CortThick

This tool is made for measuring the cortical thickness of the brain, which means to assess the distance between the white matter and grey matter in each point. CortThick can be used with the graphics user interface, but also with command lines.

This document is a presentation of the methods used to calculate the cortical thickness.

Measuring the cortical thickness consists in assessing, measuring the distance between the white and the grey matter. The picture hereafter shows the distance between the blue layer (grey matter exterior) and the yellow layer (referring to the white matter boundary).

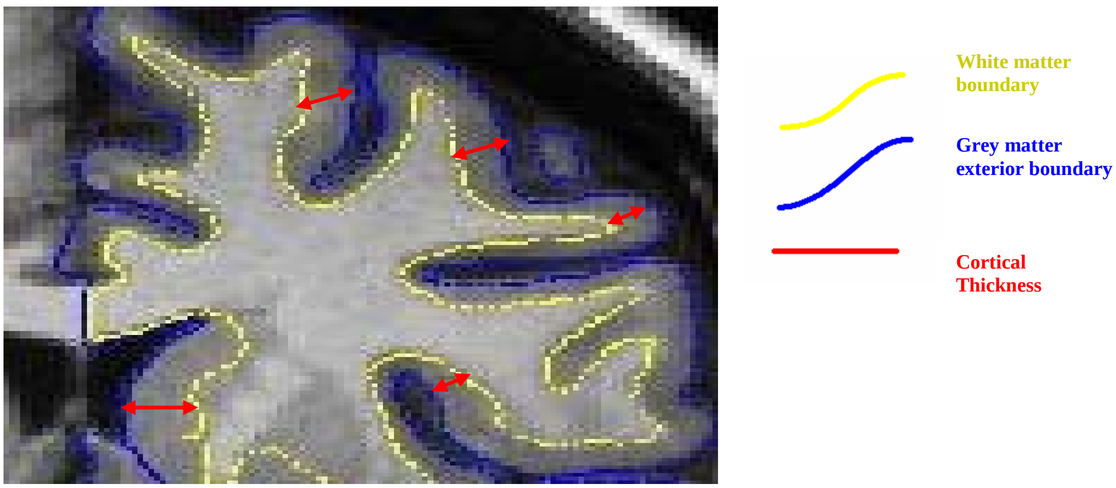


Figure 1 Calculate cortical thickness means measuring the distance between the blue layer and the yellow layer

Several techniques are already used to perform this measure. But the difficulties of doing a right measure are due to the segmentation step. In fact there is a loss of geometry information, exterior boundary within foldings disappear.

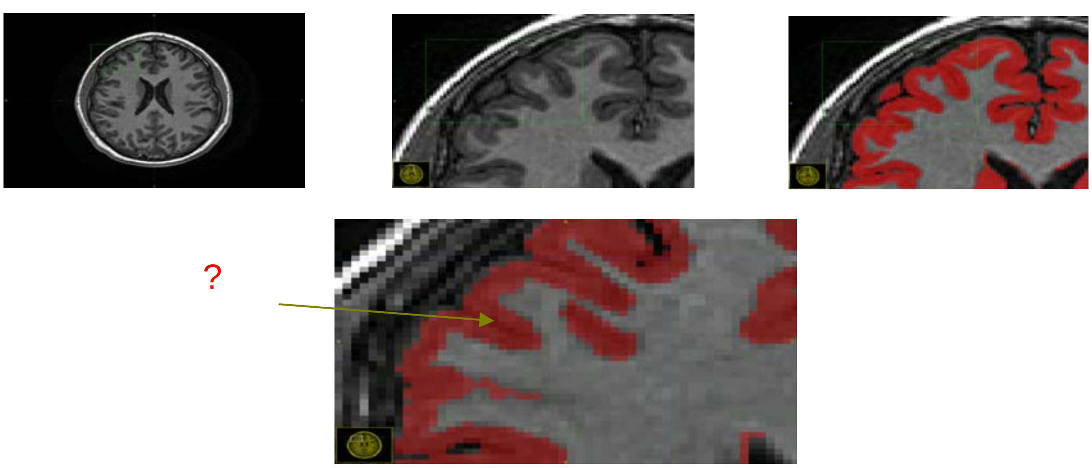


Figure 2 During the segmentation step, there is a loss of geometry information which leads to difficulties to calculate the cortical thickness

1. Pipeline:

The method used here, is to apply a Danielsson distance transform on the white matter image, which is a binary image. A vector map is obtained. Combining it with the grey matter image permits to know for each grey matter pixel the closest white matter boundary pixel. Then the calculation of the cortical thickness is done by a simple maximum operator.

To calculate the thickness of the brain, this following pipeline is used:

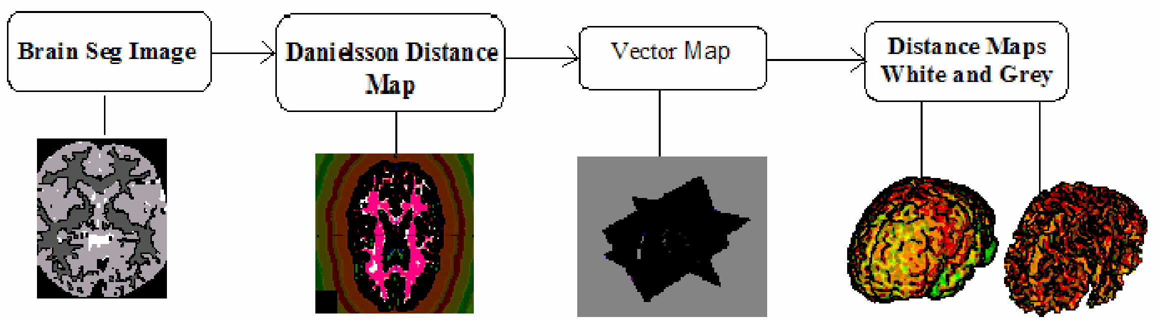


Figure 3 Pipeline cortical thickness

2. Danielsson Distance transform:

2.1. Brief description of distance transform:

The distance transform is an operator normally applied to binary images. The result of the transform is a grey level image that looks similar to the input image except that the grey level intensity of points inside foreground are changed to show the distance to the closest boundary for each point.

One way to think about the distance transform is to think about a propagation of a level set.

2	2	1	1	1	2	2
2	1	1	0	1	1	2
2	1	0	1	0	1	1
1	1	0	1	1	0	1
1	0	1	1	1	1	0
1	0	1	2	2	1	1
0	1	1	2	2	2	2

1	1	1
1	0	1
1	1	1

Figure 4 Distance map using chess-board (or 8-neighbour) distance

There are several different sorts of distance transform depending upon which distance metric is being used to determine the distance between pixels. The example shown in figure 4 uses the chessboard distance metric.

2.2. Danielsson's algorithm:

The algorithm proposed in 1980 by Danielsson to compute Euclidean distance functions is a sequential type relies on the following two principles:

- The image pixel is scanned in a predefined order, generally from upper left to bottom right and from bottom right to upper left.
- The new value of the current pixel, determined from the values of the pixels in its neighbourhood, is written directly in the same image, so that it is taken into account to determine the new values of the not yet considered pixels.

