Local Extraction of Extra-Axial CSF from structural MRI

Tahya Deddah[a], Martin Styner[a,b], and Juan Prieto[a]

[a]Department of Psychiatry, University of North Carolina, Chapel Hill, North Carolina, United States

[b]Department of Computer Science, University of North Carolina, Chapel Hill, North Carolina, United States

ABSTRACT

The quantification of cerebrospinal fluid (CSF) specially the extra-axial cerebrospinal fluid (EA-CSF), which is the CSF in the subarachnoid space surrounding the cortical surface of the brain, plays an important role in the detection of autism spectrum disorder (ASD) in infants, where a previous study showed an increase of the global volume of EA-CSF in children with ASD compared to normal children.

However, measuring the global volume of EA-CSF still abstract and does not provide a specific anatomical location of the effect. A localized EA-CSF extraction would provide more accurate and exploitable measurements. Indeed there is a recent study which provide a local EA-CSF extraction by using a pipeline that combines probabilistic brain tissue segmentation, cortical surface reconstruction and streamline-based local EA-CSF quantification.

A graphical user interface is necessary to facilitate the usage of this pipeline and make it available for the general public.

The purpose of this article is to implement a graphical user interface tool (Local EACSF) which allows the user to easily run the previous pipeline in order to quantify locally the EA-CSF and control the quality of this quantification, It also adds some improvements and corrections to the pipeline to optimize the computation of EA-CSF. LocalEACSF gives a results similar to the original pipeline and allows neuroimaging labs to a local extraction of extra-axial CSF in their neuroimaging studies in order to investigate its role in normal and atypical brain development.

Keywords: Cerebrospinal Fluid, Extra-axial CSF, Open-Source Software

1. INTRODUCTION

Cerebrospinal fluid (CSF) is a clear, colorless body fluid found within the tissue that surrounds the brain and spinal cord of all vertebrates. The fluid is made by a group of cells, called the choroid plexus, and distributed in two distinct spaces: • The subarachnoid space (between the pia mater and the arachnoid) which is a space external to the central nervous system. This part of CSF is called extra-axial cerebrospinal fluid (EA-CSF) and is the object of our actual study. • The ventricular system which is a space inside the brain.

Cerebrospinal fluid plays an essential role in the development and the function of the brain as well as its protection in both prenatally and throughout the lifespan. Indeed the development and the function of the brain are insured by the CSF circulation that allows:[1] (1) the delivery of growth factors and other signaling molecules necessary for healthy neural growth (2) the cleaning of the brain by removing neurotoxins and metabolic waste by products of neuronal function.

Previous studies[2] have indicated that the EA-CSF is a promising marker for the early detection of children at risk of neurodevelopmental disorders such as autism spectrum disorders (ASD) by showing an increase in the global volume of EA-CSF in infants at high familial risk of ASD.

The finding of the previous studies indicate that a global quantification of EA-CSF is important in understanding the CSF pathology and its relation to ASD symptoms but still not allowing us to go further and do more localized analysis of EA-CSF. Hence the need for a local EA-CSF quantification.

In this article, we will explain the existing pipeline for a local extraction of EA-CSF from MRI , correct and improve it then build a graphical user interface to facilitate the execution of this pipeline.

2. METHODS

2.1 Existing Pipeline:

The following method is used to compute the EA-CSF (see original paper for more details[3]):

As a first step, a probabilistic tissue segmentation of the white matter (WM), the gray matter (GM) and the cerebrospinal fluid (CSF) is extracted from a magnetic resonance imaging (MRI). Models of CSF outer surface, gray matter and white matter surfaces are constructed from the tissue segmentation.

A partial differential equation is solved between a defined inner surface and the outer surface of the CSF to generate the streamlines connecting those two surfaces.Then, throughout each of the streamlines, the CSF space is sampled and the CSF probability values are integrated to generate a local EA-CSF measurements at each point on the cortical surface. (Figure 1).

