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PHYSICS CONTRIBUTION

LOCAL SETUP ERRORS IN IMAGE-GUIDED RADIOTHERAPY FOR HEAD AND NECK CANCER PATIENTS IMMOBILIZED WITH A CUSTOM-MADE DEVICE

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Purpose: To evaluate the local positioning uncertainties during fractionated radiotherapy of head-and-neck cancer patients immobilized using a custom-made fixation device and discuss the effect of possible patient correction strategies for these uncertainties.

Methods and Materials: A total of 45 head-and-neck patients underwent regular control computed tomography scanning using an in-room computed tomography scanner. The local and global positioning variations of all patients were evaluated by applying a rigid registration algorithm. One bounding box around the complete target volume and nine local registration boxes containing relevant anatomic structures were introduced. The resulting uncertainties for a stereotactic setup and the deformations referenced to one anatomic local registration box were determined. Local deformations of the patients immobilized using our custom-made device were compared with previously published results. Several patient positioning correction strategies were simulated, and the residual local uncertainties were calculated.

Results: The patient anatomy in the stereotactic setup showed local systematic positioning deviations of 1–4 mm. The deformations referenced to a particular anatomic local registration box were similar to the reported deformations assessed from patients immobilized with commercially available Aquaplast masks. A global correction, including the rotational error compensation, decreased the remaining local translational errors. Depending on the chosen patient positioning strategy, the remaining local uncertainties varied considerably.

Conclusions: Local deformations in head-and-neck patients occur even if an elaborate, custom-made patient fixation method is used. A rotational error correction decreased the required margins considerably. None of the considered correction strategies achieved perfect alignment. Therefore, weighting of anatomic subregions to obtain the optimal correction vector should be investigated in the future. © 2011 Elsevier Inc.

Head-and-neck cancer, Registration, Setup uncertainties, Radiotherapy, Image-guided radiotherapy.

INTRODUCTION

Head-and-neck tumors have remained a challenge for radiotherapy (RT) because of the vicinity of the tumor to surrounding multiple organs at risk (OARs). The introduction of highly conformal radiation techniques such as intensity-modulated RT has enabled dose escalation to the planned target volume, with simultaneously sparing of the OARs. When using intensity-modulated RT, patient positioning needs to be performed accurately for each treatment fraction to prevent degradation of the planned dose distribution.

Most current approaches to correct for patient positioning errors have been based on the assumption that the patient's anatomy is rigid. However, the neck is flexible, and deformations are likely to occur, leading to additional dose smearing. Also, the weight loss of the patient during RT might further contribute to this dose degradation. To minimize the occurrence of deformations, various external patient fixation devices have been used. The amount of deformations emerging in the head-and-neck region for patients immobilized with commercially available Aquaplast masks has been previously described (1–4). Up until 2008, at the German Cancer Research Center, patients undergoing RT for head-and-neck cancer were immobilized with a customized fixation device composed of a scotch-cast mask and a vacuum mould. This combination was introduced with the intention of reducing the potential deformations and movements in

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this region. However, in daily use, anatomic deformations became apparent on the control computed tomography (CT) scans acquired during the treatment course to verify patient positioning.

We, therefore, evaluated the actual deformations and positioning uncertainties observed in patients immobilized with this fixation. The present evaluation helped to clarify whether a firmer head fixation would result in less pronounced deformations compared with the commercially available masks. We also discussed possible patient correction strategies on the basis of the obtained results.

METHODS AND MATERIALS

Treatment procedure

Patients. The data from 45 head-and-neck cancer patients consecutively treated between 2005 and 2008 were retrospectively selected for the present analysis. All patients underwent intensity-modulated RT for oropharyngeal, laryngeal, or locally advanced nasopharyngeal cancer. Approximately one third of all patients underwent placement of a percutaneous endoscopic gastrostomy tube before the start of, or during, RT to prevent excessive weight loss during RT. A median of 30 fractions was delivered to each patient.

Patient fixation. Each patient was immobilized with an individually customized fixation device. It consisted of a vacuum mould complemented by a tight scotch-cast head mask. An example of the patient fixation is shown in Fig. 1. Care was taken to ensure a good imprint of the shoulders, and additional small tattoos were placed on both shoulders to ensure correct shoulder positioning in the mould. The oropharyngeal cancer patients were provided with a tongue depressor to expand the space between the tongue and the palate. No bite blocks were used.

Treatment device, planning, and delivery. The patients underwent RT with a linear accelerator combined with an in-room CT scanner (Siemens Primatom, Siemens OCS, Malvern, PA). The CT scanner was a single-slice spiral scanner on rails arranged perpendicular to the linear accelerator gantry axis. The CT scanner met the image quality of diagnostic standards.

