3D Atlas Building in the Context of Head and Neck Radiotherapy Based on Dense Deformation Fields

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Abstract

In this paper we present a methodology to build a computational anatomical atlas based on the analysis of dense deformation fields recovered by the Morphons non-rigid registration algorithm. The anatomical atlas construction procedure is based on the minimization of the effort required to register the whole database to a reference. The suitability of our method is demonstrated for atlas construction of the head and neck anatomy. In this application, CT is the most frequently used modality for the segmentation of organs at risk and clinical target volume. One challenge brought by the use of CT images is the presence of important artefacts caused by dental implants. Such artefacts make the use of most atlas building techniques described in the literature impracticable in this context. The results have shown that our model is faithful for representing the shape variability presented in human nature with the advantage that our anatomical atlas does not have any degree of smoothness.

1. Introduction

The introduction of intensity modulated radiation therapy (IMRT) into clinical practice has allowed a better control of dose distribution over tumoral areas and the reduction of normal tissues jeopardizing. An efficient application of this technology in clinical practice raises the issues of adequacy and accuracy of the selection and delineation of the Clinical Target Volumes (CTVs) as well as surrounding Organs at Risk (OAR) to be preserved. Such delineation is typically performed by trained experts and is an extremely time consuming task. Manual segmentation also raises the risk of introducing intra- and inter-rater variabilities.

Atlas based segmentation is a well known paradigm to assist the radiologist in the segmentation task. In this paradigm, shape and intensity characteristics are encoded in the atlas which is warped on the patient under investigation by a spatial transformation. Using this warping, volumes of interest (VOI) defined in the anatomical atlas can be projected onto the patients' coordinate system.

Significant efforts have been directed toward the development of templates for atlas based segmentation, mainly for the human brain using magnetic resonance (MR) as the main modality [13], [16], [8]. Some methods use a single subject anatomy, as in [2], [3], [11], which can not cope with the complexity of the image data and the variability of the structures under study. In these cases the atlas will be biased towards the anatomy of the chosen image.

A widely used atlas of the human brain is the MNI atlas, that is the standard atlas template in SPM [15]. This atlas was constructed using spatial normalization by linear registration with 9 degrees of freedom. Linear registration does not compensate for local shape differences in the brain, which induces blurring, not only in the averaged Magnetic Resonance (MR) template but also in the tissue distribution maps obtained by averaging segmentations over all subjects. This makes linear atlases not suited as a mean shape template for brain morphometry approaches that are based on non-rigid atlas-to-subject image registration.

What we propose here is the use of the deformation field as the main feature to build an anatomical atlas. Atlas construction based on deformation field analysis has been an important topic of research [5], [16]. More closely related to our work is the one in Guimond et al [5], where it is proposed to build an average shape and average intensity atlas from a set of subjects. In this work, one image is chosen as the reference from a set of 5 magnetic resonances. An elastic registration between the reference and all the subjects in a data set is then performed. Residual and affine registrations are extracted from this registration. The average shape model is found by averaging the residual deformations. The average of residual transformations is then applied to the averaged intensity image, repeating this process until the atlas is unbiased due to the choice of the first reference image. They have shown convergence of the choice of the reference image on the final atlas template after 2 iterations. However, only five images were used for template construction; such limited database may not be enough to assess local shape differences or to generalize the fast convergence into an unbiased template.

In this paper, contrary to [5], we do not perform intensity average. This is mainly motivated by the fact that the main modality in the context of head and neck radiotherapy is CT, in which dental implants may cause metal artifacts in the volumes, making impracticable to average intensities as performed in most proposed methods [15]. Moreover, instead of choosing one image from the database to start the registration process and then applying the average deformation field iteratively to remove the bias caused by the choice of the first image, we propose to find an optimal template based on the deformation field average.

The paper is organized as follows. In the next section we briefly describe the anatomical atlas building model and the non-rigid registration method used called Morphons. In section 3, numerical results are presented and a qualitative evaluation of our method is illustrated. Finally, discussions and conclusions are presented in Section 4, also pointing out future work.

2. Atlas Building

The aim of anatomical atlas construction is to have an image/volume that represents a population anatomy of the head and neck from a database of 3D CT images, assuming that the database is representative of the population of interest. The goal of the atlas in head and neck radiotherapy is to automatically segment the zones at risk and also the regions with high probability of tumoral propagation in the fatty tissues [4].

