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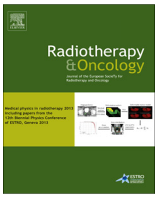

Adaptive radiotherapy

Adaptive radiotherapy with an average anatomy model: Evaluation and quantification of residual deformations in head and neck cancer patients

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ABSTRACT

Background and purpose: To develop and validate an adaptive intervention strategy for radiotherapy of head-and-neck cancer that accounts for systematic deformations by modifying the planning-CT (pCT) to the average misalignments in daily cone beam CT (CBCT) measured with deformable registration (DR).
Methods and materials: Daily CBCT scans (808 scans) for 25 patients were retrospectively registered to the pCT with B-spline DR. The average deformation vector field (<DVF>) was used to deform the pCT for adaptive intervention. Two strategies were simulated: single intervention after 10 fractions and weekly intervention with an <DVF> from the previous week.

Methods and materials: The model was geometrically validated with the residual misalignment of anatomical landmarks both on bony-anatomy (BA; automatically generated) and soft-tissue (ST; manually identified).
Results: Systematic deformations were 2.5/3.4 mm vector length (BA/ST). Single intervention reduced deformations to 1.5/2.7 mm (BA/ST). Weekly intervention resulted in 1.0/2.2 mm (BA/ST) and accounted better for progressive changes. 15 patients had average systematic deformations >2 mm (BA): reductions were 1.1/1.9 mm (single/weekly BA). ST improvements were underestimated due to observer and registration variability.
Conclusions: Adaptive intervention with a pCT modified to the average anatomy during treatment successfully reduces systematic deformations. The improved accuracy could possibly be exploited in margin reduction and/or dose escalation.

Intensity modulated radiotherapy (IMRT) has been widely adopted for the irradiation of head-and-neck cancer (HNC) patients. The highly conformal dose distributions offer superior sparing of organs-at-risk (OARs) while malignant tissue is optimally irradiated [1]. Moreover IMRT has been used for dose escalation to clinically demonstrated areas of radioresistant hypoxia [2].

Practically, the benefits of IMRT are limited by the accuracy with which the anatomy of the patient from the planning-CT (pCT) can be reproduced during treatment. Small misalignments, random or systematic, resulting from patient setup, posture or anatomy changes, can significantly influence the position and shape of the dose distribution delivered to the patient. To account for these geometrical uncertainties safety margins are applied [3]. A reduction of geometrical uncertainties allows smaller margins and may increase the therapeutic ratio. With image guided radiation therapy, patient setup errors can be determined and corrected with an opposite shift of the treatment couch. Daily imaging allows for near-perfect correction of patient setup errors, while with a limited amount of imaging the systematic component can be estimated and minimized with an offline correction protocol [4]. Anatomy and posture changes however, are non-rigid and therefore require a different approach.

With adaptive radiotherapy (ART) the treatment plan is adjusted to account for changes in anatomy and posture (deformations). At present, adaptive radiotherapy for HNC mainly deals with treatment response (progressive changes), such as weight loss or tumor shrinkage [5–7]. Therefore a properly timed repeat CT-scan (rCT) during treatment is a suitable basis for plan adaptation to account for treatment response. On the other hand, substantial systematic deformations, up to 3.5 mm, are present with HNC patients, despite extensive immobilization [8–10]. A rCT-scan is a snapshot of the patient's anatomy, subject to random deformations. By freezing an arbitrary pose of the patient, (new) systematic deformations are introduced that cannot be corrected with a couch shift. A rCT-scan is therefore inappropriate to correct systematic posture misalignments [7].

We propose a new adaptive strategy to reduce systematic deformations by modifying the pCT to the average anatomy (AA)

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observed in a repetitive imaging series during the initial fractions of radiotherapy as estimated with deformable registration (DR): the AA-model. Cone beam CT often provides such a repetitive imaging series as it is routinely acquired for patient position verification. Although CBCT image quality is typically somewhat lower than fan-beam CT, considerable improvements have been achieved in recent years (e.g. scatter correction [11,12]) and reconstruction (e.g. compressed sensing [13]). Moreover, various publications demonstrated that for the head-and-neck region current CBCT image quality is adequate for deformable image registration [14,15], dose recalculation in CBCT-scans [16,17], contour propagation to the CBCT [18,19], dose remapping [20], and adaptive replanning [21]. In this study we evaluated a CBCT based AA-model to account for systematic deformations and quantified the reduction in geometrical uncertainties on anatomical landmarks for various adaptive approaches.