Treatment plans were generated using the in-house treatment planning system VIRTUOS (5) and the inverse planning tool KonRad (Siemens Oncology Care System).

The patients were positioned using a stereotactic setup approach (6). For target point localization, a stereotactic head frame was attached to the mask for image acquisition of the planning CT scan and all subsequent control CT scans. With the localizers of the stereotactic frame, each control CT scan could be automatically correlated with the corresponding planning CT scan in the treatment planning system. The stereotactic setup ensured the accurate positioning of the patient immobilization device. Thus, theoretically, the remaining positioning error of the mask and mould after stereotactic registration between the planning and subsequent CT scans would be zero. In reality, quality assurance of the stereotactic setup guaranteed a geometric uncertainty (*e.g.,* due to frame distortion or reattachment procedures) of <1.5 mm radial distance.

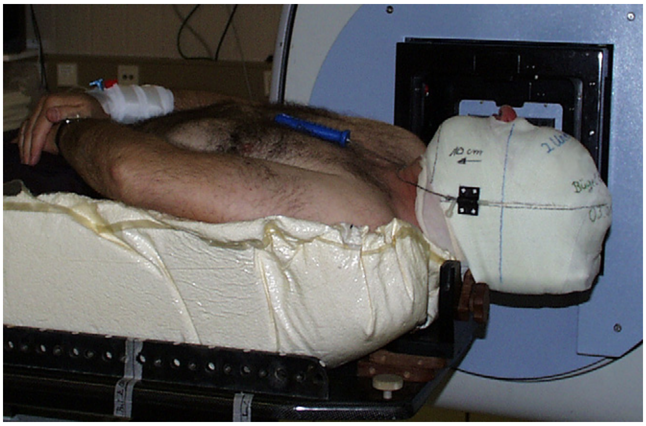

Fig. 1. Patient fixation with vacuum mould and scotch-cast mask.

Control CT scanning procedure. During the treatment course, every patient had a control CT scan done before RT on the first treatment day and at least once each week. The scanned volume included the whole target volume plus a margin of $\leq$2 cm above and below in the craniocaudal (CC) axis. The CT slice thickness was 3 mm, with an in-slice resolution of 0.98×0.98 mm^2. The nose, mandible, and jugular notch were included in all CT scans. A total of 488 CT studies from 45 patients were obtained. On average, 10 scans for each patient were evaluated. The control CT scans were not used for image-guided on-line setup correction. However, they were acquired to deduce the margins needed for treatment of stereotactically positioned patients. Additionally, they enabled the identification of patients with excessive weight loss, for whom replanning on the acquired control CT scan was performed.

Quantification of positioning accuracy

Quantification of global positioning accuracy using target registration box. For each patient, a target registration box (TRB) for the overall setup error was defined. The TRB completely surrounded the target volume plus a 1-cm margin in the CC axis, but without a margin in the right–left and anteroposterior (AP) axes (Fig. 2). The control CT scans were stereotactically correlated with the respective planning CT scan, making the coordinates for both CT cubes directly comparable. Next, the anatomic positioning error was evaluated by matching the control CT cube to the planning

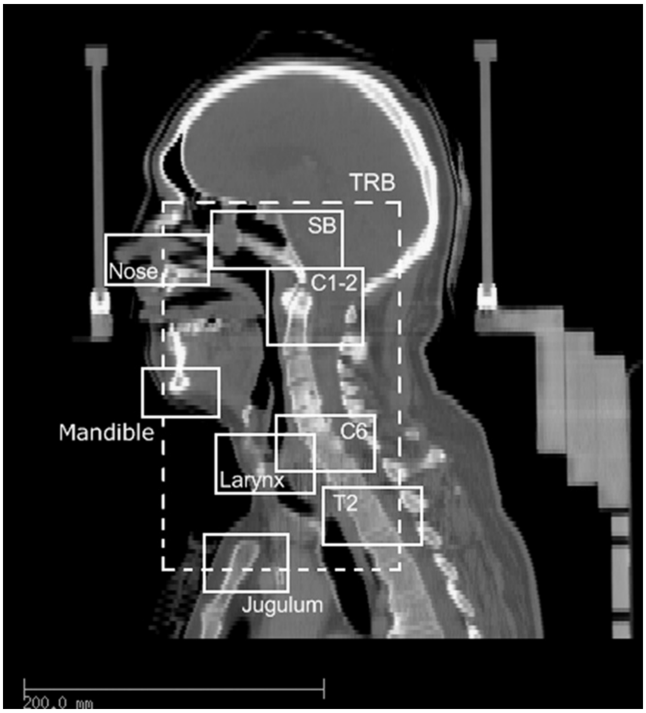

Fig. 2. Definition of registration boxes in sagittal view on planning computed tomography scan, including stereotactic frame.

