Design of a synthetic database for the validation of non–linear registration and segmentation of magnetic resonance brain images

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ABSTRACT

Image registration and segmentation are two important tasks in medical image analysis. However, the validation of algorithms for non–linear registration in particular often poses significant challenges:[1,2]

Anatomical labeling based on scans for the validation of segmentation algorithms is often not available, and is tedious to obtain. One possibility to obtain suitable ground truth is to use anatomically labelled atlas images. Such atlas images are, however, generally limited to single subjects, and the displacement field of the registration between the template and an arbitrary data set is unknown. Therefore, the precise registration error cannot be determined, and approximations of a performance measure like the consistency error must be adapted. Thus, validation requires that some form of ground truth is available.

In this work, an approach to generate a synthetic ground truth database for the validation of image registration and segmentation is proposed. Its application is illustrated using the example of the validation of a registration procedure, using 50 magnetic resonance images from different patients and two atlases. Three different non–linear image registration methods were tested to obtain a synthetic validation database consisting of 50 anatomically labelled brain scans.

Keywords: synthetic ground truth, validation of non–linear image registration and segmentation, magnetic resonance imaging, brain images

1. DESCRIPTION OF PURPOSE

A number of methods have been proposed for the generation of ground truth, which can be applied for the validation of automated image registration and segmentation approaches. One possible approach involves use of finite element method (FEM) simulations to produce tissue deformations.[3] However, significant uncertainties arise in estimating both the elastic properties of the tissues, and the boundary conditions. Furthermore, this approach requires a significant amount of human interaction and computational resources. An alternative approach[4,5] generates a ground truth for the validation using a simulating brain tissue atrophy. Since this approach used correspondences between images for the generation, the method is not suited to the generation of ground truth database consisting of multiple patients.

This work introduces an approach for generating a synthetic database. The target application selected in this work was morphometry of the brain. Therefor the novel approach is applied to generate a database with 50 MR brain images from different patients and two different atlases. However, different applications areas may be treated in a similar fashion. The database is constructed in such a way that all necessary information required to validate methods for non–linear registration and segmentation is available and thus represents a ground truth

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for such validations. The ground truth includes anatomical labeling based on magnetic resonance brain scans for the validation of the segmentation as well as displacement fields for the validation of the registration.

2. MATERIAL

This work is based on a set of 50 T1 magnetic resonance scans as well as two atlas scans.

The scans (see Fig. 1 (d)) are coming from the Alzheimers Disease Neuroimaging Initiative (ADNI) database (www.loni.ucla.edu/ADNI). The patients are without known neurodegenerative disease.

The first atlas scan is the single-patient magnetic resonance image with associated anatomical labels, made available by the International Consortium for Brain Mapping (ICBM).[6] The atlas scan is based on a single patient and is thus only of limited use for multi-patient-studies. Furthermore, the skull is only partially visible (see Fig. 1 (a))) and cannot be used for the image registration task.

The second atlas scan (ASP) is a multi-patient non-segmented customized magnetic resonance image[7] which has been aligned using a linear transformation to the Montreal Neurological Institute (MNI)[8] reference space (see Fig. 1 (c)). The advantage of this atlas scan is that in contains information about anatomical variability. The multi-patient atlas from the SPM toolbox[9] (see Fig. 1 (b)) may have been another option. However, it is not used here, because it is constructed from different patient scans resulting in a somewhat blurred appearance which is not well suited for segmentation.

3. METHODS

In this section we start out by describing the employed registration methods followed by a detailed outlining of the algorithm generating the ground truth database.

3.1 REGISTRATION

The image registration problem is defined as follows. Given a reference image R and a template image T to be transformed, we wish to find a smooth transformation (displacement field) y. To generate the ground truth database, we will make use of three different non–linear registration methods, which will be briefly described.

