History of proton radiography and tomography

The energy-loss method of proton radiography is the most widely used technique to create proton images. The well-defined range of protons is used to create a high-contrast projection image of the object being radiographed. Variations in density within the patient or phantom affect the energy of the protons that leave it. Protons traversing a region of increased density will lose more energy than otherwise, and will exit the phantom with lower energy. These protons will also have a shorter residual range. By either measuring the energy of the exiting protons or their residual range, one can ‘observe’ the internal increase in density. Because the range of unperturbed protons is so well-defined, a single proton provides a fairly accurate indication of how much the internal density has changed.

Another feature of energetic protons is that their paths are altered by the atomic nuclei in the water. Although the protons are usually deflected a small amount in any single interaction, there are innumerable interactions, which can accumulate to produce a significant change in path. This process, called multiple Coulomb scattering, limits the spatial resolution achievable in proton radiography. For example, multiple Coulomb scattering will cause a pencil beam of 230-MeV protons passing through 30 cm of water to spread to a full-width at half maximum (FWHM) of 14 mm.

One way to reduce this loss of image resolution in proton tomography is to measure the lateral exit position of individual protons and take this position into account in the reconstruction algorithm, which constrains the protons to follow a much narrower curved path through the phantom. Even better is to also measure the direction of the entering and exiting proton, which would further constrain the interior proton path.

Another approach is to employ ions (charged nuclei) instead of protons. Because of their higher mass, these particles are deflected less than protons, thereby significantly improving image resolution. Because their range is even better defined than protons for a given imaging situation, ions can reduce the dose required to achieve a given density resolution relative to protons.

One of the first papers about charged-particle radiography was written by Bélanger and Bélanger in 1959 [1]. They took radiographs of thin slices of tissue, including human specimens, using Po-210 as a source of alpha particles. The 5.3-MeV alphas, with a range of 0.04 g/cm^2 produced exquisite radiographs on fine-grained film, which permitted microscopic examination.

Andreas (Andy) Koehler, who had done numerous physics experiments with the Harvard Cyclotron in Boston [Cambridge, Massachusetts], also performed proton radiography. Among other things he took a proton radiograph of a lamb chop, which became famous because it vividly showed structural details in the tissue that were invisible in the best x-ray radiograph. In the 1970s, Andy Koehler teamed up with William Steward to radiograph human specimens. A physician, Steward had long been interested in proton radiography; he was adept at preparing the human specimens. In a series of experiments performed around 1973, Steward and Koehler radiographed a variety of specimens and showed that proton radiography could be used to visualize soft-tissue anatomy, as well as abnormalities [2–4].

In his famous paper, Allan Cormack [5] demonstrated the feasibility of imaging cross sections of the human body through computed tomography. He suggested that one of the ways to obtain the required projection data would be to measure the energy lost by protons (or heavy ions) after passing through the body. His concept was realized in 1972 when Michael Goitein [6] developed a least-squares reconstruction algorithm and used it to reconstruct a phantom from alpha-particle scan data measured by John T. Lyman and colleagues. Lyman et al. scanned an anthropomorphic chest phantom with an 840-MeV alpha-particle beam at the Lawrence Berkeley Laboratory cyclotron, measuring the energy lost by the alpha particles as they traversed the phantom. The phantom was rather coarsely scanned at 41 lateral positions for each of 19 angles, making the reconstruction problem fairly difficult. Nevertheless, Goitein’s reconstruction was of good quality and showed a clear delineation between the phantom’s soft tissue and lungs and spine.

In another experiment at Berkeley, Kenneth Crowe and his collaborators used a 900-MeV alpha particle beam to scan phantoms and human subjects. A water bath helped to even out the variable thickness of the subject. The positions of the alphas were measured with a multi-wire proportional chamber and their residual range determined with a stack of planar scintillators. They scanned many phantoms, but in 1975, their greatest achievement was to scan a human brain sample with the alpha beam [7]. The reconstruction showed many of the details seen in an x-ray CT scan obtained at the Mayo Clinic with an EMI scanner. They estimated the dose for the alpha scan to be around 50 times lower than for the EMI scan.

