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Review paper

# Review of technologies and procedures of clinical dosimetry for scanned ion beam radiotherapy

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ABSTRACT

In the last few years, the use of ions in radiation therapy is gaining interest and it is being considered medically necessary for a growing subset of tumours. Concurrently, the technologies involved in a particle therapy treatment are rapidly evolving, as well as the accuracy in the dose delivery in spite of the increased complexity.

Since nowadays, the pencil beam scanning technique is showing very interesting features in terms of dose conformation and overall treatment outcome, the present review is intended to summarize the main procedures, detectors and tools adopted for the clinical dose verification. A list of dose measurements is provided, with the aim of being a valuable guidance for starting and future particle therapy facilities.

Absorbed dose to water, relative dose, fluence and surrogates of the delivered dose are the main quantities measured by means of different detectors, specifically developed for point-like, 1D or 2D measurements.

The dosimetric procedures are here categorized according to their purpose, distinguishing between system commissioning and clinical quality assurance. A separate discussion is dedicated to patient specific, in vivo and 4D dose verification, which aim at assessing the actual delivered dose.

Together with the description of the currently used methods, challenges and perspectives toward an increasingly accurate and fast dose verification strategy are discussed.

## 1. Introduction

Any radiation therapy modality aims at delivering the prescribed amount of dose to a tumour, sparing the surrounding tissues as much as possible. To better pursue this goal, charged particle radiation therapy is generally acknowledged to be medically necessary [1], above all, for those tumours close to organs at risk where a high conformality and steep gradients are essential or when resistance to other types of radiation is an issue. Exemplary cases are chordomas, chondrosarcomas [2–7], eye tumours [7–11] as well as treatments where the dose to the healthy tissues must be very limited, such as central nervous system and paediatric tumours [12–15].

At present, proton and carbon ion beams accelerated up to a few hundred MeV/u and delivered with the Pencil Beam Scanning (PBS) technique are showing very interesting performances in terms of dose conformation due to their favourable physical properties [7,16–19]. Moreover, their increased biological effectiveness represents an additional appealing feature of this technique, even though the biological uncertainty is still matter of a large research effort.

Nevertheless, besides these proved benefits, several controversies related to particle therapy outcomes still exist, mainly due to the limited literature in respect to conventional radiation therapy, especially for carbon ions, and to the lack of phase III clinical trials [18–20]. Moreover, from a technical point of view, complex modulated particle dose distributions have important drawbacks such as the increased sensitivity to beam delivery uncertainties [21], pencil beam dose calculation [22–24], patient setup and movement [25,26], range uncertainties [22,27] and dose verification [28,29].

To date, approximately thirty and five facilities are treating patients worldwide using actively scanned proton and carbon ion beams respectively, and these numbers are rapidly growing [30].

In order to assure the safe, effective and consistent radiation delivery, medical physicists have to carry out dedicated and accurate measurements of absorbed dose in several scenarios. The primary quantity used in radiation therapy is the absorbed dose to water ($D_w$) and one goal of dosimetry is a direct determination of the dose delivered in water under reference conditions. In addition, dose measurements under non-reference conditions are mandatory to verify the dose delivered in more realistic as well as more practical experimental conditions. These include the use of tissue equivalent materials rather

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than water, patient-specific fields rather than uniform geometrical fields, and specific measurements for beam characterization, such as longitudinal and transversal dose profiles in air for different beam energies.

Before clinical practice is allowed to start, acceptance tests verify the system performance specifications, and the commissioning is done in order to characterize the beam and the dose delivery capabilities in terms of delivered dose. The results of the commissioning procedures also provide data to optimize the analytical beam model, used by the Treatment Planning System (TPS) and by Monte Carlo (MC) simulation to predict, i.e. to calculate, the dose distributions for the specific beam line setup.

After clinical routine has started, dosimetric Quality Assurance (QA) measurements are periodically performed to verify if the system is delivering the dose properly with respect to its capability and within acceptable tolerances. For example, each morning, before treatments, daily QA is carried out to verify some pencil beam characteristics, such as the range, the position and the size for a subset of the available conditions.

Then, less frequent tests, i.e. monthly and yearly QA, are required to control specific system features such as beam monitor linearity, uniformity and reproducibility, beam contamination and stability of the overall system.

Due to the high sensitivity to planning and delivery uncertainties of the so called intensity modulated particle therapy (IMPT) treatments [22,31], a detailed patient-specific QA program [28,29] is mandatory to perform a pre-treatment verification of each 3D–optimized treatment plan. In addition to the measurements, pre-treatment independent dose calculations and log-files analysis have been recently introduced to improve and speed up the QA procedures [28,32].

