Atlas based segmentation: Atlas generation using Elastix

Medical Image Registration and Applications
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I. Introduction

Atlas-based segmentation is a widely used image segmentation approach in medical imaging that aims to benefit from prior knowledge about the structures to be segmented during the segmentation process. This prior knowledge usually comes from one or more reference images of the same structure to be segmented that were previously annotated (for example manually). These images are called atlases and they can be divided into two types: topological and probabilistic. The prior information provided by the Atlas is then embedded to a segmentation algorithm such as Expectation-Maximization in order to improve its performance.

II. Objective

The objective of this first part of a two-part laboratory work is to build a *probabilistic atlas* and use it to extract tissue models for brain MRI tissue segmentation. This process involves brain volumes registration, label propagation and atlas generation. The Elastix registration tool will be used in this work.

III. Theoretical Background

A. Atlas

An atlas can be defined as the combination of an intensity image (template) and its segmented image (the atlas labels). [1]. The images to be segmented will be registered to the template then the transformation obtained will be applied inversely on the labels of the atlas to generate the segmentation result of the target image, this process is called *labels propagation*. The way of propagating the labels depends on the type of the atlas used. In the literature, we can distinguish two types of atlases:

1) Topological Atlas

Topological, single-subject or deterministic atlas approaches use a single template intensity image and its corresponding ground truth to infere the segmentation of a target unlabeled image of the same structure. The selection of the single image to be used can be random or based on a similarity measure where the closest image to the target in the dataset is used as a reference. The target image is registered to the template and the resulting segmentation is obtained by applying the inverse transformation of the registration on the atlas labels. In this scheme, the atlas assigns deterministic labels to each voxel in the target volume which identifies the region to which it belongs.

2) Probabilistic Atlas

Probabilistic atlases are obtained using multiple reference images, therefore they are used in multi-atlas segmentation approaches. The atlas is generated after registering all the images in the dataset to a single instance and propagating their labels to the common registration space. The choice of the fixed image in the registration process can be random or based on an error or similarity measure. The reference intensity image of the atlas can be the instance used as a fixed image or the mean image obtained after averaging all the registered intensity images. The atlas labels are a fusion of the propagated labels of all the images in the train set. There exist two major approaches of fusing the labels:

- *Averaging*: this is obtained by taking the average of the propagated labels for each class to obtain a membership probability map that gives for each voxel location the probability of that voxel belonging to the region in question.
- *Majority Voting*: this approach assigns to each voxel the most frequent label that appears at its location among the training set images.

We are mainly interested in this type of atlas and we will only consider this type in the remaining parts of this report.

B. Atlas Generation

To generate a multi-atlas, several training images are needed. From a dataset we can either use all the images provided or select some of them based on a metric, for instance, the ones that maximise the similarity with the target image.

The process of building a multi-atlas consists of three major steps:

- 1. *Registration*: in this phase, a single image from the population is chosen as a fixed image. The remaining images will be registered with respect to this fixed image to move all the images to a common space.
- 2. *Label propagation*: in this step, the transformation parameters obtained in step 1 for each instance are applied to the corresponding labels to move them to the registration space.
- 3. *Atlas generation*: in the last step, the registered images are used to build the atlas. As previously mentioned, The template can be the fixed image selected to perform the registration or the mean of all the image. The labels are obtained by fusing the propagated labels of the training images either by averaging or majority voting.

C. Tissue Models

Tissue models are the conditional probabilities of the voxel class given its intensity $p(\omega|x)$. This probabilities can be obtained by using the ground truth label assignment for each volume. The tissue models, can be later used to generate a segmentation of the brain based uniquely on intensities or to perform a better initialization in Expectation Maximization algorithm.

