additional silicon strip plane was sandwiched between the drilled slab and the subsequent one to study the effect of 7.5 cm of PMMA on multiple Coulomb scattering. The distances between the Si planes were as follows: 3 cm between p1 and p2, 13.5 cm between p1 and p5, 24 cm between p1 and p3, and 27 cm between p1 and p4 (see fig.1). This arrangement will be indicated as “test configuration A”.

The second phantom was a commercial imaging phantom (QC-3, Masthead Imaging Corporation, Canada) with size 10.5×12×2 cm³, which was originally conceived for density and spatial resolution studies with photons. It consisted of inserts of different density (lead and polyoxymethylene plastic) spaced in close proximity (see Fig. 2, right). Five different regions were present with a minimum spatial frequency of 0.1 lp/mm to a maximum one of 0.7 lp/mm. In this phantom, six regions of lead and Delrin were introduced sideways for noise measurements. Measurements with this phantom were performed using the configuration shown in Fig.3 (test configuration B).

**Results**

Since protons are charged particles, they undergo multiple-Coulomb scattering causing a non-straight trajectory. In order to reconstruct precise images, a correction is therefore needed to take into account the real path traversed. Because of the random nature of this process it is not possible to calculate the precise trajectory of the proton through the target, but just the most likely path...
(MLP) along with a probability envelope. A semi-analytical method to predict the MLP was introduced by Williams [17]. A recent study comparing this method with experimental data and Monte Carlo simulation demonstrated its accuracy [18]. In this work, we used the MLP method to take into account the effect of multiple scattering when reconstructing the radiographic phantom images using the spatial information from the last plane of the tracker and the residual energy from the calorimeter. The images were reconstructed on a 2D grid of pixels consisting of 2×2 strips; the spatial distribution of the proton residual mean energy formed the basis for the image reconstruction.

Fig. 4 shows the phantom image obtained from the raw data obtained with test configuration A; the proton residual energy is plotted versus the proton coordinates in the most distal Si plane. Not surprisingly, the raw data from the last tracking module, obtained without any correction for multiple scattering, are blurred, most of the phantom details are lost, and only the large central hole can be distinguished. The situation is strongly improved when Coulomb scattering is taken into account by back-projecting the proton coordinates on the last tracking plane to the level of the special phantom using the MLP (Fig. 5). In this case, it is possible to distinguish additional details of the phantom, in particular, the two holes above and below the central hole. The smallest holes are hidden by noise, due to insufficient proton histories in the periphery of the phantom.

The thickness sensitivity of the non-corrected image at the level of the last plane is 12% of the total phantom thickness, dominated by the poor spatial resolution. The resolution at the level of the intermediate plane, just downstream the drilled phantom, is 4%. The limiting thickness resolution depends also on the number of proton histories, the overall thickness of the phantom stack, the initial energy and the intrinsic calorimeter resolution, therefore 4% is the maximum resolution we can reach using this experimental set-up. An estimation of the reconstruction errors is shown in Fig. 6. The proton's positions measured on the intermediate module, are compared to the MLP predicted positions at the level of p3 plane. The error histogram of the x-measuring detector has a mean of 0.02 mm and a standard deviation of 0.63mm; the y-measuring detector has a mean of 0.24 mm and
a standard deviation of 0.63mm.

Applying the same procedures to the raw data coming from test configuration B we get an image of the QC3-phantom on the last plane (Fig. 7). Again, the spatial resolution of this image is too poor to be evaluated, while the radiographic image at the level of plane 3 (Fig.8) is of better quality and it is possible to distinguish different regions of the QC3-phantom. Since it is possible to distinguish the region on the left with 0.45 lp/mm, the spatial resolution of the radiography based on MLP reconstruction which takes into account the multiple scattering, is about 1.1 mm.

Conclusions

In the context of quality assurance in proton therapy, proton radiography (pCR) and tomography (pCT) images may be used in the future to improve the range accuracy of proton dose calculations compared to X-ray CT and to verify the correct positioning of the patient. The results of our experiments obtained with 200 MeV protons show that a thickness resolution of at least 4% can be achieved with a PMMA phantom of 15 cm thickness. When using the MLP approach to reconstruct proton images, the spatial resolution obtained with the commercial resolution phantom QC3 was 1.1mm. Our results confirm the validity of the method proposed by D. Williams, which has also been validated using Monte Carlo simulations [18]. It is expected that the pCR apparatus developed within the PRIMA-PRIN06 project, which will be optimized with respect to performance, will start taking data at the end of this year.

Reference


Fig. 1. Sketch of pCR system, in the test configuration A. The telescope (planes p1 to p4), the calorimeter (b) and a phantom (c) are shown. The phantom is composed of 12 PMMA homogeneous slabs, except one as indicated by the gray one. The plane p5 is sandwiched between the drilled slab and the subsequent one. A possible proton trajectory (a) is indicated as an illustration.

Fig. 2. Left: details of the drilled slab of the phantom used in the test configuration A. Right: QC3 phantom realized assembling material of different density. The red square indicates the area covered by the xy plane.

Fig. 3. Sketch of pCR system, in the test configuration B.
**Fig. 4.** Image of the PMMA phantom reconstructed on the last plane of the telescope

**Fig. 5.** Image of the PMMA phantom reconstructed on p5 of the telescope taking account of the multiple scattering.
Fig. 6. Reconstruction error histogram of the x and y measuring detector relative to the test configuration A.

Fig. 7. Image of the QC-3 phantom reconstructed on the last plane of the telescope
Fig. 8 Image of the QC-3 phantom reconstructed on p3 of the telescope taking account of the multiple scattering.