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An automatic deformable registration method to evaluate parotid glands shrinkage during radiotherapy treatment in Tomotherapy

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Abstract— **The aim of this study is to provide a method to track the anatomical alterations of parotid glands during radiation treatment. The method we implemented is based on an intensity-based free-form deformable registration to realign the planning kilo-Voltage CT (kVCT) and the daily Mega-Voltage (MVCT) image sets and on an automatic contour propagation algorithm based on surface construction by triangular mesh. The accuracy of the method was evaluated through visual inspection and comparison with manual contours drawn by expert physicians. The uncertainties of automatic contours were similar to those of manual contours, in terms of parotid volumes and center-of-mass distances. The parotid volumes decreased with a median total loss of 21.7%. We observed an average medial shift of parotid center-of-mass of 3.1 mm from the external part toward the midline. The deformable registration method presented in this work provides an accurate tool for the automatic evaluation of parotid changes occurring during a radiotherapy treatment period.**

I. INTRODUCTION

Head and neck cancers (HNC) have always presented a challenge to the radiation oncologist. Survival depends upon local control with high-dose radiation, yet the tumor is surrounded by critical, dose-limiting normal tissues. Reduced salivary output and permanent xerostomia have been reported to be most common side effects of radiation for HNC and a major cause of decreased quality of life.

The recent availability of new IMRT delivery techniques using a much larger number of segments and degrees of freedom, such as Helical Tomotherapy (HT) may open new fields of exploration for the radiotherapy of HNC due to the ability of these techniques in creating very deep dose gradients and in tailoring very sharp dose distributions around the target volumes. The most important result of a few investigations is that HT has the potential to significantly improve the quality of the dose distribution both in terms of better dose homogeneity within the planning target volume and more efficient sparing of spinal cord, parotids and mandible [1].

During the course of radiation treatment, HNC patients may undergo significant anatomical changes: a significant decrease of parotids volume and their migration towards the high-dose region with a distance change of few mm; due to these anatomical modifications the parotids can receive a total dose significantly higher than the planned one. Overdosing to organs at risk due to the anatomic changes during the RT course can determine severe acute side effects with a treatment interruption and a subsequent decrease in local tumor control probability.

On the other hand, daily image-guidance by CT is nowadays possible, by using HT (with Mega-Voltage CT, MVCT) or other systems, with the potential to better understand the impact of these modifications and of adapting the treatment according to these anatomical changes.

For this reasons having an accurate method for the evaluation of parotids modifications is very important. The aim of this study is to provide a deformable registration between the planning kilo-Voltage CT (kVCT) and the daily MVCT image sets and a contour propagation algorithm able to track the anatomical alterations of parotid glands during radiation treatment. The registration method is based on intensity-based free-form deformation [2]-[3]. In this work we carry out a validation of the methods in terms of qualitative assessment and quantitative comparison between deformed and manual contours drawn by a few expert physicians. Moreover, we provide a preliminary evaluation of parotid alterations in terms of volume and distance changes and in terms of local shrinking and stretching.

II. MATERIALS AND METHODS

A. Patient characteristics

The study consisted of 3 patients treated for head and neck cancer on a helical tomotherapy unit (HiArt 2 Tomotherapy, Madison, Wisconsin). Patients were treated with radiation therapy and with concurrent chemotherapy.

For this study we used the planning kVCT scans of each patient and 2 daily MVCT images. MVCT images were acquired prior to each treatment fraction and were clinically used for patient alignment. For the purpose of this study one MVCT scan at the beginning of the treatment and one at the end (fraction 30) were considered.