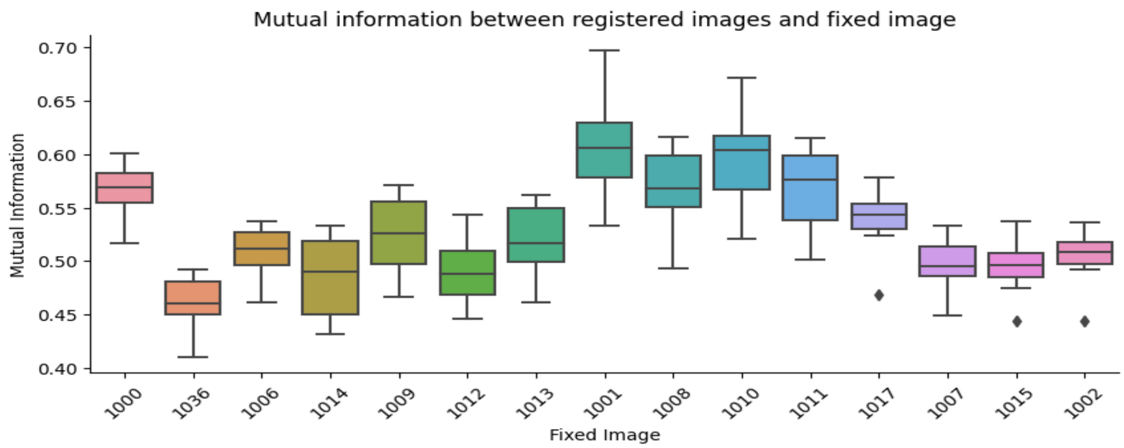

Fig. 1. Mutual Information of the resulting registration for each fixed image

IV. Project Management

The project was executed in not more time than the assigned one in classes. We first installed and explored the Elastix package and used it to perform registration. After trying the SimpleITK version of Elastix, we finally decided to keep using the executable binaries provided by Elastix, mainly due to the automatic handling of deprecated parameter map arguments available in the second and not in the first. After the first lab session, registrations were run overnight and we then proceeded to the label propagation step. In the second session we built the atlases using the resulting registration images and we visualised the results. The remaining time was used to prepare the report.

V. Implementation

In this lab work, we built a probabilistic atlas for brain tissue segmentation from scratch based on a training set of 15 brain MRI volumes. We used Python as a programming language. The source code is available in https://github.com/kakou34/mira_lab lab_2. The main file containing the implemented functions is *utils.py* and we refer to it in the following lines except explicit mention of the contrary.

A. Registration

The Elastix [2] open-source software was used to perform the registration of the brain volumes to a common space. This is achieved using the *elastix_wrapper* function [lines 10-52]. This function takes the paths to the moving image, fixed image and transformation parameters as arguments and uses the subprocess package to execute the elastix command in order to perform the registration. Elastix automatically saves the registered image and the final transformation parameters that were used to obtain the optimal registration. We modified the transformation parameters to save the images in Nifty format for easier visualization of the results.

B. Label Propagation

The Transformix extension of Elastix was used in this step. Similarly to the previous step, the function *transformix_wrapper* [lines 55-88] was created. This function takes the paths to the original labels and the transformation parameters files (generated by Elastix in the previous step) as arguments and uses them to execute the registration command on the labels. We modified the transformation parameters to save the images in Nifty format and to use a nearest-neighbors interpolator in order to preserve the categorical nature of the labels volumes during the label propagation step. The results are automatically saved in a predefined folder. The resulting label is a single image that assigns a different label to each tissue type.

C. Atlas Generation

The atlas generation is performed in the *registration_elastix* jupyter notebook. The template image is obtained by averaging the registered brain images. The probabilistic atlas is obtained by first splitting each propagated categorical label volume in four binary label volumes, one for each class. Then, the average of the propagated labels of each tissue was computed across all subjects in the population. The result is 4 membership probability maps, one for each tissue type (CSF, GM, WM) and one for the background class. The majority voting atlas is obtained by applying *argmax* over the array of concatenated probabilistic atlases. In other words, each voxel is associated to the tissue that gives the highest probability in the corresponding voxel's location in the probabilistic atlas.

D. Tissue Models

Once we propagate the labels of each volume, we can use the labels assignment to generate the likelihoods for each voxel $p(x|w_k)$, which are the conditional probabilities of a voxel intensity (x) given a tissue class (w_k). The mentioned probability density function is obtained by normalizing the histograms by the total number of samples used to construct it (see figure 7 for an example). Once the *pdf* is obtained, the posterior probability can be obtained by applying Bayes rule and assuming a non-informative prior:

$$p(w_k|x) = \frac{p(x|w_k)p(w_k)}{\sum_k p(x|w_k)p(w_k)} \tag{1}$$

given that $p(w_k)$ is the same for all classes, the expression simplifies to:

$$p(w_k|x) = \frac{p(x|w_k)}{\sum_k p(x|w_k)} \tag{2}$$

which is equivalent to divide elementwise the obtained likelihoods by the sum of the likelihoods of all classes (see figure 8 for an example).