Danielsson's algorithm requires four image scanning and it does not propagate distances, but vectors: it yields a vector image j where each pixel p is assigned a vector v such that p-v is (one of) its closest feature pixel in the original image I. To get an actual distance function form j, it suffices to take is norm.

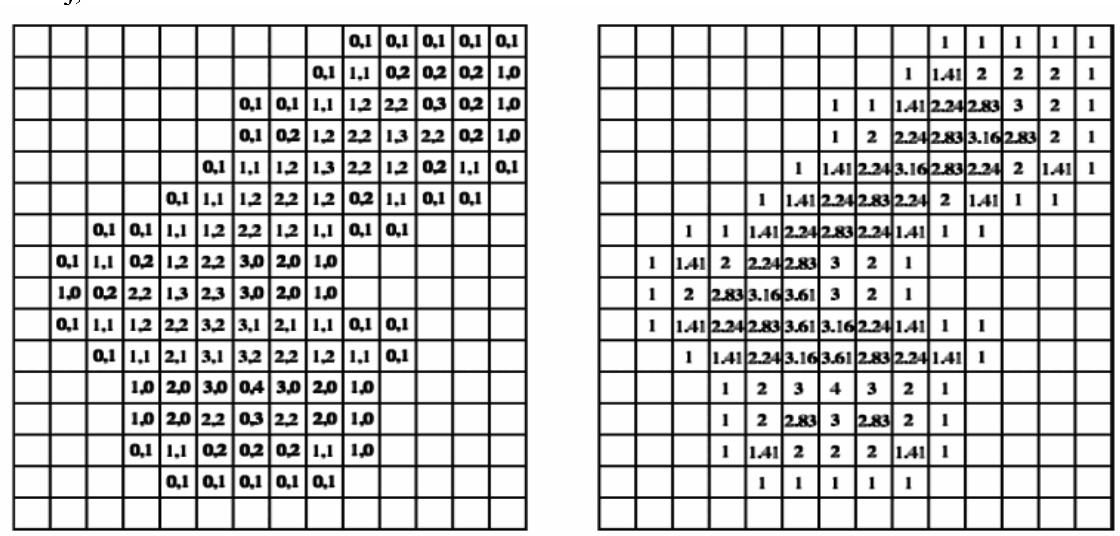


Figure 5 Danielsson distance transform propagate the vectorial information of the location of the nearest pixel of a set S

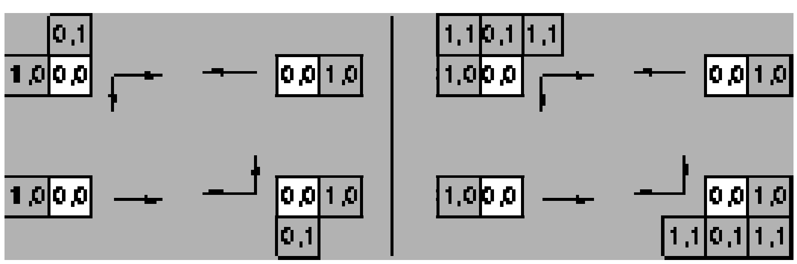


Figure 6 Danielsson distance transform needs tow raster scan, one from the upper left to the bottom right and one to the bottom right to the upper left using the mask shows on the figure. So the image is scanned four times.

To calculate the thickness after running the Danielsson distance transform, the Euclidian distance is used.

3. Vector map:

Once the Danielsson distance map is applied on the white matter image, the vector map can be obtained.

To do it, the Danielsson distance map image is combined with the grey matter image to find for each grey matter point, closest white matter points.

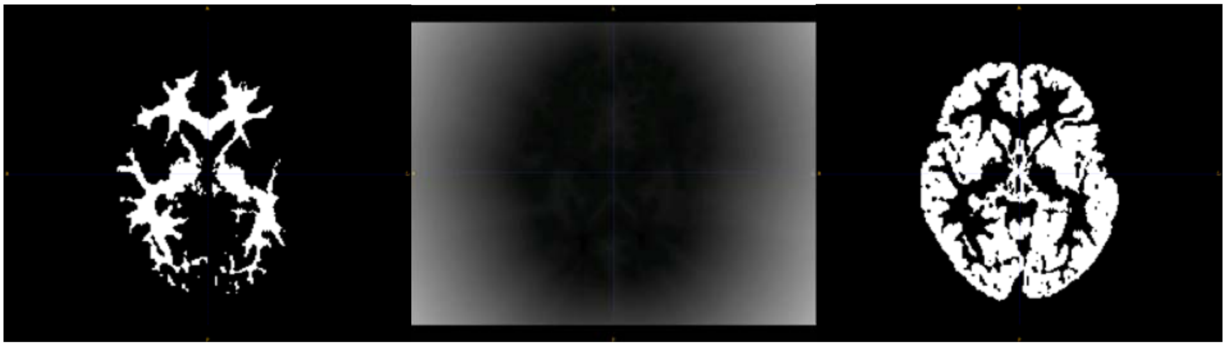


Figure 7 left: VECTOR MAP: white matter image, middle: distance map image, right: grey matter image. At each grey matter voxel, "known" the distance to the white matter => at each grey matter voxel, store the vector to the closest point.

4. Distance map white and grey:

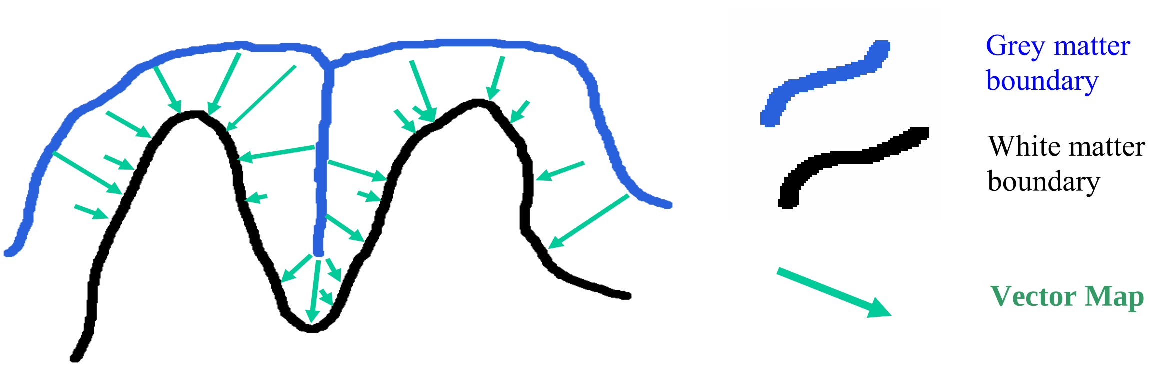


Figure 8 cortical thicknesses, there is several grey matter voxel pointing on one white matter voxel

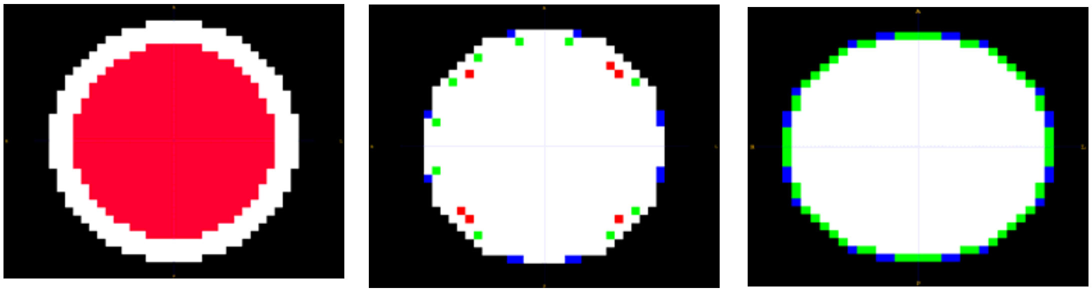
After calculating the vector map, each grey matter voxel points to white matter surface. So there are several grey matter voxel pointing on the same white matter voxel. The aim is to select only the grey matter boundary voxel.

