

## POLITECNICO DI TORINO

# METHOD AND ALGORITHM FOR CHIARI MALFORMATION DIAGNOSE 

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## Summary

The research was developed in the medical image processing to segmentation of specific regions of the brain. These segmentations can help to improve the accuracy and time saving in Arnold-Chiari malformation diagnosis.

Currently are used the manual approaches to Chiari diagnosis by the neurosurgeons while the computer vision systems can be more effective. One automatic approach can have same behaviour in different images, therefore, their behaviour are more predictive than manual approaches.

We focus on a recommended diagnosis method, that is based on recognizing the Posterior Fossa Midline, Intracranial Midline and Cerebellum Midline areas. In this method the neurosurgeons decide about Chiari malformations types by these regions anatomy. Today, the main problem is the different manual segmentation regions by different neurosurgeons. Therefore, we tried to suggest one automatic approach that decreased these errors.

Our research proposes a method based on Atlas-Based Segmentation to segment regions and detected some their features that can be helped in classification Chiari type.

This work is divided into 8 chapters. The first three chapters are described the Brian anatomy, Arnold-Chiari malformation diagnostic and pathology and chapter 4 are described computer vision systems approaches. Chapter 5 describes the proposed method for segmentation. The subsequent chapters are the validation and features analysis.

## Introduction

Arnold-Chiari is a malformation of the skull and cerebellum. In this malformation, the cerebellum parts are extended into the upper spinal canal and below the foramen magnum. In some case, part of the skull can be smaller than normal and pushed the cerebellum into the foramen magnum and spinal canal, it creates the pressure on the cerebellum and brain that can be disturbed on their functionally. Generally, Chiari cause is the genetic mutations or maternal diet during fetal development and in some patients, it can be occurred thought traumatic injury, disease, or infection. In the past, was it was difficult to diagnose, generally there was one Chiari case in every 1,000 births. But today with the medical image technology and image processing have been positive effect on diagnostics.

The current standard for Chiari malformation diagnose is a check patient history, observation of symptoms and diagnostic tests such as: X-ray, that is able to detect frequent anomalies, The Magnetic Resonance Imaging (MRI), that generates high quality image to extent of Chiari malformation and it development and CT scan to find about cerebral ventricles size and revealing blockages on foramen magnum and the possibility of evaluating the posterior fossa or spinal cord.

## Proposed Study

The proposed study is divided into two parts, the first is the brain segmentation of the regions of interest, the second is the extraction and analysis of features, which may be able to help in the automatic identification of Chiari types. So this method does not need a manual selection of an initial area, differentiating it from semi-automatic segmentation schemes. Used the Atlas-Based Segmentation technique, and used with the Demons method, where the test patient images are compared with a reference image, previously drawn by the doctor or radiologist. This method generates as output three masks segmentation: Cerebellum Mask (MC), Brain Mask (MB) and Mask of the Posterior Fossa(MPF). Only the masks would be of great help to who should identify the disease. With the masks we extracted important morphological characteristics, in order to be able to classify in
corresponding classes with the types of the disease.
Has been developed new diagnose method to improve Chiari malformations diagnose. This method tries to understand about Chiari malformations and their type thorough identifying the cerebellum (MC), posterior fossa (MPF) and brain (MB) and In this study, we try to propose as automated approach for this diagnose aid method. This approach is based on the Atlas-Based Segmentation and extract features.

## Chapter 1

## Brain Anatomy

In this chapter, we can see the anatomical structure of the brain to better understand the segmentation algorithm and its relation to ArnoldChiari Syndrome in subsequent chapters.

The brain is an organ of nervous system central to control the body activates, interpreting and coordinating the information which receives. It has bilaterally symmetric structure (Figure 1.1) that surrounded by its meninges into cranium to protect the central nervous system.


Figure 1.1: The brain bilateral symmetric structure.

The brain is able to grow during the life. The brain weighs at the birth has less than 400 g , and when adult increase between $1,250 \mathrm{~g}$ and $1,450 \mathrm{~g}$. Also, its weighs can be different in males and females. However, the males brain weigh generally is more than the females [5].

There are three large regions in brain: cerebrum, cerebellum, and brainstem. The Figure 1.2 shows the regions.


Figure 1.2: The main parts in brain: cerebrum, cerebellum, and brainstem.

### 1.1 Cerebrum

The Cerebrum is the superior and major part of the brain. The cerebrum consists of four different lobes, the Frontal, Occipital, Parietal and Temporal (Figure 1.3), that are able to processing different sensory information.


Figure 1.3: The main brain lobes: Frontal, Occipital, Parietal and Temporal.
Its surface layer calls the cerebral cortex, that composes of a highly folded collection of gray matter. In deep cortex, there are the white matter (Figure 1.4). Its function is a transportation cortex and cortical responses information to other regions of the central nervous system (CNS). The cerebrum situates in the cerebral hemispheres that called right and left lateral ventricles [25].