In particular for this labwork, after building the atlases, we built the tissue models using two different approaches. In both of them the procedure for one tissue involves computing the histogram of the voxel intensities under the desired tissue mask for all cases in the atlases collection. The different methods use different tissue masks:

- *Using the atlas*: For each image in the dataset, the tissue regions are defined by the majority voting atlas in the registered space.
- *Using the labels*: For each image in the dataset, the intensities inside each region are defined by the propagated labels in the registered image.

VI. Experiments

A. Fixed Image Selection

To choose the best subject to be used as a fixed image, we performed a set of 15 experiments where in each of them a different subject was used as a fixed image and all the others were registered to it. The average mutual information metric -given by equation 3- between reference and registered image was used for evaluation.

$$MI(If, Im) = \sum_{i,j} p(i,j) log(\frac{p(i,j)}{p(i)p(j)}) \quad (3)$$

where p(i, j) is the normalised 2D histogram between the fixed image and the registered image, p(i) is the marginal for i over j and p(j) is the marginal for j over i

From the boxplots in figure 1, we can see that the choice of the fixed image is important as some volumes in the provided dataset are more similar to the overall population and thus provide better registration results. This is the case for subject 1001, where a higher average MI, indicates better general alignment of the other volumes to it. In other cases, for instance 1036, the average mutual information obtained was very low compared to the other experiments. Based on these results, the subject 1001 was used as a fixed image in the next steps.

B. Registration

After selecting the fixed image, we registered the remaining images to image 1001. Two registration methods were tried: a rigid transformation (using the Rigid Parameters file from Par0025[1]) and an affine transformation (using the Affine Parameters file from Par0009[2]). Figure 2 shows example registration results (slice n° 130) of subjects 1006, 1013 and 1036 (rows in the image) using both techniques.

It can be seen from the images that the registration results are satisfactory in both cases, with the affine transformation outperforming the rigid one (see case 1006 where the size and the ratio between the dimensions of the brain area in the result of rigid transformation are different from the fixed compared to the result of the affine transformation). This observation was confirmed after an inspection of the average Mutual Information between the fixed and registered images. The results of the comparison can be seen in the boxplot in figure 3 where we can clearly see that using the affine transformation parameters provides better results.

[1] https://elastix.lumc.nl/modelzoo/par0025/
[2] https://elastix.lumc.nl/modelzoo/par0009/

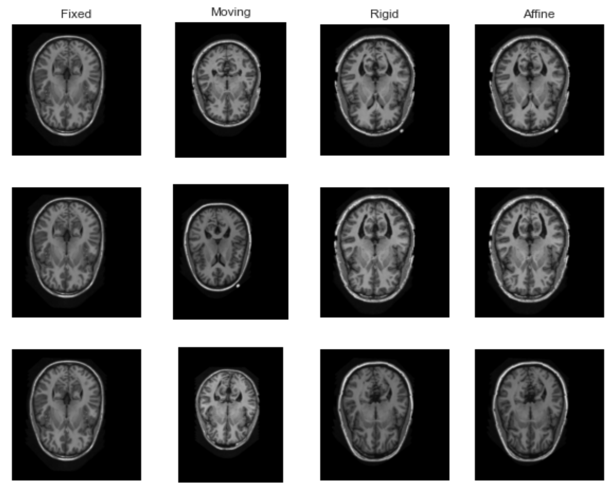

Fig. 2. Example registration results using rigid and affine transformations (slice n°130).