CT cube. Thus, a widely accepted rigid body registration algorithm implemented in VIRTUOS and based on mutual information was applied, considering both translational and rotational shifts (7). This method has been evaluated in phantom studies and achieved subvoxel accuracy (8). The bounding box did not include the stereotactic frame to avoid the influence of the frame on the registration result.

Multiple regions of interest analysis. To analyze the local positioning uncertainties, we used an approach similar to that described in a previous study (6). For each patient, local registration boxes (LRBs) one to eight were introduced into the planning CT scan. These LRBs contained different anatomic structures that are expected to show interfractional positioning variations. To define the small registration boxes, anatomic landmarks were identified on the planning CT scan of every patient. The corresponding LRBs surrounded these landmarks. The LRBs included (Fig. 2): C1-C2, the skull base (SB), mandible, nose (including the anterior parts of both maxillary sinuses), C6, T2, larynx, and jugulum right (*i.e.,* the medial part of the right clavicle). Six patients had undergone laryngectomy; thus, the corresponding LRB was not scored in the statistical analysis for these patients. All LRBs were rectangular but varied in size. Each LRB was symmetrical around the predefined landmark; thus, the landmark was the center of this LRB. An exception was made in the two "nose" and "mandible" LRBs. The registration boxes were asymmetrical in the AP direction because of the stereotactic frame that needed to be excluded from the image content. Otherwise, it would have influenced the registration results by aligning the stereotactic frame, instead of the anatomic features.

Quantification of registration measurement error. Whenever evaluating geometric errors, a measurement error assessment is needed. We assumed that no deformations or motions would occur between the anatomic nose LRB (including both anterior maxillary sinuses) and the SB LRB, because theses are rigidly connected anatomically. The distance between the two landmarks was determined on each CT scan, and the standard deviation of this distance was calculated for each patient. These values were averaged for all patients, resulting in a mean value of 0.2 ± 0.1 mm, which was assumed to be our registration measurement error. However, the registration accuracy for the different LRBs might not be exactly the same, because these boxes differed in content and contrast. In particular, for the LRB larynx, one would expect greater registration inaccuracy owing to the lower bony contrast compared with the SB, for example.

Mathematical analysis

Calculation of deformations. Rigid body movements are described by a transformation that preserves the mutual distance of two arbitrary points inside the object. This type of transformation can be expressed by a 4 × 4 matrix, T_{rigid}, consisting of entries deduced from the six parameters describing the translation of the object in all three directions and the rotation around the three axes in respect to a reference point. The correction simulation of a patient model (*e.g.,* a CT scan) is performed by applying the inverse error matrix T^{-1}_{rigid}. To quantify the occurred deformation for a LRB i, a deformation vector d_i is used:

$$d_i = T^i \cdot r_i - r_i \tag{1}$$

where d_i originates at each respective landmark with the landmark position r_i (representing the center of the LRB) on the planning CT scan. The superscript of the transformation indicates its reference structure. The residual deformation vector after a rigid target point correction (TPC) in respect to a reference structure s represented by the corresponding landmark is then calculated as follows:

$$d_i^s = (T^s)^{-1}(T^i r_i) - r_i = \left((T^s)^{-1} T^i - I\right) r_i \tag{2}$$

Statistical analysis of cohort. All LRBs are subsequently registered using each control CT to determine the parameters of the corresponding transformations and resulting deformations. To analyze the results, the systematic and random deformations $\Sigma_{p,i}$ and $\sigma_{p,i}$ of each patient p, and each LRB i is calculated as the mean displacement and its standard deviation, respectively. To combine the outcomes to group specific values, the group mean, systematic, and random error M_i, Σ_i, and σ_i for each LRB i are calculated according to a previously reported manner to allow comparison (1, 9).

Local positioning uncertainties

Quantification of stereotactic positioning errors. After stereotactic correlation of the planning and control CT scans, LRBs one to eight were registered separately using the rigid body registration algorithm. The results reflected the positioning errors of the anatomic subvolumes represented by the LRBs in the absence of any correction procedure.

Quantification of deformations referenced to C1-C2. To assess the deformations referenced to a specific anatomic point, all LRB translations were referred to LRB 1, containing the cervical vertebral bodies C1 and C2. This allows for a comparison of our results with previously reported studies (3). Both translational and rotational errors were considered.

Quantification of deformations in regard to target bounding box. The residual errors of the individual LRBs after TPC using a registration of the TRB were assessed using the registration results of acquired data and Eq. 2. The TPC included a correction of the translational and rotational errors.