The first method is representative for the class of non-parametric registration schemes. It is a member of the Flexible Image Registration Toolbox (FLIRT)[10] and is based on the following minimization problem

$$D(y; R, T) + \alpha \cdot S(y) \to \min!$$

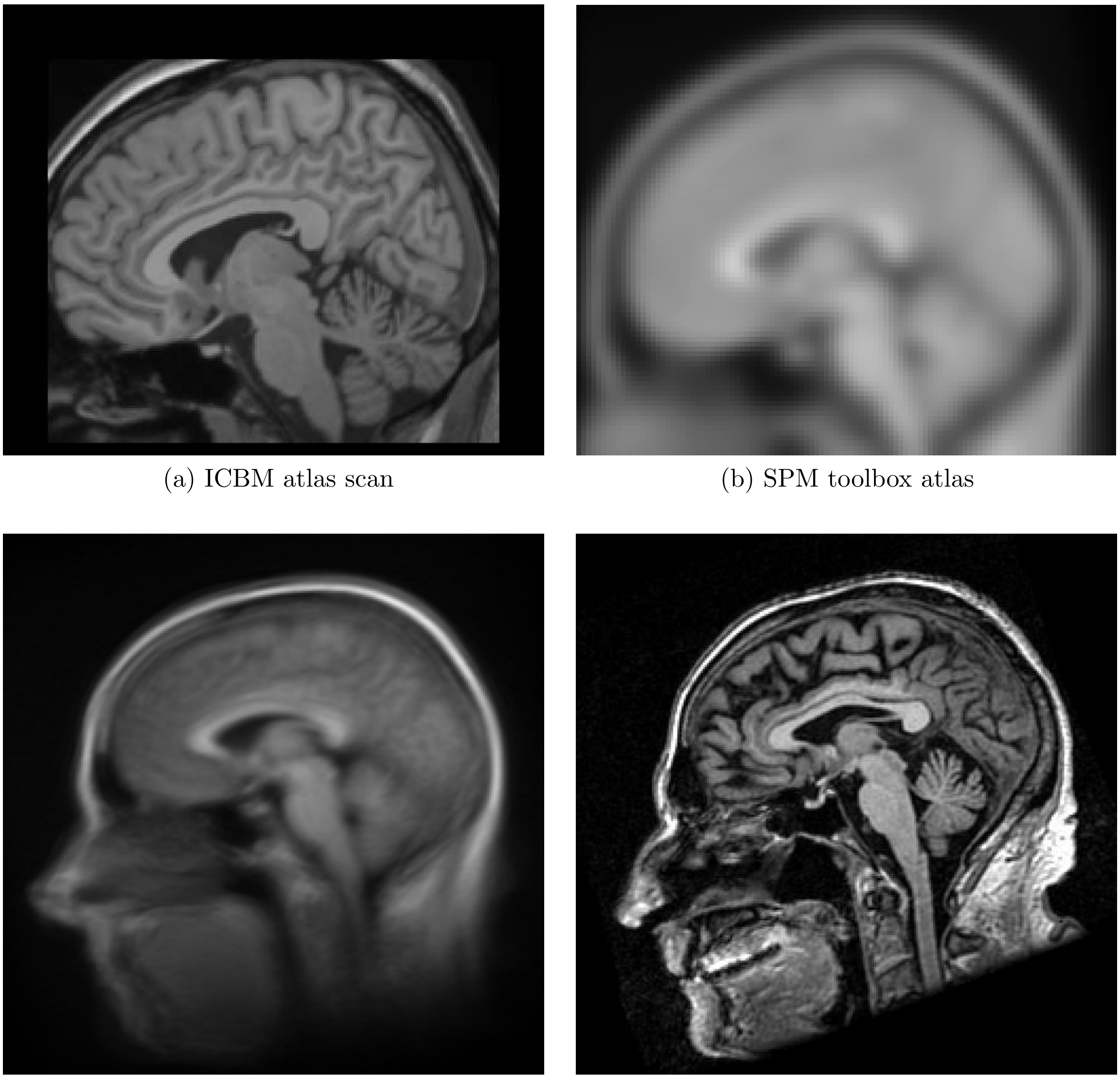
Here, S denotes a regularizer for the displacement field y. The specific choice of the regularizer is not critical for this work (for an overview see[11]). In the examples presented below, the so-called elastic smoother[12]

$$S(y) = \int_\Omega \frac{\mu}{4} \sum_{i,j=1}^{3} \left(\partial_{x_i} y_j + \partial_{x_j} y_i\right)^2 + \frac{\lambda}{2} (\text{div } y)^2 \; dx,$$

is used, where μ and λ are known as Lamé-constants encoding elasticity properties. D is a distance measure measuring the similarity between the reference image and the deformed template image $T \circ y$. Here, we employed the so-called cross–correlation (CC)[13] measure given by

$$D(y; R, T) = \int_\Omega \frac{R(x) - E(R(x))}{\sigma(R(x))} \cdot \frac{T(y(x)) - E(T(y(x)))}{\sigma(T(y(x)))} \; dx,$$

where E denotes the expected value and σ the standard deviation. Again, we may have used other terms like a mutual information based measure,[14,15] but, as we will see, the validity of the ground truth database does not