Therefore, the solution is to choose the grey matter voxel with maximum distance. So a maximum operator is used, for each white matter point, find the furthest grey matter point.

5. Delete point:

Because of a discretization issues, some wrong points appear. So a cleaning is necessary.

Figure 9 A cleaning is necessary to delete wrong points



Two spheres **Result before cleaning** **Result after cleaning**

The cleaning is done before calculate the white and grey distance map. The aim is to delete wrong points. In order to determine which is right and which one is wrong, vectors are used. In fact during the vector map step, vectors are stored so it is easy to use it.

For each grey matter point, there is one or two or more closest white matter point, so there are one or two or more vectors at the same point. The goal is to calculate the angle between vectors and keep the point if the angle calculated is superior to threshold determined by a function *f*. The furthest the point is the smaller the angle is.

$$f(x)=b*\exp(-a*x) \qquad a=\frac{1}{(spmin-5/10*Distmax)}$$

$$b=\Pi*e^{a*spmin}$$

With spmin = spacing minimal = distance min

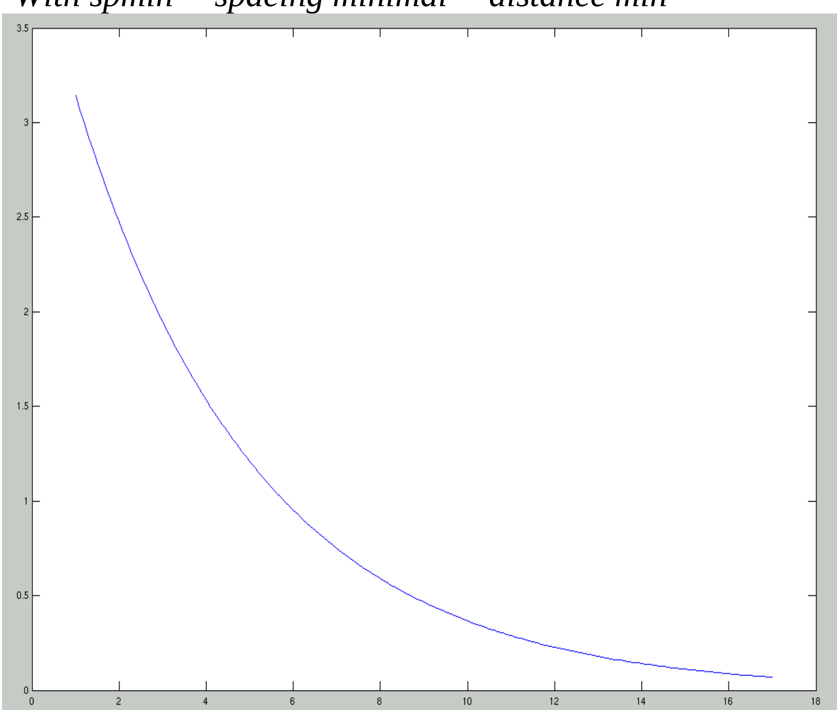


Figure 10 Function *f* to calculate the threshold angle

The algorithm can be break up like that:

For each grey matter point, keep it if:

1. It is a boundary point
2. It is in a folding: to know if it is in a folding or not, calculate the angle of vectors, the angle founded is α.
3. Then calculate the angle, which will correspond to the threshold, the angle founded is μ.
4. Keep the grey matter voxel if α > μ.

Thus a new vector map is calculated. This step is very important to have better results. As you can see in the figure 9, depending on the geometry of the brain, results can be very different with or without the delete step.

6. Visualization options:

To visualize the cortical thickness map on the white matter, an interpolation is necessary. In fact, due to a discretization issue and due to the delete step, some white matter surface points won't have distance information (figure 10).

So the interpolation is a surface averaging interpolator.

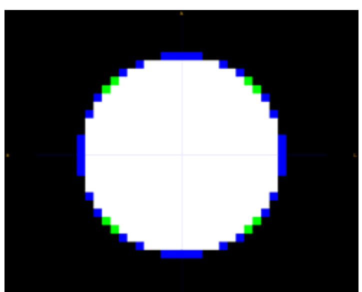


Figure 10 Before Averaging

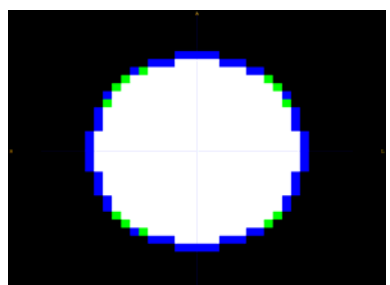


Figure 11 After averaging

7. Validation step:

A validation step is used to ensure the distance can be trust.

The method consists in using two kinds of test images: a sphere and a smooth white matter surface. Both structures are dilated by knowing the distances. For each structure obtained, the cortical thickness is calculated and results are compared.

7.1. Comparison of each structure to the initial one:

Each structure is compared to the initial one. Normally, the thickness should be just a peak but because of a discretization issue, the thickness is a distribution.

For the sphere, peaks are really explicit and so the average. In opposition, the folding re-appears for the brain. As you can see in the figure 15, the thickness is not a peak or just a distribution. In fact as folding reappears, distances are smaller and so the average.

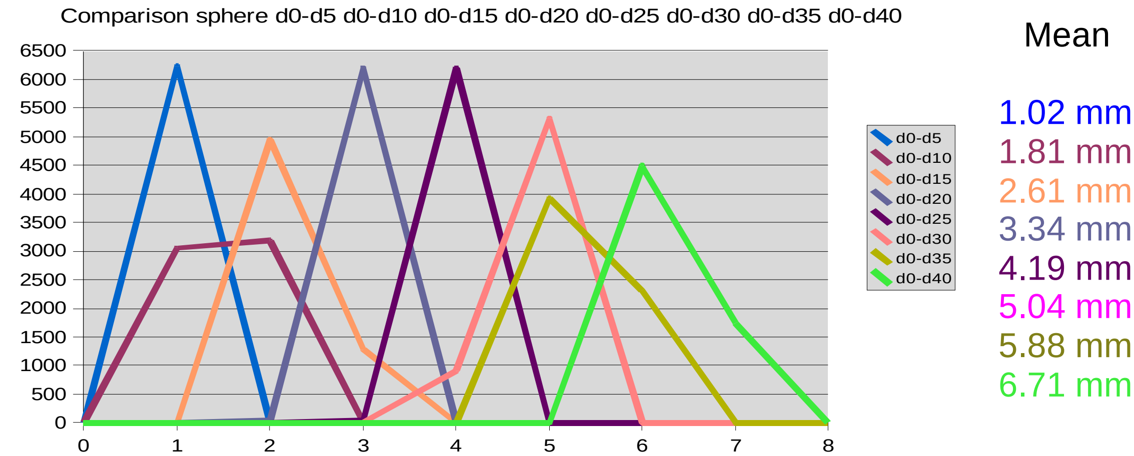


Figure 12 *SPHERE*: thickness of the sphere, thickness between the initial structure and others. Because of a discretization issue, it is not just a peak but also a distribution.

