PHYSICS CONTRIBUTION

AUTOMATIC DELINEATION OF ON-LINE HEAD-AND-NECK COMPUTED TOMOGRAPHY IMAGES: TOWARD ON-LINE ADAPTIVE RADIOThERAPY

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Purpose: To develop and validate a fully automatic region-of-interest (ROI) delineation method for on-line adaptive radiotherapy.

Methods and Materials: On-line adaptive radiotherapy requires a robust and automatic image segmentation method to delineate ROIs in on-line volumetric images. We have implemented an atlas-based image segmentation method to automatically delineate ROIs of head-and-neck helical computed tomography images. A total of 32 daily computed tomography images from 7 head-and-neck patients were delineated using this automatic image segmentation method. Manually drawn contours on the daily images were used as references in the evaluation of automatically delineated ROIs. Two methods were used in quantitative validation: (1) the dice similarity coefficient index, which indicates the overlapping ratio between the manually and automatically delineated ROIs; and (2) the distance transformation, which yields the distances between the manually and automatically delineated ROI surfaces.

Results: Automatic segmentation showed agreement with manual contouring. For most ROIs, the dice similarity coefficient indexes were approximately 0.8. Similarly, the distance transformation evaluation results showed that the distances between the manually and automatically delineated ROI surfaces were mostly within 3 mm. The distances between two surfaces had a mean of 1 mm and standard deviation of <2 mm in most ROIs.

Conclusion: With atlas-based image segmentation, it is feasible to automatically delineate ROIs on the head-and-neck helical computed tomography images in on-line adaptive treatments. © 2007 Elsevier Inc.

INTRODUCTION

Dose escalation has been shown to be effective in improving the outcome of cancer radiotherapy (RT) at various sites (1–6). However, collateral damage to normal tissue limits the maximal dose that can be safely delivered (7). RT planning uses computed tomography (CT) images, which represent a snapshot of the anatomic geometry at the time of the treatment planning CT scan. Because of setup variations and anatomic changes, a considerable motion margin must be applied to compensate for patients’ anatomic variations. Consequently, a large volume of normal tissue is irradiated by approximately the same radiation intensity as that received by the target. In recent years, image-guided RT (IGRT) has become an important technique in tightening the planning target volume margin (8, 9). On-line imaging modalities, such as ultrasonography, megavoltage CT (10), cone-beam CT (CBCT) on-gantry (11), and CT-on-rail (12), provide on-line volumetric images of the patient during IGRT sessions.

Currently, in IGRT sessions, daily on-line images are registered into planning CT images by rigid-body image registration with six degrees of freedom. Translational position errors may be corrected by shifting the treatment table. Methods have also been proposed to correct or partially correct rotational error by rotating the collimator, the gantry, and/or the table (13–15). However, when the shapes or relative positions of the target and organ-at-risk (OAR) change, simple rigid-body correction techniques may not be sufficient for high-precision RT.

On-line adaptive plan adjustment using daily anatomic geometry and position setup may compensate for target and OAR interfraction variation. A plan adjustment method has been proposed to modify the beam aperture and to deform

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Patient data
A conventional helical CT scanner (Tomoscan SR7000, Philips Medical System, Shelton, CT) was used for image acquisition. Seven HN cancer patients were enrolled in the study. In addition to the treatment planning CT images, 3–6 weekly CT images were acquired for each patient during the RT course. A total of 32 weekly images were acquired from the patients. All images had a slice thickness of 2–3 mm. The resolution was 512 × 512, and the pixel size was 0.973 mm in the transverse plane. Weekly images were used as surrogates of on-line images in the study. Unlike treatment planning CT, no intravenous contrast was administered in the weekly CT acquisitions.

Manual ROI delineation
A commercial treatment planning system (Pinnacle, Philips Medical System, Madison, WI) was used in the contouring of ROIs. A physician manually contoured all ROIs on the planning images, which included the gross tumor volume (GTV), mandible, brainstem, parotids, and lymph nodes. Another physician repeated the contouring on all planning and on-line images independently. Because of the lack of contrast and other medical information, the GTV was not contoured on the on-line images.

All ROIs were dumped into binary ROI masks for data processing. A binary ROI mask \( M \) is a three-dimensional matrix with voxels labeled 1 inside and 0 outside the ROI. It is defined as

\[
M(x) = \begin{cases} 
1 & x \in O, \\
0, & \text{elsewhere}.
\end{cases}
\]

where \( O \) is a spatial domain that manifests the ROI volume, and \( x \) is a voxel vector.