(a) ICBM atlas scan (b) SPM toolbox atlas

(c) ASP atlas (d) MRI from ADNI

Figure 1. Sagittal views illustrating the data contained in the (a) single-patient labeled ICBM atlas scan, (b) multi-patient atlas of the SPM toolbox, (c) multi-patient ASP atlas and (d) magnetic resonance brain image from ADNI database.

rely on the specific choices. The regularization parameter α represents the relative weighting of the respective terms.

The next two methods are well-known members of the so-called parametric registration scheme class. The idea is to represent the thought after displacement field

$$y(x) = \sum_{k=1}^{N} \alpha_k B_k(x)$$

as a linear combination of well selected basis functions $B_k : \mathbb{R}^d \to \mathbb{R}^d, k = 1, 2, \cdots, N$. The registration task then boils down to the optimal selection of the coefficients α_k via the solution of the following minimization problem

$$D(y; R, T) \to \min!$$

where again the CC-measure is used.

The most prominent parametric schemes goes back to Rueckert et al.[16] It is known as free form deformation method (FFD) and uses cubic B-splines as basis functions. Here, we make use of the implementation of Kabus et al.[17] Finally, we employed the method provided by the statistical parametric mapping toolbox (SPM). It is widely used in the context of brain-imaging and is based on discrete cosine transform basis functions.[18] Let us note, that if the basis functions resemble a linear mapping, the notion linear registration is used.

3.2 GENERATION OF SYNTHETIC GROUND TRUTH

The idea is to generate a synthetic database which is on one hand as close as possible to real brain scans and on the other hand does not implicitly contain any bias towards a specific registration method and/or specific brain atlas.

Therefore, the method for the generation of the database consists of three independent steps. In the first step, we linearly registered the ADNI data, ASP atlas scan, and the ICBM atlas scan to the same coordinate system given by the previously mentioned MNI space.

In the second step (compare Fig.2(a)) we first registered with the help of the outlined FLIRT routine the ICBM-T1-image onto the ASP atlas scan. The resulting displacement field is called y_1. Next we applied all three registration methods (FLIRT, FFD, SPM) to obtain a registration from the ASP atlas scan onto each of the 50 ADNI database MR-images. The resulting 150 displacement fields are called $y_{2,i}^k, i = 1, 2, 3; k = 1, 2, \ldots, 50$. We abbreviate this set of fields by $\{y_2\}$.

In the final step (compare Fig. 2 (b)) we transformed the ICBM-T1-image and its labels with the help of the concatenated displacement fields $\{y_2\} \circ y_1$. This results in a set of 150 perfectly segmented images, which resemble a MR scans, and build the wanted synthetic database. Note, that both the labeling of the template and reference are known as well as the underlying displacement fields. Therefore, the set is perfectly suited for the validation of registration and segmentation methods for magnetic resonance brain images.

Fig. 3 gives three examples of the synthetic ground truth generated with introduced approach and FFD for the registration. The columns from left to right correspond to the synthetic scans developed with ICBM atlas scan and three representative datasets from ADNI database. Finally, Fig. ?? displays the corresponding labeling.

Obviously, the employed registration schemes may be either substituted by other schemes or their ingredients may be altered.

4. A REGISTRATION VALIDATION

We are now in a position to validate registration as well as segmentation schemes. To give an idea on how one might perform these tasks we consider a sample validation for the used FLIRT scheme.

To this end we take advantage of the displacement fields associated with the FFD and SPM methods in our synthetic database. We abbreviated them by y_n (see Fig. 2 (c)). Next we computed the (direct) registration from ICBM to the related database entries by the FLIRT method and call the obtained displacement field y.

The first error measure is the so-called registration error,[19] which is given by

$$\mathrm{Err}_{\mathrm{Reg}} = ||y - y_n||_{L_2}.$$

It actually measures the difference between the ground truth and and the computed displacement field.

