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Lymphatic Eyes Project

September 27, 2015

1 INTRODUCTION

Registration/lymphatics/MRI project focuses on tracking cerebrospinal fluid which injected into animals' brain to establish how the fluid communicate with components of the brain and to verify if the fluid get into the eyes via the optic nerves. Each dataset considered in this project contains volumes (frames) which are the images of the brain sampled after injecting the cerebrospinal fluid. Since the areas occluded by the fluid have higher intensity than others, looking at the changes over time of the brain volume actually helps to investigate how the fluid is transferred inside the brain.

One simple approach to extract the changes is to compare every frame with the baseline. Ideally, with clear and perfectly aligned volumes, it is feasible to see the changes caused by the fluid by simply subtract each volume with one among several first volumes which have no liquid injected. This simple approach is relevant indeed since the data is sparsely sampled which is not suitable for tracking methods.

The main challenge is the quality of the data due to the scanner, the misalignment of the volumes, and the movement of the animal itself. The constant movement of the eyes especially makes the surrounding area become even harder to observe the changes.

Thus the main targets of this project are:

- Enhancing the visual quality of data: reducing noise, correcting the intensity bias.
- Correcting the anatomical misalignment: registering each volume to one reference frame.
- Developing visualization method to observe the changes effectively.

The registration part takes an important role in this project since the perfect registration ensures that displacements between frames solely come from the effect of the fluid. We evaluate two main approaches for registration, namely intensity-based and gradient-based registration.

2 Dataset and data pre-processing

There are two main dataset considered in this project, namely supine NIDA 072115B and supine 072414A, which contains 44 and 61 frames respectively. Each frame is a volume of size 256x256x256. The first three frames of each dataset are selected as baseline since they are images of the brain when the fluid is not injected yet. One frame of supine 072414A dataset is shown in figure 2.1, visualizing 2D images of one volume at different slices taking from all 3 dimensions.

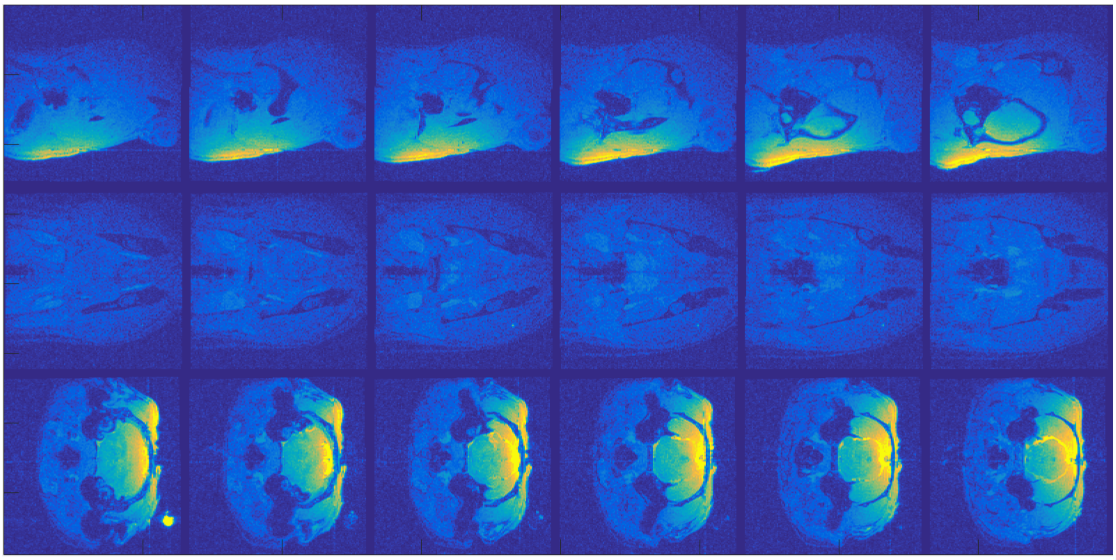


Figure 2.1: 2D slices of supine 072414A dataset

It is clear that the dataset is affected by the intensity non-uniformity artifact which usually occurs in MRI. Noticeably, intensity non-uniformity significantly affects gradient-based and thresholding methods.

