Automatic Inter-subject Registration of Whole Body Images

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Abstract. 3D inter-subject registration of image volumes is important for tasks such as atlas-based segmentation, deriving population averages, or voxel and tensor-based morphometry. A number of methods have been proposed to tackle this problem but few of them have focused on the problem of registering whole body image volumes acquired either from humans or small animals. These image volumes typically contain a large number of articulated structures, which makes registration more difficult than the registration of head images, to which the vast majority of registration algorithms have been applied. This paper presents a new method for the automatic registration of whole body CT volumes, which consists of two steps. Skeletons and external surfaces are first brought into approximate correspondence with a robust point-based method. Transformations so obtained are refined with an intensity-based algorithm that includes spatial adaptation of the transformation's stiffness. The approach has been applied to whole body CT images of mice and to CT images of the human upper torso. We demonstrate that the approach we propose can successfully register image volumes even when these volumes are very different in size and shape or if they have been acquired with the subjects in different positions.

1 Introduction

Image registration is an essential tool in order to be able to follow the progression of diseases, to assess response to therapy, to compare populations, or to develop atlas-based segmentation methods. The latter involves segmenting structures in one reference volume, commonly called the atlas, and using this reference volume to segment these structures in other volumes. This necessitates being able to register the atlas to the volumes that need to be analyzed. Because it involves a number of subjects, non-rigid registration methods are required to address this problem. A number of methods and techniques have been developed over the years to achieve this; chief among them are intensity-based techniques and more specifically, methods that rely on Mutual Information (MI) [1][2]. However, most automatic methods that have been proposed have been applied to head images only. This is because head images are relatively simple compared to whole body images. Head images contain one single major identifiable structure (the cranium) as opposed to whole body images that contain many articulated

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structures (the bones). In head images the cranium surrounds the brain, therefore constraining the deformation. In whole body images, the situation is the opposite: soft tissue surrounds the bones, leading to very large inter-subject size and shape differences. All these differences make the registration of whole body images much more difficult than the registration of head images. Despite these difficulties non-rigid registration techniques for extra-cranial applications have been proposed for specific applications such as the registration of breast, abdomen, lung, or prostate images. For instance, Camara et al. [3] use a Free-Form Deformation (FFD) approach guided by a gradient vector flow combined with a grey-level MI non-linear registration algorithm for thoracic and abdominal applications. Rueckert et al. [4] also use FFD to register breast images acquired before and after contrast injection; these are image volumes acquired from the same subject. Cai et al. [5] present a validation study of CT and PET lung image registration and fusion based on the chamfer-matching method; this study also involves images acquired from the same subject.

In general, however, fully automatic inter-subject or even intra-subject registration of whole body images remains a challenge. One of the main reasons is that, in practice, non-rigid registration algorithms need to be initialized with a rigid or affine transformation. If the image volumes do not contain articulated structures, as is the case for head images, a single transformation is sufficient. If, on the other hand, these image volumes contain a number of bony structures, which are rigid but whose relative position changes from acquisition to acquisition, a single transformation is insufficient. A number of transformations need to be computed, one for each element in the articulated structure. These transformations then need to be somehow combined. This is the approach followed by Little et al. [6]. These authors present a technique designed for the intra-subject registration of head and neck images. Vertebrae are registered to each other using rigid body transformations (one for each pair of vertebrae). Transformations obtained for the vertebrae are then interpolated to produce a transformation for the entire volume. One problem with the approach is that it requires segmenting and identifying corresponding vertebrae in the image volumes. Because corresponding vertebrae are registered with rigid-body transformations, the approach is also applicable only to intra-subject registration problems. Martin-Fernandez et al. [7] propose a method, which they call articulated registration. This approach requires the labeling of landmarks to define wire models that represent the bones. A series of affine transformations are computed to register the rods, which are the elements of the wires. The final transformation for any pixel in the image is obtained as a linear combination of these elementary transformations with a weighting scheme that is inversely proportional to the distance to a specific rod. This technique has been applied to the registration of hand radiographs. Arsigny et al. [8] also propose an approach in which local rigid or affine transformations are combined. They note that simple averaging of these transformations leads to non-invertible transformations, and they propose a scheme that permits the combination of these local transformations, while producing an overall transformation that is invertible. Their method is applied to the registration of histological images. The authors comment on the fact that their method could also be used for articulated structures but do not present examples. Recently, Papademetris et al. put forth an articulated rigid registration method that is applied to the serial registration of lower-limb mouse images [9]. In this approach, each individual joint is labeled and the plane in which the axis of rotation for each joint lies is identified. A transformation that blends piecewise rotations is then computed. The authors comment of the fact that piecewise rigid models often lead to transformations that are discontinuous at the motion boundaries, which produces folding and stretching. The approach they propose produces a transformation that is continuous at these interfaces. The authors have applied their method to the registration of lower limbs in serial mouse images. They suggest that their technique could be used to initialize an intensity-based algorithm but do not present results.