Deformable image registration
Deformable image registration maximizes the similarity between the reference image \( R \) and the floating image \( T \) by warping the floating image and, also, keeps the displacement vector fields smooth. A general form of the objective function of grayscale-based deformable image registration is given by the following equation (22):

\[
F(u) = D(R, T(u)) + \alpha S(u), \quad \alpha > 0
\]

where \( D \) is the measure of similarity with respect to the image intensity, \( S \) is the smoothness regularizer, \( u \) is the displacement vector field, and \( \alpha \) is a regulation parameter that controls the relative weights between the two components in the function \( F \).

We chose the sum of the square difference between the two images as the measure of similarity \( D \) and the sum of the square gradient of voxel displacement as the smoothness regularizer \( S \), which are defined as

\[
D = \int_{\Omega} ||R(x) - T(x + u(x)||^2 dx, \quad (3)
\]

\[
S = \int_{\Omega} \frac{\partial u}{\partial x} \frac{\partial u}{\partial x} dx, \quad (4)
\]

where \( \Omega \) is the domain of the registration. We used a variational-based optimization scheme, in which the local minimum of the objective function was obtained by solving Euler-Lagrange equations (21, 22).

Principally, deformable image registration searches the global minimum of the objective function. Even though locally \( R \) and \( T \) have different values, the optimization algorithm will still be able to find the best global matching between the images. Thus, the deformable image registration algorithm is applicable to the images with different voxel intensities, such as CT images with and without contrast or helical CT images vs. CBCT images.
Multiresolution approaches have been widely used in deformable image registration to alleviate the problem of local minima. We used a multigrid approach to register the image pair with coarse to fine grids at different registration levels (23). As well as maintaining the smoothness of displacement field, the existence of the smoothness regularizer $S$ also limits the range of deformation. The algorithm can be reluctant to match the regions with low contrast and large deformation. To remedy this problem, we reset the displacement fields to zero when registration was completed at each registration level and used the deformed images as new floating images in the next registration level. The displacement fields were saved before resetting.

Automatic image segmentation

Deformable image registration transforms floating images with the displacement map $u$. Thus, we used the planning CT images as floating images and the on-line images as reference images in deformable image registration, so that the displacement map $u$ could be directly used to transform ROI masks on planning images without reversion. The ROI masks on planning images $M_p$ were transformed onto the on-line images according to

$$M_f(x) = M_p(x + u),$$

where $M_f$ is the ROI masks on daily on-line images.

We used a Pinnacle Script to generate binary masks of reference ROIs. The reference ROI masks were transformed onto on-line images using displacement maps from deformable image registration. As a consequence, target images were segmented automatically. We used a custom-developed algorithm to convert the ROI masks into Pinnacle’s ROI file format so that the ROIs can be displayed in Pinnacle.

Dice similarity coefficient index

The dice similarity coefficient (DSC) index (24) has been widely used in the evaluation of deformable image registration results. In this study, manually contoured ROIs were compared to automatically contoured ROIs using the DSC index. The DSC index is defined as

$$\text{DSC} = \frac{2a}{2a + b + c} \quad \text{where} \quad a = n\{O_1 \cap O_2\}, \quad b = n\{O_1 \setminus O_2\}, \quad c = n\{O_2 \setminus O_1\}$$

$$n(O)$$ is the number of voxels in $O$, $O_1$ is the set of voxels of manual (reference) ROI, $O_2$ is the set of voxels of automatic (test) ROI, $a$, representing proper delineation, is the number of voxels common to both data sets; $b$ is the number of voxels unique to $O_1$; $c$ is the number of voxels unique to $O_2$; and $n(O)$ is the number of voxels in $O$. The DSC conformationality index approaches 1 when the reference ROI and test ROI overlap exactly.

