Radiotherapy and Oncology 100 (2011) 356–359

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Respiratory motion

Comparative study of respiratory motion correction techniques in cone-beam computed tomography

Simon Rit [a,*], Jasper Nijkamp [b], Marcel van Herk [b], Jan-Jakob Sonke [b,**]

[a] *Université de Lyon, CREATIS, France;* [b] *Department of Radiation Oncology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands*

ARTICLE INFO

Article history:
Received 25 July 2011
Received in revised form 16 August 2011
Accepted 22 August 2011
Available online 15 September 2011

Keywords:
Cone-beam computed tomography (CT)
Respiratory motion
Motion compensation
4D image
Image-guided radiation therapy (IGRT)
Stereotactic body radiation therapy (SBRT)
Stereotactic ablative radiotherapy (SABR)

ABSTRACT

Background and purpose: To validate the clinical usefulness of motion-compensated (MC) cone-beam (CB) computed tomography (CT) for image-guided radiotherapy (IGRT) in comparison to four-dimensional (4D) CBCT and three-dimensional (3D) CBCT.
Material and methods: Forty-eight stereotactic body radiation therapy (SBRT) patients were selected. Each patient had 5–12 long CB acquisitions (4 min) and 1–7 short CB acquisitions (1 min), with a total of 349 and 150 acquisitions, respectively. 3D, 4D and MC CBCT images of every acquisition were reconstructed. Image quality, tumor positioning accuracy and tumor motion amplitude were quantified.
Results: The mean image quality of long short acquisitions, measured using the correlation ratio with the planning CT was 74%/70%, 67%/47% and 79%/74% for 3D, 4D and MC CBCT, respectively; both 4D and MC CBCT were corrected for respiratory motion artifacts but 4D CBCTs suffered from streak artifacts. Tumor positioning with MC CBCT was significantly closer to 4D CBCT than 3D CBCT ($p < 0.0001$). Detailed patient analysis showed that motion correction was not required for tumors with less than 1 cm motion amplitude.
Conclusions: 4D and MC CBCT both allow accurate tumor position analysis under respiratory motion but 4D CBCT requires longer acquisition time than MC CBCT for adequate image quality. MC CBCT can therefore advantageously replace 4D CBCT in clinical protocols for patients with large motion to improve image quality and reduce acquisition time.

Image-guided radiotherapy (IGRT) has been a rapidly growing field of this past decade [1]. Among other techniques, cone-beam (CB) computed tomography (CT) has been developed to improve the localization of treatment targets [2]. This is particularly important in stereotactic treatments which deliver high doses in a very few fractions [3]. One difficulty is the respiratory motion which causes blur and streaks in CBCT images around moving organs and limits the accuracy of tumor positioning.

Respiratory motion artifacts have been an early concern in the development of CBCT scanners for IGRT and have led to the development of several correction techniques. The first solution that has been investigated is 4D respiration-correlated CBCT [4]. 4D CBCT consists in sorting CB projections prior to reconstruction according to a respiratory signal. Subsets of CB projections are then used to reconstruct frames of the 4D CBCT representing different phases of the respiratory cycle. However, 4D CBCT images suffer from streak artifacts due to large angular gaps between consecutive projection images. Streak artifacts can be reduced by slowing down the gantry rotation to improve the sampling of projection images [4].

Another class of correction techniques is motion-compensated (MC) CBCT. MC CBCT uses an estimate of the respiratory motion, generally described by a deformation vector field (DVF), to compensate for the respiratory motion during the reconstruction of a single 3D CBCT image [5,6]. For clinical usability, we have proposed the use of a prior motion model to reconstruct the MC CBCT during the CB acquisition and obtain the resulting image within a few seconds after the acquisition [6]. The model uses the 4D DVF estimated on the 4D planning CT and assumes similar motion during planning and CBCT acquisition.

For SBRT treatments of lung cancer patients, 4D CBCT had been used since 2006 in clinical practice, using 4 min of acquisition time [4,7]. MC CBCT is a promising new technique to improve image quality while reducing the acquisition time to 1 min [6]. The purpose of this study was to validate the clinical usefulness of MC CBCT in comparison to 4D CBCT and 3D CBCT on a large set of SBRT patients.

