Radiotherapy and Oncology 110 (2014) 529–537

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Lung cancer RT

Validation of the mid-position strategy for lung tumors in helical TomoTherapy

Marie Wanet [a], Edmond Sterpin [a], Guillaume Janssens [a], Antoine Delor [b], John Aldo Lee [a], Xavier Geets [a,b,*]

[a] Center of Molecular Imaging, Radiotherapy and Oncology, Institut de recherche expérimentale et clinique, Université catholique de Louvain; and [b] Department of Radiation Oncology, Cliniques universitaires Saint-Luc, Brussels, Belgium

ARTICLE INFO

Article history:
Received 6 August 2013
Received in revised form 18 October 2013
Accepted 20 October 2013
Available online 11 January 2014

Keywords:
Lung cancer
Tumor motion
TomoTherapy
Monte Carlo simulation
Geometric uncertainties

ABSTRACT

Purpose: To compare the mid-position (MidP) strategy to the conventional internal target volume (ITV) for lung tumor management in helical TomoTherapy, using 4D Monte Carlo (MC) plan simulations.
Materials and methods: For NSCLC patients treated by SBRT ($n = 8$) or SIB-IMRT ($n = 7$), target volumes and OARs were delineated on a contrast-enhanced CT, while 4D-CT was used to generate either ITV or MidP volumes with deformable registrations. PTV margins were added. Conformity indexes, volumetric and dosimetric parameters were compared for both strategies. Dose distributions were also computed using a 4D MC model (TomoPen) to assess how intra-fraction tumor motion affects tumor coverage, with and without interplay effect.
Results: PTVs derived from MidP were on average 1.2 times smaller than those from ITV, leading to lower doses to OARs. Planned dose conformity to TVs was similar for both strategies.
4D MC computation showed that ITV ensured adequate TV coverage (D_{95} within 1% of clinical requirements), while MidP failed in 3 patients of the SBRT group (D_{95} to the TV lowered by 4.35%, 2.16% and 2.61%) due to interplay effect in one case and to breathing motion alone in the others.
Conclusions: Compared to the ITV, the MidP significantly reduced PTV and doses to OARs. MidP is safe for helical delivery except for very small tumors (<5 cc) with large-amplitude motion (>10 mm) where the ITV might remain the most adequate approach.
 Radiotherapy and Oncology 110 (2014) 529–537

Helical TomoTherapy is an appealing irradiation modality to treat unresectable locally advanced stage II–III as well as inoperable stage I non-small cell lung cancer (NSCLC) patients. Indeed, it combines an advanced technique of intensity-modulated radiation therapy (IMRT), leading to highly conformal dose distributions, with an accurate imaging device for patient positioning, based on megavoltage computed tomography (MVCT). These features allow target volumes to be irradiated with sharp dose gradient, and thus help deliver high dose while sparing healthy surrounding tissues.

However, tumor motion caused by breathing may jeopardize treatment quality. In that regard, on-line management of respiratory tumor motion requires dedicated methodologies and techniques, like breath hold, gating [1], or tracking [2], which are not yet available in TomoTherapy systems [3]. Thus, treatment plan robustness against breathing motion still relies on the definition of specific volumes, like an internal target volume (ITV) or the mid-position (MidP), which are expanded with safety margins.

The ITV approach is widely used in clinical practice [4–6]. The ITV encompasses all tumor positions during the breathing cycle and can be determined from a four-dimensional computed tomography (4D-CT). A planning study with four-dimensional (4D) Monte Carlo (MC) has demonstrated that an expanded ITV can be safely applied in TomoTherapy [3]. In particular, interplay effect between beam and tumor motions did not significantly affect the delivered dose distributions. However, the ITV approach is known to overestimate the safety margins, and thus may lead to unnecessary irradiation of healthy tissues [7,8].

The MidP, on the other hand, involves a volume that corresponds to the time-weighted mean position of target volumes during the breathing cycle [8]. This approach provides several theoretical advantages over the ITV and partly overcome the issues encountered with the ITV. First, by using a 4D-CT, it eliminates the systematic error that would otherwise occur with a fast 3D CT that is merely a snapshot at some point of the respiratory cycle, possibly polluted by artifacts. In contrast with the ITV approach, the random uncertainty about tumor motion is added in quadrature to the other random geometric uncertainties in the formula for the Planning Target Volume (PTV) margin calculation proposed by van Herk et al. [9]. As a result, this approach allows the margins to be significantly smaller and therefore comparable to those obtained with gated radiotherapy [8]. Furthermore, the MidP approach allows the treatment planning and delivery workflow to remain the same as in other approaches based on margins.

* Corresponding author. Address: Department of Radiation Oncology, Cliniques Universitaires Saint-Luc, Avenue Hippocrate, 10, B-1200 Brussels, Belgium.
E-mail address: xavier.geets@uclouvain.be (X. Geets).

0167-8140/$ - see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.radonc.2013.10.025

To our best knowledge, MidP has never been implemented for helical TomoTherapy of moving lung tumors, nor compared to ITV for this treatment modality. In this context, we designed the present study to assess the potential gain of MidP over ITV in terms of margin and PTV reduction. As a second objective, we investigated whether these volumetric changes in the PTV actually lowered the irradiation of the organs at risk using clinically relevant dosimetric parameters. Finally, we also computed motion-corrected dose distributions for both scenarios using a previously validated 4D Monte Carlo (MC) model based on TomoPen [3]. The latter was used to assess the plan quality, especially the potential impact of intra-fraction motion and treatment delivery mechanics on tumor coverage when margins were reduced.

Materials and methods

Fig. 1 illustrates the complete workflow from image acquisitions to treatment planning.