Distance transformation

A distance map is an image in which the value of each voxel is the distance from the pixel to a given set or object. A Euclidean distance transformation (DT) is an algorithm that computes an Euclidean distance map from a binary image representing this set of voxels (25). In this study, two DTs were performed on the binary masks of manually contoured ROIs. The first DT yielded a distance map with Euclidean voxel distances outside the ROI surfaces. Then, the ROI masks were reversed so that the ROI volumes were labeled with 0 inside and 1 outside. A second DT of the reversed ROI masks yielded the Euclidean voxel distances inside the ROI. The two distance maps were combined with positive distances outside and negative distances inside the ROI. The nearest distances between the reference ROI surfaces and target ROI surfaces were obtained by overlaying the target ROI surface voxels onto the distance matrix of the reference ROI. The distance value at each corresponding surface voxel position was the nearest distance of this surface voxel to the surface of the reference ROI. In this study, the manually contoured ROIs were used as references and the automatically generated ROIs were used as the target ROIs. The DT validation method is shown schematically in Fig. 2.

Three-dimensional DT transformations were performed on binary ROI masks. However, for some ROIs, the ends of the manual contour on the transverse CT slices were not well defined in the images and involved large human variations. To avoid that, the superior end of the brainstem and the inferior end of the spinal cord were masked out in the evaluation.
RESULTS

Deformable image registration

Daily CT images and planning CT images were used as reference images and floating images in deformable image registration, respectively. The results of deformable image registration are shown in Fig. 3. Each image registration process took 10–15 min using a Dell computer workstation with a 3.0-GHz Intel Xeon CPU and 8-G memory. As shown in Fig. 3, the images were different before image registration and highly similar after registration. Minor dis-

Fig. 3. Deformable image registration of head-and-neck computed tomography images. Images (Left) before and (Middle) after deformable image registration. (Right) Postregistration images by tiled views (gray, reference images; green, floating images).

Fig. 4. (Top) Manually drawn contours on planning computed tomography images and (Bottom) automatically delineated regions of interest on on-line images. Contours on on-line images transformed from planning computed tomography images by fully automatic atlas-based image segmentation. Note the consistency of delineation of gross tumor volumes in on-line images. Red indicates gross tumor volume; light blue, nodes; purple, parotid glands; green, spinal cord; and blue, mandible.
crepancies likely stemmed from the intrinsic differences between the image pairs. For example, the dental filling artifacts in the image pairs caused difficulty in registration.

Automatic segmentation

With the deformation information from deformable image registration, the daily images were automatically delineated according to Eq. 5. Figure 4 shows examples of the manually (physician) contoured atlas and automatically contoured on-line images at a treatment day. Qualitatively, the automatically delineated ROIs on on-line images were consistent with manually delineated ROIs on planning images.

Quantitative validation

Another physician also contoured daily CT images. The manually contoured ROIs were used as references. Automatically generated contours were compared with the corresponding manual contours. The discrepancies between the manually and automatically generated contours might have been caused by image registration errors, as well as human variation. Figure 5 shows an example of the three-dimensional surfaces of the manually and automatically delineated ROIs of the same image data set.

The discrepancies between the manual and automatic contours were evaluated with the DSC index. The human-delineated ROIs on the daily images were used as references. The DSC indexes of each ROI in each daily image data set were calculated (Fig. 6).

Discrepancies between the manual and automatic delineation were also measured by DT. Figure 7 shows the histograms of the distances between the manually and automatically contoured ROI surfaces for a typical patient. The distances between the two surfaces were centered close to zero, and the variations were mostly within 2–3 mm. Table 1 lists the mean values and standard deviations of all ROI discrepancies for all patients. The discrepancies between the manual and automatic ROIs all had a mean of 1–3 mm and standard deviation within 2 mm.

Automatic delineation of GTV

Automatic delineation of the GTV is also necessary for on-line adaptive treatment. One major advantage of atlas-based image segmentation is that the boundaries of the ROIs are not necessary located on image features such as the edges. Figure 4 shows the automatically delineated GTVs on the on-line images.

However, manual delineation of targets in HN cancer may not be consistent (26, 27). In some cases, because of its low contrast to surrounding normal tissue, the GTV can be difficult to be delineated on the on-line images without additional information, such as positron emission tomography and magnetic resonance imaging. Moreover, the on-line CT images used in this study were acquired without intravenous contrast. Therefore, the GVT was difficult for the physician to contour with the limited information provided. Thus, automatic segmentation of the GTV was not compared with the manual contours, as was done for the other ROIs in the present study. Physicians visually inspected the GTV contours on the on-line images and accepted the automatic segmentations of the GTV.