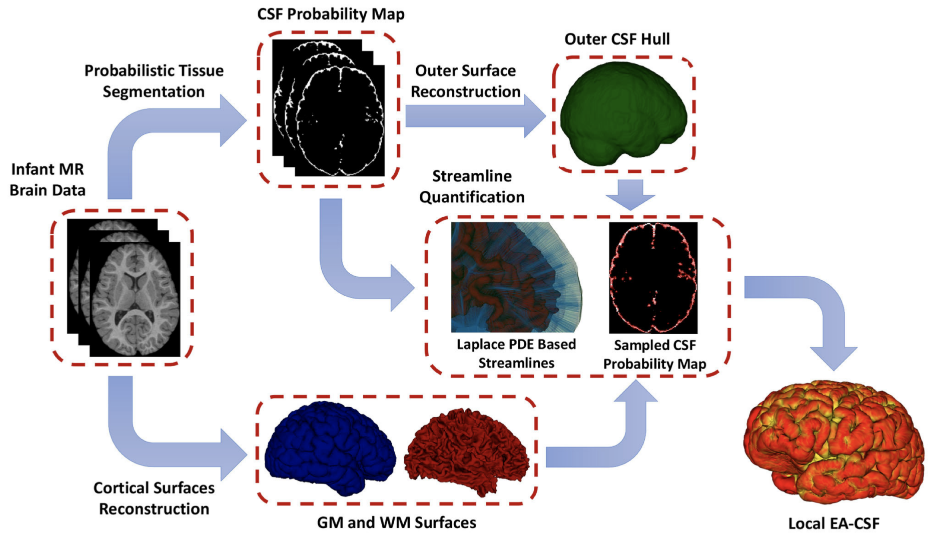


Figure 1: The proposed framework for the extraction of local EA-CSF from structural MRI.

2.1.1 Surfaces construction :

For the creation of CSF outer surface the two hemispheres are treated separately. For each hemisphere, the tissue segmentation is "thresholded", closed then dilated to create a binary image : outer image (Figure 2). The outer image is converted to a VTK format then smoothed to generate the CSF outer surface. However, no creation is needed for the gray and white matter surfaces, they are assumed to be given as an inputs.

2.1.2 Generation of streamlines:

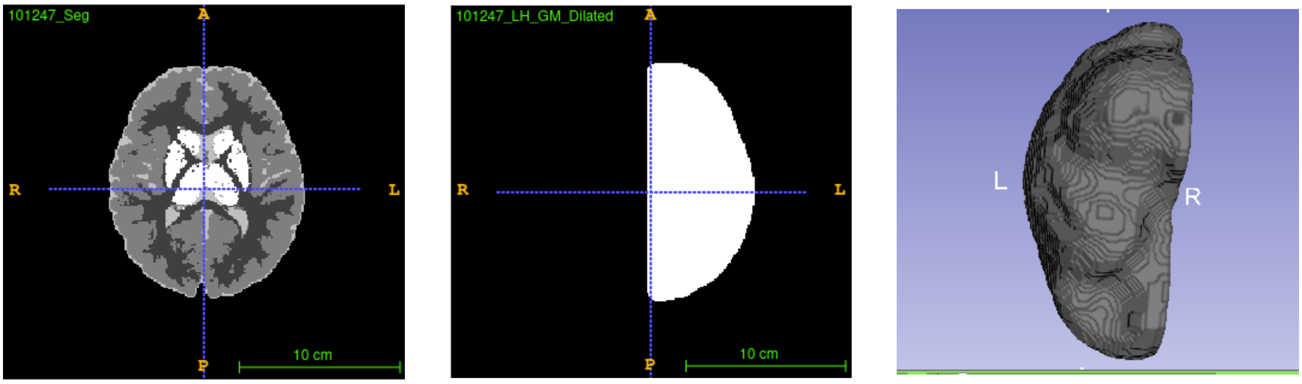
After the construction of the surfaces, we define the outer surface as the CSF outer surface and the inner surface as the average between the gray and white matter surfaces (middle surface) to reduce the margin of error in the gray matter segmentation.

A Laplacian equation is solved to obtain the gradient field enclosed between the two cortical surfaces surrounding the EA-CSF (inner and outer surfaces).

Laplace equation is a second order partial differential equation whose formula is as follows:

$$\Delta u = \nabla^2 u(x) = 0 \tag{1}$$

Once we have the gradients field, we generate the streamlines connecting the inner and outer surfaces. The streamlines are orthogonal to the gradients directions, parallel to each other and generated by a fourth-order Range-Kutta integration of the gradients field.



(a) Tissue segmentation (b) Left hemisphere outer image (c) Left hemisphere CSF outer surface

Figure 2

2.1.3 EA-CSF density computation:

A local measurement of the EA-CSF is computed for each vertex v by sampling the streamline l_v associated with it in many points then integrating all the probabilities of CSF in this sample. The probabilities values are obtained from a CSF probability Map image. A linear approximation is used to compute the probabilities for the non-uniformity of the streamlines.

$$EA - CSF_v = \sum_{k \in l_v} \frac{(P(k) + P(k+1))\Delta_k}{2} \tag{2}$$

Where Δ_k representing the Euclidean distance between the point k and its successor k + 1 in the sample.

To ensure that the CSF is calculated only between the two surfaces, a mask is used to limit the boundaries of the streamlines, this mask is the outer image computed previously.