Moreover, the efficient use of Graphic Processing Units (GPUs) for PBS dose calculation allows for further optimizations and investigation of both the treatment plan and the delivered doses, e.g. in the case of four-dimensional (4D) treatments optimization [33], time-demanding applications such as patient-specific QA or, looking at the future, online dose reconstruction [34,35].

Among the methods to assess the actual dose delivered to each patient, the in vivo dosimetry [36,37], which exploits the emission of secondary radiation as surrogates of the absorbed dose, is also considered.

This paper is intended to summarize the procedures, detectors and tools adopted for the delivered dose verification in different scenarios concerning scanned ion beam radiotherapy, showing the novelties and considering as reference the previous review by Karger et al. [38].

Section 2 provides a description of the key concepts and an overview of the dosimeters used. Section 3 focuses on the commissioning and the clinical QA, while patient specific QA and 4D-dosimetry are discussed in Sections 4 and 5 respectively.

## 2. Key concepts and detectors

In modulated PBS, narrow pencil beams, coming directly from the beam line, are transported to a specific position inside the patient to achieve elementary depositions of dose [31]. The tumour is covered by the superposition of thousands of different beams, each one delivering a defined number of particles at a defined position, called spot, within the 3D target volume. Therefore, the latter is segmented in several iso-energy slices which in turn are segmented in several spots each irradiated by a proper pencil beam. Beams with different energies penetrate at different depths delivering the particles as planned, to different slices (Fig. 1), while the beam positioning across the transverse plane is obtained by means of two independent scanning dipoles controlled by the dose delivery system [39–41]. The latter manages a bundle of detectors, i.e. beam monitors, placed just in front of the patient to measure the beam fluence, position and lateral size repeatedly in real-time. Therefore, as described in the following, clinical dosimetry includes also measurements to characterize, calibrate and test the beam monitors.

Most of the measurements performed in PBS dosimetry are devoted to single pencil beam characterization. Additionally, uniform monoenergetic 2D-fields and geometrical 3D-fields, usually square and cubes respectively, have to be measured to verify the cumulative dose deriving from the superposition of different pencil beams.

Both the dose distributions and the beams characteristics depend on the optimization methods used in the dose calculation, which is selected among the available choices in the clinical TPS. Briefly, in the single-field uniform dose approach, each field is individually optimized to deliver a uniform dose distribution over the entire target volume. Otherwise, in the multiple-field optimization, generally referred to as Intensity Modulated Particle Therapy (IMPT) [22,31], the spot weights and positions are simultaneously optimized for all the fields to produce the desired dose distribution. As a result, the single IMPT fields often show a highly inhomogeneous dose distribution, which increases the complexity of the verification measurements and demand higher detector performance due to the presence of steep dose gradients. Moreover, with the quasi-discrete scanning technique in which the beam is not turned off between consecutive iso-energy spots, the accuracy of the delivered dose also depend on the adopted scanning path optimization [42,43].

This review mainly focuses on the dosimetry for IMPT.

Among the available dosimeters, we can distinguish the detectors for beam monitoring from the independent ones used on the patient table, which measurements depend on the beam monitor performance.

A brief overview of the beam monitors is following in Section 2.1 while the different detectors available for dosimetry are described in Section 2.2.

### 2.1. Beam monitors

The detectors for beam monitoring have the crucial role of continuously measuring the number of particles and their transversal distribution, in order to guide the irradiation and correcting or interrupting it in case the values exceed the clinical tolerances. In particular, the beam monitors have the tasks of measuring:

- number of particles, i.e. integrated beam flux, often expressed in terms of monitor units (MU);
- transversal beam position, i.e. Centre Of Gravity (COG);
- transversal beam size, i.e. Full Width at Half Maximum (FWHM).

Arrays of parallel plate ionization chambers, with either a single large electrode or electrodes segmented in strips or pixels [44–47], together with multi wire ionization chambers [48–50] are the most widely adopted detectors for beam monitoring of PBS technique.

The goal of each beam flux monitor is to ensure a charge collection efficiency greater than 99%. Due to various recombination effects, the relation between the number of particles and the signal of the ionization chamber may not be linear; therefore, the monitor chambers have to be calibrated [48,51,52] during the commissioning phase. Then, as part of the clinical QA, the calibration factors are periodically verified [48,53].Variations of the daily factor below 2% are not taken into account since the effect on delivered dose is negligible to achieve a ± 5% accuracy in the absolute dose [48].

The beam position monitors are characterized by 1.5–5 mm strips/wires pitch aiming a spatial resolution within 0.3 mm. The time requirements depend on the beam intensity and pencil beam weights, which determines the dose rate and the time spent by the beam in each single spot. For a review of the procedures for beam monitors calibration and QA, see Section 3.4.

In the existing beam monitors, the charge corresponding to a count,