In summary, a survey of the literature shows that only a few methods have been proposed to register images including articulated structures. The general approach is to compute piecewise rigid or affine transformations and to somehow blend and combine these transformations. Unfortunately, this approach is often not practical because it requires identifying various structures in the images such as joints or individual bones. In this paper we propose a method that does not require structure labeling. This method can thus be automated, and we demonstrate its performance on small animal and human images.

2 Methods

There are two steps in the automatic registration method we propose. In the first step, we register only bony structures and the outside body surfaces. The transformation we compute in this first step is then used to initialize an intensity-based registration algorithm. Because our aim is to develop a fully automatic technique, we have ruled out methods that require identifying and labeling homologous structures. These methods would indeed require developing general and robust feature extraction algorithms, which is not easy to achieve. Hence, in our first step, we have chosen to rely on the robust point-based registration algorithm proposed by Chui et al. [10]. This algorithm takes as input two clouds of points and iteratively computes a correspondence between these points and the transformation that registers them, without requiring manual labeling. In addition, the two sets of points also do not need to have the same cardinality and the algorithm can deal with the problem of outliers. Correspondence is computed with the softassign algorithm proposed by Gold et al. [11]. Once correspondence is determined, a thin plate spline-based non-rigid transformation is computed to register the points. Because we use this algorithm as an initial step, the transformation it produces does not need to be extremely accurate. Point clouds in the two volumes can thus be selected in a somewhat arbitrary fashion.

In the approach we have tested so far, bone surfaces are first extracted, which can be done easily in CT images with a simple threshold. We do this in both image sets and sample the two surfaces to create the two clouds of points. Currently, we do not use any geometric feature, such as the surface curvature, to select the points. Results will show that this approach leads to acceptable results even when the skeletons are in very different positions. We then extract the external surface of the body. This is also easily achieved with an intensity threshold. As is the case for the bone surfaces, the whole body surfaces are sampled to create a second cloud of points that is added to the first one. This leads to two clouds of points, one per image volume, that typically contain 1000 to 3500 points, which are registered using the robust point-based approach of Chui et al.

The second step in our approach relies on an intensity-based registration algorithm we have proposed recently [12], which we call ABA for adaptive bases algorithm, to refine the results obtained in the first step. In this algorithm, the deformation field that registers the two images is modeled as a linear combination of radial basis functions with finite support. Coefficients for these basis functions are computed that maximize the normalized mutual information (NMI) between the images. As is often the case for non-rigid registration algorithms based on basis functions, our algorithm includes mechanisms designed to produce transformations that are topologically correct (i.e., transformations that do not lead to tearing or folding). This is done by imposing constraints on the relative value of the coefficients of adjacent basis functions. Furthermore, we compute both the forward and the backward transformations simultaneously, and we constrain these transformations to be inverses of each other. In our experience, this leads to transformations that are smooth and regular.

In our application, there are two broad categories of structures: bones and soft tissues. Because we are dealing with inter-subject registration issues, both bones and soft tissues need to be deformed (in the intra-subject registration case, individual bones can be registered with rigid-body registration methods). However, the amount of deformation typically observed for bony and soft tissue structures is very different, i.e., two livers can have vastly different shapes and sizes when the overall shape and size of individual bones vary little across subjects. This suggests using transformations whose physical properties vary spatially. These transformations should be relatively stiffer for bony structures than they are for soft tissue structures. Our algorithm allows us to do pre-cisely this. As mentioned above, regularization of the deformation field in our algorithm is obtained by imposing constraints on the relative value the coefficients associated with adjacent basis functions. In practice, we impose a threshold on the difference between the values of these coefficients. The smaller the threshold, the stiffer the transformation is. We can thus define what we call stiffness maps, which are maps that specify the value of this threshold in various regions of the image. In previous work [13], we have shown that this feature improves atlas-based segmentation results when the patient image volume contains very large ventricles or space-occupying lesions. Here, we create a simple binary stiffness map: the transformation is constrained to be stiffer over bony structures than over soft tissue structures. Results obtained when using two stiffness values, one for the bones and the other for soft tissue, improve when compared to those obtained with a single value.