2.2 Transforming the pipeline into an interface-based tool:

A graphical user interface is added to the pipeline in order to make it easier to run and user-friendly. The GUI is implemented by using C++ and Qt and is a stand-alone tool (Figure 3)

2.2.1 Inputs:

The tool's inputs can be given as a Json file and are the following:

- A tissue segmentation file of the gray matter, the white matter and the CSF to create the CSF outer surface.
- The inner surface for resolving the Laplace equation, this inner surface can be the middle or the 75P surface. The last one is the average between the middle and the gray matter surfaces.
- The CSF probablity map which contains the values of CSF probability necessary to compute the CSF density along each streamline.

Parameters and paths to all the executables used by the tool are set by default and editable.

The tool can be run locally or in a server with specifying the time, the number of nodes and the memory to use.

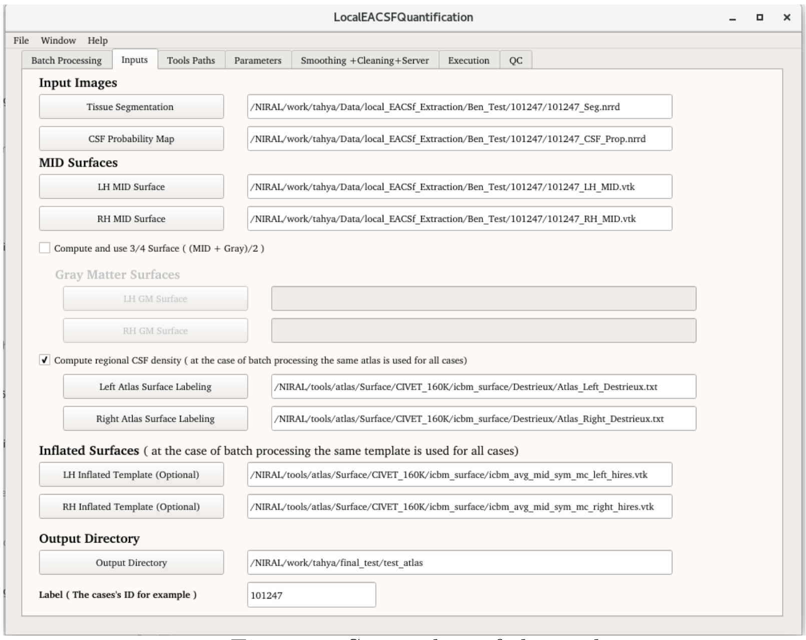


Figure 3: Screenshot of the tool

2.2.2 Outputs:

The two hemispheres are processed serially to reduce the memory usage. For each hemisphere, a directory, where the input data is copied and the following outputs are generated,is created :

- A text file containing the density value of CSF at each vertex of the cortical surface.
- A VTK file with the values of CSF density added as scalars to visualize it.
- A visitation map which is a binary file indicating all the voxels visited while computing the EA-CSF density.

The tool takes at least 8 hours to create all the outputs which makes sense given the time necessary for the generation of streamlines. While this time the progress can be watched in real time in the output and error text files.

The tool also has a clean up option that remove all the intermediate outputs generated when solving the Laplace equation. Those intermediate outputs occupy a large storage space

2.2.3 Batch Processing:

The tool features a batch processing where it treats a group of data with the same parameters and without the user interaction. This processing consists of a CSV file creation mechanism followed by the execution of the tool for each case in this file. The CSV file creation mechanism requires the provision of a directory containing the group of data to be processed. This mechanism can be skipped if a CSV file is provided directly to the tool. Batch processing can be executed locally or on server, serial or in parallel.

2.2.4 Quality Control QC:

The quality control is done by the visualization of the outputs and a comparison between the volume and the sum of EA-CSF densities:

1. visualization:

   The CSF density for both hemispheres are view-able in a surfaces visualization tool called ShapePopulationViewer (Figure 4), the CSF probability map is compared to the visitation map to ensure that all the

EA-CSF voxels from the first have been visited during the EA-CSF calculation. This comparison is made by visualizing the two images simultaneously in MriWatcher (Figure 5). Batch processing creates a CSV file with the outputs of the data group in question, ensuring a simultaneous visualization of it for a group analysis (Figure 6).