B. Deformable image registration method

An elastic image registration method was implemented for this study. The method was the one proposed in [3], adapted in terms of grid resolutions and gaussian smoothing to accommodate kVCT and MVCT image registration and it was entirely implemented in C++ based on the medical image processing library ITK (National Library of Medicine Insight Segmentation and Registration Toolkit). The method

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was formulated as a two-stage process: first, the global motion was corrected using a rigid transformation. The global motion then became the starting estimate for the second stage, where the local motion was further modeled using free-form deformations (FFD) based on B-splines [2]-[3].

$$T(x, y, z) = T_{global}(x, y, z) + T_{local}(x, y, z) \quad (1)$$

The basic idea of FFD's is to deform an object by manipulating an underlying mesh of control points. The resulting deformation produces a smooth and C^2 continuous transformation. To define a spline-based FFD, we define a sparse, regular grid of $n_x \times n_y \times n_z$ control points $\phi_{i,j,k}$. The resolution $\rho = [\rho_x, \rho_y, \rho_z]$ of the deformation determines the spacing of the grid. We denote the domain of the image volume as $\Omega = \{(x, y, z) \mid 0 \leq x \leq X, 0 \leq y \leq Y, 0 \leq z \leq Z\}$. Then, the FFD can be written as the 3-D tensor product of the 1-D cubic B-splines

$$T_{local}(x, y, z) = \sum_{l,m,n=0}^{3} B_l(u) B_m(v) B_n(w) \phi_{i+l,j+m,k+n} \quad (2)$$

where $i = \lfloor x/\rho_x \rfloor, j = \lfloor y/\rho_y \rfloor, k = \lfloor z/\rho_z \rfloor, u = x/\rho_x - \lfloor x/\rho_x \rfloor, v = y/\rho_y - \lfloor y/\rho_y \rfloor, w = z/\rho_z - \lfloor z/\rho_z \rfloor$. B_l represents the lth basis function of the cubic B-spline. Note that only those $\phi_{i,j,k}$ corresponding to the 64 control points nearest (x, y, z) contribute to the summation in (2).

As similarity measure, we used of mutual information (MI) in the form proposed by Mattes *et al.* [3] and a multiresolution strategy of the image and of the deformation grid to avoid local minima. For the optimization, the L-BFGS-B optimizer [4] was used.

C. Contour propagation

A method to automatically propagate contours from the planning kVCT to the daily MVCT scans was implemented in C++ based on the libraries ITK and VTK (The Visualization Toolkit). The contour propagation method requires the parotid glands contours which are manually drawn slice-by-slice on the transversal view of the kVCT image by a physician. Starting from these contours we constructed a surface triangular mesh of the object using the approach proposed in [5]: this method first approximate the medial axis transform of the object and then use an inverse transform to produce the surface representation. As opposed to contours, the triangular mesh preserves the relations among vertices, edges and faces after a 3D deformation. The surface deformation is as simple as displacing the vertices of the surface according to the displacement map from the deformable registration. The deformed surface is supposed to match the same volume of interest in the MVCT image since its deformation is based on the results of deformable registration. The deformed contours were obtained by cutting the deformed surface through planes corresponding to the MVCT slices.

D. Evaluation of the method

In order to assess the accuracy of the deformable registration method, the registered MVCT images were compared to the kVCT planning images by visual inspection of two expert physicians.

The deformed kVCT contours on daily MVCT scans were also qualitatively, i.e. visually, inspected to ensure that they were within established anatomic boundaries of the parotid glands.

In addition, the deformed contours were compared with the manual contours directly outlined on MVCT images by three observers. None of the observers had knowledge of contours outlined by the other observers. Since manual contours have also inherent uncertainties, it was assessed if the uncertainties of the automatic contours fall within those of the human observers. The uncertainties were estimated in terms of volume, center-of-mass (COM) and spatial overlap.

The average volume of the left and right parotid glands and the distance between their centers-of-mass (COM distance) were used to compare the deformed parotid with the parotid contoured by the observers. The COM distance should be preferred over the absolute coordinates as observed in [6].

For the spatial overlap evaluation, both intersecting (common) volume and encompassing volume were calculated. The intersecting volume was defined as the largest volume common to all parotids delineated by the three observers. The encompassing volume was the smallest volume encompassing all three volumes (i.e. the union of all three parotids volumes, obtained using the contours of each of the three observers). We visually verified if the deformed contours were between the common and the encompassing volume.