3 Results

Our approach has been evaluated on two types of images: whole body mouse scans and upper body human scans. We used an Imtek MicroCAT II small animal scanner to generate two 512x512x512 mouse CT volumes, with a voxel resolution of $0.125 \times 0.125 \times 0.125 mm^3$. Human data sets are 512x512x184 CT volumes with a voxel resolution of $0.9375 \times 0.9375 \times 3 mm^3$. Figure 1 shows results obtained with the skeletons of mouse volumes. The left panel shows the two skeletons in their original position. The right panel shows the same but after point-based registration. Figure 2 illustrates results obtained when both steps are applied. The left panel shows one CT slice in one volume (the source) and the right panel is the corresponding slice in the other volume (the target); note the large differences in size, shape and posture between these volumes. The middle panel shows the results we obtain when registering the source volume to the target volume. To facilitate the comparison, yellow contours of the lung have been drawn on the target image and copied on all the other ones.

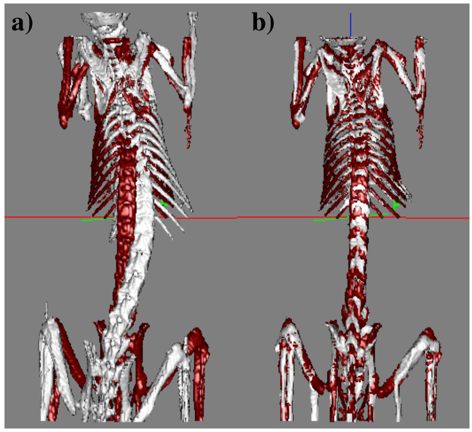

Fig. 1. Bony structures in two CT volumes a) before the registration and b) after the registration

Figures 3 and 4 show results we have obtained with upper torso CT images, and they illustrate the advantage of using two stiffness values. In both figures, the left panel is the source image, the right panel the target image. The second, third and fourth panels show the source volume registered to the target volume using (1) a stiff transformation, (2) a very elastic transformation, and (3) a transformation with two stiffness values. In figure 3, only bones are shown. In figure 4, the entire images are shown. When a stiff transformation is used, bones are deformed in physically-plausible ways, but soft tissues are not registered very accurately (arrows on the second panel of figure 4). When a more elastic transformation is used, bones are deformed incorrectly (regions highlighted in the third panels from the left). Using two stiffness values permits transformations to be computed that lead to satisfactory results both for the bony and soft tissue regions.

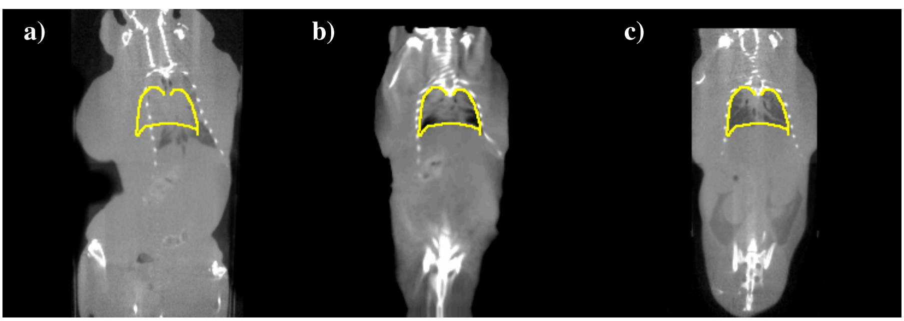

Fig. 2. One coronal slice in the source volume (left); the corresponding slice in the target volume (right) , and the transformed source image after registration (middle)