2. Comparison :

   The global volume of EA-CSF is computed and compared to the sum of EA-CSF densities. Global volume is computed by using the CSF Probability Map. this one is multiplied by the visitation map in order to remove the lateral ventricles (LV) CSF from it, then the result is normalized and the global volume is computed by adding the volume of each voxel multiplied by the its CSF density :

$$GlobalVolume = \sum_{v \in CSFvoxels} P(v) * Volume(v) = \sum_{v \in CSFvoxels} P(v) * D_x(v) * D_y(v) * D_z(v) \quad (3)$$

   Where $D_x(v)$, $D_y(v)$ and $D_z(v)$ are the voxel's sizes following x,y and z and P(v) the probabilty of EA-CSF at the vertex v. The asymmetries of the volume and the sum of the densities between the two hemispheres are calculated and compared with each other:

$$X_{Asymmetry} = 2 * \frac{(X_{left} - X_{right})}{X_{left} + X_{right}}$$

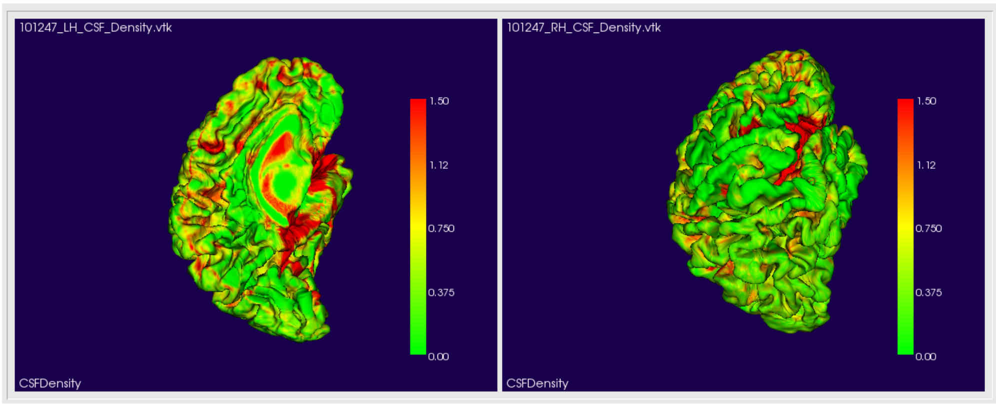


Figure 4: Left and right EA-CSF in ShapePopulationViewer

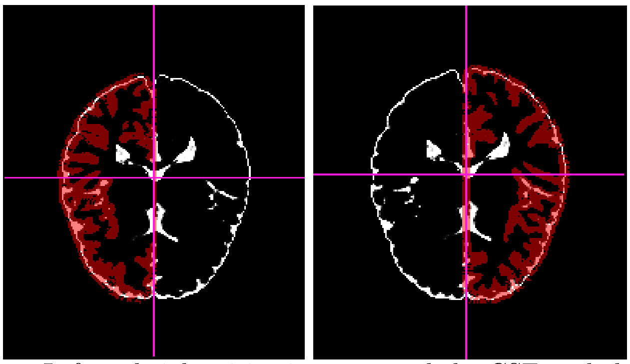


Figure 5: Left and right visitation map and the CSF probability map

2.2.5 EA-CSF regional computation:

The tool compute the mean and the sum of the EA-CSF in each region of the brain in order to allow a regional analysis of EA-CSF. The regions of the brain should be provided as an input text file (Figure 7).