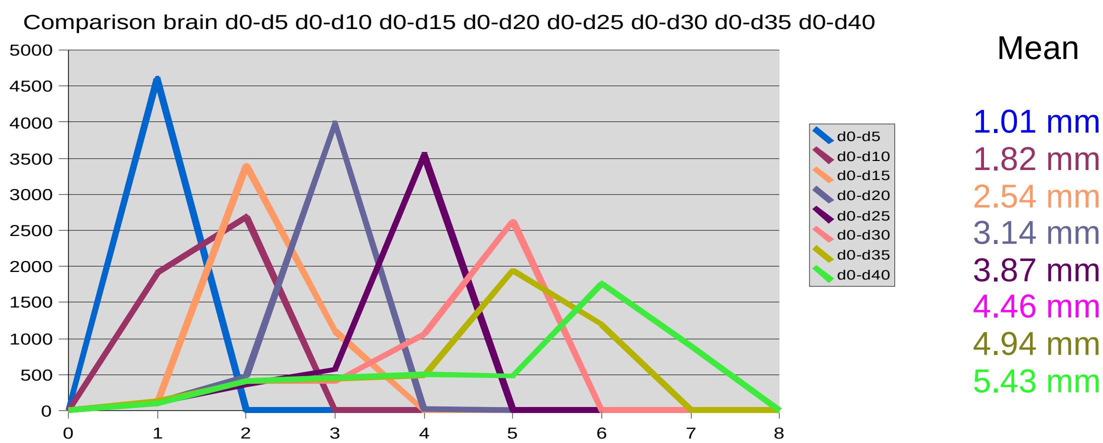


Figure 13 *BRAIN*: the difference with the sphere is due to a rebuilt of folding. So distances are smaller.

Results look different due to the shape of structures; in fact, the growing of the brain is not exactly the same as the growing of the sphere. The sphere is only a concave structure, so all thickness points belong to the grey matter exterior boundary. Or the brain contains convex surface which lead to, because of the aim of the algorithm, inside thickness point (voxels which don’t belong to the grey matter surface). As you can see in the following images, the grey matter points belonging to the thickness point of the sphere, are on the surface of the grey matter, instead of grey matter points belonging to the to the thickness point of the brain, are on the surface and inside.

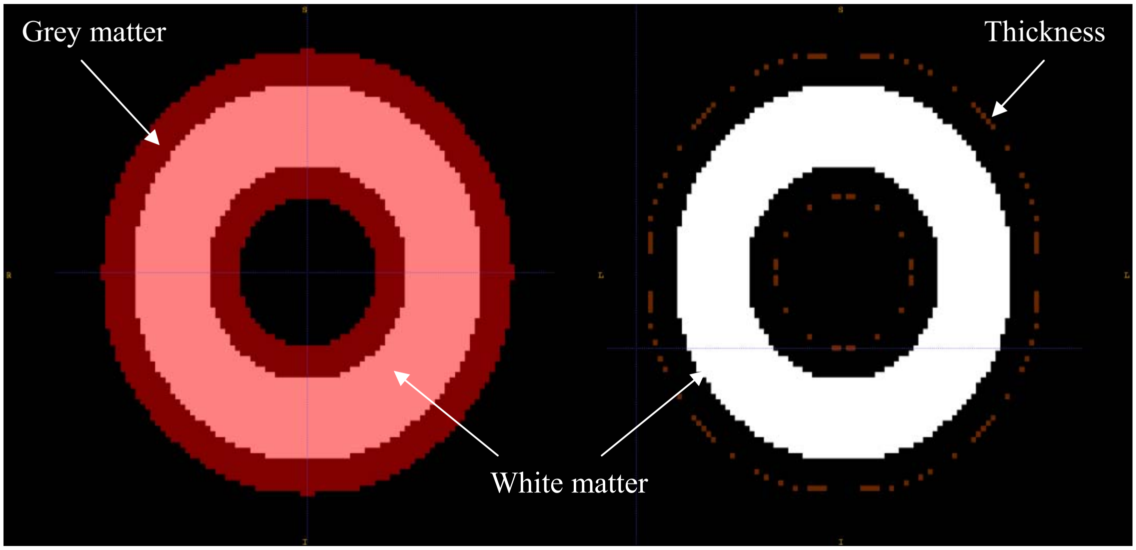


Figure 14 Thickness of the sphere, as the sphere is concave; voxels which belong to the thickness are on the surface.

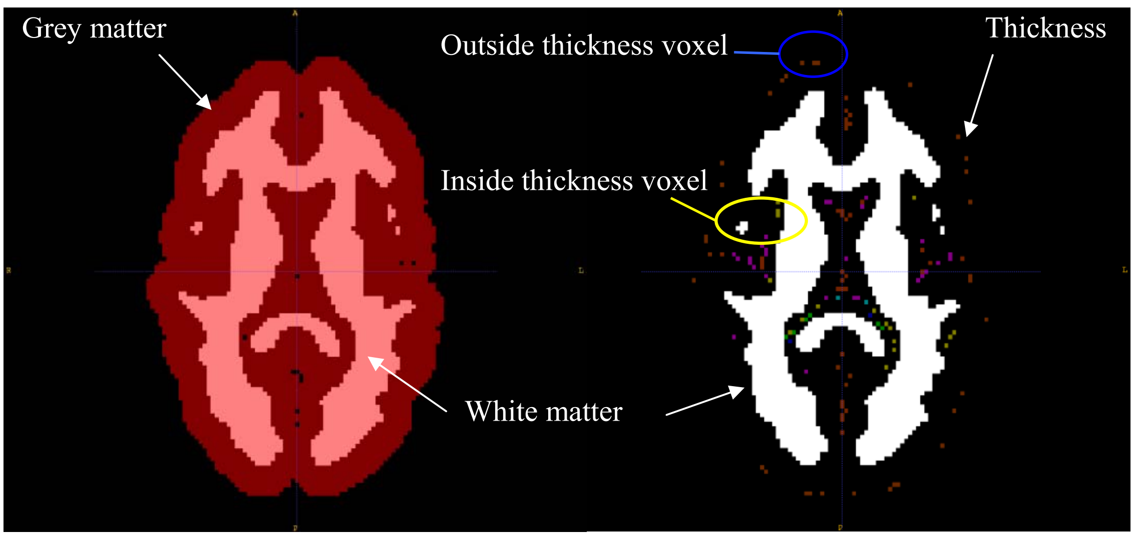


Figure 15 Thickness of the brain, there is some voxel which don't belong to the surface

To really compare results, a separation between inside and outside voxel was done. So histograms were recreated with only outside voxels and results look more similar according to the average and the shape of histograms.