To resolve this problem, we use N4 algorithm [5] to correct the image bias. Assuming that all frame in the dataset is corrupted uniformly where they are captured from the same MRI scanner, the calibration field is firstly calculated from the first frame which tries to create homogeneous intensity field over 3D isotropic volume. Then this calibration field is applied to all frame in the dataset to get B1 corrected volumes. As can be seen from figure 2.2, intensity bias correction significantly improves the quality of the images. Since intensity non-uniformity contain no valuable information, all experiment is performed on intensity corrected volumes.

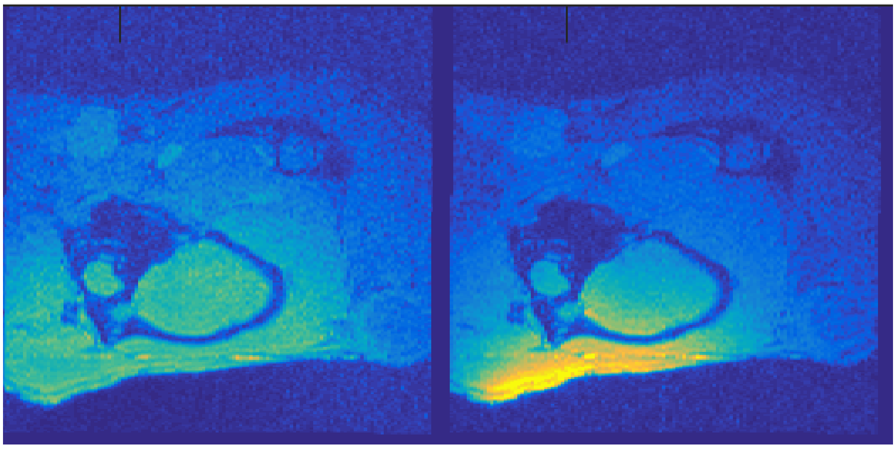


Figure 2.2: Image intensity bias correction by N4 algorithm. Left: before, right: after.

3 Registration configurations

The registration is done by using the software at www.mrf-registration.net, which uses discrete optimization method based on [2],[3],[4]. The algorithm is controlled by 3 groups of parameters to define the transformation model, search space for displacements, and optimization method respectively.

Spatial parameters mainly define the transformation model used for registration:

- Set distance (mm): Initial control point distance in millimeters
- Image levels: total number of image pyramid levels.
- Grid levels: total number of control grid levels

Label set settings defines search space for displacements:

- Sparse/Dense Sampling: generating model for displacements. For sparse sampling, only 6 main directions (on x, y, z axis) are used. For dense sampling, displacements distributed over an cubic.
- Link Maximum To Grid: Set the maximum range of the displacements.

Optimization Settings define the cost function which is subject to minimization, including similarity measure and regularization function:

- Similarity measures: the measure to calculate the quantity distance between two volumes
  - SAD: Sum of Absolute Differences
  - SADG: Sum of Absolute Differences plus Sum of Gradient Inner Products
  - GRAD: Sum of Gradient Inner Products

- NCC: Normalized Correlation Coefficient

- Regularization function: The penalty function for deformation field.
  - Pott's model penalizes deviations in the displacement assignments.
  - Truncated Absolute Difference penalizes neighboring control points.
  - Approximated Curvature Penalty penalizes the second order derivatives of the displacement field.
  - Distance Preserving penalizes changes in the distances between neighboring control points.