It is common to measure as well the so-called consistency error developed by Christensen and Johnson[20]

$$\mathrm{Err}_{\mathrm{Cons}} = ||y_n \circ y_b - I||_{L_2},$$

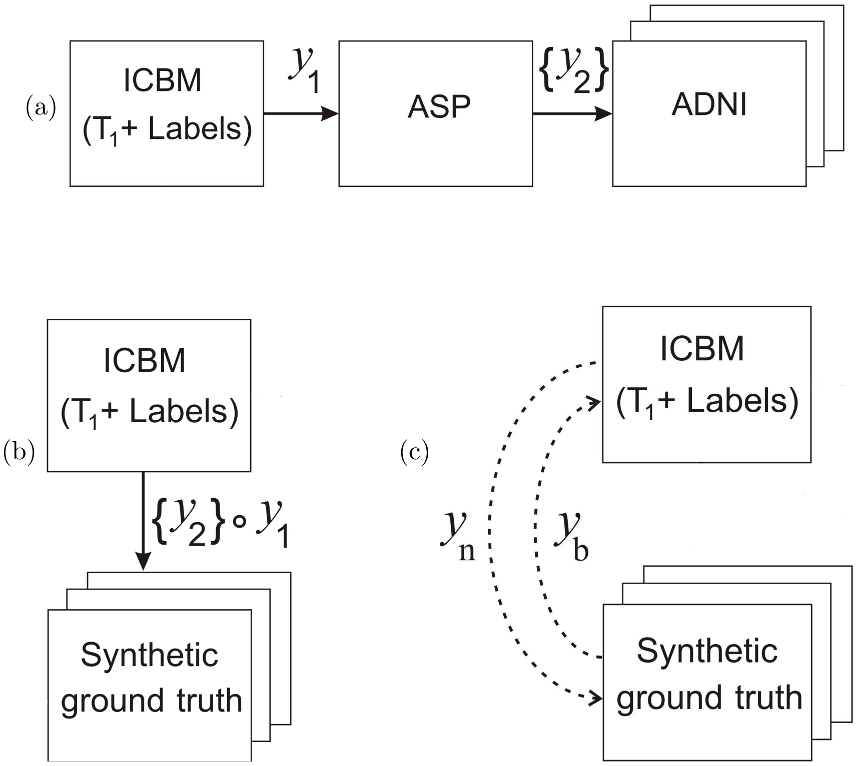


Figure 2. Schematic overview of proposed approach for the generation of the synthetic database. Illustration of the randomly synthesized images are displayed in Fig. 3. The labels are shown in Fig. 4.

where y_b denotes the (direct) registration from the database entries to the ICBM image by the FLIRT method (see Fig. 2 (c)) and I denotes the identity transformation. The consistency error describes the deviation from the identity transformation after a cyclic sequence of image registrations. The advantage of this error measure is that no ground truth is required.

Finally, we validate the segmentation performance of the FLIRT method by comparing the volume of its labels (A) with the ground truth ones (B),[21] via

$$\mathrm{Err}_{\mathrm{Seg}} = \frac{A \cap B}{A \cup B}.$$

To be a little more specific, we are using this measure for comparing volumes of ventricles $\mathrm{Err}_{\text{Seg-Vent}}$ and gray matter $\mathrm{Err}_{\text{Seg-GM}}$. To judge the computed error, the total volume of the ventricle and of gray matter is 1572 mm^3 and 147102 mm^3, respectively.

Table 1 shows the obtained results. It can be seen that all introduced errors are consistent. Of course, these numbers have to be compared to the numbers obtained by different registration methods. We plan to perform such a comparison in a forthcoming paper.

5. CONCLUSIONS

This paper presents an approach for the generation of a synthetic ground truth database of magnetic resonance brain images for the validation of non–linear image registration and segmentation methods. The method is illustrated for the validation of an image registration scheme. These early results indicate the potential of the proposed scheme. In the future we plan to extend our database with different data sets and to come up with sound validation study.

Registration Method	$\mathrm{Err}_{\mathrm{Reg}}$	$\mathrm{Err}_{\mathrm{Cons}}$	$\mathrm{Err}_{\mathrm{Seg\text{-}Vent}}$	$\mathrm{Err}_{\mathrm{Seg\text{-}GM}}$
FFD - FLIRT	3.53	2.96	0.75	0.72
SPM - FLIRT	2.81	2.57	0.78	0.73

Table 1. Registration, consistency and segmentation errors.