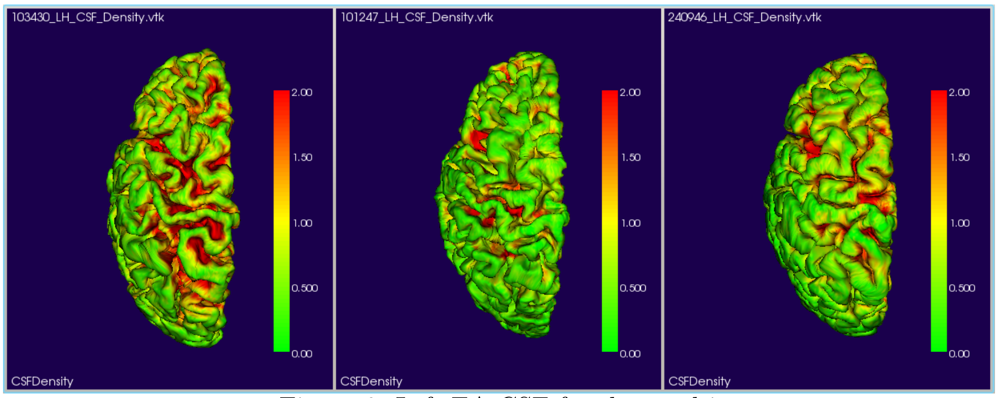


Figure 6: Left EA-CSF for three subjects

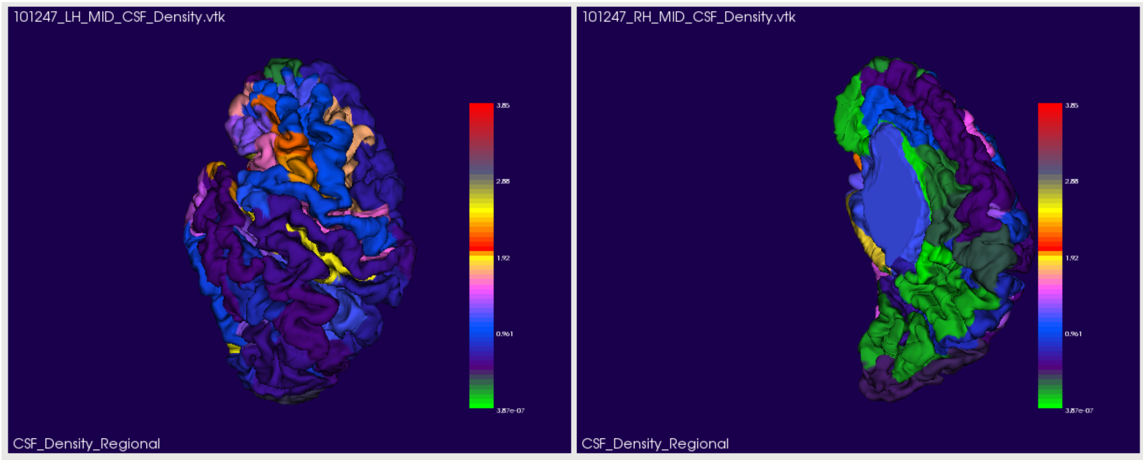


Figure 7: EA-CSF regional mean

2.3 Improvement of the pipeline:

Since the GUI works well, the following improvements and corrections are introduced to the pipeline in order to optimize the computation of the EA-CSF:

2.3.1 Smoothing:

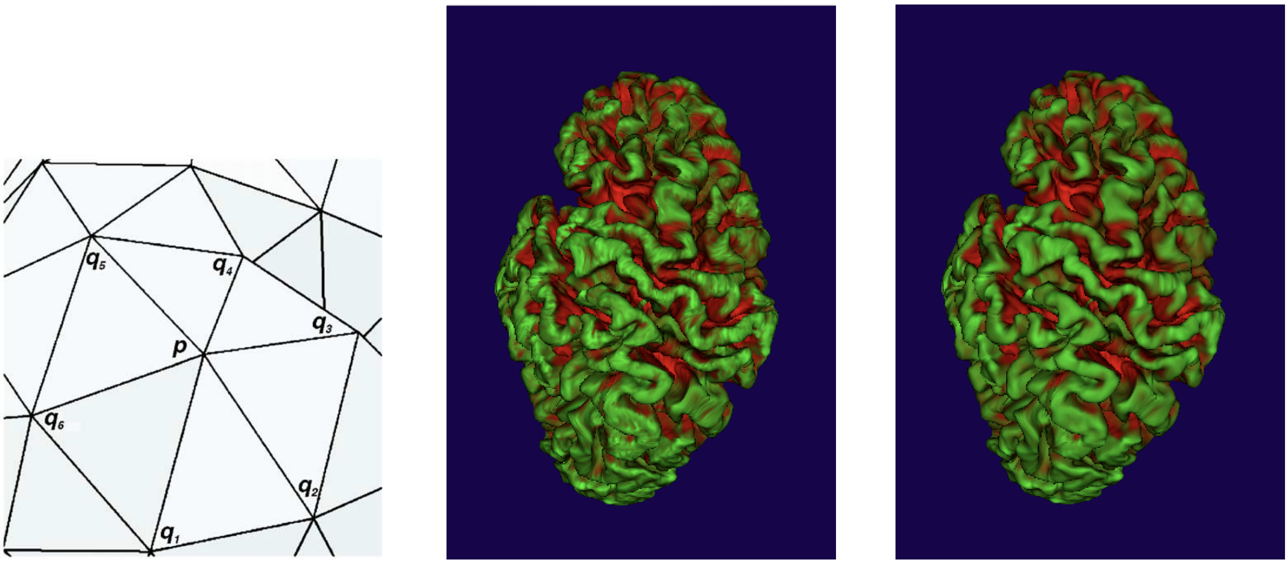
To smooth the computed CSF a heat kernel smoothing[4] was applied. The method of this smoothing is the following:
Let P be a vertex, to smooth the value of CSF at P: we consider the set Np {q0, q1, q2 .... qm} of vertices adjacent to it (Figure 8). For each element of Np the geodesic distance of P d(p,qi) is defined by 3D Euclidean distance $\|p - qi\|$. Considering σ the bandwith, the weight of every vertex in Np is given by :

$$W\sigma(p, qi) = \frac{exp(-\frac{d(p,qi)^2}{2\sigma^2})}{\sum_{q \in N_p} exp(-\frac{d(p,q)^2}{2\sigma^2})} \tag{4}$$

and the smoothed CSF density at the specific vertex P is:

$$CSFDesnity(p) = \sum_{q \in N_p} W\sigma(p, q) * CSFDensity(q) \tag{5}$$

This process is repeated N times until having the desired result. The bandwith σ and the number of iteration N are settled by default and are editable.