E. Assessing the geometrical changes of parotid glands

For each patient the volume and position changes were evaluated between the begin-of-treatment and the end-of-treatment MVCT.

Furthermore, in this work we propose a method for the local evaluation of parotid deformations. With this method we are able to easily distinguish among areas that are differently affected by modifications. In particular we are interested in a clear representation of parotid areas that are mostly affected by shrinkage during therapy.

The method uses the Jacobian of the deformation field produced by the registration algorithm [7] and its visualization on the parotid surface. The Jacobian function is defined at each point of a structure of interest i.e. the parotid in the kVCT image, and reflects the size difference between a voxel in the kVCT image and its corresponding voxel in the MVCT image.

In detail, the registration algorithm provide the deformation field $T(x, y, z) : (x, y, z) \longmapsto (X, Y, Z)$, that maps the point (x, y, z) in kVCT image domain to the point (X, Y, Z) in MVCT image domain. If $T(x, y, z)$ is known, it can be defined the Jacobian J of the transformation

$$J(x, y, z) = det(\nabla T(x, y, z)) \quad (3)$$

where ∇ denotes the gradient of a vector funcion and $det(\cdot)$ denotes the determinant of the matrix. For the principles of continuum mechanics, if $J > 1$ at a point (x, y, z), then an infinitesimal volume around (x, y, z) expands. Similarly,

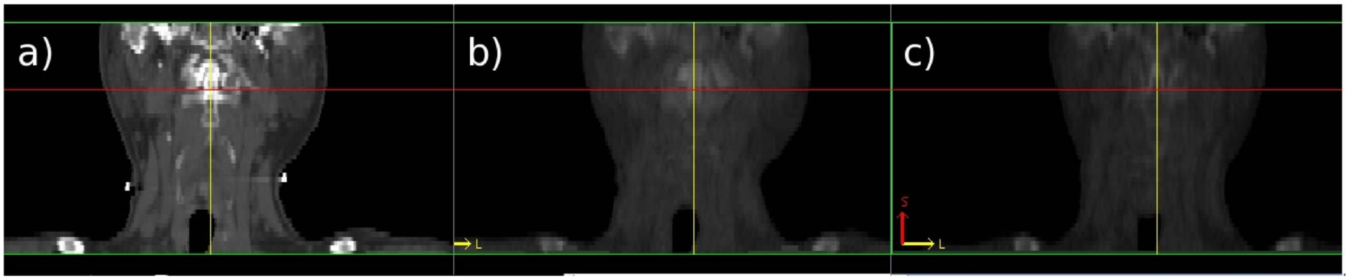

Fig. 1. Coronal view of Patient-1. (a) Planning kVCT, (b) end-of-treatment MVCT after deformable image registration and (c) end-of-treatment MVCT after rigid registration.

if $J < 1$, then a local shrinking around (x, y, z) occurs. So, the Jacobian J, evaluated in the parotid volume, gives a measures of the stretching or shrinking of the gland during the course of treatment. The mapping of J over the parotid sections provides a representation of the areas that are most involved in anatomical modifications, i.e. parotid areas most affected by shrinkage.

III. RESULTS

A. Validation of the deformation algorithm

Fig. 1 shows the kVCT and MVCT images relative to Patient-2 , after rigid and elastic registration, in order to qualitatively verify the spatial correspondence of anatomical structures in this study.

The visual inspection performed by two physicians judged a correct spatial correspondence of the parotid glands after deformation, whilst a rigid registration was considered insufficient.

A quantitative evaluation of deformation accuracy can be obtained by the analysis of the volume and COM distance of the automatically generated contours in comparison to those manually drawn. In terms of COM distance, the automatic contours were always within the manual uncertainties (Fig. 2a). The automatic deformed volumes were generally within the corresponding manual volumes drawn by the experts (Fig.2b). The only exception was found in the case of the begin-of-treatment volume for Patient-1 and Patient-2. Here the automatic volume slightly overestimated (8% and 9%) manual volumes. However a deepest investigation showed that those overestimations were located in anatomical areas presenting a very low contrast among soft tissues (i.e. areas that were more difficult to discriminate and where a manual contouring can be mostly prone to errors).

