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Impact of physiological breathing motion for breast cancer radiotherapy with proton beam scanning – An *in silico* study

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ABSTRACT

This study investigates the impact of breathing motion on proton breast treatment plans. Twelve patients with CT datasets acquired during breath-hold-at-inhalation (BHI), breath-hold-at-exhalation (BHE) and in free-breathing (FB) were included in the study. Proton plans were designed for the left breast for BHI and subsequently recalculated for BHE or designed for FB and recalculated for the extreme breath-hold phases. The plans were compared from the point of view of their target coverage and doses to organs-at-risk. The median amplitude of breathing motion determined from the positions of the sternum was 4.7 mm (range 0.5–14.6 mm). Breathing motion led to a degradation of the dose coverage of the target (heterogeneity index increased from 4–7% to 8–11%), but the degraded values of the dosimetric parameters of interest fulfilled the clinical criteria for plan acceptance. Exhalation decreased the lung burden [average dose 3.1–4.5 Gy (RBE)], while inhalation increased it [average dose 5.8–6.8 Gy (RBE)]. The individual values depended on the field arrangement. Smaller differences were seen for the heart [average dose 0.1–0.2 Gy (RBE)] and the LAD [1.9–4.6 Gy (RBE)]. Weak correlations were generally found between changes in dosimetric parameters and respiratory motion. The differences between dosimetric parameters for various breathing phases were small and their expected clinical impact is consequently quite small. The results indicated that the dosimetric parameters of the plans corresponding to the extreme breathing phases are little affected by breathing motion, thus suggesting that this motion might have little impact for the chosen beam orientations with scanned proton beams.

1. Introduction

The favourable potential of protons resulting from finite range and practically zero dose deposition beyond the Bragg peak has made this radiation modality an interesting candidate to reduce the radiation burden and hence the risk of complications from radiation therapy. This is quite relevant for breast cancer patients where radiotherapy has been shown to improve local control and overall survival [1], increasing the concern for late cardiopulmonary toxicity in long-term survivors. Several studies have investigated the potential of scanned proton beams for breast radiation therapy showing that the technique could increase target conformity and thus reduce doses to the normal tissues of interest [2–6]. The finite range of protons and the strong dependence of their interaction properties to the medium make proton dose distributions quite sensitive to physiological motion raising concerns regarding the impact of breathing on the dose distributions [7].

Motion management techniques are available including abdominal compression and respiratory gating, but they are not universally suited to breast cancer patients. Thus, abdominal compression could reduce motion, but might increase interfractional variations and could also limit some beam directions [8]. Similarly, gating, either as enhanced inspiration gating (EIG) or as deep inspiration breath hold (DIBH), could help maintain a fixed geometry relative to the beam and could also reduce the doses to organs-at-risk (OARs), but not all patients comply with or are suitable for the gating procedure [5,9,10]. An alternative to reducing motion amplitude is to investigate whether the changes in dose distributions caused by breathing are likely to have a clinical impact. Little information exists on this topic, with few studies

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investigating the changes in proton dose distribution resulting from simulated breathing motion in breast patients [12,11]. The present study therefore aims to add to the existing knowledge by investigating the impact of breathing on dose distributions for breast cancer radiotherapy with scanned proton beams.

2. Methods and materials

The study population consisted of twelve thoracic patients in a body immobilisation system with abdominal compression, who were imaged on a computed tomograph (CT) in three breathing modes: breath-hold-at-inhalation (BHI), breath-hold-at-exhalation (BHE) and free-breathing (FB). The CT image sets were acquired without contrast, using 2 mm slice thickness, with the patients in head-first-supine position with both arms placed above the head. Targets and OARs were delineated on each CT dataset by an experienced radiation oncologist according to RTOG guidelines. The PTV was defined from the referenced clinical left breast at time of CT, including the apparent CT glandular breast tissue and a margin of minimum of 10 mm, but cropped 5 mm from the skin surface. The lungs, heart and LAD were defined as OARs and when necessary their delineation was based on linear interpolation between adjacent slices. This approach led to three datasets available for each patient, one for each breathing mode.

Each patient was first planned in the Eclipse treatment planning system (Varian Medical Systems) with proton scanned pencil beam on the BHI dataset, using either one field-techniques with fields at 0° or 45° or with single field uniform dose (SFUD) and intensity modulated proton therapy (IMPT) with a previously described three-field technique with beam angles 20°, 60° and 340° [4,5]. A relative biological effectiveness (RBE) of 1.1 was assumed for protons [12]. The plans were normalised to 50 Gy (RBE) in 25 fractions as mean dose to the PTV. The plans were subsequently calculated on the corresponding BHE datasets to investigate the impact of the full breathing amplitude on the proton dose distribution. Similarly, the patients were also first planned on the FB datasets, and changes in dose distributions were evaluated by recalculating the plans for BHI and BHE CT datasets to investigate the impact of breathing motion relative to FB mode.