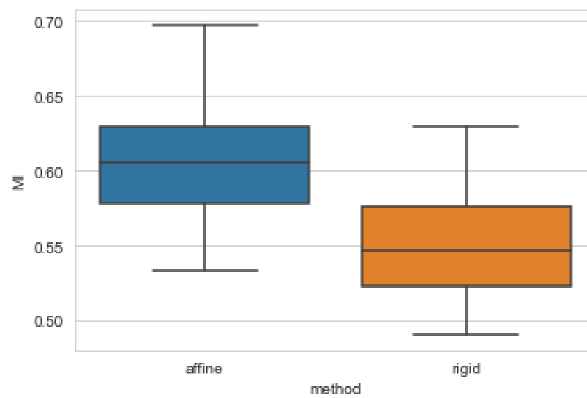

Fig. 3. Example registration results using rigid and affine transformations

C. Label propagation

After performing the registration on the brain images with respect to subject 1001, we perform label propagation as explained in the previous section. Figure 4 shows the results of this step for the previously selected subjects (slice n°130).

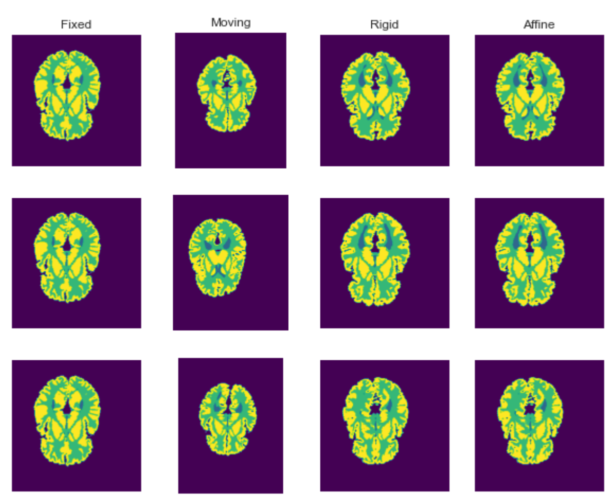

Fig. 4. Examples of labels propagation results using rigid and affine transformations (slice n°130).

D. Atlas generation

Next we generate the multi-atlases using all the images in the training set both by averaging the propagated labels to obtain a probabilistic atlas and by majority voting. This was done using both the rigid and the affine registration results. For better visualisation, we provide example atlas generation results in the appendix in figure 5 for the rigid and figure 6 for the affine case.

E. Tissue models

In the last step, we generated the tissue models as described in the previous section both using the majority voting atlas and the propagated labels of each image. Figures 8 and 9 show the resulting tissue models obtained using the rigid registration results while figures 10 and 11 show the results for the affine registration case. We can appreciate from the figures that using the labels of each image provide more smooth distributions for all the tissues compared to the results obtained using the majority voting-based atlas, but the resemblance of both plots is consistent. This last observed variability is due to the natural differences of the real tissue classes and the multi-atlas majority voting label assignment. Note that the high probabilities given to the background class for intensity levels higher than 130 is due to the presence of skull and soft tissues in the background surrounding the brain tissues, those correspond to few voxels which have high intensity values.

References

[1] M. Cabezas, A. Oliver, X. Lladó, J. Freixenet, and M. Bach Cuadra, "A review of atlas-based segmentation for magnetic resonance brain images," *Computer Methods and Programs in Biomedicine*, vol. 104, no. 3, pp. e158–e177, 2011. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0169260711002033

[2] S. Klein*, M. Staring*, K. Murphy, M. A. Viergever, and J. P. Pluim, "elastix: a toolbox for intensity-based medical image registration," *IEEE Transactions on Medical Imaging*, vol. 29, no. 1, pp. 196 – 205, January 2010.