Effect of correction of rotational error on positioning accuracy of subvolumes using TPC. TPCs were usually applied by correcting the translational errors only. Rotational errors were recorded but were not compensated. The influence of a rotational error correction on the remaining translational errors for each control CT scan was assessed for all LRBs after the initial TRB registration.

Margins for five different correction scenarios. Patient positioning deviations compromised the conformal coverage of the clinical target volume (CTV). Therefore, the security margins are typically applied to extend the CTV to a planning target volume (PTV). The size of those margins depends on the extent of the occurring positioning uncertainties. To illustrate the effect of the local positioning errors on the treatment planning process, the corresponding margins for LRBs one to eight were determined. The margins were calculated using the margin recipe for rigid body setup inaccuracies (10).

The margins for all LRBs were calculated for five different correction strategies. First, the margins required for patient positioning using stereotactic setup only (no correction strategy). Second, a registration with the TRB was performed, considering both translational and rotational errors. We listed the margins required if only the translational errors were corrected and the margins necessary if both translational and rotational errors were corrected.

The remaining two correction strategies implied to position the patient such that the maximal anatomic alignment is achieved in the planned high-dose area. Therefore, two boost sites in the head-and-neck region were chosen, including the oropharynx and nasopharynx. The mandible and SB LRBs were chosen to simulate positioning and correction of the oropharynx and nasopharynx. For

Table 1. Translational and rotational global positioning errors resulting from registration using TRB

	M (mm)			Σ (mm)			σ (mm)		
Error	RL	AP	CC	RL	AP	CC	RL	AP	CC
Translation (mm)	−0.2	−1.0	0.2	1.0	1.1	1.3	0.7	1.2	1.1
Rotation (°)	−0.5	0.0	0.1	0.7	0.5	0.7	0.6	0.4	0.5

Abbreviations: TRB = target registration box; M = group mean error; Σ = group systematic error; σ = group random error; RL = right–left; AP = anteroposterior; CC = craniocaudal.

the other LRBs, the positioning variance and resultant margins were calculated.

RESULTS

Quantification of positioning accuracy

Analysis of global positioning errors using target bounding box. The global error for the PTV was determined using registration of the control CT scans with respect to the planning CT scan using the TRB (Fig. 2). The results are listed in Table 1. The reported values refer to the isocenter of the CTV.

Local positioning errors

Stereotactic errors. For the different anatomic subvolumes, different movements are possible, determined by both patient fixation and anatomic range of motion of the respective region. To evaluate the positioning accuracies of the LRBs, we determined the translational and rotational errors separately for each LRB. The translational errors are summarized in Table 2. The reported deviations demonstrated the positioning variability of the individual subregions with regard to the stereotactic frame (not referenced to a particular anatomic structure).

Deformations referenced to C1-C2. To extract the pure anatomic deformations, the local positioning errors must be referred to one anatomic structure. The residual errors with respect to LRB C1-C2 are summarized in Table 3. The residual error of LRB C1-C2 was zero in this scenario.

Deformations after TPC. To cope with interfractional positioning errors, a rigid body correction strategy performing a TPC is imaginable. The residual errors of each LRB after TPC are reported in Table 4, showing that for neither LRB

Table 2. Local stereotactic translational errors of all LRBs

	M (mm)			Σ (mm)			σ (mm)		
LRB	RL	AP	CC	RL	AP	CC	RL	AP	CC
SB	0.0	−0.4	0.0	0.5	0.7	1.3	0.5	0.6	1.1
Nose	−0.3	−0.4	0.2	1.3	0.9	1.5	1.0	0.7	1.4
C1-C2	−0.2	−0.2	−0.1	0.7	0.8	1.5	0.6	0.9	1.2
Mandible	−0.1	−0.3	0.3	0.8	1.2	1.2	0.6	0.9	1.2
C6	−0.2	−1.2	−0.3	2.4	2.6	1.6	1.6	2.9	1.3
Larynx	−0.3	−1.6	0.5	1.6	2.3	2.2	1.2	2.2	1.7
T2	−0.1	−1.7	−0.2	3.3	1.9	2.1	4.2	2.4	1.6
Jugulum right	−0.5	−3.3	0.5	2.4	3.5	2.8	1.8	3.8	2.0

Abbreviations: LRB = local registration box; SB = skull base; other abbreviations as in Table 1.