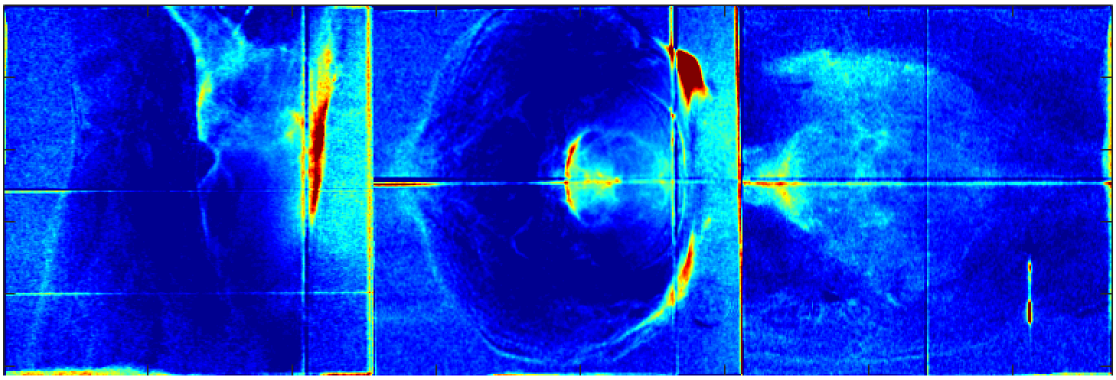
Recommended configurations which is mainly used in this project is shown in table 3.1.

Table 3.1: Recommended configurations

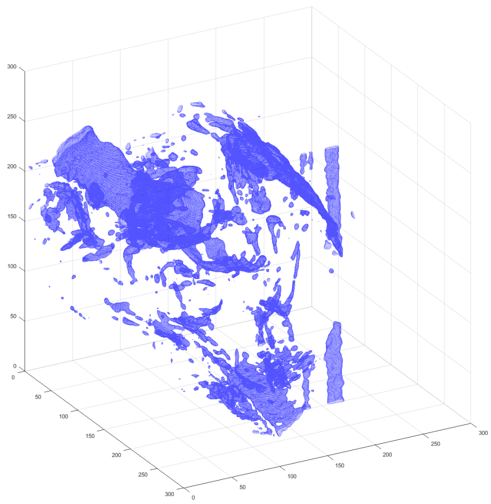
grid	= 20	%control point spacing in mm
imagelevels	= 3	%number of image pyramid levels
gridlevels	= 3	%number of control grid levels
mindim	= 32	%minimum size for any dimension within an image pyramid
iterations	= 5	%optimization iterations per level
max_dis	= 5	%maximum displacement
steps	= 5	%number of steps from min to max displacement
lab_factor	= 0.5	%label space rescale factor applied after each iteration
data	= 0	%data term: 0=SAD
dist	= 1	%distance term: 0=Pott's, 1=Trunc. Absolute Difference,
truncation	= 0	%truncation value for distance term
lambda	= 0.01	%weighting between data and smoothness term
gamma	= 0	%additional weighting
optimizer	= 0	%optimization method: 0=FastPD (currently only one optimizer)
locallabels	= 0	%local label set computation: 0=OFF 1=ON
interpolation	= 0	%deformation interpolation method: 0=Cubic B-Splines
invprojection	= 1	%inverse projection method: 0=Cubic B-Splines, 1=Linear
linkmax	= 1	%indicates if the maximum displacement is linked to the control point spacing
increg	= 1	%incremental regularization: 0=OFF 1=ON
update	= 0	%indicates the field update mode: 0=ADDITIONAL
sampling	= 0	%indicates the displacement space sampling mode: 0=SPARSE 1=DENSE
bins	= 32	%number of bins used for histogram based data terms (e.g. NMI, CR, HD)
margin	= 0	%image border margins (in millimeters) exluded from data cost computation
sigma	= 1	%sigma for Gaussian image pyramid

4 REGISTRATION RESULTS

Performing a registration technically generates a deformation field to correct any displacement between two instances. For lymphatics dataset, there are three possible kinds of displacements between frames: the global offset due to sampling process, the movement/rotation of anatomical components of the animal, and the intensity changes which subject to the effect of the fluid. Figure 4.1 gives an insight of these kinds of displacement by demonstrating the percentage change values computed for each voxel. As can be seen from figure 4.1b, only a small proportion of displacement comes from the effect of the fluid which is the flow in the middle. Regarding the purpose of the project, a good registration is defined in the sense that it should correct only the first two kinds of displacement and preserve the third one.