Figure 1.4: The grey and white matter in the cortex

### 1.1.1 Frontal lobe

The frontal lobe is largest cerebral lobe of cortex. It is situated at the front of the brain. The central and lateral sulcus separated it from parietal and temporal lobe respectively. It contains the most dopamine-sensitive neurons that is responsible for selecting sensory information which arrive from the thalamus to the forebrain. It has main role in voluntary movement, regulates activities such as walking and expressive language [11]. In addition, the frontal lobe is able to calculate the future consequences resulting from current actions in order to solve problems and is responsible for emotional control and our personality.

### 1.1.2 Occipital lobe

The occipital lobe is located in the back of brain. It is the visual processing center to receives and interprets information from the eyes.

### 1.1.3 Parietal lobe

The parietal lobe is located above temporal lobe and behind the frontal lobe. It has main role to integrate and process sensory information that receives from various parts of the body, such as taste, temperature, pain and touch. Also it is part of the processing language, mathematical operations, and spatial orientation.

### 1.1.4 Temporal lobe

The temporal lobe is located behind the ears. It has role to receives sensory information to comprehend or understand their meanings in visual memory and language comprehension. Then, the temporal lobe is able to processing auditory information and memory encoding.

### 1.2 Cerebellum

The cerebellum is located above the brainstem, just below the occipital lobe. It is composed in two cerebellar hemispheres right and left. The cerebellum outer and deep similar to cortex this means that it consists of folded gray matter and white matter. Cerebellum has a main role in balance, equilibrium and body control, and it is responsible for fine movement coordination, muscle tone and sense of body position [9].

### 1.3 Brainstem

The brainstem consists of the midbrain, pons, and medulla oblongata that shows in the Figure. It Is responsible for some automatic functions such as breathing, heart rate, body temperature, and etc.


Figure 1.5: The main brainstem parts: midbrain, pons, and medulla.

The brainstem connects cerebrum with cerebellum and other hindbrain structures by the midbrain. To transfer the neural messages between the brain and spinal cord by pons and medulla. Then, it is important role to connect the brain motor and sensory system [1].

### 1.4 Skull

The skull protects the brain and vision, taste, hearing, equilibrium, and smell organs from injury. It consists of 8 cranial and 14 facial bones. The skull inside consists of three areas: anterior fossa, middle fossa, and posterior fossa, also a hole where pass the cranial nerves, arteries, veins that is called the Foramen magnum. It is main hole that connects the brain to spinal cord. The Figure 1.6 shows the skull areas structure.


Figure 1.6: The Skull structure.

## Chapter 2

## Arnold-Chiari Syndrome

Arnold-Chiari syndrome or Arnold-Chiari malformation, refers to a rare congenital malformation of the central nervous system (CNS). This condition is caused by a lower displacement of the cerebellar tonsils, passing through the occipital opening at the base of the skull (posterior fosse, Figure 2.1), leading in many cases to hydrocephalus as a consequence of the obstruction of cerebrospinal fluid circulation. It was first described by the Austrian pathologist Hans Chiari at the end of the 19th century. Him described three distinct types of this disorder: type I, II and III. Subsequently, other researchers added another type to the syndrome in question, type IV [3].


Normal Brain Structure


Chiari Malformation

Figure 2.1: Chiari Malformation.
Type I syndrome is typically asymptomatic during childhood. When there are symptoms, it is characterized by headache, sore throat, unsteady ambulation. The malformation consists of the descent, or herniation of the
cerebellar tonsils in the upper part of the vertebral column through the foramen magnum of at least $3-5 \mathrm{~mm}$ [10] (Figure 2.2). In some cases, the lower part of the bulb can descend.


Figure 2.2: Chiari Malformation type 1. The herniation of the cerebellar tonsils in yellow through the posterior fosse in blue.

In type II a lumbar myelomeningocele or tonsillar hernia may be found below the foramen magnum. This can lead to paralysis below the spinal defect. This type is more common in females, and the symptomatology, when present, makes a serious debut in the neonatal period or during early childhood and more subtly in adolescence [10].


Figure 2.3: Chiari Malformation type 2. The herniation of the cerebellar tonsils in red through the posterior fosse in blue.

Arnold-Chiari syndrome type III is rare, associated with the presence of syringomyelia. It can be considered a 'cervical bifid spine' in which the entire cerebellum is herniated through a bone defect involving the foramen magnum, to form a myelo cerebellum syringomyelia (Figure 2.4). It manifests at birth and is burdened by a poor prognosis both for early mortality and for severe neurological disability at a distance [35]. The syndrome type III is linked to an occipital encephalocele, containing a variety of abnormal neuroectodermal tissues. In this type the symptoms described in type I and II, besides neurological deficit are observed [4].