Material and methods

Patients

We retrospectively analyzed lung cancer patients that underwent stereotactic body radiotherapy at the Netherlands Cancer

* Corresponding author. Address: Université de Lyon, CREATIS, CNRS UMR5220, Inserm U1044, Centre Léon Bérard, 28 rue Laënnec, 69008 Lyon, France.
** Principal corresponding author.
E-mail addresses: simon.rit@creatis.insa-lyon.fr (S. Rit), j.nijkamp@nki.nl (J. Nijkamp), portal@nki.nl (M. van Herk), j.sonke@nki.nl (J.-J. Sonke).

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doi:10.1016/j.radonc.2011.08.018

Institute-Antoni van Leeuwenhoek Hospital (NKI-AVL) between February 2008 and November 2009. The treatment protocol is detailed in [7], we focused in this study on image guidance for patients with relatively large tumor motion measured on the 4D planning CT [8]. We only selected the group of patients with a peak-to-peak amplitude greater than 5 mm in one of the three directions of the image coordinate system. In total, 48 patients were selected for this study.

Planning image

Respiration-correlated images were acquired on a helical CT scanner (24-slice Somatom Sensation Open, Siemens, Forchheim, Germany) synchronized to the respiration using the temperature variations in a nasobuccal mask [9]. The field-of-view encompassed the whole lungs. 4D CTs were reconstructed with a voxel resolution of $1 \times 1 \times 3$ mm^3 in 10 frames.

The respiratory motion was retrospectively estimated on each 4D CT by registering the 5th frame (exhale) of the 4D CT to the other frames using deformable registration, resulting in a 4D deformation vector field (DVF). The 4D DVF was used to process a time-averaged mid-position (MidP) 3D CT image [10] which was used as reference image during registration.

Image guidance

Cone-beam (CB) CT images were acquired in the treatment room using a scanner attached to the gantry of the linear accelerator (Elekta Synergy 4.2; Elekta Oncology Systems Ltd., Crawley, West Sussex, UK). Three CB images were acquired during each of the three fractions. The first CBCT image was acquired to assess and correct the misalignment of the time-weighted average position of the target and avoid critical structures with respect to the treatment plan. The second CBCT image was acquired to validate the target alignment after couch shift and prior to the treatment delivery. The third CBCT image was acquired at the end of the treatment fraction to measure the intrafraction stability.

CB acquisition time was 4 min for the first two acquisitions and 1 min for the last acquisition. The long acquisitions were obtained by slowing down the gantry for improved image quality of 4D CBCT [4]. The short acquisitions were acquired at the standard gantry speed for 3D CBCT. The rest of the acquisition parameters were 120 kVp, with various exposures ranging from 0.16 to 0.64 mAs per frame.

Adjustments in the guidance protocol were allowed depending on the course of the treatment, e.g. the need for an extra CBCT image to confirm the setup, failures in adequately setting up the patient, or patient intolerance to the length of the fraction. As a consequence of such events, extra CBCT images were acquired, a few fractions were adjourned, or the last CBCT image was not acquired, respectively. All images were analyzed, regardless of those events.

Each patient had 5–12 long acquisitions and 1–7 short acquisitions. In total, there were 349 long and 150 short acquisitions.

Image reconstruction

Three different CBCT reconstruction techniques were retrospectively investigated. The first technique was standard 3D CBCT filtered backprojection reconstruction, without respiratory motion correction [11]. The second technique was 4D respiration correlated CBCT [4] which is in current clinical use for SBRT of tumors moving more than 8 mm with breathing [7]. The third technique was motion-compensated (MC) CBCT based on the 4D DVF derived from the 4D planning CT as a prior model [6]. The resulting 3D MC CBCT represents the time-averaged anatomy of the patient during the CB acquisition.

Tumor registration

Image guidance requires the assessment of tumor position at treatment time. Each CBCT image was automatically registered on the MidP reference CT image in the two-step procedure detailed in [7] which is clinically used at the NKI-AVL. First, the rigid motion (translations and rotations) of the bony anatomy were assessed in a rectangular region of interest (ROI) encompassing a large part of the spine. Second, the translations of the gross tumor volume (GTV) enlarged with a 5 mm margin were estimated assuming similar rotations as the bony anatomy for robustness to round-shaped tumors. For 4D CBCT images, each frame was separately registered and the time-averaged displacement was used to derive the couch correction. At each step, the registration was visually checked and, when failing, was reinitialized until the target of the step, i.e. bony anatomy or tumor, was accurately aligned by the automated registration.