Table 3. Deformations referenced to LRB C1-C2

	M (mm)			Σ (mm)			σ (mm)		
Variable	RL	AP	CC	RL	AP	CC	RL	AP	CC
SB	0.0	0.1	−0.1	0.2	0.3	0.5	0.2	0.4	0.5
Nose	0.0	0.2	−0.6	0.7	0.4	1.5	0.6	0.5	1.5
C1-C2	0	0	0	0	0	0	0	0	0
Mandible	0.0	0.3	−0.6	0.6	1.3	1.6	0.6	1.1	1.4
C6	0.1	1.2	0.3	1.6	2.2	0.7	1.1	2.3	0.7
Larynx	0.2	1.7	−0.5	1.1	2.1	1.9	0.9	1.7	1.6
T2	0.0	2.0	0.3	3.5	2.5	1.6	4.2	2.7	1.4
Jugulum right	0.5	3.5	−0.6	2.2	3.8	2.4	1.7	4.1	1.9

Abbreviations as in Tables 1 and 2.

was perfect alignment achieved. These errors reflect the extent of elastic deformations that cannot be covered by the rigid body registration procedure.

Deformations after TPC including rotational error correction. We investigated to what extent small rotational errors in rigid correction strategies would contribute to the overall positioning uncertainties. Figure 3 illustrates the influence of the correction of the rotational error on the remaining translational errors for all LRBs. The occurring rotational errors were small and <1° around each axis if averaged for all patients (Table 1); 95% of the individual rotational errors were <1.7° (data not shown). Despite these small values, the variance of almost all residual translational errors decreased noticeably after a rotational error correction.

Margins. The margins for five different correction scenarios were calculated, applying the margin recipe $m = 2.5\Sigma + 0.7\sigma$ for the rigid body setup inaccuracies (3, 10) to each LRB, with m indicating the margin, and $\Sigma$the systematic and σ the random error. Table 5 lists the results for the different correction strategies. The required margins were labeled "stx" if the patient was positioned using the stereotactic setup only. The columns labeled "TRB trans" and "TRB trans/rot" show the margins required if only the translational errors or both the translational and rotational errors, respectively, were corrected after registration with the TRB. The next two columns contain the margins for the last two positioning scenarios.

DISCUSSION

Local positioning uncertainties

One patient setup correction strategy is a simple TPC, including correction of the translational and rotational errors determined by the registration using a TRB. However, applying this three-dimensional transformation differently pronounced local deformations remain unconsidered. The results of the registration of the LRBs reflected that the local positioning errors exceeded the global patient setup error determined by the TRB registration. This is because the global registration vector originates from averaging over all regional uncertainties, thus playing down the true local positioning inaccuracies. Previous other studies analyzing local positioning uncertainties in head-and-neck patients using a different patient fixation came to the same conclusion (2, 3).

Table 4. Residual deformations after registration of TRB and its correction

	M (mm)			Σ (mm)			Σ (mm)			M (°)			Σ (°)			σ (°)		
Variable	RL	AP	CC	RL	AP	CC	RL	AP	CC	RL	AP	CC	RL	AP	CC	RL	AP	CC
SB	0.0	0.2	0.2	0.2	0.5	0.6	0.2	0.6	0.5	−0.1	0.0	0.0	0.4	0.2	0.8	0.3	0.2	0.5
Nose	0.1	0.1	0.8	0.8	0.7	1.9	0.6	0.6	1.4	0.0	0.0	0.0	0.4	0.2	0.3	0.4	0.3	0.3
C1-C2	−0.1	−0.3	0.3	0.3	0.5	0.6	0.3	0.5	0.5	0.2	−0.1	0.0	0.6	0.5	0.8	0.6	0.4	0.6
Mandible	0.0	−0.7	0.4	0.6	1.4	1.7	0.6	1.1	1.4	−0.2	−0.1	0.0	1.1	0.6	0.1	1.0	0.5	0.2
C6	0.0	−0.1	0.3	1.2	1.5	0.7	1.0	1.9	0.6	−0.2	−0.0	0.1	1.1	0.6	1.0	1.1	0.6	1.1
Larynx	0.1	0.3	−0.2	0.9	1.4	1.8	0.7	1.1	1.5	−0.1	0.0	0.0	0.4	0.3	1.2	0.6	0.6	1.1
T2	−0.2	0.0	−0.1	2.4	1.7	1.7	3.9	2.0	1.4	0.0	−0.1	0.0	0.5	0.6	0.4	0.6	1.3	0.5
Jugulum right	0.3	1.4	−0.3	1.4	2.3	2.0	1.4	2.6	1.9	0.1	0.3	0.3	0.4	0.8	0.7	0.6	1.1	0.9

Abbreviations as in Tables 1 and 2.

Stereotactic errors

The predominant content of the LRBs is not subject to deformations because the boxes are defined on the bony anatomy. However, these LRBs are representative parts of larger anatomic structures (*e.g.,* the cervical spine), which can deform or show progressive anatomic changes.