Indeed, from the analysis of the encompassing and common volumes we noted that even when the automatic volumes overestimated the manual ones, the automatic contours were always within established anatomic boundaries (i.e. the zygomatic arch, the external auditory meatus, the mastoid process and the masticator space). In these cases, the automatic contours were greater than the encompassing contours only in areas where the manual uncertainties were maxima. In all the other cases, the automatic contours fell between the encompassing and the common contours as can be appreciated in Fig. 3.

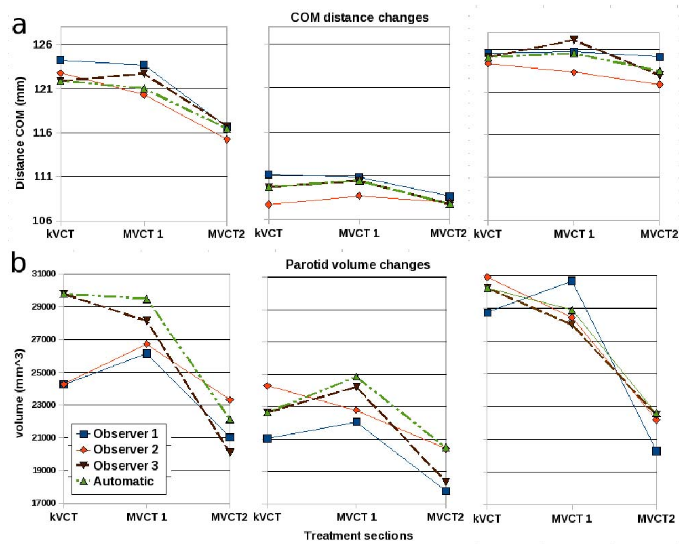

Fig. 2. Comparisons of the automatic parotid contours with three manually drawn contours over treatment sections: planning (kVCT), begin-of-treatment (MVCT 1) and end-of-treatment (MVCT 2). The automatic contours were created deforming the contours drawn by Observer3 on planning kVCT. (a) Center-of-mass (COM) distance and (b) average parotid gland volumes changes.

B. Evaluation of parotid deformations

A decrease in parotid volume was observed for all three patients. The percent volume loss was of 17.6%, 21.7% and 24.9% respectively. The median volume loss of 21.7% is similar to the results reported by Lee *et al.* [6] over 10 patients, obtained using a different registration method. The differences in the lateral and axial directional COM distances were very negligible. The main direction of parotid migration was from the external part toward the mid-line. We observed an average medial shift of parotid COM of 3.1 mm. This result is reasonable in agreement with Barker *et al.* [8] that observed a median medial shift of 3.1 mm in 14 patients.

The spatial distribution of deformation in parotid glands can be observed in Fig. 4 where we show, in blue on a red background, the regions in which the Jacobian function for Patient 1, was smaller than 0.85 corresponding to a shrinkage greater than 15%.