Quantitative assessment

Image quality of the three reconstructed CBCTs was assessed using the correlation ratio between the evaluated CBCT image and the MidP image after registration within the ROI used for tumor registration, which corresponds to the optimum of the similarity measure found by the automated tumor registration.

Accuracy of tumor registration was assessed with respect to 4D CBCT registrations which are currently used in our clinical protocols as the most accurate estimate of the tumor under respiratory motion (submillimetric for a moving phantom [12]). The accuracy of 3D and MC CBCT tumor registration was measured as the difference between the derived couch corrections of these methods compared to the 4D CBCT analysis.

Accuracy of the prior motion model used for MC CBCT was assessed by reconstructing a 4D MC CBCT, i.e. applying motion compensation but sorting the projections and reconstructing image frames in the same way as in 4D CBCT. If the assumption of the *a priori* motion model were correct, the respiratory motion would have been perfectly compensated for and 4D MC CBCT would not display any residual motion. Therefore, the amplitude of the tumor motion was measured on 4D CBCT and 4D MC CBCT using the aforementioned registration technique to assess the accuracy of the *a priori* motion model.

Results

Fig. 1 illustrates the three CBCT techniques for a long and a short acquisitions with respect to the MidP reference CT and Table 1 summarizes the quantitative assessment of the image quality. The results were significantly different between reconstruction techniques ($p < 0.0001$, paired *t*-test). 4D CBCT images had the lowest image quality in the correlation ratio sense due to streak artifacts. 3D CBCT image quality was better although it does not account for respiratory motion. MC CBCT had the best image quality because it uses all projection images and corrects for motion blur. Long acquisitions were only slightly superior for 3D and MC CBCT with 3.5% and 5.5% difference on average ($p = 0.09$ and $p = 0.006$, unpaired *t*-test) but the difference was larger and very significant for 4D CBCT with 20.6% difference ($p < 0.0001$). In many cases, the low image quality of 4D CBCT images with short acquisitions made automated registration and its visual inspection difficult. Therefore, short acquisitions were not part of the subsequent quantitative analysis.

Table 2 contains the quantitative assessment of tumor registration accuracy using 4D CBCT registrations as a reference. The group means were not significantly different from 0 ($p > 0.36$) except the cranio-caudal positioning with 3D CBCT ($p = 0.0001$) which was significantly worse than MC CBCT ($p < 0.0001$) with a 0.7 mm group

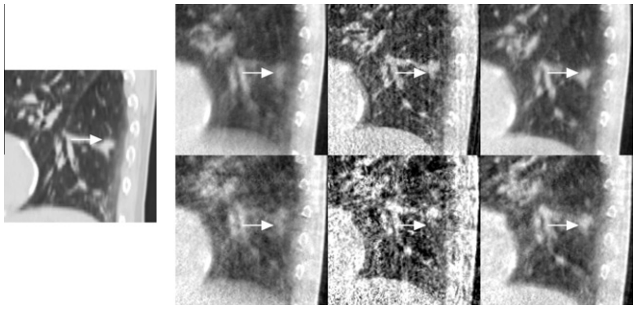

Fig. 1. Sagittal slices of, from left to right, the MidP CT, the 3D CBCT, the end-exhale frame of the 4D CBCT and the MC CBCT reconstructed from a long (top) and a short (bottom) acquisition of the patient with the largest average tumor motion. The MidP CT and the CBCTs have been registered on the bony anatomy. The arrows indicate the same point around the tumor location which illustrate the baseline variations and the breathing motion [12].

Table 2
Difference between 3D/ MC CBCT registrations and 4D CBCT registrations for images reconstructed from long acquisitions in terms of group mean (GM), systematic error (Σ) and random error (σ).

	Left–right (mm)	Craniocaudal (mm)	Anteroposterior (mm)
3D CBCT			
GM	−0.0	0.7	0.1
Σ	0.2	1.2	0.4
σ	0.2	0.7	0.3
MC CBCT			
GM	−0.0	−0.0	−0.0
Σ	0.2	0.6	0.2
σ	0.1	0.3	0.2

mean, i.e. an average offset of the estimated position towards the cranial direction (exhale) with respect to the time-averaged position. Both the systematic (Σ) and random (σ) errors of 3D CBCT were larger than those of MC CBCT. Inter-patient variability (Σ) was larger than intra-patient variability (σ) which indicates that registration errors are mainly patient dependent.

