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The impact of breathing amplitude on dose homogeneity in intensity modulated proton therapy

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ABSTRACT

Background/purpose: Intensity-modulated proton therapy (IMPT) dose distributions can be severely degraded in targets moving with respiration due to the interplay, range and blurring effects. In this study we investigated the joint and disentangled impact of these effects as a function of the motion amplitudes.
Materials/methods: Single-fraction time-resolved proton treatment delivery was simulated using an in-house developed 4D-motion simulation platform. The respiratory induced anatomical changes were described by deformation vector fields (DVF) derived from 4D-Computed Tomography (4D-CT) scans scaled to different motion amplitudes. Based on the individual spots exported from IMPT plans for 10 lung cancer patients, three dose distributions with different combinations of motion effects were generated. The doses were subtracted from each other to study the separated impact of individual effects over the planning target volume (PTV). The results were evaluated using univariate and multivariate regression models including amplitude, tumour size and location.
Results: The interplay effect led to an average dose error of 7% for motion amplitude of 20 mm, whereas range and blurring effects were smaller at 2.6% and 2.5%, respectively. These effects increased linear-quadratically with amplitude and were significantly associated with tumour volume or location.
Conclusion: Single-fraction dose variations due to interplay effects dominate other respiratory-induced variations for a large range of motion amplitudes.

1. Introduction

Proton therapy delivers highly conformal dose to the target, while sparing the surrounding normal tissues and outperforms photon therapy in the intermediate and low dose levels [1]. Pencil Beam Scanning (PBS) is currently the most advanced technique, capable of delivering Intensity Modulated Proton Therapy (IMPT) [2–4]. An IMPT plan consists of different energy layers covering the target from distal to proximal side which are populated with a variable number of spots. Each spot has a weight that determines how many protons should be delivered at that position. The plan is delivered by a narrow pencil beams, scanning at these spot positions laterally to the beam direction by magnetic deflection and longitudinally on each layer by adjustment of the beam energy. The delivery process requires time for settling of the magnets, delivering the protons and energy adjustment.

The use of the PBS technique in thoracic and upper abdominal regions is challenging, as the targets move with respiration, affecting the dose delivery [5]. Besides the dose blurring effect caused by target motion perpendicular to the beam direction which is well described for photon therapy [6,7], the finite range of the protons makes them highly sensitive to density changes along the beam path over the respiratory cycle. In addition, target motion relative to the pencil beams setting causes interplay effects further degrading the delivered dose distributions [8–11] .

The impact of motion effects has been evaluated in several studies [5,8,9] demonstrating that dose uniformity depends more on the amplitude than other parameters of tumour motion. Lambert et al. [8] concluded that the PBS technique should not be used for targets that have motion amplitudes bigger than 1cm. Newer study demonstrated that PBS might be used for motion up to 2cm if delivered with bigger spot sizes [10]. Both studies [8,10] were based one original motion amplitude per patient. Although all previous studies reported the impact of interplay effects they

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actually studied the combined impact of blur, range and interplay effects since they were not separated.

The purpose of this study was therefore to disentangle respiratory motion effects in lung cancer IMPT into its three components and quantify their amplitude dependence. To that end, a motion simulation platform was developed which estimated the dose deposition of individual proton spots while respiratory motion takes place. A wide range of amplitudes was modelled in each patient anatomy. This relationship between amplitude and motion effects was assessed to derive rules of thumb for the necessity of different motion compensation strategies.

2. Materials and methods

We used the following CT data sets: Mid-Position CT (MidP-CT) scan for treatment planning and synthetic-phase-CT (SynPhCT) scans to simulate the different motion amplitudes in patient geometries. The SynPhCT scans were generated from 4D-Computed Tomography (4D-CT) scans by scaling the original deformation vector fields (DVFs) with the motion amplitudes up to 3cm cranio-caudal (CC) peak-to-peak amplitude of the GTV. The original DVFs describe deformation of the MidP-CT scan over the respiratory cycle (10-phase 4D-CT) [12].

2.1. Patients and treatment planning

Ten Non-Small-Cell-Lung-cancer patients with primary tumours with peak-to-peak amplitude exceeding 1cm on the 4D-CT were included in this study (Table S.1). The lymph nodes were not studied here for simplicity as their motion is not always in the phase with the primary tumour [13,14].

To characterize the tumours, the planning target volume (PTV) (123-1239cc), CC position and depth were calculated. The CC tumour position (0.41–0.78) was calculated from the CC distance of the centre of the mass in the tumour volume (GTV) to the diaphragm normalized to the length of the lung. The tumour depth (6.2–15.4 cm) was measured along the beam path from the thorax to the centre of mass for both beams and the mean value was calculated.