(a) 2D mean images over 3 dimensions



(b) 3D volume

Figure 4.1: Volume contains percentage change values of supine 072414A dataset

The registration is done by registering each frame to the only one reference. We choose the middle frame to be the reference since its distances to others are smallest. The results then is evaluated based on following criteria:

1. Anatomical correctness.

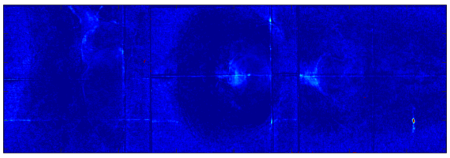
2. Registration performance which respect to misalignment correction.

3. Fluid area's preservation.

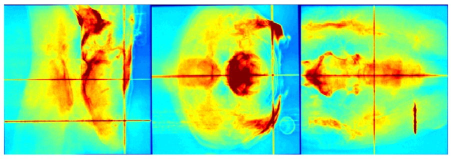
4.1 Intensity-based registration

In this experiment, registration algorithm is applied directly on original data, using similarity measure based on absolute differences. This measure is clearly more pronounced in the contrast enhanced areas since the displacement of high value voxels penalizes higher than normal voxels. Therefore, it is more likely that the third criteria which is fluid area's preservation is violated since the fluid area always have higher intensity values.

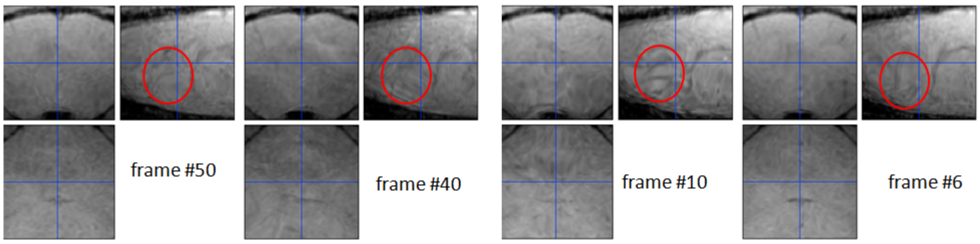
Empirical results which is shown in figure 4.2 show the same conclusions. While the registration drastically reduces the differences between frames (figure 4.2a) since there is almost no chages in percentage of voxels in volume, there are two major problems. As can be seen from figure 4.2b, the changes mainly focus on high contrast area. The second problem is that the changes caused by contrast agent misleads the control grid of registration system, creating distortions on anatomical components of the brain.



(a) Percentage changes of registered dataset



(b) Sum of differences (SOD) between registered and original dataset



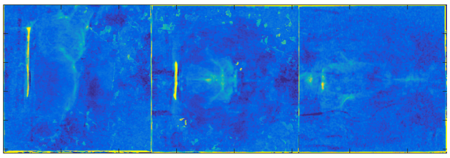
(c) Anatomical distortion of registered volumes, red circles mark over-deformed areas

Figure 4.2: Analysis of registered supine 072414A dataset using intensity-based registration

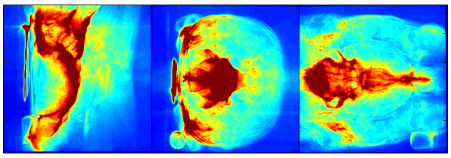
4.2 Gradient-based registration

4.2.1 Gradient image

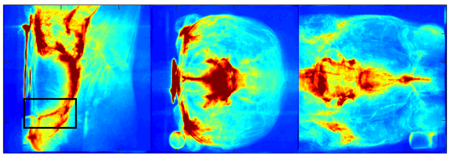
One approach to reduce the effect of high contrast area is using gradient image which is directional change in the intensity or color in an image. The gradient image mostly preserves the edges and therefore helps the registration focusing more on general structure. Gradient images registration can be done by using GRAD similarity measures or using gradient images as source-target instances to compute deformation field.