Materials and methods

Patient data

Twenty five HNC patients were retrospectively selected. Regular IMRT planning had been performed on a planning CT (Somatom Sensation Open, Siemens AG, Erlangen, Germany) with an in-plane voxel size of 1×1 mm^2 and slice distance of 3 mm. Daily CBCT-scans (Elekta Synergy, Elekta Oncology Systems Ltd., Crawley, UK) were available (33 median, range 21–35), reconstructed at a voxel size of 1 mm^3. Patients were immobilized with a 5 point thermoplastic mask and positioned with a knee support and a standard head-rest (Civco Medical Solutions, Kolona, USA).

Adaptive treatment modification with an AA-model

In the AA-model we describe the local misalignment at position $\mathbf{r}$ and fraction f by $u_f(\mathbf{r})$. The complete set of displacement vectors for a particular fraction is called the deformation vector field (DVF). In this study we determined the DVF with CT-to-CBCT deformable registration (DR).

As with conventional patient setup [3], a series of local misalignments contains a systematic and a random component, quantified by the average and the standard deviation respectively. Consequently we estimated systematic deformations in a series of N fractions with the average local misalignment:

$$\langle u(\mathbf{r})\rangle = \frac{1}{N+1}\sum_{f=1}^{N} u_f(\mathbf{r}) \tag{1}$$

Extending this to all positions is equal to averaging the deformation vector fields: <DVF>. We divided by $N + 1$ since the pCT is also considered a sample of the random position of the anatomy.

For adaptive treatment modification, we applied the <DVF> to the pCT to propagate the local systematic misalignments and thereby generated a sharply defined mCT in which the systematic deformations were eliminated (Fig. 1). Note that the technique to generate a new CT-scan from a set of DVFs is already clinically practiced for treatment planning of lung cancer patients where the mid-position anatomy is derived from all phases of a 4D-CT [22].

Discrepancies in the remainder of the treatment are due to (1) imprecise measurements of the local misalignments, (2) residual uncertainties in the estimation of the systematic local misalignments (limited statistical power in estimating the mean value of a distribution), and/or (3) progressive changes (a non-stationary distribution).

Treatment simulation

To quantify the geometrical accuracy with which the patient anatomy is reproduced during treatment, we started by defining a set of atlas-based landmarks in the pCT. Subsequently, these landmarks were identified in the daily CBCT-scans (see below). As baseline geometrical accuracy, we calculated the residual landmark misalignment (CBCT minus pCT position) after online couch shift corrections (referenced further by shift corrections). Next we simulated two possible adaptive approaches with the AA-model: single intervention and weekly intervention. The simulation was performed as follows: upon an intervention we repositioned the landmarks in the pCT according to the displacements from the AA-model. Next, the residual landmark misalignments for the remaining fractions after the intervention were calculated by subtracting this new position from the CBCT position. Simulations did not require actual replanning and were thus independent of a planning technique. With weekly interventions, we hypothesized that we could better follow progressive changes than a single intervention protocol. In addition, we simulated a regular repeat CT intervention by repositioning the pCT landmarks according to the deformations of a single fraction. Finally, to quantify the optimal achievable performance given the finite accuracy of landmark identification and deformable image registration, we calculated the AA from all fractions and determined the residual systematic misalignments over all fractions relative to this AA (validation series).

Anatomical landmark definition and identification

The proposed protocols were validated with the residual misalignments of clearly identifiable, atlas-based, landmarks on bony anatomy (BA) and soft tissue (ST). Per patient 47 BA landmarks were defined on 12 bony structures (collected in 4 groups) in the pCT. The high contrast of the BA landmarks allowed the use of an automatic method to define these landmarks in the pCT and identify them in all available fractions with sub-millimeter precision [23]. Additionally, 14 ST landmarks were defined on the planning CT for 11 patients by an expert research technologist. Two observers independently identified these landmarks in weekly CBCT-scans. With two observers quantification of observer variability was possible (see below). ST Landmarks describing similar anatomical structures were taken together into 9 subgroups. More details on landmark definition and identification can be found in the supplement in the online version.

Deformable registration

Non-rigid registration was performed with in-house developed software, applying B-spline deformations as described by Rueckert et al. [24], Mattes et al. [25] and Kybic and Unser [26] with correlation ratio [27] as cost function and regularization terms [28] to cope with limited CBCT quality. The registration was performed after setup corrections, in the frame of reference of the pCT with a region of interest encompassing the anatomical landmarks. A 5 step coarse-to-fine multi-resolution approach was applied with a final B-spline control grid spacing of 1 cm. The BSpline control point positions were optimized with a gradient descent method with feedback step size adjustment [26]. Quantifying the precision of our B-spline DR implementation was part of this study.

Observer and registration variability

Observer and registration variability influence the landmark identification and may increase the residual errors in the simulations. We distinguish accuracy (average of repeated