Our reported deviations showed the positioning variability of the individual subregions with regard to the stereotactic frame, not referenced to a particular anatomic structure inside the patient. In the absence of daily imaging and patient correction, the CTV needs to be expanded by margins derived from these uncertainties. These margins again consist of two parts. First, the margins need to cover the stereotactic rigid body positioning uncertainties and second, those due to anatomic deformations within the patient and motion of the patient within the immobilization device. In the present study, it was not possible to definitely separate between the two contributions, because even between the planning CT and first control CT scans, deformations might occur. For intracranial treatment at the SB, at which no deformations between these two CT scans, would be expected, the stereotactic error has been estimated to be 1.8 ± 0.6-mm radial distance (11). Overall, the stereotactic setup uncertainties of the LRBs indicated a lesser range of motion and deformations within the scotch-cast mask

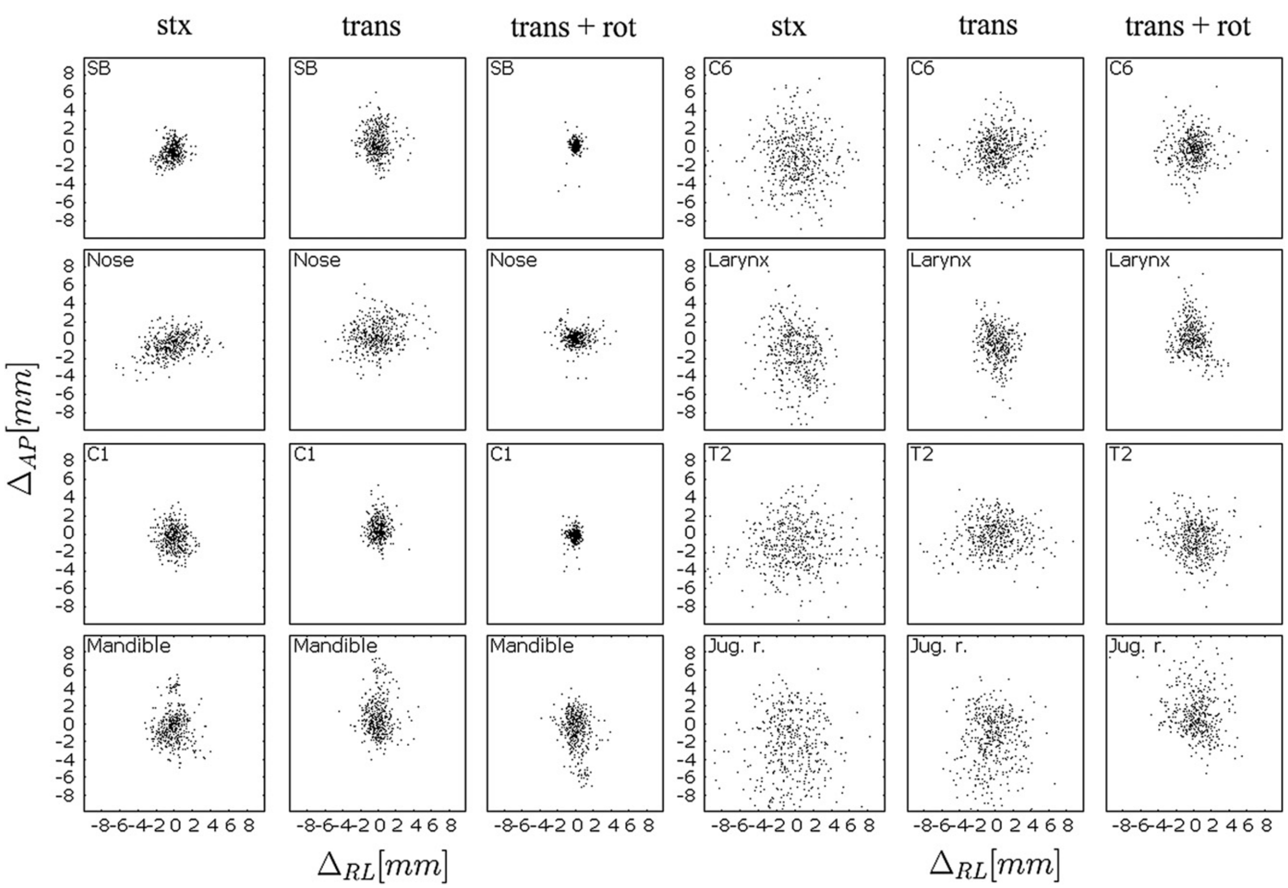

Fig. 3. Comparison of local translational positioning errors without any correction (stereotactic [stx]) and remaining errors after target point correction using registration of target registration box neglecting (trans) or including (trans+rot) rotational error correction. Axial deviations of all patients and fractions shown.