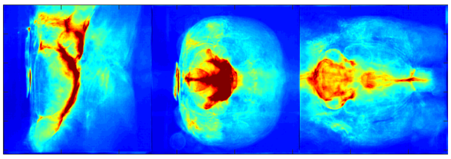
(a) Percentage changes of gradient registered dataset



(b) SOD between original and intensity registered dataset



(c) SOD between original and gradient registered dataset



(d) SOD between gradient and intensity registered dataset

Figure 4.3: Analysis of registered supine NIDA 072115B dataset using gradient images registration in comparison with intensity registration

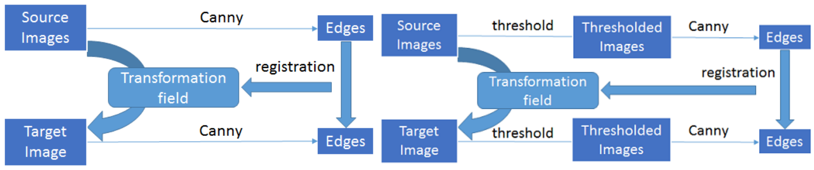
As can be seen from the registration results of supine NIDA 072115B dataset visualized in figure 4.3, the percentage changes of gradient images registered dataset are generally larger than intensity-based registered dataset. This decrease indicates that there is less deformation which partly addresses the over-deformation problem. Noticeably, a proportion of the fluid area still preserves the displacement shown as high percentage change values in figure 4.3a.

Figure 4.3b, figure 4.3c and figure 4.3d show the differences of intensity-based and gradient images registration methods. While intensity-based registration makes changes over the whole volume, gradient images registration focuses more on the boundaries which are visualized as the clear edges in figure 4.3c. This mechanism helps prevent the anatomical distortions.

On the other hand, figure 4.3c and figure 4.3d indicates a major drawback of registration using gradient images. Even though using gradient images for registration helps reducing the deformation on fluid area, the optic nerves which is marked by rectangle in figure 4.3c, still gets immensely deformed. In fact, registration regards optic nerves' area of original data and gradient data relatively the same since the optic nerves can be considered as small edges and thus they are preserved in gradient images.

4.2.2 Binary thresholding-gradient image

Registration using gradient images shows that gradient representation helps balancing the registration by leveling the high contrast areas into high value edges. The empirical results however shows that the deformation field is still affected by the intensity enhancement of the fluid. Thus it is essential to normalize the values of voxels. To acquire that, Canny Edge detector [1] is used to extract edges with binary values, marking only voxels whose gradient value satisfies defined thresholds. Since the edges only have binary value, the effect of intensity enhancement vanishes. Besides, we also evaluate the effect of high contrast voxels to Canny Edge detector by removing high value voxels out of the volumes before utilizing edges detector. From each pair of target/source volumes, they will be put though a threshold to get rid of high contrast areas, then the edges are extracted which then are used to compute the deformation field. The threshold is selected so that the high contrast area mostly contains fluid areas. For supine NIDA 072115B dataset, the threshold value chosen is 1500, which contains the area visualized in figure 4.7. The summary of these two pipelines are summed up in figure 4.4.



1

(a) Edge detector (b) Edge detector + thresholding

Figure 4.4: Registration process using edge detector and edge detector after thresholding images

As can be seen from figure 4.5, the deformation field is less pronounced in the fluid area. As expected, the difference between figure 4.5 and figure 4.3c shows the advantages of edge registration method over gradient images registration method where the optic nerves are less affected by the deformation field.

Figure 4.6 visualizes in 3D the accumulative sum of changes over time after using different registration methods on supine NIDA 072115B dataset, and therefore summarizes the performances of gradient images registration methods used in this project. Figure 4.6a shows the accumulative changes of original data. It shows that the area around the eyes and outer skin of the animal have significant changes due to the movement of the animal and the misalignment of volumes respectively. The changes across the optic nerve are actually can be observed in figure 4.6a. Unfortunately, this changes possibly can be caused by the misalignment and movement as well.