(a) Vertices adjecents to P (b) CSF before smoothing (c) CSF after smoothing

Figure 8

2.3.2 Interpolation:

To facilitate the generation of the streamlines between the inner and the outer surfaces, the surfaces are divided into several images with a given dimension treated separately.
The dimension of the images was set to a constant value in the original pipeline. By varying this dimension two interesting findings were found out (Figure 9):

- The average of EA-CSF densities decreases as the images dimension increases becoming more accurate due to the reduction of (I AM NOT SURE : artifacts errors). However, increasing the dimension costs in terms of time and memory.
- While the images dimension used in the original pipeline works perfectly for some cases, we observe a drop of EA-CSF densities average for others due to (NOT SURE: the motion artifacts).
  To solve this issue a linear interpolation is done. In fact now the CSF density is computed for three different values of image dimension: The original one (for example 300) and two other values symmetrical to each other with respect to the original value (for example: 280 and 320). An interpolated CSF density is computed using the two last densities (for example: 280 and 320) :

  $$CSFDesnsity_{Interpolated} = \frac{CSFDesnsity_{maximumvalue} + CSFDesnsity_{minumumvalue}}{2}$$

  The average of the original densities and the average of the interpolated densities are calculated and compared to each other, the one with higher average will be retained as the final density to avoid the drop of EA-CSF.
  The original, interpolated and final densities are stored in files and added to a vtk file to be viewable for the quality control.
  It should be noted that the three previous densities are calculated in parallel and the tool always offers the possibility of not doing this interpolation.

2.3.3 Elimination of double counting:

As indicated before, during the creation of CSF outer surfaces , the tissue segmentation is dilated, closed then converted to a vtk format for both hemispheres. this dilation causes an interference between the left and right

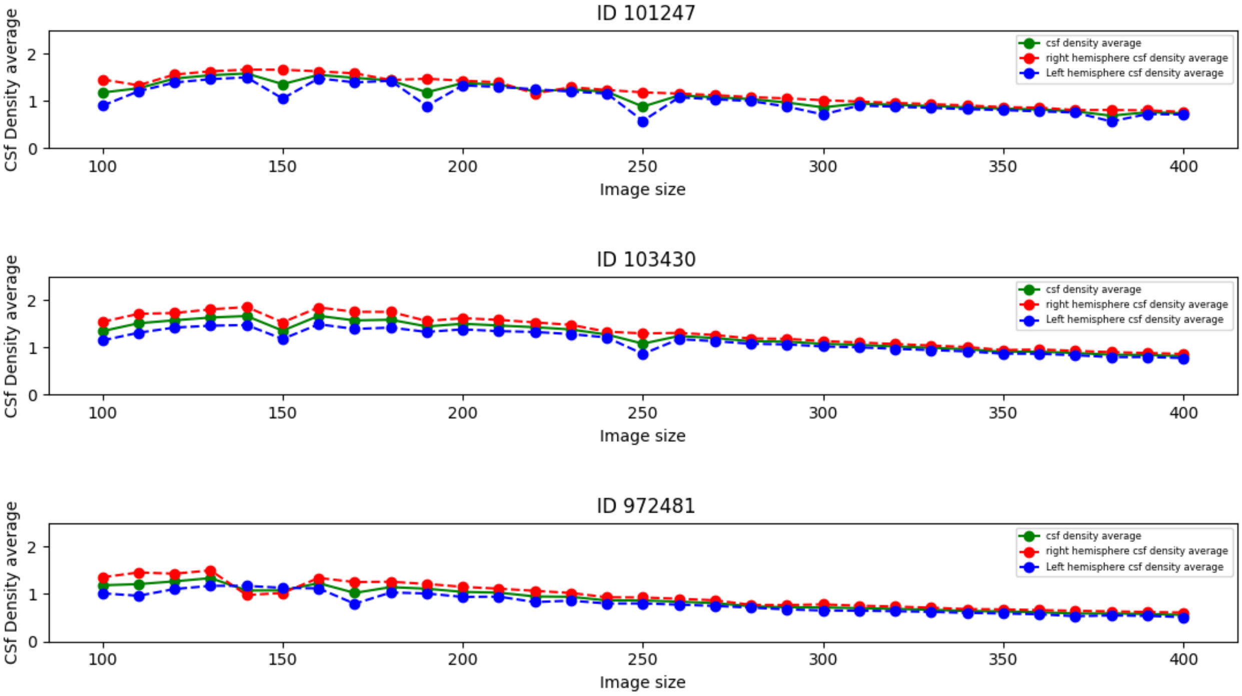


Figure 9: EA-CSF density average by the image size

outer images and then a double counting of CSF in this common area in both hemispheres. To eliminate the double counting, a mid-sagittal plan is fitted between the two outer images. Each point of the common area (intersection) is considered in the left or the right image according to its position regarding the plan.
The method used to fit the plan is to find a normal and a point of it which minimize the sum of the squares of the distances between each point of the intersection and the plan:
Let X be a point of the intersection and X_i its projection in the plane, finding the plan is equivalent of finding the normal and a point that minimize this quantity :