Table 5. Local margins for five different correction strategies

	stx (mm)			TRB trans (mm)			TRB trans/rot (mm)			Mandible (mm)			SB (mm)		
Variable	RL	AP	CC	RL	AP	CC	RL	AP	CC	RL	AP	CC	RL	AP	CC
SB	1.7	2.2	3.9	2.5	3.8	1.8	0.8	1.6	1.8	2.0	3.9	3.5	—	—	—
Nose	3.9	2.7	4.7	4.5	3.7	4.1	2.4	2.1	5.6	2.7	3.6	5.2	1.8	0.9	2.4
C1-C2	2.1	2.6	4.5	1.7	3.1	1.8	0.9	1.6	1.9	2.0	3.3	4.3	1.1	1.5	1.5
Mandible	2.4	3.7	3.9	2.5	4.5	4.1	2.9	4.3	5.1	—	—	—	2.8	3.5	3.8
C6	7.0	8.4	5.1	4.8	5.7	1.9	3.7	5.1	2.2	6.9	8.9	5.5	6.0	6.5	2.4
Larynx	4.7	7.4	6.7	2.9	4.8	5.4	2.7	4.3	5.6	4.5	8.2	6.5	4.1	7.5	4.7
T2	11.3	6.6	6.4	10.1	5.3	4.1	8.8	5.7	5.2	11.6	8.9	8.1	11.0	7.5	4.7
Jugulum right	7.2	11.4	8.4	5.2	8.7	6.2	4.4	7.6	6.4	7.4	12.9	7.5	7.2	11.6	6.9

Abbreviations: stx = patient positioned using stereotactic setup only; TRB trans = margins required if only translational errors corrected after registration with TRB; TRB trans/rot = both translational and rotational errors corrected after registration with TRB; other abbreviations as in Tables 1 and 2.

compared with the lower neck area. This can partly result in a greater amount of bony anatomy and the lesser amount of soft tissue (*e.g.,* fat), especially in the SB region, making the skull less susceptible to the anatomic changes caused by weight loss. In contrast, patient positioning is more affected in the neck area where, for example, fat catabolism during RT can be observed. Initially, the scotch-cast masks were designed for stereotactic intracranial treatment and high-precision carbon ion treatments at the skull base. Because of the proven good repositioning accuracy at the SB (11), they were used also for head-and-neck cancer treatment. For these treatments, the patient fixation was completed by a vacuum mould to avoid shoulder movement. No neck rest was placed between the mask and the mould and distance between both positioning devices was fixed. Because of this fixed distance between the mask and mould, the bending of the neck would be slightly different in all patients, depending on the length of the patient's neck.

To our knowledge, no published data exist to make our stereotactic subregion head-and-neck uncertainties directly comparable to those of other patient cohorts. However, a similar approach was applied by Zhang *et al.* (1) for evaluation of local uncertainties using a thermoplastic mask with radiopaque markers attached to the mask as an external reference point. Comparable in both studies was the positioning uncertainties of the LRBs C1-C2 and C6. The results of the LRB "palatine process" in the study by Zhang *et al.* (1) were compared with those of our "nose" LRB, which also included the anterior parts of both maxillary sinuses. The reported systematic and random shifts for the C6 LRB (outside the mask) were similar in magnitude to ours. A noticeable difference, however, was seen in the errors of C1-C2 LRB in the AP and right–left direction and in the AP and CC direction for the "nose" LRB, in which the systematic and random errors of our patient cohort were about three times smaller. These findings might be explained by the reduction of the ability for the skull to nod in the firm scotch mask.

Deformations referenced to C1-C2

Depending on the applied patient fixation method, a different extent of possible deformations among the LRBs can be expected. This primarily affects the deformations caused by movements of the anatomic structures. It is, therefore, of interest to evaluate the extent to which the applied patient fixation might have influenced the observed deformations. To compare the results obtained with our patient fixation with those of previous published studies, the setup inaccuracies of the subvolumes were referenced to C1-C2 LRB in accordance with the study by van Kranen *et al.* (3). They performed a similar study using a commercially available five-point thermoplastic fixation mask with shoulder fixation. In contrast to this mask, our patient fixation consisted of a very firm mask combined with a mould but without a neck rest. Five of our LRBs were defined on similar anatomic positions and therefore were directly comparable. On balance, the systematic and random errors for the subvolumes of the patient cohort were similar. However, the large positioning variation of the larynx and the mandible seen by van Kranen *et al.* (3) in the CC direction could not be observed in our patient cohort. Our results show that despite an elaborate patient fixation, considerable deformations occur in head-and-neck cancer patients.