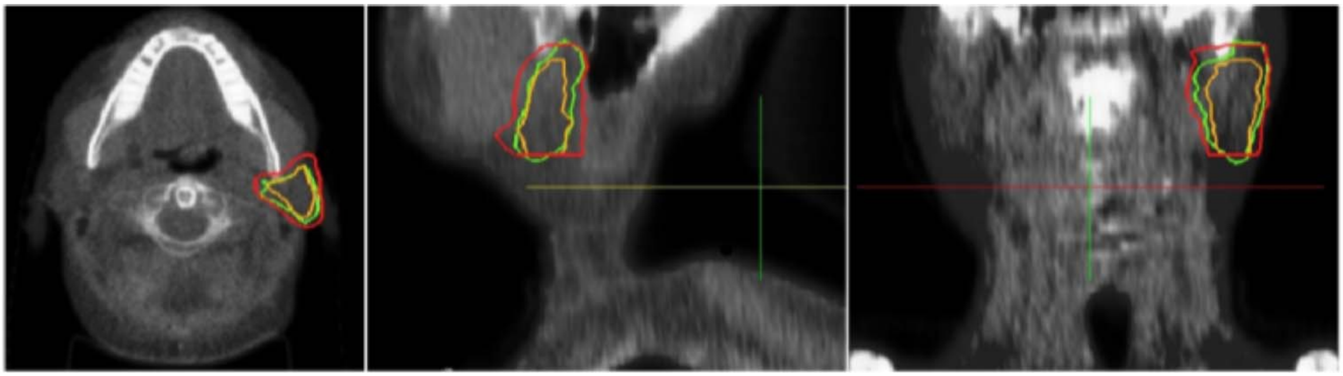

Fig. 3. Encompassing contour (red), common contour (yellow) and automatic contour (green) are shown in end-of-treatment MVCT, for Patient-1, right parotid. Note the consistency of delineation of parotid glands: deformed contour is always inside anatomical boundaries i.e. the zygomatic arch.

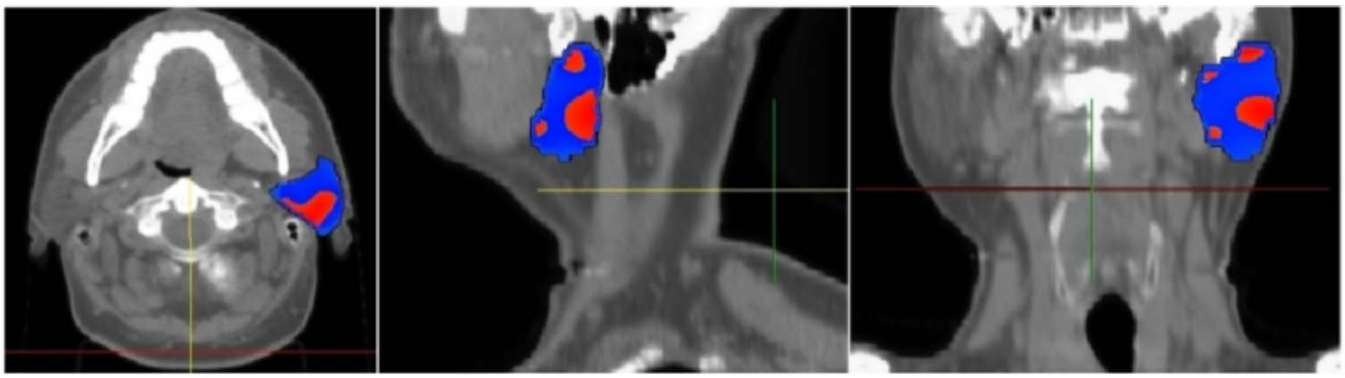

Fig. 4. Axial, sagittal and coronal views of kVCT for Patient-1 with the overlapped Jacobian function calculated in right parotid. In blue Jacobian function smaller than 0.85 corresponding to a shrinkage greater than 15%. In this case we noted a maximal shrinkage in the anterior, internal and inferior areas.

IV. DISCUSSION AND CONCLUSIONS

In this work free-form deformable image registration and automatic contour propagation were used to analyze anatomical alterations of parotid glands during radiotherapy treatment. The deformed contours were considered to be reasonable in shape and location by two physicians. A multi-observer study also showed that volume and COM distance of the automatically generated contours were typically within the uncertainty obtained with manual contouring.

Anatomical alterations of parotid gland were analyzed in terms of volume and COM distance changes from the beginning to the end of the radiotherapy treatment. These changes resulted consistent with what had been previously reported.

The Jacobian determinant of the transformation was mapped in the parotid glands volumes to estimate which regions are more affected by variation during therapy. This method was judged to be able to highlight anatomical areas that underwent different changes during the therapy.

The deformable registration process presented in this work provides an accurate tool for the automatic evaluation of parotid changes occurring during a radiotherapy treatment period.

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