Although several methods have been proposed to create a brain atlas, their extensions to head and neck exist only in theory and have not been demonstrated in practice. In fact, in our application we encountered some difficulties that do not exist in brain MR images, which limits the straight application of most proposed methods in head and neck CT. Firstly it is prohibitive to have CT images/volumes of normal subjects due to the nature of the exam. The other problem is the presence of several artefacts in the database, which makes impossible to use the same methodologies as proposed for brain atlas building.

2.1. Registration

Registration is the process of finding a transformation T that best matches two images according to a criterion of similarity. One image is the reference, which remains fixed during the registration process, while the other is deformed in the geometric space of the reference. The reference image is also called fixed or target image and the transformed image is called the moving image.

For the atlas building, it is important to use a very accurate registration methods. The non-rigid algorithm used in this application is the Morphons algorithm. This method was chosen based on our previous work [12], in which we have shown with with quantitative results the capability of this non-rigid multi-modality registration method to segment regions of interest in head and neck CT images. Even though all images are only CT volumes, the reason to use a multi-modality method in this application is the noisy database containing artefacts that may cause intensity variations. These artefacts are being illustrated in Figure 1, which shows slices of an axial and a sagittal view, respectively, from a subject of the database.

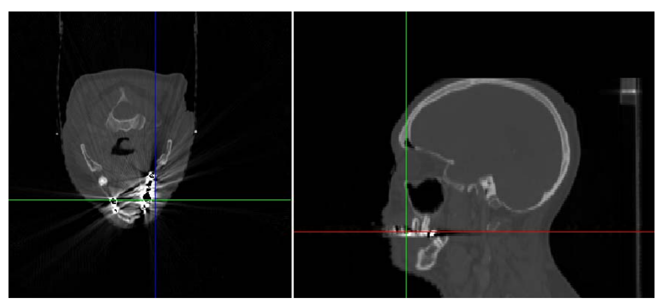

Figure 1. Slices of an axial and a sagittal view of one image of the Database showing metal artefacts from dental implants.

2.2. Morphons

The Morphons method is a non-rigid registration method using an iterative deformation scheme where the displacements estimation are found from local phase difference [17], [7]. To find local phase information, a set of quadrature filters, each one sensitive to structures in a certain direction, is applied to the fixed image and the atlas respectively. Registration with Morphons involves iterative accumulation of a dense deformation field under the influence of certainty measures. These certainty measures are associated with the displacement estimates found in each iteration.

The output from filtering a signal $\mathbf{s}$ with one quadrature filter $\mathbf{q}$ is:

$$\mathbf{q} = (\mathbf{q} * \mathbf{s})(\mathbf{x}) = A(\mathbf{x})e^{j\phi(\mathbf{x})}$$

where $j = \sqrt{-1}$.

The phase difference between two signals after filtering with a quadrature filter can be found according to:

$$\mathbf{q}_1\mathbf{q}_2^* = A_1 A_2 e^{j\Delta\phi(\mathbf{x})} \tag{1}$$

The phase difference is the argument of this product, $\Delta\phi(\mathbf{x}) = \phi_1(\mathbf{x}) - \phi_2(\mathbf{x})$. The local displacement estimate $d_\imath$ in a certain filter direction $\imath$ is proportional to the local phase difference of the filter responses in that direction, $d_\imath \propto \Delta\phi(\mathbf{x})$.

A displacement estimate is found for each pixel and for each filter in the filter set. Thus, a displacement field $d_\imath$ is obtained for each filter direction $\hat{\mathbf{n}}_\imath$. These fields are combined into one displacement field by solving a least square problem:

$$\min_{\mathbf{d}} \sum_\imath \left[c_\imath(\hat{\mathbf{n}}_\imath^T \mathbf{d} - d_\imath)\right]^2 \tag{2}$$

where $\mathbf{d}$ is the sought displacement field, $\hat{\mathbf{n}}$ is the direction of filter $\imath$, and $c_\imath$ is the certainty measure (equal to the magnitude of equation 1).