IMPT plans were optimized in Pinnacle^3 research version 9.100 (Philips, Best, the Netherlands) on the MidP-CT scan for each patient. We used two co-planar beams and an internal gross tumour volume (IGTV) override [15] with the density of water. Ideally a different IGTV and corresponding IMPT plan should be generated for each of the motion amplitudes. However, to manage the workload we only performed a single IGTV expansion (15 mm in CC direction) for each patient. Plans were designed to deliver 95% of the 66 Gy-prescribed doses to 99% of the PTV in fractions of 2.75 Gy. Details of our treatment planning technique are described in the Supplementary material S1.

As the IGTV doesn't exist in reality, the treatment plan was recalculated on the MidP-CT without IGTV override. Then, the 3D dose distribution of each individual proton spot was exported using a customized plug-in and was used as an input planned dose in our motion simulation platform.

2.2. 4D-motion simulation platform

Dose re-calculation on 10 different SynPhCT sets combined with the motion effects (interplay, range and blur) for a range of amplitudes in a treatment planning system (TPS) is a time consuming process. Therefore we developed a 4D-motion simulation platform to estimate the impact of respiratory motion on IMPT plans. It has three main components: 1) spot delivery timing estimation, 2) spot dose range correction and 3) deformation & accumulation (Fig. 1).

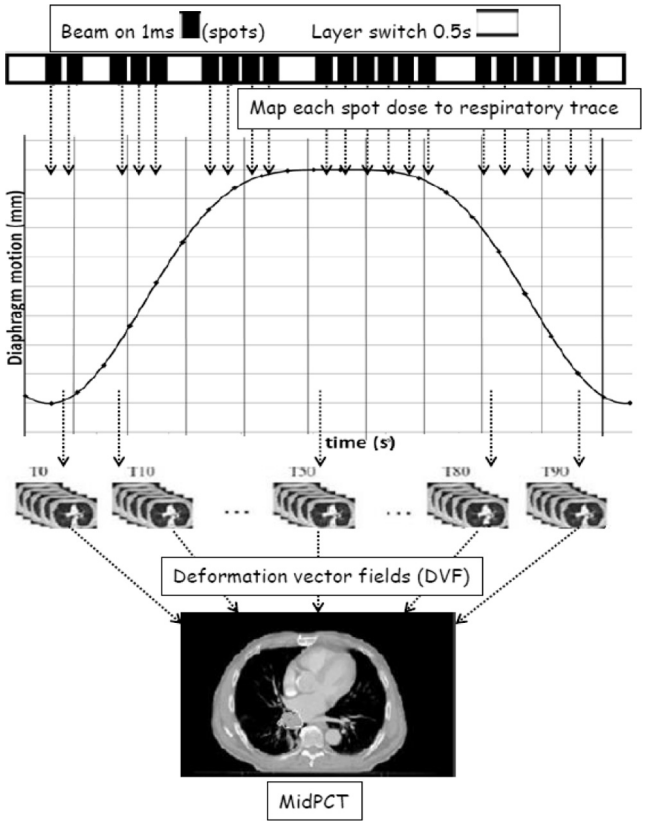

Fig. 1. Schematic overview of the 4D-Motion simulation platform. Each breathing cycle is separated into 10 phases and according to the time stamp the spots are range corrected considering the anatomy of a particular phase and deformed & accumulated back to MidPCT reference anatomy as exemplified by the arrows.

1. For estimation of spot delivery timing we used a periodic respiratory trace (T = 4 s) generated in MATLAB Release 2016a (The Math Works, Inc., Natick, MA). Each cycle was separated into 10 phases (each 400 ms) and linked with the corresponding phase from the 10 SynPhCT sets explained above. We simulated plan delivery based on the timings of a Pronova SC360 proton therapy system (Pronova Solutions, Maryville, TN, USA): for longitudinal scanning 0.5 s to switch the energy layer; for lateral scanning 1 ms to settle the magnets and varying spot delivery time (typically 1–5 ms; see Supplementary material S2 for details) depending on the number of protons per spot. Previous studies also demonstrated that the starting respiratory phase during treatment has significant impact on the observed interplay effect [9,16–18]. To address this issue the mid-starting phase that was closest to the average interplay effect per patient was chosen for the remainder of the analysis (see Supplementary material S3 for details).
2. Spot dose distributions were range corrected for a density changes in the beam path for each SynPhCT. The effect of density changes on proton spot dose distributions was approximated using a water equivalent path length (WEPL) strategy [19,20] (see Supplementary materials S4 for details). To estimate the error introduced by the WEPL assumptions used in our motion simulation platform we compared the dose calculated using our platform for a motion amplitude of 3cm (as a worst case), with the corresponding dose recalculated in the TPS for all 10 patients.
3. Finally, spot doses of each phase were deformed and accumulated onto the reference MidP-CT anatomy.