The generated synthetic ground truth database can be made available upon request.

6. ACKNOWLEDGMENTS

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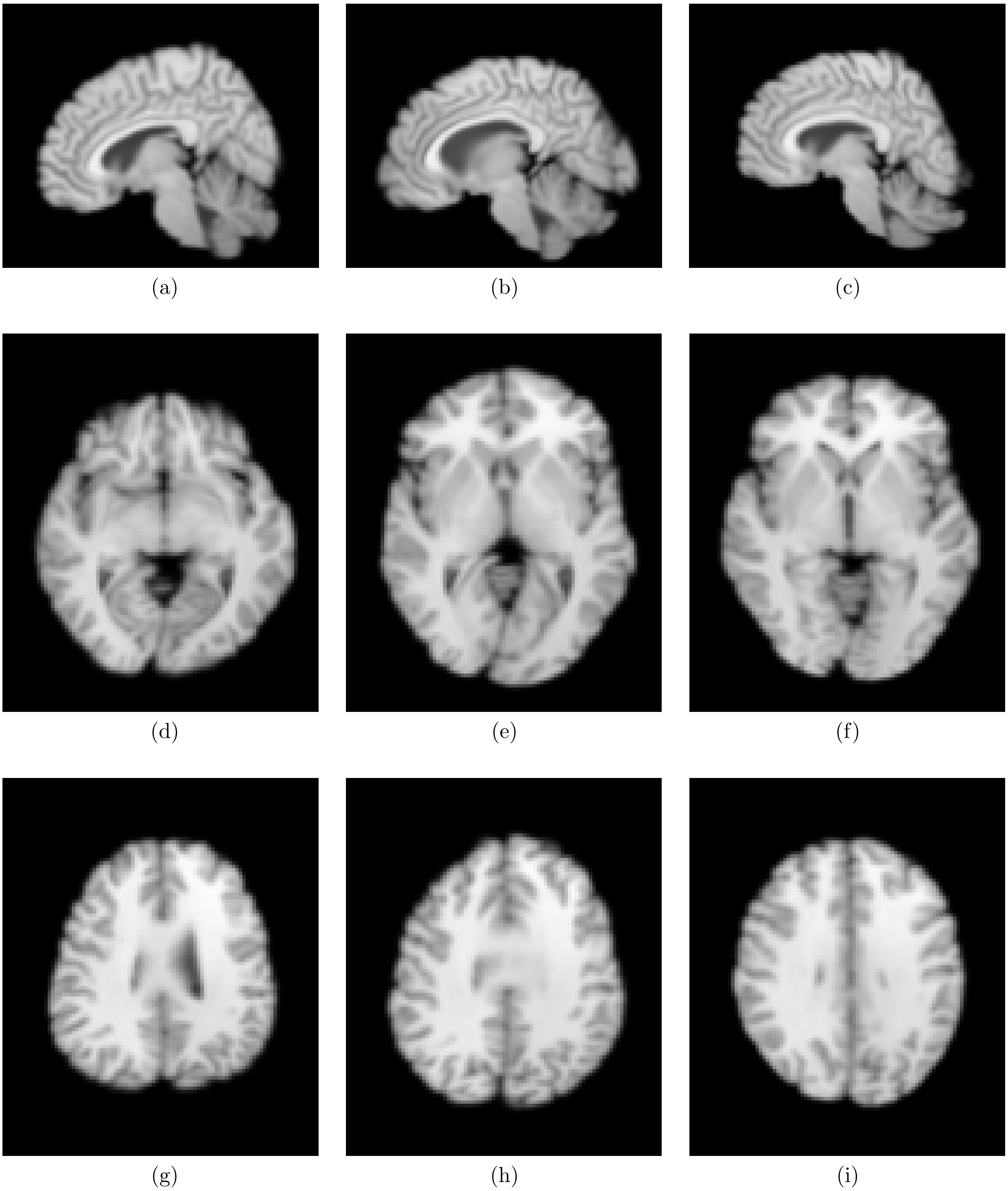

Figure 3. Illustration of the randomly synthesized images. Sagittal (a - c) and transversal (d - i) slices from three different representative datasets of synthetic ground truth generated with introduced approach and FFD for the registration. The columns from left to right correspond to the synthetic scans developed with ICBM atlas scan and datasets from ADNI database. The labels of images are displayed in Fig. 4.