Fig. 2 displays the average amplitude per patient of the registration differences relative to the average tumor motion amplitude. 3D CBCT registration errors were greater than 1 mm in 10 patients, up to 5 mm for one patient. These errors increase with tumor motion amplitude (Pearson's linear correlation coefficient $R = 0.71$, ($p < 0.0001$). Motion compensation reduces this error below 1 mm, except for 3 patients for which the average errors were 1.1, 1.2 and 3.4 mm. The errors of MC CBCT registrations were not correlated to tumor motion amplitude ($R = 0.41$, $p = 0.004$).

The peak-to-peak tumor motion amplitude measured on 4D respiration-correlated CBCT, i.e. the maximum extent of the estimated tumor displacement, is compared before and after compensation in Fig. 3. The median/95th percentile of the tumor amplitudes was 9.2/18.9 mm and 3.8/10.3 mm before and after compensation, respectively, showing large compensation of the tumor motion with the *a priori* motion model. However, substantial residual motion was observed and the compensation increased the motion in the few cases that are above the identity line. The residual motion measured on 4D MC CBCT was further investigated by taking a signed version of the peak-to-peak amplitude, i.e. the signed difference between the peak positions around the exhale and inhale phases after projection on the main direction of motion. The distribution was not significantly different from 0 ($p = 0.5$) and the outliers mainly correspond to under-compensation of the motion.

Discussion

We have investigated the use of CBCT reconstruction techniques to account for breathing motion in image guided stereotactic body radiotherapy of lung tumors. Both 4D and MC CBCT visually correct for the respiratory blur of 3D CBCT (Fig. 1). Image quality results (Table 1) were in agreement with our previous investigations on a few patients [4,6]: 4D CBCT requires long acquisitions to limit streak artifacts (4 min), whereas MC CBCT provides sufficient image quality with short acquisitions normally used for 3D CBCT (1 min).

Table 1
Group mean (standard deviation) of the image quality measure, i.e. the correlation ratio between the MidP reference CT image and registered CBCT images in the tumor region.

	Long acquisitions (%)	Short acquisitions (%)
3D CBCT	73.5 (11.3)	70.0 (11.2)
4D CBCT	67.4 (11.4)	46.8 (12.1)
MC CBCT	79.0 (9.8)	73.5 (10.8)

The image quality of CBCT images was assessed using the similarity measure used for target registration, i.e. the correlation ratio with the MidP CT in the GTV with 5 mm extra margins. Thereby, we assumed no tumor changes during the course of the SBRT, which is the best option in our opinion for these short treatments (about 10 days between the first and the last fractions) because the MidP image accurately represents the tumor [10] and tumor changes would impact all reconstruction techniques. Another limitation was the greater sensitivity of the correlation ratio to streak artifacts of 4D CBCT images than motion blur of 3D CBCT. In our clinical experience, this does not necessarily reflect human perception which is generally more disturbed by motion blur than streak artifacts because the latter are obviously non-anatomical. Studies with human observers would be required for finer analyses.

CBCT images are primarily used in clinical protocols for target positioning. The accuracy of tumor registration was assessed with respect to our best reference, currently used in the SBRT protocol of the NKI-AVL, i.e. registrations of 4D CBCT images reconstructed from long acquisitions [7] which are time-resolved and, therefore, explicitly account for inter-fraction variations of the tumor motion pattern. Both the group mean and the variability of the registration accuracy was improved with MC CBCT compared to 3D CBCT (Table 2). The average cranio-caudal offset of 3D CBCT registrations can be due to the longer time spent at end-exhale than at any other phase of the breathing cycle [13], which implies that end-exhale is better defined in the blurred image and registration will lock on this position. The variability of the registration is due to the uncertainty underlying the registration of blurred objects and is another motivation for using motion correction techniques in CBCT imaging.

The largest variability of registration errors was inter-patient (Table 2, Σ). Detailed analysis of registration errors on a patient basis confirmed disparities in the registration accuracy (Fig. 2). Below 1 cm average tumor motion amplitude, differences between 3D and 4D CBCT were lower than 1 mm and the use of 4D CBCT would not be justified. Tumor motion greater than 1 cm caused larger errors which were reduced by the use of MC CBCT. In 3 patients, the average residual error of MC CBCT was greater than 1 mm. Retrospective analysis of these patients indicated that all 3 corresponding targets were located on the posterior side of the patient near the pleural boundary where large sliding motion occurs [14]. Visual inspection of the prior motion models, computed with deformable registration of 4D CTs, displayed misregistrations of these tumors and under-estimated motion amplitudes, which is in accordance with ouliers of the signed amplitude distribution. Improvement of the deformable registration accuracy at sliding