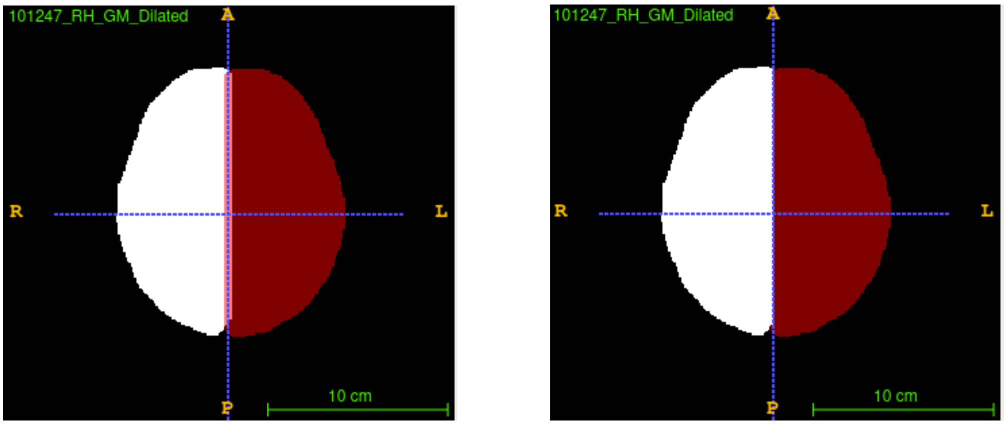
$$\sum(X - X_i)^2 = \sum(\frac{\vec{OX}.\vec{n}}{||\,\vec{n}\,||})^2 \tag{6}$$

where $\vec{n}$ is the plane normal and O is a point of it. The point O is initialized as the center of the intersection and the normal as the vector connecting the centers of two outer images. A minimizer is used to find the optimal values of these two variables. This plane is adjusted after solving the Laplace equation to avoid the intersection between the inner and outer surfaces which could create problems in the computation of the Laplacian (Figure 10 and 11).

2.3.4 Correction of EA-CSF density :

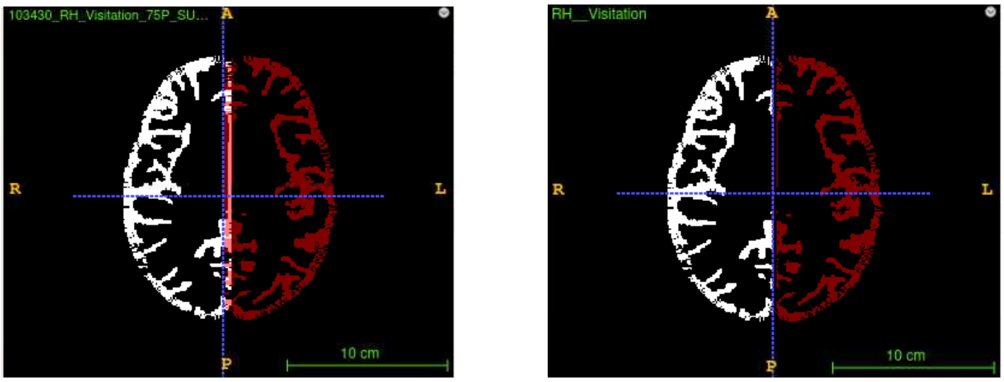
The method followed in the EA-CSF computation is to accumulating the CSF for all streamlines passing through the voxel in question. This method gives a sum of density very superior to the global volume of EA-CSF due to the overlapping between the streamlines. A density correction has been made. It allows a relative density to be assigned to each voxel by dividing the value of its density by the sum of the lengths of streamlines passing through it So instead of (2) we use the following equation to compute the EA-CSF:

$$EA - CSF_v = \sum_{k \in l_v} \frac{(P(k) + P(k+1))\Delta_k}{2 * TotalLength} \tag{7}$$



(a) Outer images before fitting the plane (b) Outer images after fitting the plane

Figure 10



(a) Visitation map before fitting the plane (b) Visitation map after fitting the plane

Figure 11

where TotalLength is lenghth total of the streamlines passing through the voxel.
This correction reduce the overlapping between the streamlines so the over-counting of EA-CSF and also give us a sum of density which is almost equal to the volume (a difference smaller than 5%).