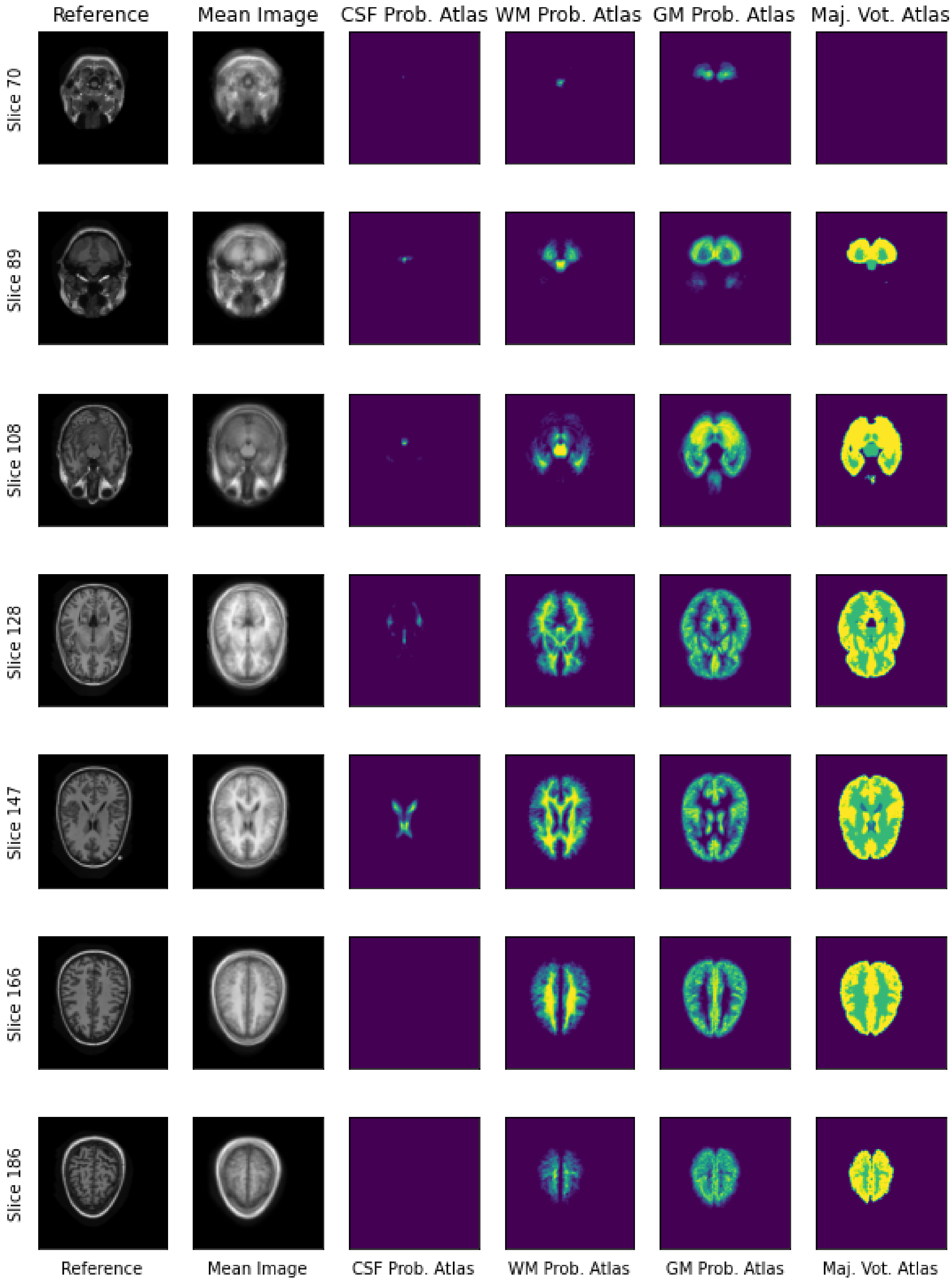

Fig. 5. Examples of Atlases generated using rigid registration.