Iterative accumulation of a dense deformation field is done under the influence of certainty measures:

$$\mathbf{d}_a^{'} = \frac{c_a\,\mathbf{d}_a + c_k\,(\mathbf{d}_a + \mathbf{d}_k)}{c_a + c_k} \tag{3}$$

where $\mathbf{d}_a^{'}$ indicates the *updated* accumulated deformation field, $\mathbf{d}_a$ is the accumulated field from the previous iteration and $\mathbf{d}_k$ is the displacement estimates $\mathbf{d}$ derived in the current iteration k. c_a and c_k are certainty estimates associated with the accumulated deformation field and the displacement estimates, respectively. c_k is the sum of certainty values $c_\imath$ in equation 2 for all filter directions. c_a is found by an accumulation procedure by using the certainty values as certainties of themselves:

$$c_a^{'} = \frac{c_a^2 + c_k^2}{c_a + c_k} \tag{4}$$

2.3. Atlas Model

The atlas building consists in finding a subject that represents anatomically a population. The ideal situation is to have an unambiguous numerical criterion which indicates that a certain image is the most representative in size/shape of human anatomy, this image being then chosen as the Atlas.

Non-rigid registration accounts for the differences in the coordinate systems of the two subjects due to size/shape variation, enabling the deformation of each of the subjects to be quantitatively and qualitatively compared. Based on it, deformation fields will be the main feature to discriminate the best subject to be the atlas. A subject for which the average of the deformation field is near zero, after having all other subjects being registered into him, is the optimal shape template or Atlas. This is the principle of our method, assuming that all the images in the database are geometrically aligned. Let us now introduce formally our methodology.

A deformation field is a function that represents a correspondence between two different subjects. Let $\mathbf{D}(x, y, z)$ be the deformation field for the whole image/volume, and each point (x, y, z) in $\mathbf{D}(x, y, z)$ have a displacement vector associated in each of the three directions: x, y and z. Note that it differs from $\mathbf{d}$ in Eq. 2, which represents the displacement for a given pixel/voxel.

To simplify the notation, a point in the space will be denoted as $\mathbf{x} = (x, y, z)$; i and j are the indices of the subjects in a database of N images. The displacements from subject j to subject i in each direction x, y and z are respectively defined as:

$$D_{x_{ij}}(\mathbf{x}) \in \Re^m \times \Re^n \times \Re^p$$
$$D_{y_{ij}}(\mathbf{x}) \in \Re^m \times \Re^n \times \Re^p$$
$$D_{z_{ij}}(\mathbf{x}) \in \Re^m \times \Re^n \times \Re^p$$

where $m \times n \times p$ are the image dimensions. This triplet defines the deformation field that register subject j into subject i and represents how much a subject has to be deformed to have the same size/shape of the other.

After all subjects j have been registered in a certain subject i, the average of all the deformation fields will be found. The average displacements in each direction x, y and z are, respectively:

$$\overline{D}_{x_i}(\mathbf{x}) = \frac{1}{N-1} \sum_{j=1, j\neq i}^{N} D_{x_{ij}}(\mathbf{x}) \tag{5}$$

$$\overline{D}_{y_i}(\mathbf{x}) = \frac{1}{N-1} \sum_{j=1, j\neq i}^{N} D_{y_{ij}}(\mathbf{x}) \tag{6}$$

$$\overline{D}_{z_i}(\mathbf{x}) = \frac{1}{N-1} \sum_{j=1, j\neq i}^{N} D_{z_{ij}}(\mathbf{x}) \tag{7}$$

Where $\overline{\mathbf{D}}_i(\mathbf{x}) = (\overline{D}_{x_i}(\mathbf{x}), \overline{D}_{y_i}(\mathbf{x}), \overline{D}_{z_i}(\mathbf{x}))$ is the average deformation field for the subject i.

A subject i whose average of the deformation field is closest zero is the optimal shape template. Based on this, we would like to measure it in a concisely manner, since $\overline{\mathbf{D}}_i(\mathbf{x})$ is a very dense information. So we do that using the norm of the magnitude, as defined in the following equations.

$$|\overline{\mathbf{D}}_i(\mathbf{x})| = \sqrt{\overline{D}_{x_i}(\mathbf{x})^2 + \overline{D}_{y_i}(\mathbf{x})^2 + \overline{D}_{z_i}(\mathbf{x})^2} \tag{8}$$

The norm of the magnitude of the average deformation field for each subject i is:

$$\mathcal{D}_i = \frac{1}{m \times n \times p} \sqrt{\sum_{x=1}^{m} \sum_{y=1}^{n} \sum_{z=1}^{p} |\overline{\mathbf{D}}_i(\mathbf{x})|^2} \tag{9}$$

Subject i which requires the minimum average displacement in the equation bellow is the optimal shape template or Atlas:

$$\min_i \mathcal{D}_i \tag{10}$$

The block diagram in Figure 2 illustrates the atlas building process. In this scheme, let the boxes in grey be a subject in a database of 6 images. The boxes are disposed by their size/shape in relation to the centre image, this latter being the most central anatomy in this database. The subjects around the centre image have a varying anatomy, being smaller or bigger. Since we don't know a priori which image has the most representative size/shape, everyone at a time will be the fixed image and all the 5 subjects left will be non-rigidly registered into him.