Figure 4.6b effectively demonstrates the drawback of registration method based on gradient image. Although the registration corrects the majority of changes caused by the volumes' misalignment and eyes' movement, it also removes the flow of fluid getting into the eyes. Comparing figure 4.6b and figure 4.6c shows that the improvement of edges registration

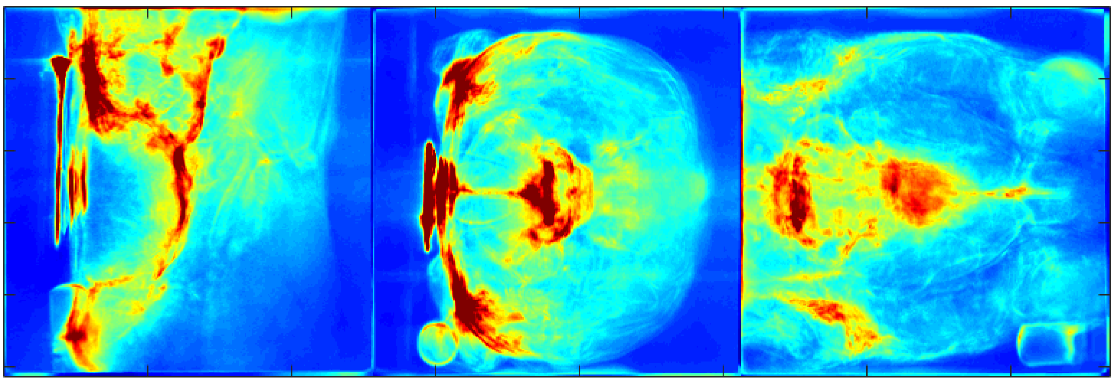
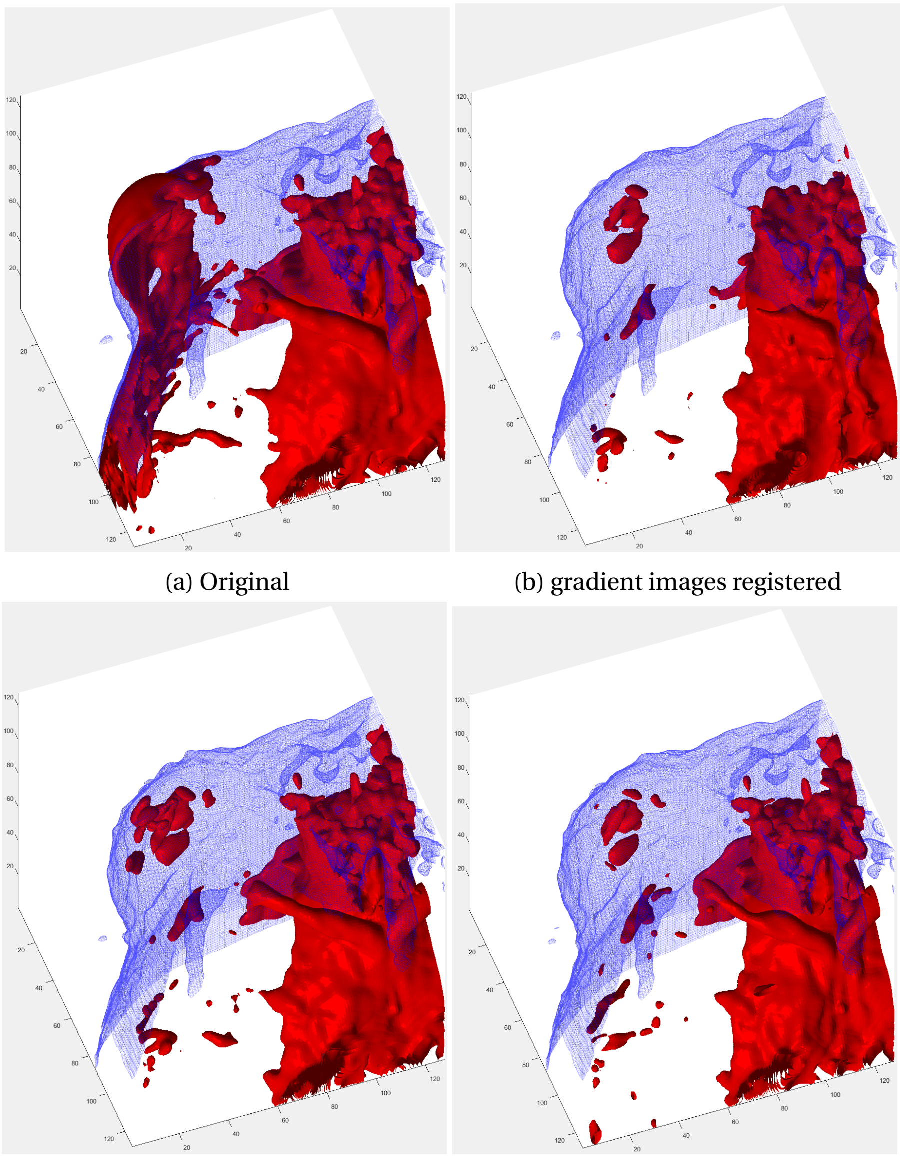