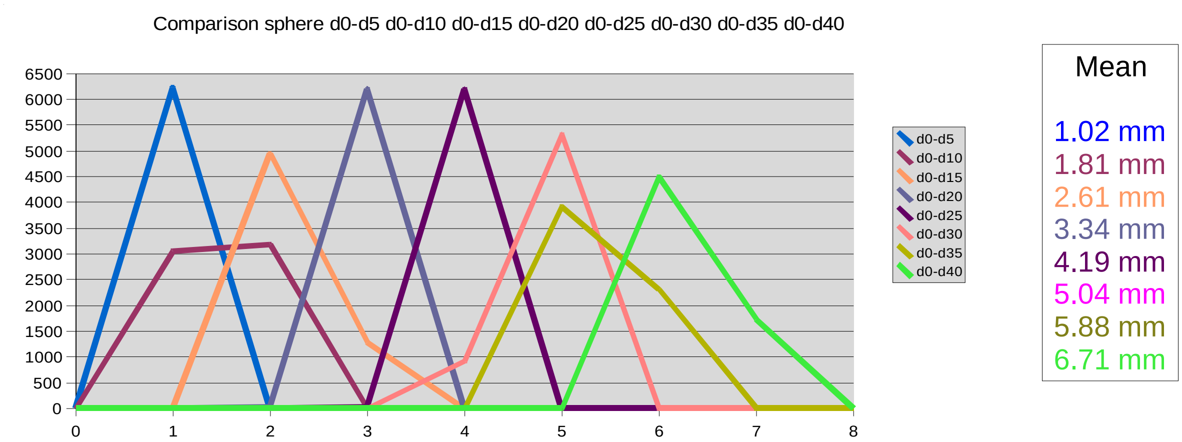


Figure 16 Thickness of the sphere.

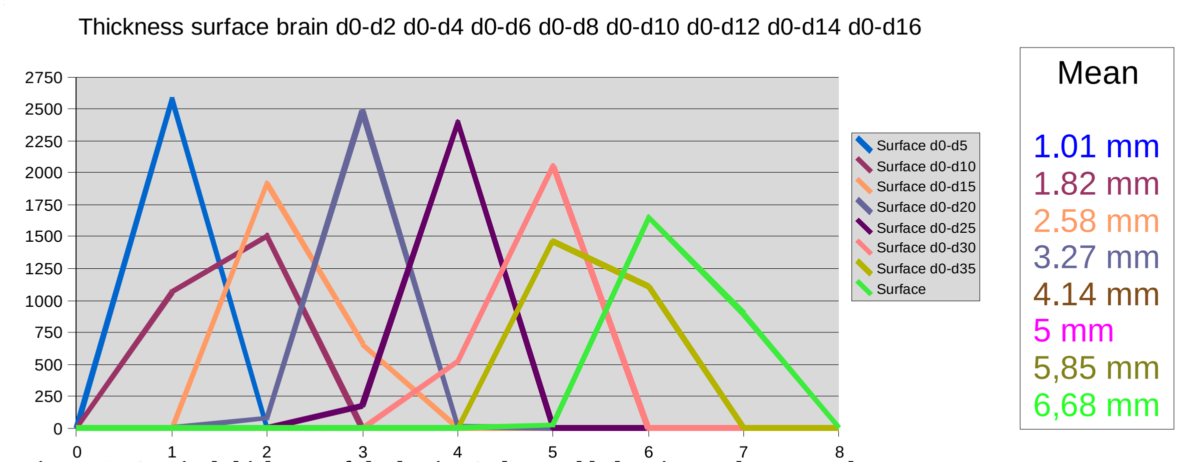
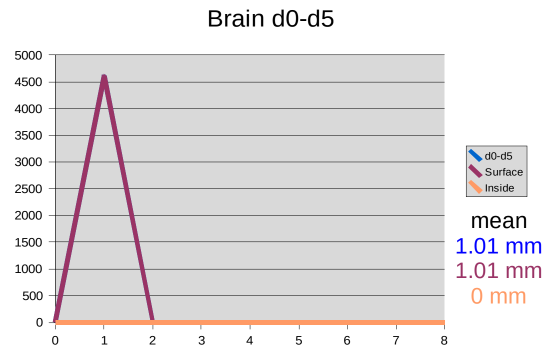
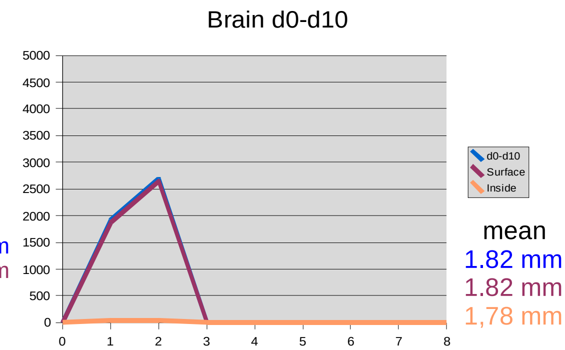
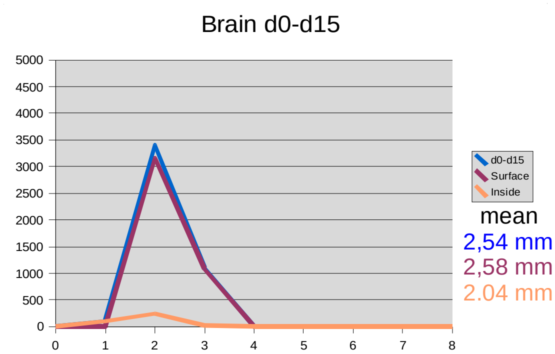


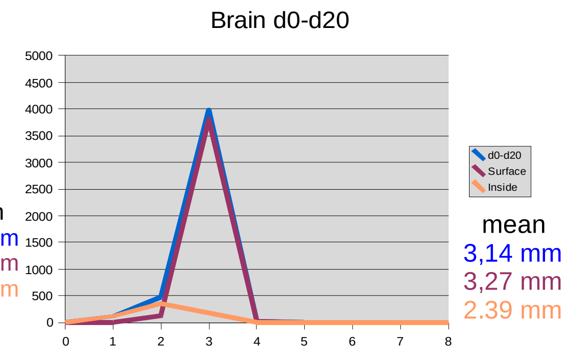
Figure 17 Cortical thickness of the brain. Only voxel belonging to the external grey matter boundary thickness are used here.

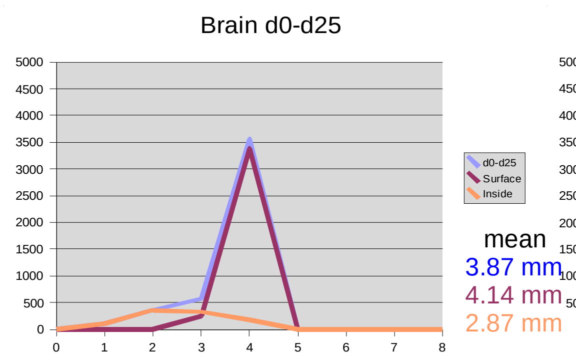
Moreover, for each structure, the histograms comparing inside and outside thickness voxel was built. The thicker the grey matter is, the more inside voxel there is. So the average is not as big as the sphere because of a recreation of foldings.