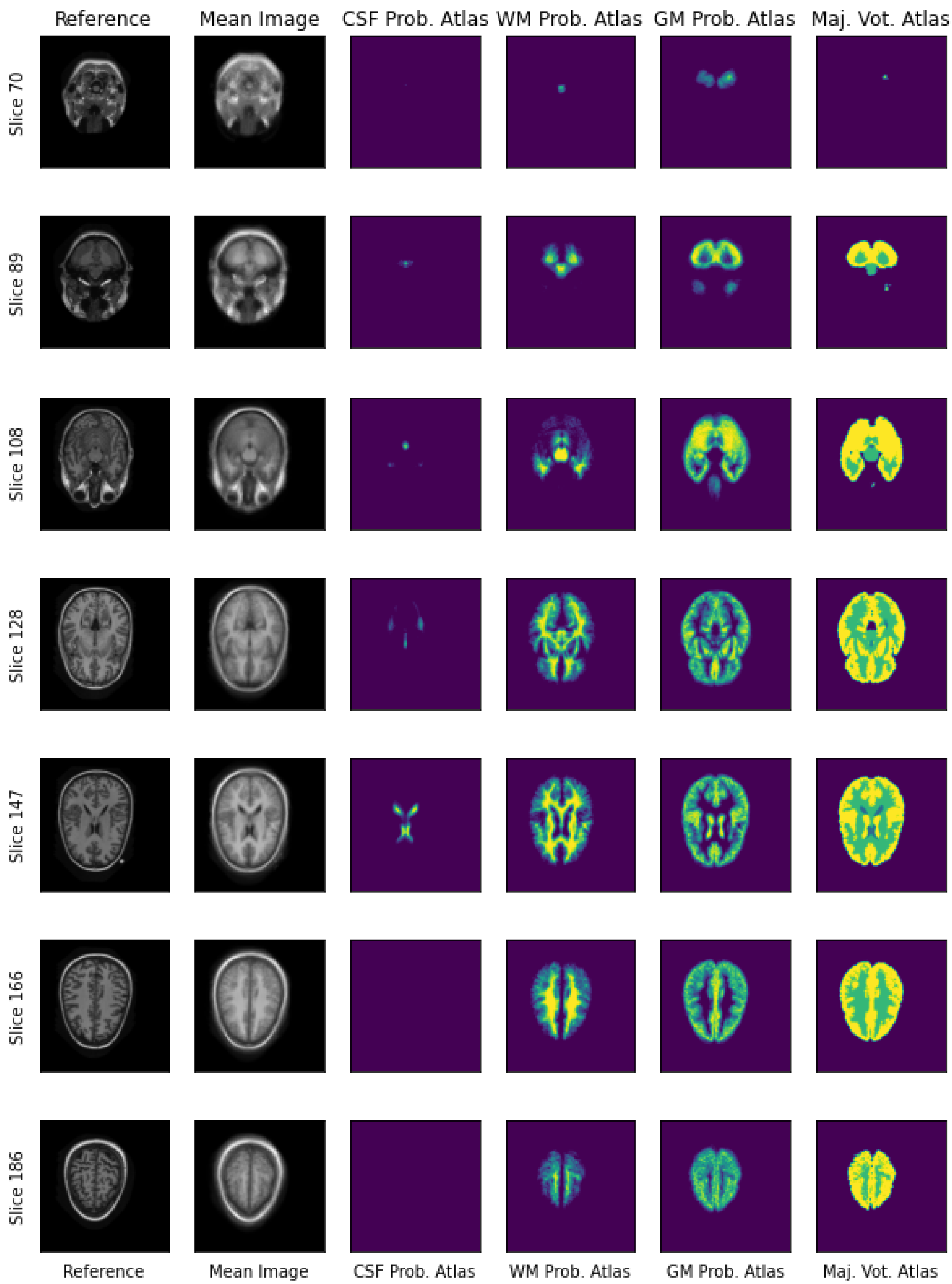

Fig. 6. Examples of Atlases generated using affine registration.

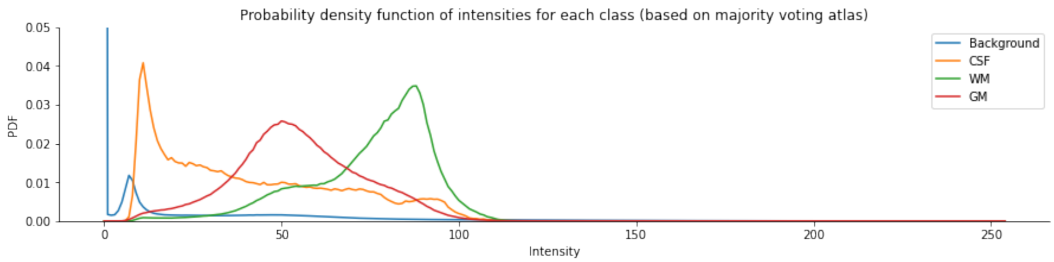

Fig. 7. Probability density functions obtained using rigid transformation and the majority voting atlas.