Since Allan Cormack had already suggested using protons to perform CT, it was natural that since he lived near the Harvard Cyclotron Lab, he would work with Andy Koehler to conduct a proton CT experiment. In 1976, they measured the energy lost by 158-MeV protons in traversing a circularly symmetric 9.52-cm-diameter Lucite phantom as a function of radius. They showed that density variations as small as 6 mg/cm^3 relative to the average phantom density of 1.17 g/cm^3 were easily seen in the reconstruction [8]. From their graphs, one could tell that the limit of their density resolution was many times smaller than that, perhaps around 0.1%. Thus, their experiment successfully demonstrated that protons could achieve density resolutions far superior to those attained in contemporary commercial x-rays scanners, which was about 1%.

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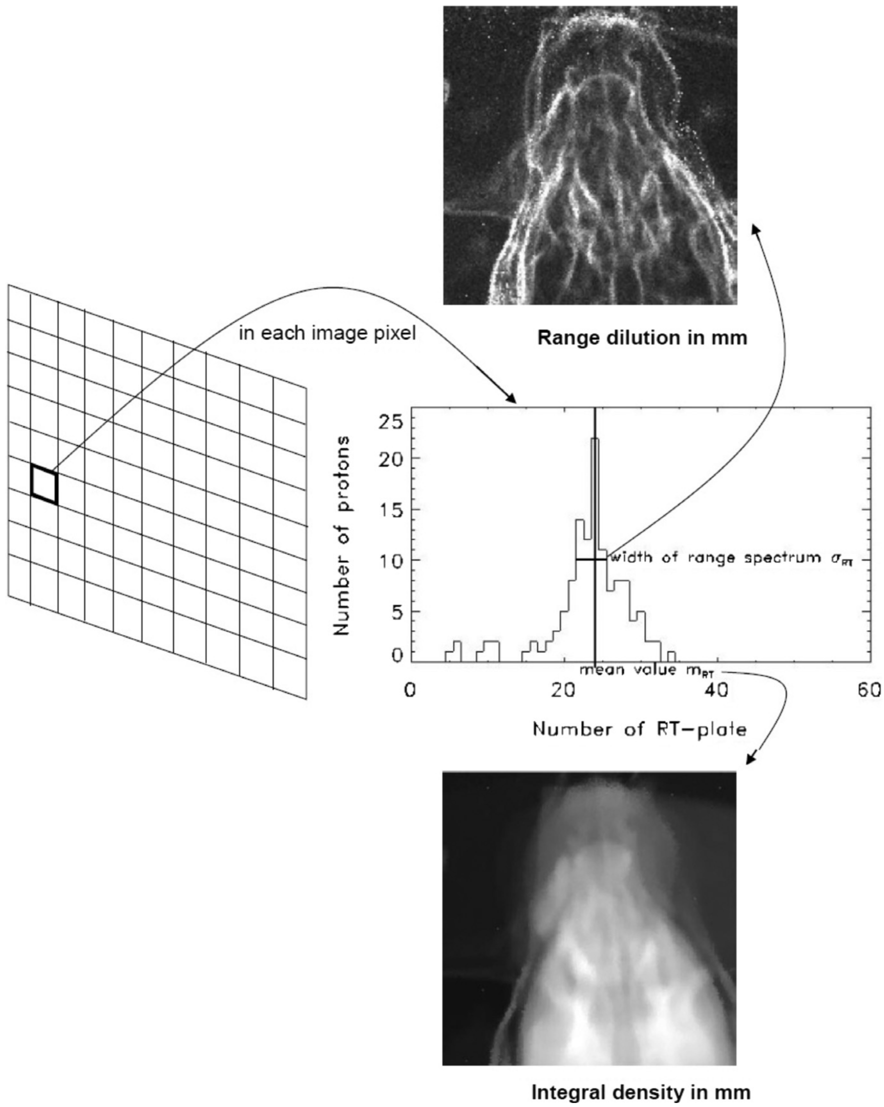

Figure 1. Reduction of the information of the measured proton range spectra to create proton radiographies of a canine patient treated for a nasal tumor with proton therapy at PSI. The bottom image shows the mean range ("density image") and the top image shows the range variations ("range dilution image"). Both images can be used for QA in proton therapy [14].