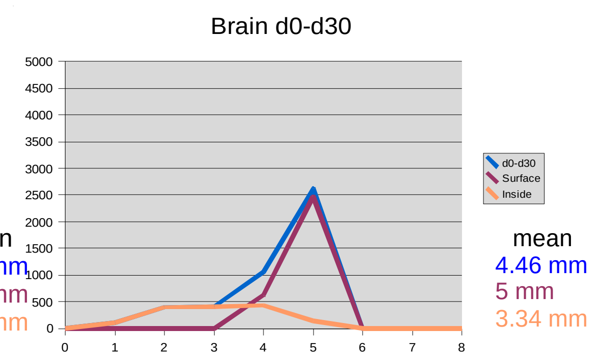

Brain d0-d5
d0-d5
Surface
Inside
mean
1.01 mm
1.01 mm
0 mm

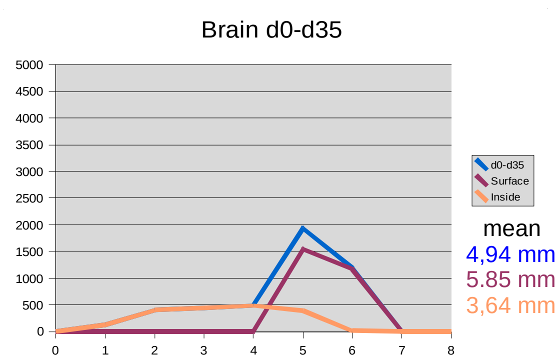

Brain d0-d10
d0-d10
Surface
Inside
mean
1.82 mm
1.82 mm
1,78 mm

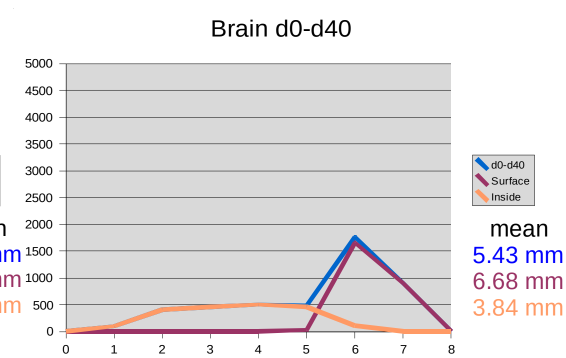

Brain d0-d15
d0-d15
Surface
Inside
mean
2,54 mm
2,58 mm
2.04 mm


Brain d0-d20
d0-d20
Surface
Inside
mean
3,14 mm
3,27 mm
2.39 mm


Brain d0-d25
d0-d25
Surface
Inside
mean
3.87 mm
4.14 mm
2.87 mm


Brain d0-d30
d0-d30
Surface
Inside
mean
4.46 mm
5 mm
3.34 mm


Brain d0-d35
d0-d35
Surface
Inside
mean
4,94 mm
5.85 mm
3,64 mm


Brain d0-d40
d0-d40
Surface
Inside
mean
5.43 mm
6.68 mm
3.84 mm

8. Results:

After the validation of the algorithm, the tool is used to measure the cortical thickness for different cases. Thus some results obtained confirme the truth of the calcuation of thickness

8.1. Longitudinal study :

For this study, four cases were used. One neonate, one at one year, one at two years and an adult. The one year and the two years brain come from the same child.

So in those cases, and for each one, a distribution of the thickness is obtained. The following graphics show that the thickness of the neonate is really thin. Apparently the 2 years old is thicker than the adult. Moreover, the thickness was mapped on the grey matter for each case. However, a problem of segmentation of the motor brain is constated. In fact, this part of the brain is really thin, so it is hard to segment it.

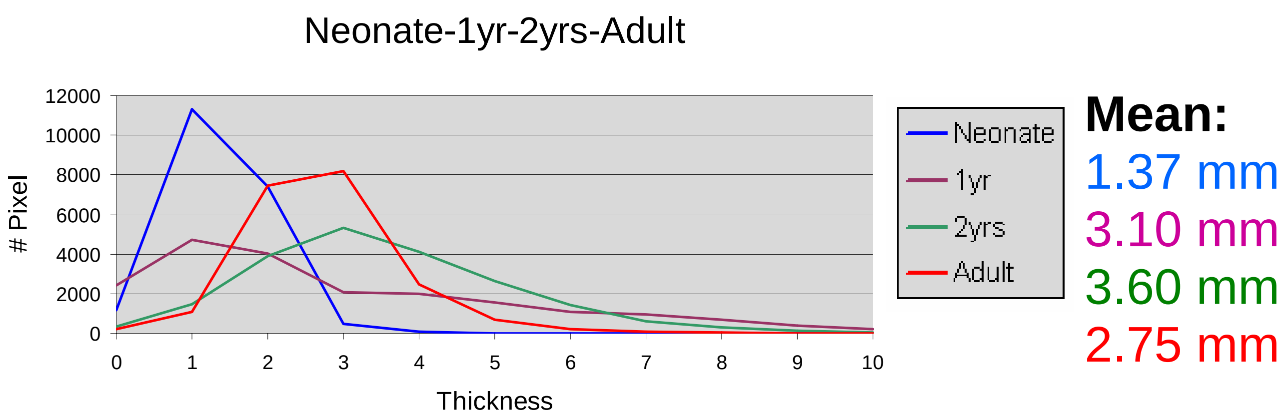


Figure 18 Calculation of the thickness for four different brains, a neonate, a one year old, a two year old and an adult. The cortical thickness for the neonate is really thin and for the adult, the cortical thickness is thicker than the two years

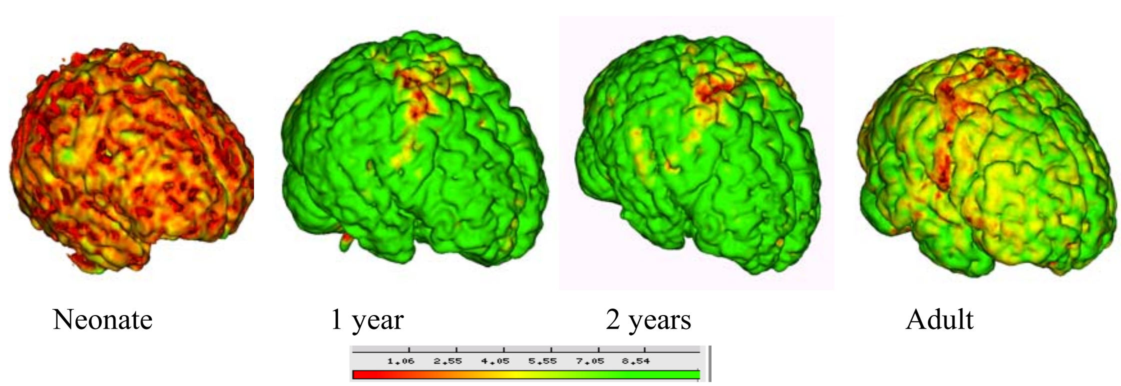
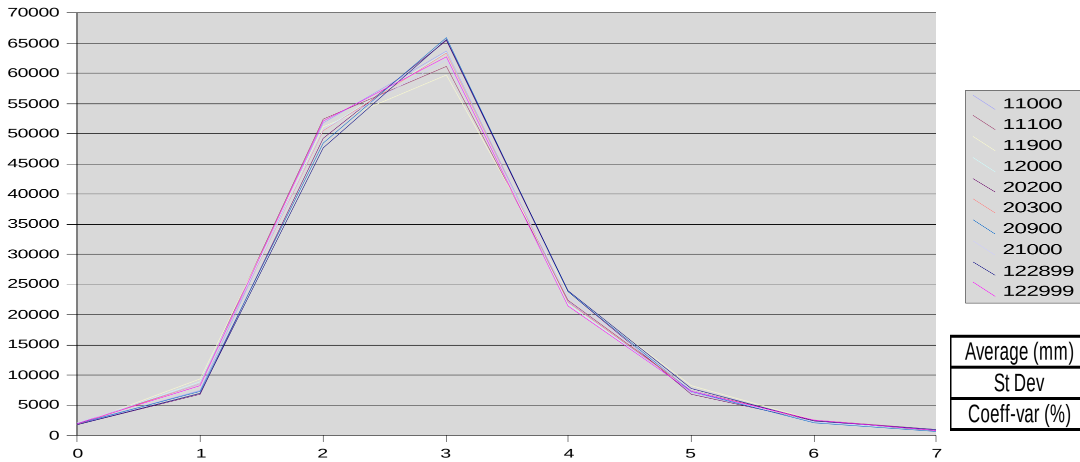