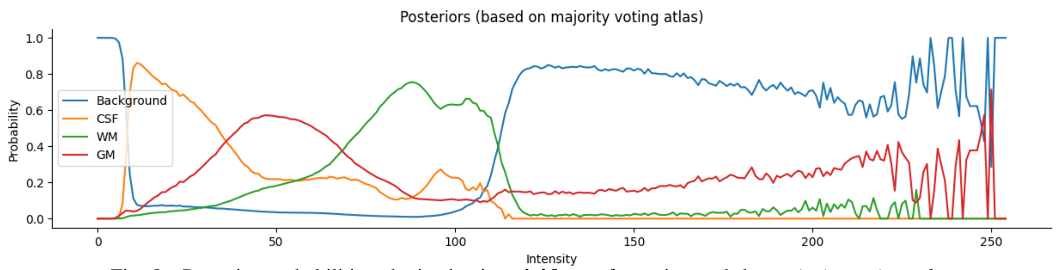

Fig. 8. Posterior probabilities obtained using **rigid** transformation and the *majority voting atlas*.

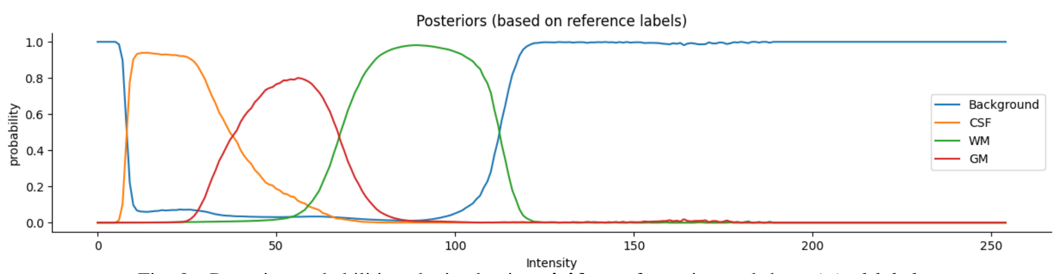

Fig. 9. Posterior probabilities obtained using **rigid** transformation and the *original labels*.

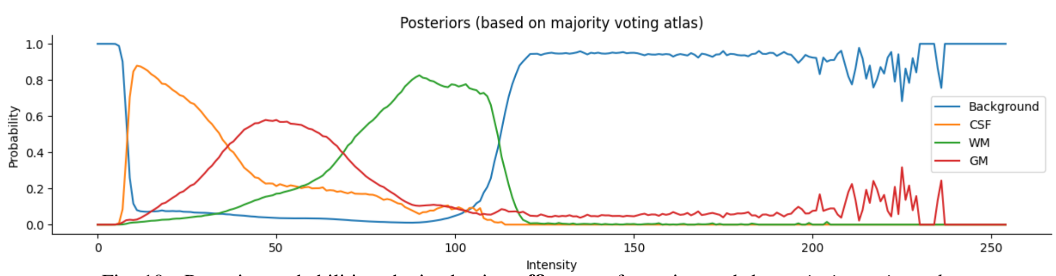

Fig. 10. Posterior probabilities obtained using **affine** transformation and the *majority voting atlas*.

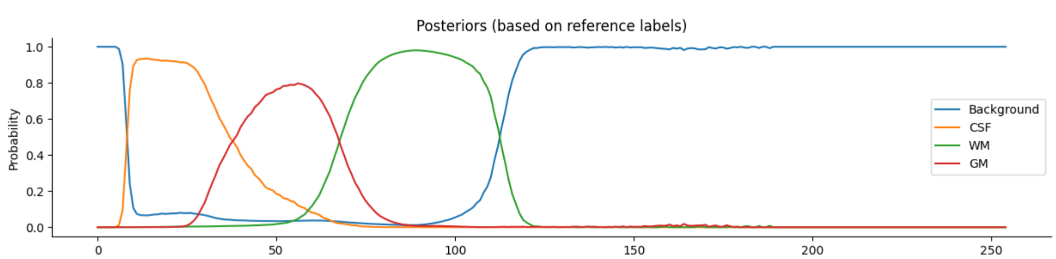

Fig. 11. Posterior probabilities obtained using **affine** transformation and the *original labels*.