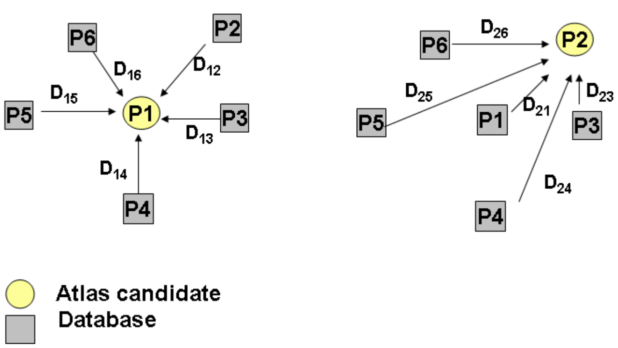

Figure 2. Scheme that illustrates the atlas building process. See text for details.

Based on left diagram of Figure 2, subject P1 starts being the altas candidate. The deformation field resulting from registering image P2 into P1 will be denoted by $\mathbf{D}_{12}$, to register image P3 into P1 will be denoted by $\mathbf{D}_{13}$, and so on. After all images have been registered to P1, equations 5, 6 and 7 are calculated for the set of deformation fields $\mathbf{D}_{1j}$ from all registrations pairs $1j$. Then the equation 9 is computed for subject $P1$. To find an image that represents the central anatomy between all the others in the database, each subject at a time has to be an atlas candidate. Next, all steps described above have to be repeated considering P2 as the fixed image or the atlas candidate, as shown in the right scheme of Figure 2. The subject i that gives the minimum value in equation 10 is the Optimal Shape Template or the Atlas.

In order to illustrate our atlas construction procedure, we took a real image of a hand and artificially created two others to have an enlarged and a reduced version of it. Figure 3 shows the real hand in the top, the enlarged version in the left bottom and a reduced one in the right bottom. In the hand experience, the enlarged hand was registered at the original one and the norm of the deformation field was calculated, providing a value of $2,254$. Then the reduced hand was registered at the original hand and the norm of the deformation field was calculated, providing a value of $1,929$. After registering both modified hands at the original one, we calculate the average deformation field described and finally the norm of it, founding a value of 241. The norm of the average deformation field was around 10 times smaller than the norm of the deformation field of the enlarged hand being registered at the original hand, and also smaller than the norm of the deformation field of the reduced hand being registered at the original hand. This corroborates the expected behaviour of our method, showing that our metric is capable of finding the image with a central anatomy in the population.

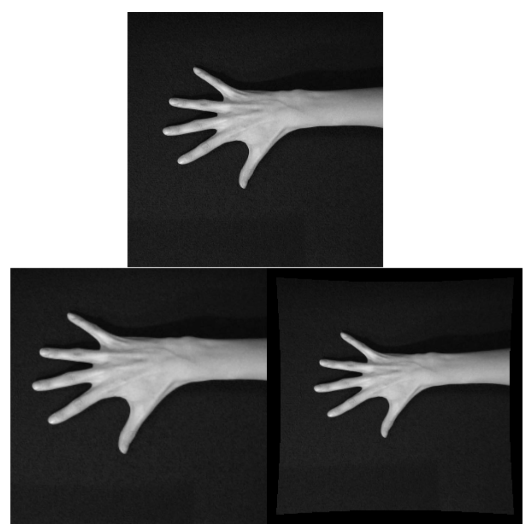

Figure 3. Database of hands. Top: original Hand; Left Bottom: artificially enlarged hand; Right Bottom: Artificially reduced hand.

3. Results

3.1. Database

A database of 31 patients of 3D CT images previously segmented by a radiologist has been used to build the atlas. The size of the CT volumes is of 256x256x128 pixels with a voxel size of 0.9765 x 0.9765 x 2.1093 mm^3. All images in this database are male patients with the age between 50 and 70 years old.