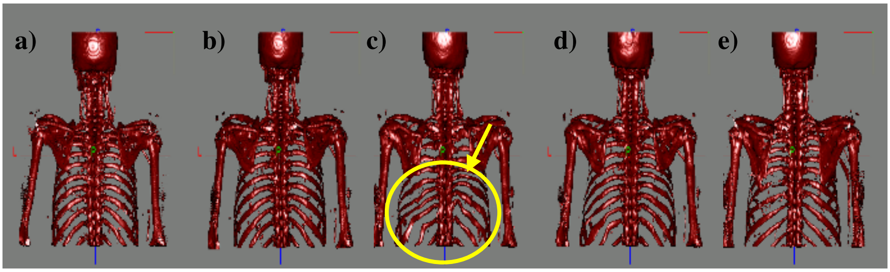

Fig. 3. a) Skeleton of the source image, e) skeleton of the target image. b), c), and d) source skeleton registered to target skeleton using a stiff transformation, a very elastic transformation, and two stiffness values, respectively.

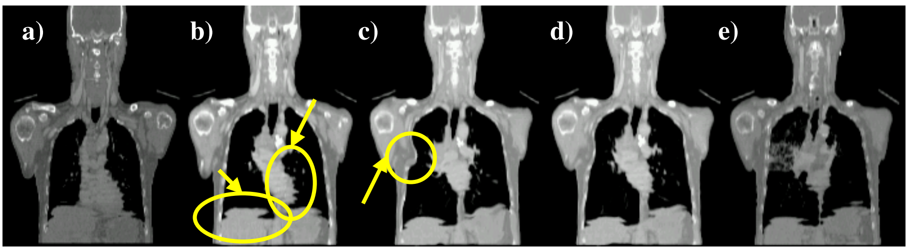

Fig. 4. a) One coronal slice in the source volume, e) corresponding slice in the target volume, b), c), and d) source image registered to target image using a stiff transformation, a very elastic transformation, and two stiffness values, respectively

Figure 5 illustrates results we have obtained with another set of upper torso volumes. The left panel shows one sagittal image in one of the volumes (the source). The right panel shows the slice with the same index in the second volume (the target) prior to registration. The second, third, and fourth panels show results obtained with our intensity-based algorithm alone, results obtained with point-based registration alone, and results obtained when both approaches are combined, respectively. The second panel shows typical results obtained when non-rigid registration algorithms cannot be initialized correctly. The overall shape of the registered volume appears correct but

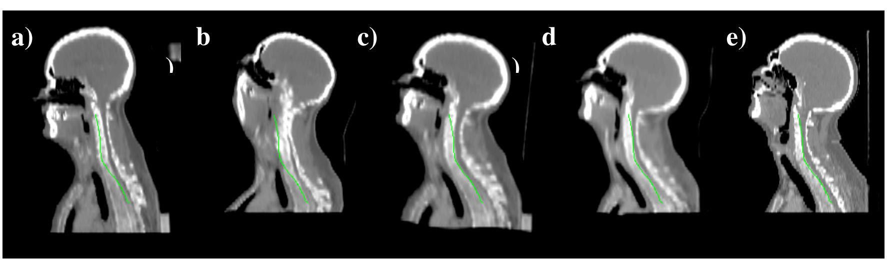

Fig. 5. a) One sagittal slice in the source volume, e) the corresponding slice in the target volume, b), c), and d) registration results obtained with intensities alone, points alone, and with both methods combined, respectively

bones have been deformed incorrectly. A closer inspection of the deformation field (not shown here for lack of space) also shows that the deformation field is very irregular. The deformation field obtained with the point-based registration is smooth but the registration relatively inaccurate, as shown in the third panel. As can be seen in this panel, the shape of the head and its size are not exactly similar to those shown in the right panel. Similarly, the sizes of the vertebrae are incorrect. The fourth panel shows that the best results are obtained by combining both approaches.

4 Conclusions

In this paper, we present what we believe is the first automatic approach for the registration of articulated structures applicable to inter-subject registration problems. Existing work typically relies on a combination of piecewise rigid body transformations, which requires localizing joints in the image accurately. This is time-consuming and hard to automate. In our method, the process can be fully automated by registering first the entire skeleton using a point-based method that does not require labeling of homologous points. This produces a transformation, which may not be extremely accurate but is nevertheless sufficient to initialize an intensity-based non-rigid registration algorithm. The second step leads to an accurate registration. We also show that better results can be obtained with two stiffness values than with one. Future work includes improving the way points are selected for the point-based registration algorithm and conducting a quantitative evaluation and comparison of these algorithms.

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