Figure 4.5: SOD between original and edge registered dataset



(a) Original (b) gradient images registered

(c) Edges registered (d) Edges registered +threshold

Figure 4.6: Accumulative sum of changes over time after using different registration methods on supine NIDA 072115B dataset

method over gradient images registration method indeed allows the process of transferring the fluid to the eye via optic nerves to be observable.

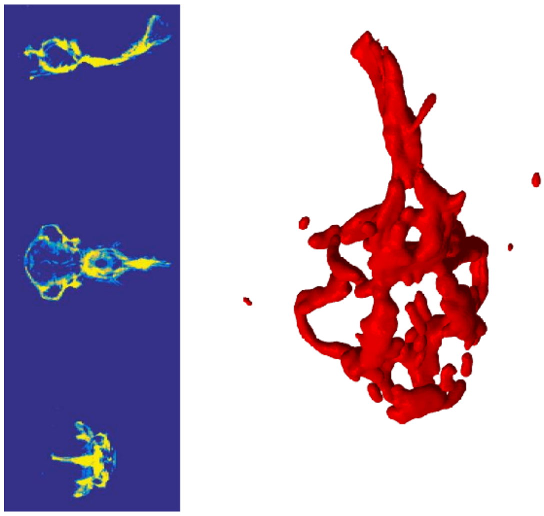


Figure 4.7: Accumulative sum of voxels which are larger than 1500 of supine NIDA 072115B dataset

REFERENCES

[1] J Canny. A computational approach to edge detection. *IEEE Trans. Pattern Anal. Mach. Intell.*, 8(6):679–698, June 1986.

[2] Ben Glocker, Nikos Komodakis, Nikos Paragios, and Nassir Navab. Approximated curvature penalty in non-rigid registration using pairwise mrfs. In *ISVC (1)*, volume 5875 of *Lecture Notes in Computer Science*, pages 1101–1109. Springer, 2009.

[3] Ben Glocker, Nikos Komodakis, Nikos Paragios, Georgios Tziritas, and Nassir Navab. Inter and intra-modal deformable registration: Continuous deformations meet efficient optimal linear programming. In *IPMI*, volume 4584 of *Lecture Notes in Computer Science*, pages 408–420. Springer, 2007.

[4] Ben Glocker, Nikos Komodakis, Georgios Tziritas, Nassir Navab, and Nikos Paragios. Dense image registration through mrfs and efficient linear programming. *Medical Image Analysis*, 12(6):731–741, 2008.

[5] N. Tustison and J. Gee. N4itk: Nick's n3 itk implementation for mri bias field correction. 12 2010.