At the Los Alamos Meson Physics Facility (LAMPF), Kenneth Hanson and his colleagues embarked on a thorough study in 1977 of the technological challenges of bringing proton CT into clinical use [9]. The experiment succeeded in demonstrating the feasibility of full 2D reconstructions with sufficient density resolution to match the capabilities of clinical x-ray scanners for phantoms with diameters up to 30 cm. A second pCT experiment was performed by Hanson *et al.* [10] with the goal to compare high-quality proton and x-ray scans of human specimens. Again, William Steward was on hand to provide specimens. A typical experimental run lasted one hour, during which 60×10^6 protons were recorded. Ken Hanson was able to reconstruct a fixed heart specimen taken from the victim of a heart attack and a brain suspended in gelatine.

Although proton imaging has tremendous advantages over X-ray CT in terms of density resolution and patient dose, proton CT scanners have not been further developed for routine clinical use. The main reasons were the high cost and space requirements for a proton CT scanner. In addition, there was the problem of limited spatial resolution, which could be improved with proton coincidence measurements, but whose technical implementation for fast imaging were anything but trivial. For all these reasons, interest in charged particle imaging died in the early 1980s and was not revived until many new proton-therapy centers began patient operations in the 1990s.

In the beginning of the 1990s, around 10 new facilities started patient treatments, including the first clinical facility in Loma Linda. This success was based on the highly desirable depth-dose distributions for therapy, mainly because the sharp fall-off of dose at the distal end of range can potentially be used to spare critical normal structures just distal to the target volume.

Michael Goitein, working at the Harvard cyclotron, was the first to recognize that charged-particle radiation therapy requires careful attention to be paid to tissue heterogeneities. Whereas heterogeneities of clinical concern alter the dose distributions of photon beams by only a few percent, their influence on charged-particle beams can result in near-zero dose being delivered to parts of the target volume, or to unintended treatment to the full target dose of critical structures distal to the target volume [11].

In the early 1990s, Eros Pedroni at PSI decided to start a feasibility study for the use of proton radiography for detecting such range uncertainties in proton therapy. In contrast to a purely diagnostic use of proton radiography and tomography, its feasibility as a quality assurance tool for proton therapy was evaluated. The first experiments using a proton radiographic set-up for quality control in proton therapy were performed at the Paul Scherrer by Uwe Schneider [12,13]. The aim was to use proton radiographs as verification images to improve the accuracy of each proton treatment. Because of the low dose given with proton radiography or tomography, this can be done for each dose fraction and the resulting radiograph can be used to detect changes in the anatomy during treatment. It can be hence a perfect tool for adaptive proton radiotherapy.

After the reliability of quantitative proton radiography was demonstrated, it was decided to build a proton radiography scanner at PSI, which was mounted on the therapy gantry. With this scanner, the first proton images of a dog subject could be acquired [14]. Dogs with cancer were treated at PSI at that time to optimize the workflow for proton therapy. The Figure 1 (bottom) shows a proton range image of one of the canine patients. The range information can be used to verify the calculated ranges of the treatment planning system. The impact of the tissue heterogeneities on the dose distribution could be quantified also with proton radiography. The width of the range spectra can be used to create a "range dilution image" (Figure 1 at top). Such "range dilution images" can be used to adjust dynamically the necessary safety margins around the target volume and to find the optimal beam directions for therapy.

In summary, the experiments and theoretical work in the 1990s have proven that proton radiography is an excellent tool for quality control in adaptive proton therapy. One major reason why no human patients in the 1990s were imaged with protons is the difficulty of integrating a proton-imaging system into an existing control system designed for therapy. The proton current that is needed for imaging is orders of magnitude lower than for therapy. As all detector systems and safety devices are usually designed for high proton currents in therapy, it is a crucial and difficult task to include low dose-rate imaging into the safety system of a therapy facility and to obtain certification of the authorities for human applications.

After a break of about 20 years, interest in proton tomography has recently rebounded. Various research groups worldwide are again conducting theoretical as well as experimental research. For this reason, this special issue of the "Zeitschrift für Medizinische Physik" reports on the latest activities in the field of proton and ion radiography and tomography.

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