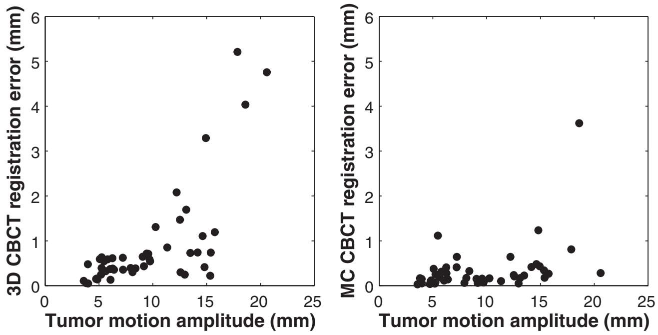

Fig. 2. Plot of the patient average amplitude of the difference between the 3D (left)/MC (right) tumor registration and the 4D CBCT tumor registration against the average amplitude of the tumor motion measured on the 4D CBCT.

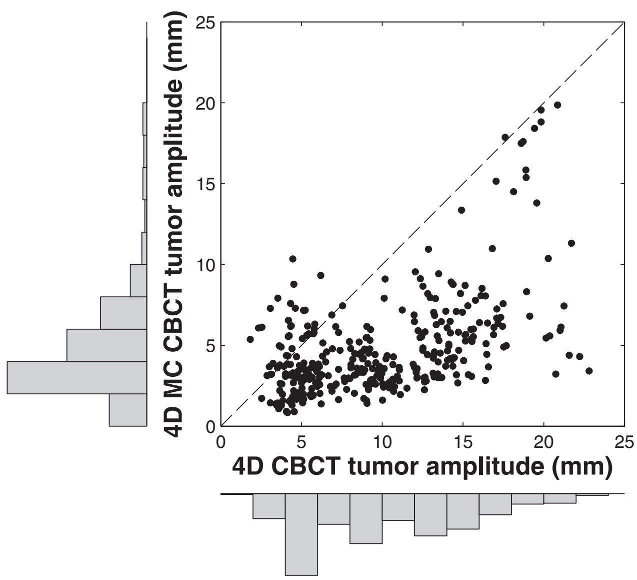

Fig. 3. Scatter plot and marginal histograms of the peak-to-peak tumor motion amplitude measured on 4D CBCT before and after compensation of the respiratory motion.

locations is needed to improve the motion compensation accuracy, e.g. using subanatomical region segmentations [15].

A large part of the motion blur is corrected by 4D and MC CBCT but there is some residual blur due to the nature of the modeling of breathing motion: they both assume periodic breathing during acquisition and MC CBCT additionally assumes a similar motion pattern during CB acquisition as the one described by the 4D planning CT. The latter assumption was validated by comparing tumor amplitude on 4D CBCT before and after compensation, which generally showed large compensation of tumor motion (Fig. 3). Residual motion was expected due to the known inter- and intra-fraction variability of the respiratory motion [13]. Patient-by-patient analysis of the residual motion measured on 4D MC CBCT can provide information on the cause of the residual motion: under- and over-estimation of the breathing motion, phase shift of the estimated motion or change in motion pattern. We did not observe any systematic cause for residual motion in all patients, e.g. by investigating signed amplitudes.

This study confirmed the clinical potential of MC CBCT and similar results are expected for other targets moving with breathing, e.g. centrally located lung tumors and upper-abdominal tumors [6]. Below 1 cm tumor motion, motion correction of CBCT images has a limited impact and the threshold for using 4D CBCT (and in the near future MC CBCT) has, therefore, been raised from 5 to 8 mm in the clinical protocols at the NKI-AVL. Above this threshold, MC CBCT is being currently implemented in place of 4D CBCT to improve image quality with reduced acquisition times from 4 to 1 min. MidP CT is used clinically for treatment planning since August 2011, providing the necessary 4D DVF for MC CBCT. The clinical workflow includes visual validation of the deformable registration of the 4D CT to detect misregisrations, e.g. due to sliding motion near the pleura.

Conclusion

Respiratory motion causes blur in 3D CBCT which leads to substantial registration errors when tumor motion is greater than 1 cm. 4D CBCT corrects for respiratory motion but requires long (4 min) acquisitions for adequate image quality. MC CBCT corrects for respiratory motion with improved image quality and allows using standard (1 min) acquisition times.

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