3. RESULTS AND ANALYSIS :

3.1 Comparison between the results of existing pipeline and the new tool :

To compare the results of the original pipeline and the new tool, both were executed for the same data (45 subjects). The new tool was executed without the improvements and with the same parameters as the original pipeline. Both provided a similar results with a difference between 0% to 10% (Figure 12). This is due to an rounding error while computing the CSF Outer surface. This error is accumulated throughout the resolution of the differential equation making the final results different. That show us the sensitivity of Laplacian to a slight difference of the inputs.

3.2 Evolution of EA-CSF in terms of age:

In order to see the evolution of EA-CSF in term of age the tool was applied for a 100 subjects at 6, 12 and 24 months, We expect to see a decrease of EA-CSF while increasing the age which was the case from 12 to 24 months but from 6 to 12 the EA-CSF increased that could be due to the difference of scan that we use for 12 and 6 months (Figure 13).

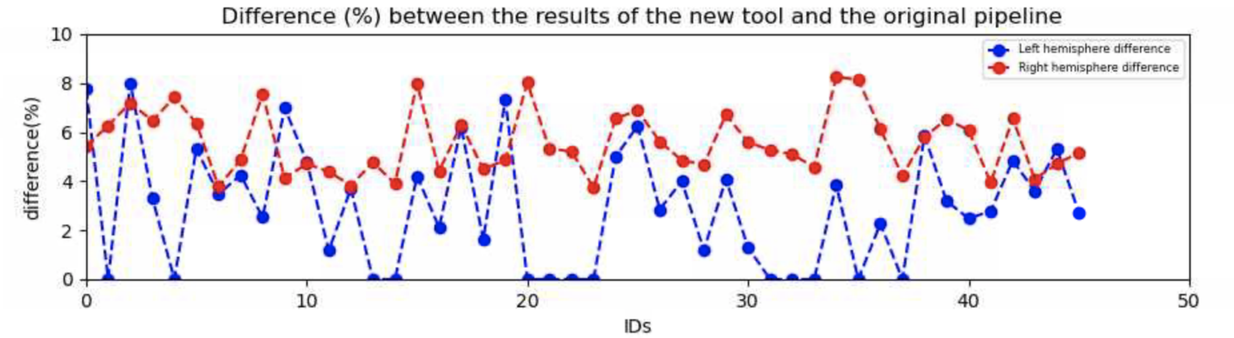
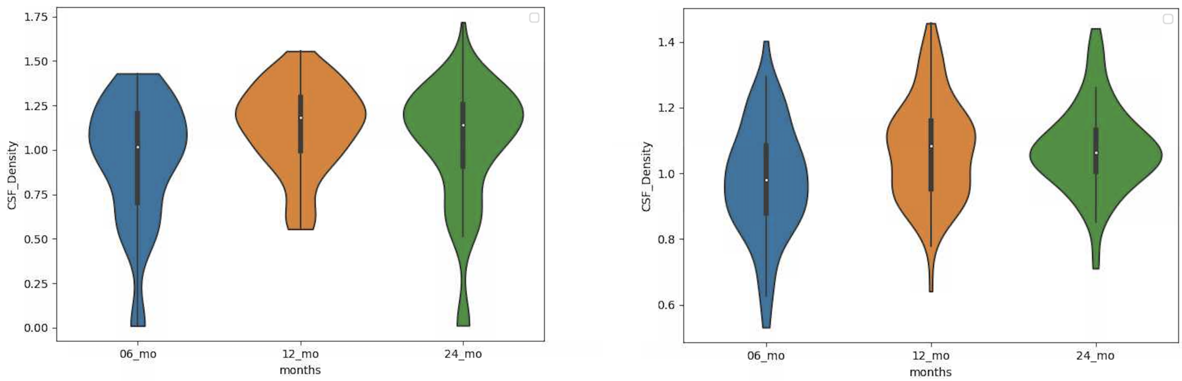


Figure 12: Difference between the results of the new tool and the original pipeline



(a) Left EA-CSF (b) Right EA-CSF

Figure 13: EA-CSF evolution in the time

4. CONCLUSION :

Here, we presented the development of a publicly available interface-based tool for a local computation of extra-axial CSF. We also presented some improvements to the existing local computation process of EA-CSF by making it more precise. However, the density remains slightly different from the volume due to the lengths of the streamlines which can sometimes be larger or smaller than the size of the voxels and the computation time still considerable (at least 8 hours). future versions of the tool should take these two improvements into account.

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