3.2. Implementation

Before performing Morphons registration, all images in the database have to be at same geometric space, a condition required by the atlas model. So we firstly apply a rigid registration; the geometrically alignment is obtained by minimizing the mutual information between the fixed and the moving image [10] using a Simultaneous Perturbation Stochastic Approximation(SPSA)[1]. The rigid transformation is a superposition of a 3-D rotation and a 3-D translation and the registration parameter is a six-component vector consisting of three rotation angles and three translation distances [9]. The rigid registration is done only once, putting all database at the same geometric space of any chosen subject. The choice of this subject can be arbitrary, because linear transformation such as the Rigid Registration preserves the anatomy of the moving image and consequently it does not affect the result.

The rigid registration algorithm was performed using ITK environment [6] and Morphons was performed using Matlab. It has been performed in total 31 rigid registrations and 31*30 non-rigid registrations.

For each image i being the fixed in the registration process, we have calculated $\mathcal{D}$ from equation 9. Table I summarizes the numerical results, the $\mathcal{D}$ values for all 31 patients, showing that subject 3 was found to give the minimal value of $\mathcal{D} = 579$. Figures 4 and 7 are an axial and sagittal views of subject 3.

To illustrate that subject 3 has indeed a central anatomy regarding the size/shape in relation to others in the database, we took two subjects with high values of $\mathcal{D}$: patient 31 with $\mathcal{D}_{31} = 2,335$ and patient 9 with $\mathcal{D}_9 = 1,823$. These high values mean that such subjects should have significant difference of anatomy to patient 3 in relation to size. In fact they have, as we can observe in the Figures 5 and 8, which are an axial and sagittal view of patient 31, and in Figures 6 and 9 which are an axial and sagittal view of patient 9.

4. Conclusions and Final Remarks

In this paper we have proposed a methodology to build an anatomical atlas that represents the size/shape variability present in human anatomy based on dense deformation field using Morphons. In our previous work we have shown that Morphons is an effective strategy for estimating non-rigid registration of the head and neck anatomy.

To illustrate that our atlas is representative in relation to size/shape of the population, we have shown some slices from the patient's volumes. It is clear that patients with high $\mathcal{D}$ value have more difference in anatomy in relation to the others, as we have shown in this paper. The results were also quantitatively validated by an oncologist.

Another important point to be discussed is the size of the database that must be representative. Ideally, the size of the population should be as large as possible. Although we

Table 1. Numerical results for each subject being the atlas template according to the scheme presented in Figure 2

	Patient	Deformation Field Metric
1	Pat1	0.934×10^3
2	Pat2	1.744×10^3
3	Pat3	0.579×10^3
4	Pat4	0.919×10^3
5	Pat5	1.259×10^3
6	Pat6	1.129×10^3
7	Pat7	1.059×10^3
8	Pat8	3.118×10^3
9	Pat9	1.823×10^3
10	Pat10	0.776×10^3
11	Pat11	1.392×10^3
12	Pat12	1.219×10^3
13	Pat13	0.753×10^3
14	Pat14	1.257×10^3
15	Pat15	0.585×10^3
16	Pat16	1.961×10^3
17	Pat17	1.280×10^3
18	Pat18	1.210×10^3
19	Pat19	0.872×10^3
20	Pat20	1.347×10^3
21	Pat21	0.965×10^3
22	Pat22	0.790×10^3
23	Pat23	2.005×10^3
24	Pat24	1.161×10^3
25	Pat25	0.966×10^3
26	Pat26	0.869×10^3
27	Pat27	0.943×10^3
28	Pat28	0.816×10^3
29	Pat29	0.784×10^3
30	Pat30	0.794×10^3
31	Pat31	2.335×10^3

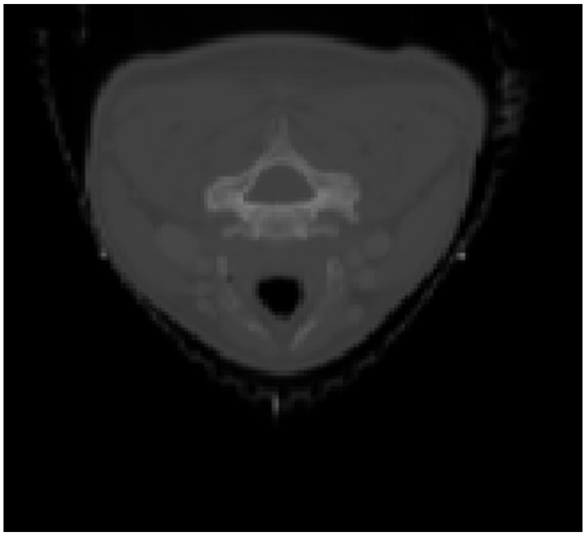

Figure 4. Axial view of patient 3.