Deformations after TPC including rotational error correction

If a TPC based on a TRB registration is performed, it should be investigated if the determined rotational error can be neglected. To clarify the effect of these rotational errors on the remaining translational errors of all subvolumes, we compared the translational errors with and without correction of the related rotational error. This influence was substantial, despite the small values of the occurring rotational errors. The variance of most residual translational errors decreased observably after their correction. This tendency was demonstrated most prominently in the two subvolumes of SB and C1-C2, in which the variance of the residual translations was halved. Thus, the results showed that for our patient fixation, it would be beneficial to correct the rotational error. Still, this influence needs to be evaluated for different head-and-neck fixation devices.

Margins

In clinical routine, it is not the averaged positioning uncertainties that are important, but the margins for target definition resulting from these uncertainties. The magnitude of the required margins for all LRBs is influenced by the selection of the LRB used for registration. This influence is discussed for five clinical patient correction strategies. Because the margin recipe for rigid body shifts (10) was used and no valid margin recipe for deforming objects exists, these values only represent the lower limit for the actually needed margins.

In the case of no correction strategy, the required margins for regions inside the scotch cast mask are mainly smaller compared with those determined from a TPC using translations only. In contrast, outside the mask (larynx, C6, jugulum), larger margins are necessary for stereotactic positioning. Using a TPC with translational error compensation, the margins for the LRBs inside the mask increase by trend, in contrast to outside the mask.

Additional correction of the rotational error in each control CT scan provides the possibility of decreasing the margins in the right–left and AP axes. The LRBs inside the mask were more affected; thus, the remaining margins can partially be halved. This trend was not seen in any of the LRBs located along the spinal cord.

In summary, if both translational and rotational errors can be corrected daily, the margins required to cover the remaining deformations can be noticeably reduced compared with the margins needed for exclusive stereotactic positioning. However, this approach necessitates daily imaging and daily translational and rotational patient positioning correction, even if the determined errors are small.

In clinical routine, it can be advantageous to choose one LRB that provides the optimal correction vector for different tumor locations. For example, in nasopharyngeal cancer, a tumor infiltration of the SB can be present, in which the tumor is in close vicinity to the brain stem or optical nerves. In these patients, a registration focused to the LRB SB is superior in terms of nearby OAR sparing compared with a TRB registration, because smaller margins are needed in the high-dose SB area. However, positioning of the other LRBs becomes worse, especially in the caudal neck, implying the need of larger margins in this area.

In oropharyngeal cancer, it can be beneficial to spare the mandible from the high-dose regions to prevent osteoradionecrosis. Optimal positioning of the mandible can be achieved if registration is focused to the LRB mandible. Again, positioning uncertainties of all remaining LRBs will increase compared with registration with the TRB. In contrast to the nasopharyngeal case, positioning uncertainties of the LRBs containing the OAR spinal cord will increase at all levels along the CC axis. However, an enlargement of the PTV margins also results an increased risk of the spinal cord to bend into the increased PTV, because it is subject to the same positioning uncertainty as the PTV. The margins necessary for the PTV close to the spinal column are about the same in size compared with those needed for stereotactic positioning only (which could be achieved without daily imaging and patient correction).

Thus, these positioning scenarios show that no general correction strategy can be recommended for all head-and-neck patients. However, an individual weighting of the relevant anatomic structures might be beneficial when performing the registration. Possible correction strategies using multiple region of interest registration were recently discussed (12, 13) and are still of great interest. We, therefore, implemented a multiple subvolumen registration tool in the research version of our treatment planning system for additional evaluation of the correction approaches. It allows choosing several, in location and size, variable registration boxes. The effect of the registration result of one of these boxes on the final three-dimensional vector can individually be weighted, depending on the necessity of an optimal alignment in the considered anatomic regions. Additionally, the dosimetric effect for the transformed and nontransformed control CT scan can be calculated to compare with the original plan. Next, the physician decides to accept or revise the proposed three-dimensional vector for TPC. However, the margin prescription for PTV delineation needs to be specified, depending on the applied correction protocol.

CONCLUSIONS

The present study quantified the local positioning variations due to deformations in the head-and-neck region. Despite the use of an individualized patient fixation device composed of a firm scotch-cast mask and a vacuum mold, local deformations occurred similar to those from reported results with Aquaplast masks. Therefore, throughout the treatment course attention should be paid to the positioning variation of the various head-and-neck subregions when using highly conformal RT techniques. None of the correction strategies achieves perfect alignment in all LRBs due to deformations. From the results for our patient fixation, a TPC based on a target bounding box, including rotational error correction, was superior to no correction or solely translational error correction. Future work will evaluate the simultaneous use of several local registration boxes for different tumor sites.

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