Figure 2.4: Chiari Malformation type 3. With the syringomyelia indicated.
The type IV, later described, is characterized by the absence of cerebellar development, which is incompatible with life.

## Chapter 3

## Neuroradiological Diagnosis

The Nuclear Magnetic Resonance (NMR) is a crucial diagnostic tool for patient diagnosed with Chiari Malformation. Radiology is a necessary part of the diagnostic considerations on the continuous patient treatment. There are key areas in the process of pathology diagnosing that require improvements to contribute to the early and adequate identification of disease at the beginning. The MRI is essential for the subsequent therapeutic choice. If the diagnosis is not correct, it can also happen that surgery performed in a technically perfect is not effective. For example, the descent of the cerebellar tonsils is caused by the anchored marrow extending the tonsils downwards or to an intracranial hypertension that "pushes" the tonsils from top to bottom, the decompression intervention (aimed at the enlargement of a small cranial fossa) may be unsuitable to solve the problem [27].

The presence of the malformation is detected by the brain image that shows the position of the cerebellar tonsils in the area of the cerebrospinal junction. In the figure 3.1 is possible to see the fourth ventricle (A), basion (B), medulla oblongata (C), cerebellar tonsils (D), opistion (E) and cerebellar hemispheres (F) are anatomical landmarks.


Figure 3.1: Cerebellar tonsils in the area of the cerebrospinal junction
The figure 3.2 shows the image of a sagittal MRI and the line that joins basion and opisthion defines the lower limit of the posterior cranial fossa, constituting the reference point (B) from which the degree of tonsillar ectopia (A) is measured.


Figure 3.2: Reference point (B) from which the degree of tonsillar ectopia (B).
To verify if the lowering of the cerebellar tonsils may be have caused by alterations or interruptions of the cerebrospinal fluid flow through the foramen magnum, a brain resonance is performed with a study of the liquor flow or of the liquor dynamics ( kinetic resonance or cine resonance or resonance with fluximetry or phase-contrast resonance), used to measure the
regularity and quantity of the flow of liquor at the brain level [37].
The Chiari malformation diagnosis is advisable to deepen the radiological studies to exclude the possible coexistence of other malformations such as: syringomyelia, hinge malformations, anchored medulla, etc. Therefore, for this purpose it is also useful to perform a complete vertebral column resonance [23]. When a syringomyelia is diagnosed (Figure 3.3), it is advisable to continue the diagnostic procedure to investigate the presence of other concomitant diseases such as scoliosis, hernias, canal stenosis, anchored marrow.


Figure 3.3: Cervical spinal MRI with syringomyelic cavity indicated by arrow.

MRI does not necessarily correspond to the clinical picture, very low tonsils or an accentuated syringomyelia can lead to few symptoms and, vice versa, slightly lowered tonsils or a small syringomyelia can cause severe symptoms. Furthermore, the neurological examination serves to assess whether the symptoms complained of by the patient may be attributable to other diseases that the patient suffers from.

### 3.0.1 Neuroradiological diagnostic criteria

The main diagnostic criterion for MR images was found to be the herniation of one or both of the cerebellar tonsils of 5 mm below the margin of the foramen; or $3-5 \mathrm{~mm}$ of herniation accompanied by syringomyelia, despite the debate remains open especially for the increasingly frequent finding of cases of Chiari 0 and "borderline". This last condition is highlighted when the cerebellar tonsils engage the foramennous with a descent between 3 and

5 mm , requiring a careful clinical and radiological evaluation over time, especially if associated with a syringomyelia or a kinking (kneeling of the bulbomidullary junction). Symptoms such as headache or signs of motor deficiency. Therefore, radiology remains a valid criterion but, only associated with a clinical evaluation, today the clinical history of a typical Chiari malformation is not understood and can be analyzed only by evaluating many cases, year after year. Furthermore, the natural history of the disease remains to be studied, and therefore it is not entirely clear what happens with a patient who has the malformation but, do not have symptoms. The $3-5 \mathrm{~mm}$ criterion is a good guiding criterion, in the great majority of cases, but sometimes there are exceptions that must be interpreted.

In conclusion, Cine-RM is a non-invasive examination that is carried out for research purposes and which can be a valid tool for indications of operability and be used as a prognostic criterion in the immediate.

### 3.1 Morphological Analysis

The most recent research assigns the herniation to a mismatch in the growth of the neural and bony elements of the posterior fossa [38]. This defect would eventually constitute a short and low posterior fossa, which would not be able to contain the nerve structures that develop.