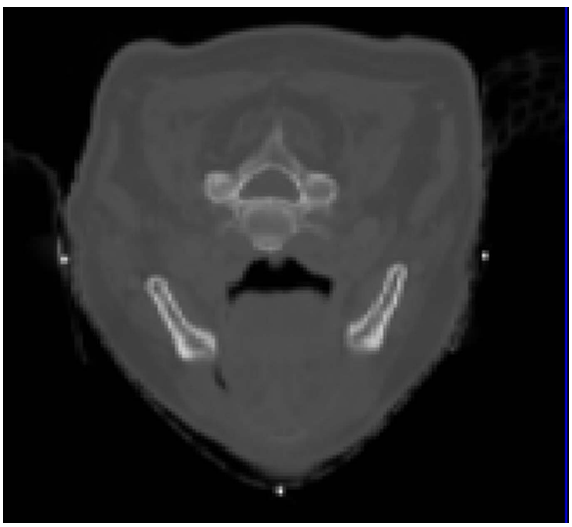

Figure 5. Axial view of patient 31.

have used 31 subjects, it is important to emphasize that the database we have used is from a very restricted population, including neither child nor females, only male adults with medium age.

Our atlas methodology could be used as a good initialization for the Guimond's method, for instance. The main advantage of our methodology is that the chosen atlas is the original image/volume and thus does not have any degree of blurriness imposed by interpolation and iterative process, which would impose problems in future registration when using it for atlas based segmentation. Another potential application of the methodology presented here is the quantitative evaluation of tumor evolution during radiotherapy treatment, including dose adaptation. Until now, to

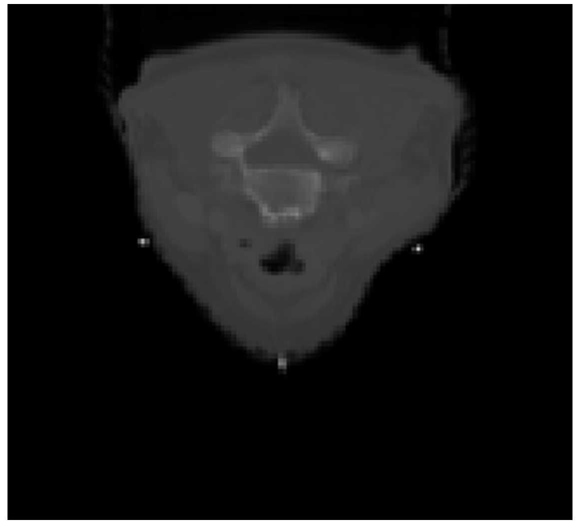

Figure 6. Axial view of patient 9.

our knowledge, the dose is kept unchanged over the entire therapy even though the tumor volume decreases over time.

Finally we need to mention the computational complexity of our method. The number of registrations to be computed is N (N - 1). All the computations were done with 2.6 GHz processor. One registration takes approximately 17 minutes. The database consists of N = 31 images. Hence the procedure approximately takes 240h . Although this method is computationally intensive this does not pose any serious problems, since our calculations are performed offline and all the registrations has to be done only once.

One of our future work objectives is to make a comparison with other approaches and a complete evaluation of our methodology. Also, we would like to investigate the use of a single anatomical atlas in comparison to a mean atlas under a very good non-rigid registration methods. At last, we intend to to build a statistical atlas based on [14].

5. Acknowledgements

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Figure 7. Slice of a sagittal view of patient 3.

Figure 8. Slice of a sagittal view of patient 31.

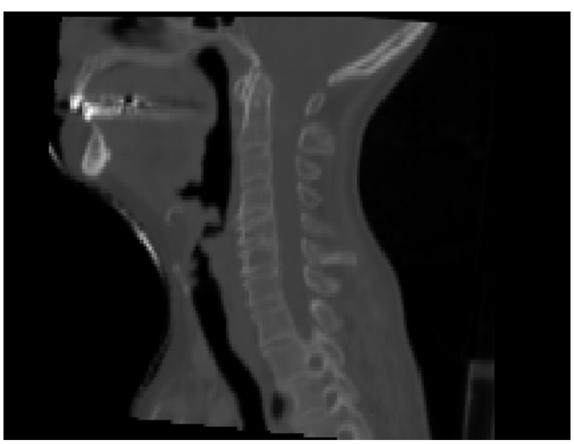

Figure 9. Slice of a sagittal view of patient 9.

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