The resulting treatments plans were compared in terms of dosimetric parameters representative for the target [13] and the OARs of interest [14,15]. The planning target volume (PTV) receiving at least 95% of the prescribed dose ($V_{95\%}$) or 93% ($V_{93\%}$), as well as the heterogeneity index (*HI*) defined as:

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{mean}}$$

where $D_{2\%}$ (the dose to 2% of the volume) is the near maximum dose, $D_{98\%}$ (the dose to 98% of the volume) is the near minimum dose and D_{mean} is the mean dose to the PTV, were used to quantify target coverage and uniformity. The statistical significance of the difference in parameters was tested with a paired, two tailed Student *t*-test.

As the patients were imaged in a body immobilisation system with abdominal compression, the amplitude of their breathing motion was determined from the positions of the sternum at the mid-level of the breasts. The analysis showed that the sternum moved between 0.5 and 14.6 mm, with a median value of 4.7 mm. This value is comparable with the amplitudes of the breathing motions found in free breathing patients in other studies [16,17] and indicates that the CT datasets used are representative for normally breathing patients. Correlations were also sought between the amplitude of breathing motions and changes in dosimetric parameters of interest.

3. Results

Changes in patient anatomy and the associated changes in dose distribution with breathing motion are illustrated in Figs. 1 and 2 for one of the patients included in the study planned on the BHI dataset and FB dataset respectively. Thus, breathing appears to change the dose distributions in and around the ipsilateral lung, the heart and the LAD. One of the most visually striking features is the variation of the dose to the lung that increases in BHI and decreases in BHE. For small separations between the PTV and the lung, the extension of the distal part of the spread-out Bragg peak (SOBP) into the lung causes a dose spill corresponding to the soft tissue equivalent length of the less dense lung tissue. Thus, as the density of the lung decreases at inhalation, the penetration increases, while the opposite effect happens at exhalation.

Changes in the dosimetric parameters considered are presented in Tables 1–4. Breathing decreased the near minimum dose ($D_{98\%}$) to the PTV from 48–49 Gy (RBE) to 46–47 Gy (RBE), as well as the $V_{95\%}$ that decreased from 99–100% to 96–98%, depending on the planning approach use (Tables 1 and 3). The P-values of Student's *t*-tests for the differences were less than 0.04 in all cases with the exception of the FB-BHE comparison for one field at 45° and three-field SFUD. The heterogeneity index (HI) also increased from 4–6% to about 8–11% at the extremes of the breathing cycle with statistically significant differences (P-values of Student's *t*-test less than 0.04 in all cases with the only exception of the FB-BHE comparison). The mean dose to the target was also affected, but the magnitude of the change depended upon the planning approach used.

Breathing motion also affected the doses to the OAR. Thus, exhaling decreased the dose burden to the ipsilateral lung, while

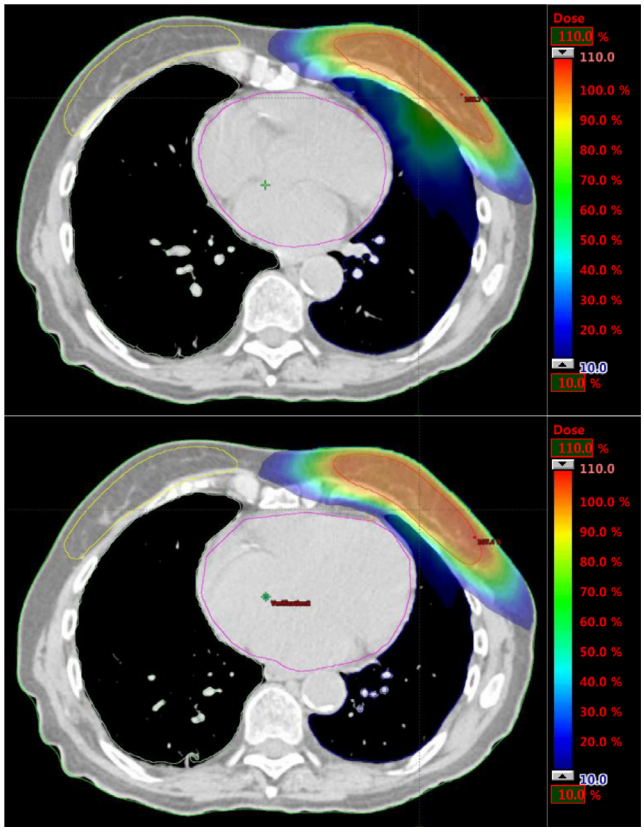

Fig. 1. Breathing induced changes in the dose distributions of the three-field IMPT plans in one patient planned on the BHI dataset (upper panel) and recalculated on the BHE dataset (lower panel). The PTV is delineated in red. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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