Patient selection

Fifteen NSCLC patients were retrospectively included in the present study. Among these, 8 patients had stage I NSCLC treated with stereotactic body radiation therapy (SBRT), while the remaining 7 patients had locally-advanced stage II–III NSCLC treated with simultaneous integrated boost (SIB) IMRT in the framework of a dose escalation protocol. The internal review board approved this study and all patients gave their informed consent.

Image acquisition

Prior to treatment, all patients underwent a planning imaging session either on a big bore CT scanner (Aquilion LB, Toshiba medical system corporation, Japan) or a combined PET-CT scanner (Gemini TF, Philips Medical system, Cleveland, OH, USA). For all acquisitions, patients were immobilized in a thermoformed plastic mask (CIVCO Medical Solutions, Iowa, USA).

A contrast-enhanced CT (CE-CT) from the entire thoracic region was acquired in free breathing mode for the purpose of delineation, and reconstructed in 2 mm-thick slices. Next, a 4D-CT was acquired and patients were audio-coached to regularize their breathing and thus reduce 4D-CT image artefacts [10,11]. In this acquisition mode, the CT scanner automatically set the optimal helical pitch according to the patient's breathing period measured from either a pressure belt (Medspira/Mayo Clinic Breath Hold™, Mayo Clinic Medical Devices, USA) or magnetic sensors (Nomics©, Liège, Belgium). The 4D-CT datasets were retrospectively binned into 10 equally distributed temporal phases, for motion management purposes. Finally, an average CT was computed by averaging all 10 phases.

For the SIB group, 4D-FDG-PET images were also acquired 60–120 min after injection of an average activity of 8.04 mCi of FDG in patients fasting at least for 6 h before examination. The breathing signal was recorded with the same devices as the 4D-CT. After correction for decay, random, scatter, and attenuation, images were reconstructed with the iterative algorithm 3D LOR-OSEM. The images had a transverse FOV of 180 mm (one bed position centered on the region of interest). The attenuation correction was performed using the averaged 4D-CT.

Motion estimation

Internal motion due to breathing was estimated with the 4D-CT images. First, the CE-CT and the end-exhale phase of the 4D-CT were non-rigidly registered using a log-domain diffeomorphic Morphon algorithm (see Appendix for more details). This method is based on the matching of the local phase (i.e., lines and edges) at different scales and is therefore insensitive to contrast differences between the CE-CT and the 4D-CT. Next, this registration algorithm was run to map the end-exhale phase of the 4D-CT with the other phases, yielding 9 non-rigid transformations [12]. The latter were used in two different ways: first, to compute the deformation between the reference phase and the mean position of the anatomy along the respiratory cycle, which will further be applied to the CE-CT-based target volumes (TVs) to generate their corresponding MidP volumes and, second, to propagate these contours on all other phases of the respiratory cycle, the union of all deformed TVs forming an individual ITV. The deformed contours were visually checked on all phases, to assess registration accuracy. For the SIB group, the combined PET/CT acquisitions allowed MidP PET images to be computed in a straightforward way, just by applying the non-rigid deformations to the PET component.

Definition of target volumes and organs at risk

For both the ITV and MidP, Fig. 1 illustrates the workflow for the definition of the target volumes (TVs) and organs at risk (OARs). It comprises the following steps:

(1) OARs, gross tumor volume (GTV_{CT}) and clinical target volume (CTV_{CT}) of primary tumors and lymph nodes were manually delineated on the CE-CT. As there is no CTV extension for the SBRT group (i.e., $CTV_{CT} = GTV_{CT}$), the GTV will be noted CTV in the rest of the text, for the sake of clarity [13,14]. Additionally, for the SIB group, a GTV_{PET}, corresponding to the boost region, was automatically segmented on PET images using a previously validated gradient-based method [15,16].
(2) The corresponding ITV_{CT} and ITV_{PET} were generated using non-rigid registration, like previously described.
(3) Then, the internal structures were computed in their mid-position, using the transformation vectors from deformable registrations as described earlier. The resulting TVs were noted $GTV_{CT\text{-}MidP}$, $CTV_{CT\text{-}MidP}$ and $GTV_{PET\text{-}MidP}$.
(4) The PTV margins were drawn using the formalism proposed by van Herk et al.

In the last step, the margin thickness formula combines different types of geometric uncertainties and can be written as

$$M_{PTV} = 2.5\sqrt{\left(\Sigma_{TM}^2 + \Sigma_{BL}^2 + \Sigma_{SETUP}^2 + \Sigma_D^2\right)} + 1.64 \times \sqrt{\left(\sigma_{TM}^2 + \sigma_{BL}^2 + \sigma_{SETUP}^2 + \sigma_p^2\right)} - 1.64\sigma_p,$$

where Σ and σ denote the standard deviations of the systematic and random errors, respectively. Subscripts TM, BL, SETUP, D and p refer to tumor motion, baseline shift, patient setup variability, delineation uncertainty, and penumbra, respectively. The coefficients in the formula ensure that the CTV receives at least 95% of the prescribed dose for 90% of patients. All standard deviations, except Σ_{TM} and σ_{TM}, were set in agreement with the literature, while also taking into account the specificities of TomoTherapy and the handling of operators in our treatment unit [17–19]. These values were similar for ITV and MidP. In the particular case of penumbra, its width σ_p for helical TomoTherapy was computed as follows. Dose profiles in transverse and longitudinal directions at 5 cm depth for a 5×5 cm^2 field were obtained with TomoPen MC simulations in a 0.33 g/cm^3 density phantom. The computed profile was fitted with the sum of two Gaussians according to Witte et al. [20]. The effect of couch motion on dose distributions can be approximated as a convolution of the beam with a square response with