Figure 19 Thickness of the brain mapped on the grey matter. A problem of segmentation appears; in fact the motor brain is really difficult to segment because it is really thin

8.2. Same patient, 10 different scanners:

In this study, the same subject was scanned ten times in ten different scanners. For each scan, the cortical thickness was calculated and the following results are obtained :



Average (mm)	2,87
St Dev	0,23
Coeff-var (%)	0,81

Figure 20 cortical thicknesses in function of the frequency, the number of voxel. Distributions are very similar.

	Average(mm)	*Median(mm)*
11000	2,8639	3,0465
11100	2,8535	3,0465
11900	2,8697	3,0465
12000	2,8522	3,0465
20200	2,9013	3,1431
20300	2,8684	3,0465
20900	2,8803	3,0465
21000	2,8566	3,0465
122899	2,9216	3,0465
122999	2,8516	3,0465

Tableau 1 Results of the 1O study. For each cases, the mean and the average of the cortical thickness is calculated

The coefficient of variance is really low, inferior to 1% which mean the reproducibly of the algorithm.

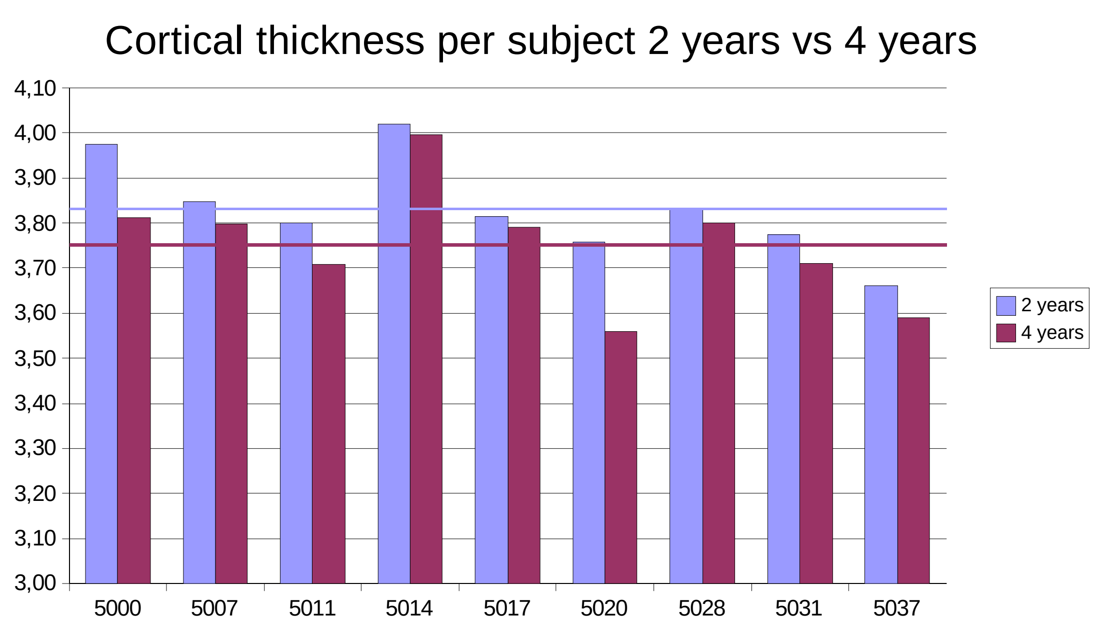
8.3. Calculate the cortical thickness for the same child at 2 and 4 years old:

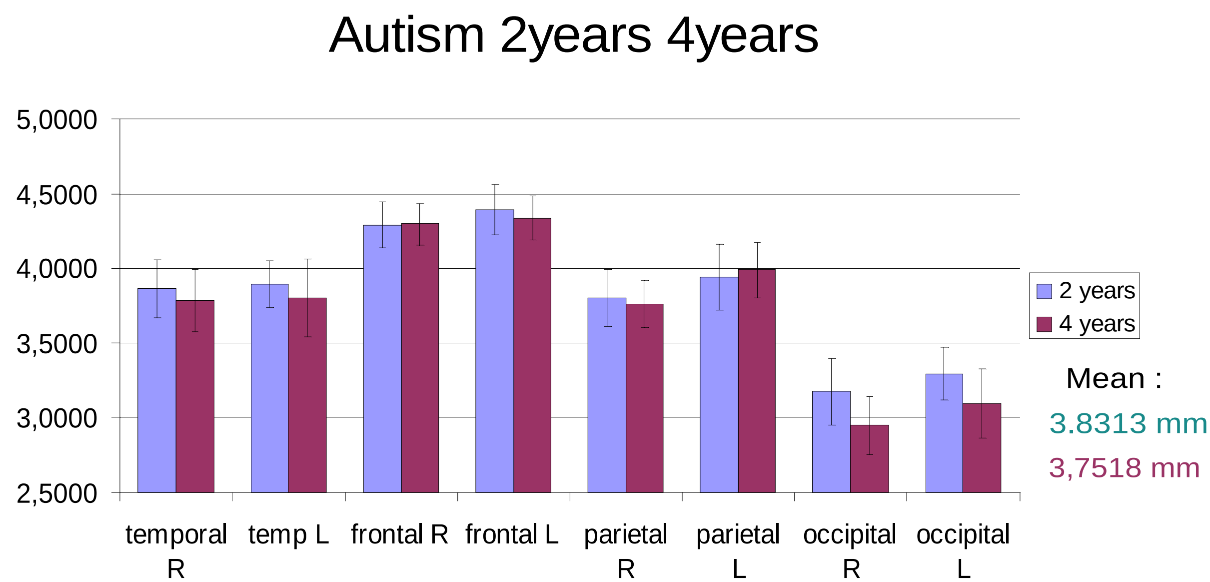
In this study, nine children are scanned at two years old and at four years old. The cortical thickness is calculated for each child and for both ages. The brain is, then, parcellated in lobes. Thus, for each child, the cortical thickness of each lobe at time one and two is known.