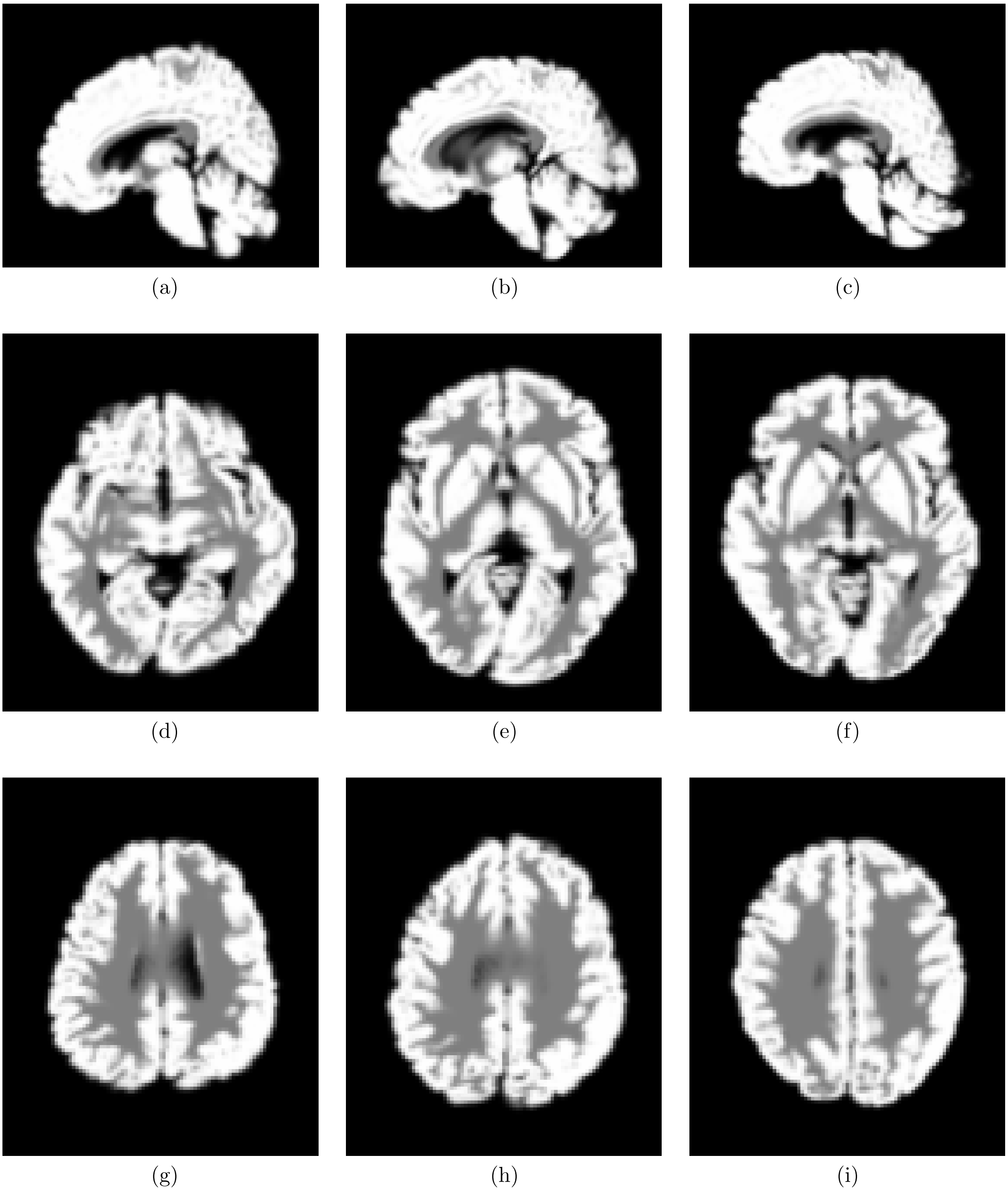

Figure 4. Labeling of the synthesized images displayed in Fig. 3. Sagittal (a - c) and transversal (d - i) slices from three different representative datasets of synthetic ground truth generated with introduced approach and FFD for the registration. The columns from left to right correspond to the synthetic scans developed with ICBM atlas scan and datasets from ADNI database.