DISCUSSION

In this study, we implemented and validated an automatic atlas-based image segmentation method to delineate the ROIs of daily HN CT images. Automatic segmentation transforms the contours on planning images into the contours on daily images. Atlas-based image segmentation has many features that are suitable for on-line adaptive treatments. These include:

1. Atlas-based image segmentation incorporates a priori knowledge about the shape and image characteristics of the ROIs.
2. Atlas-based image segmentation is able to contour the ROI with a boundary that is not located on the edge. The position of contours can be interpolated from surrounding structures.
3. Atlas-based image segmentation is able to contour all ROIs at once.

The second feature is crucially important for on-line adaptive treatment. For RT planning, some ROIs do not have significant contrast against the background. Physicians delineate these through the use of previous knowledge of the shape and relative position of the ROIs to more prominent structures. Atlas-based image segmentation mimics the knowledge of the anatomy and radiology experts. It uses *a priori* knowledge about shape and image data.
characteristics in the segmentation process. The boundary of some structures, such as the GTV, does not lie on the image edge. Atlas-based image segmentation may interpolate ROI boundaries from nearby structures with more obtrusive contrasts.

Deformable image registration relies on image quality. In the present study, we used CT images from a fan-beam CT scanner. CT-on-rail provides daily helical CT images. Our current automatic ROI delineation method can be directly applied to IGRT by CT-on-rail. Still in its infant stage, CBCT on-gantry is becoming a popular on-line imaging modality for IGRT. The image quality of CBCT is inferior to that of a fan-beam CT scanner. Both scatters and approximate image reconstruction cause significant image artifacts and distortions. More importantly, the signal/noise ratio is dramatically low compared with that of regular fan-beam CT images. Thus, additional improvements may be necessary to make the algorithm immune to the defects of CBCT.

Dental filling artifacts often exist in some HN CT images. Figure 8 shows the automatic segmentation results of HN images with dental filling artifacts. The influence of the artifacts was constrained to a proximate region of a dental filling. Only the mandible contours on a few slices were distorted. Other ROIs were not significantly affected. Many CT reconstruction algorithms have been developed to eliminate or reduce dental filling artifacts. Implementation of these techniques in on-line CT imaging modalities would be beneficial in HN on-line adaptive treatments.

Deformable image registration does not guarantee point-to-point matching. Point-to-point matching is very difficult to validate because the true information is unknown. Previous studies warped the image data set with predetermined displacement fields and then registered the warped image data set back to their original shapes (18, 21). In reality, however, organ shape changes are far more complex than any deformation model can simulate. Fortunately, exact point-to-point matching is unnecessary in on-line re-planning, in which only the ROI boundaries are used. Additional investigations are necessary for off-line adaptive RT, in which point-to-point information is mandatory to obtain accumulated doses.

We validated atlas-based segmentation through a comparison with manual delineation. The discrepancies between the reference manual contours and automatic generated contours included registration errors, as well as human variations. This quantitative validation method is only valid

![Fig. 7. Histograms of surface distances between manual regions of interest and automatic regions of interest. ROI = regions of interest.](image)

Table 1. Mean followed by standard deviation of discrepancies between manually and automatically generated contours

<table>
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<tr>
<th>Pt. No.</th>
<th>Total images</th>
<th>Brain stem (mm)</th>
<th>Spinal cord (mm)</th>
<th>Mandible (mm)</th>
<th>Right parotid (mm)</th>
<th>Left parotid (mm)</th>
<th>Lymph nodes (mm)</th>
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Abbreviations: Pt. No. = patient number; NA = not applicable.
* Nodes of Patient 5 were included in gross tumor volume and were not contoured separately.
when the ROI can be accurately defined by a human, such as has been done for the kidney (28). We have performed repeat manual delineation by two physicians on a few data sets. This limited study showed that all the ROIs, except for the GTV, can be reliably delineated using daily CT images without contrast. Larger scale of studies should be performed to quantify the component of interphysician variations in the overall discrepancies.

Automatic delineation of the GTV is extremely important for on-line adaptive treatment. We have experienced difficulty in the manual delineation of the GTV in daily images without intravenous contrast. As a consequence, automatically generated GTV contours were not quantitatively validated in the same way as the other ROIs in this study. Additional study in GTV validation is necessary for on-line adaptive RT.

CONCLUSION

Atlas-based image segmentation can automatically delineate the ROIs on daily CT images. Quantitative validations demonstrated that this method was robust in contouring ROIs in daily HN fan-beam CT images. Atlas-based image segmentation can be a key component in IGRT by way of on-line replanning, as well as for other on-line adaptive approaches.

REFERENCES