To simplify the visualization of the results, an average is calculated. Thus the following histogram presents the average of each lobe for ten children at time 1 (2 years old) and at time 2 (4 years old).

	2 years	4 years
5000	3,97	3,81
5007	3,85	3,80
5011	3,80	3,71
5014	4,02	4,00
5017	3,81	3,79
5020	3,76	3,56
5028	3,83	3,80
5031	3,77	3,71
5037	3,66	3,59
Mean	3,83	3,75

	2 years	4 years
temporal R	3,86	3,79
tempral L	3,90	3,80
frontal R	4,29	4,30
frontal L	4,39	4,34
parietal R	3,80	3,76
parietal L	3,94	3,99
occipital R	3,17	2,95
occipital L	3,29	3,10
Mean	3,83	3,75





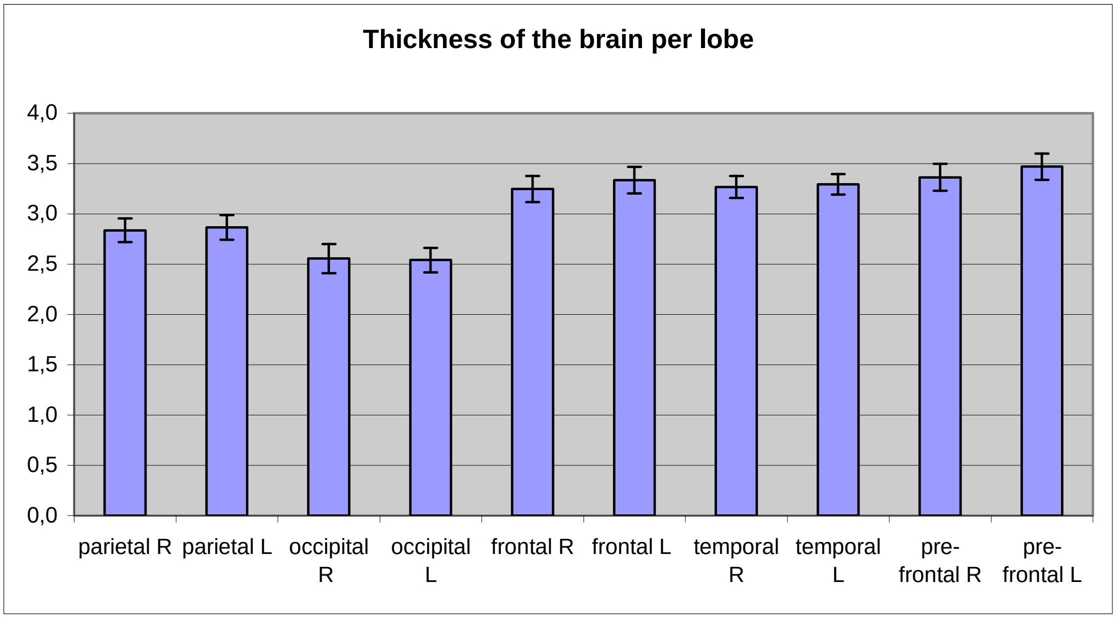
Results show a diminution of the cortical thickness at four years old for most of lobes but not for the parietal lobe, the cortical thickness seems to increase, same thing for the right frontal lobe.

8.4. Adolescent study:

In this study, 22 adolescents were scanned age between 9 to 18 years old and segmented using the same techniques. The cortical thickness algorithm was used by using the same parameters for each case. A function was used in addition to know the number of foldings voxel reconstructed. The average of the percentage of the repartition of the voxel is 7% for inside voxels (voxels which are inside the foldings) and 93% for boundaries voxel.

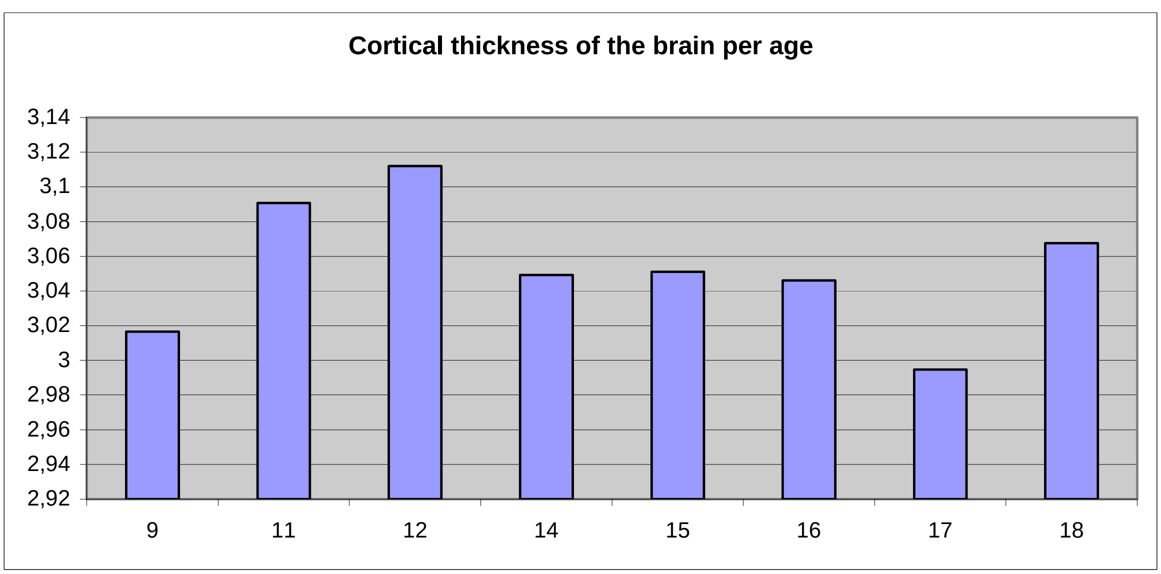
The following histogram represents the cortical thickness in function of the frequency.

	Thickness (mm)
parietal R	2,8
parietal L	2,9
occipital R	2,6
occipital L	2,5
frontal R	3,2
frontal L	3,3
temporal R	3,3
temporal L	3,3
pre-frontal R	3,4
pre-frontal L	3,5
Mean	3,05



As the age is known, the cortical thickness per age was calculated and the following histogram is obtained:

Cortical brain	nbre	Mean
Age		
9	2	3,02
11	4	3,09
12	2	3,11
14	6	3,05
15	3	3,05
16	2	3,05
17	1	2,99
18	2	3,07
	Mean	3,05



Moreover, we compare the cortical thickness of female brain and male brain. Results do not show a real difference between the two populations in term of cortical thickness.

	Male (mm)	Female (mm)
parietal R	2,85	2,83
parietal L	2,87	2,86
frontal R	3,18	3,10
frontal L	3,23	3,18
occipital R	2,58	2,54
occipital L	2,55	2,54
temporal R	3,24	3,29
temporal L	3,25	3,33
pre-frontal R	3,30	3,41
pre-frontal L	3,42	3,50
Mean	3,05	3,06