Among the first studies about this evidence, are those of Marin [26] that in 1981 showed that the encondral basicranium of fetuses with rhomboencebrain malformations, such as Chiari malformation, was shorter than normal, attributing this to the underdevelopment of the occipital bone.

With the diffusion of magnetic resonance MRI in the 1990s, radiological comparison studies also expanded. Stovner [35] studied the cranial dimensions on lateral radiographs in 33 adult patients with Chiari I Malformations and verified by MRI and in 40 controls. In this study, the size of the posterior cranial fossa was significantly lower in patients than in controls.

Other studies were published including the one by Misao Nishikawa et al. which analyzed the encumbrance of the structures within the posterior cranial fossa as a possible pathogenesis of Chiari malformation of type I [23].

In this publication the morphology of the brainstem and cerebellum within the posterior fossa (neural structures of the midbrain, bridge, cerebellum and medulla oblongata) and basicranio were considered considering their embryological development. Thirty Chiari patients and 50 control cases in a prospective study were studied by neuroimaging.

These studies are important because they were among the first to estimate the encumbrance of the posterior cranial fossa structures using a "volume ratio" in which the volume of the posterior cranial fossa (mesencephalon, bridge, cerebellum and medulla oblongata) was compared to the volume of the posterior cranial fossa enclosed by bone structures and the
tentorium (ratio between PFBV and PFCV).
The study proposed here is that of using a series of important features of the cerebellum, posterior fossa and the brain, in order to find a correlation with each type of Chiare malformation. These characteristics may be morphological or geometric, which should be separated by segmentation of the respective regions, thus generating a mask for each region, cerebellum (MC), posterior fossa (MPF) and brain (MB). Therefore, a possible classification for each patient based on the medical image.

The next chapter, will be approached the study and selection of the automatic segmentation method for MC, MB, MPF regions, and the analysis of the most appropriate features for a possible classification of the disease.

## Chapter 4

## Computer Aided Diagnosis

The computer technologies, medical images developments have helped to improve the different medical applications such as computer aided diagnosis (CAD), image-guided intervention, minimally invasive surgeries and drug monitoring treatment and disease management. One of the remarkable function in medical image applications, is the segmentation to find the interest anatomical parts in the image. Generally, to find the automatically solution for many medical problems in computer vision fields, it is necessary to use the segmentation methods. These methods have been divided in two main groups: the general segmentation algorithm, that is most frequently used in simple medical segmentation problems and the Atlas-Based segmentation that frequently is used in complex segmentation problem. In this work is necessary to use a powerful segmentation method, because it is a complex problem to solve with general methods and an automatic method does not a medical interaction [14]. Therefore, we focus on the registration Atlas-Based Segmentation.

### 4.1 Atlas-Based Segmentation

The atlas-based segmentation tries to find the similar image parts between the moving and reference image (previously segmented by the doctor or radiologist). This method is usually used for brain segmentation to individualize more complex regions. There are several atlas-based segmentation methods, that the main difference between them is their registration algorithm.

### 4.1.1 The registration method

The registration based segmentation is the robust approach that tries to adapt the transformation between the template that is known as reference image and the transformed that is known as floating or moving image. The
registration tries to map any image to the template image. The Figure 4.1 shows this process.


Figure 4.1: Registration process block diagram

According to the registration functional, is divided in several groups: The mono, multi, intra-subject and inter-subject model registration. When the reference and moving image is the same modality (generated by same medical device), the registration process is called mono-model registration and in different modality, the process is called multi-modality registration [32]. Also, the intra-subject registration defines when the reference and moving image belong to the same patient, and when they belong to the different patients, the registration process is called the inter-subject registration.

The different registration techniques are based comparing some variables between two images, such as the features, intensity, transformation, probabilistic density, and etc.

### 4.1.2 The Probabilistic method

The Probabilistic method uses the statistical or probabilistic approaches to image registration such as the estimation of the image intensity, probability density function (PDF), which defined at different points on the image domain. In order to this aim, it is applied several PDF estimation techniques for example using kernel functions, yielding a smoothed PDF estimate to alignment moving image entropies with template image.

### 4.1.3 Intensity vs feature methods

In these methods, is necessary moving the floating image to align with the template image, until the both images are matched. For this aim, it was
defined a cost function between two images and tries to minimize it. The cost function can be defined according to the Equation 4.1.

$$
\begin{equation*}
\text { Cost Function }=- \text { Similarity Measure } \tag{4.1}
\end{equation*}
$$

The Intensity method considers the intensity patterns for the similarity measure valuation. In the other side, the feature method tries to compare some features such as: points, lines, surfaces and contours between two images. In order to these valuations, it is necessary some mathematic approaches such as: the correlation metrics, squared intensity difference, distance measures, etc. In the Figure 4.2 shows the feature extracted and distance map.


Figure 4.2: Feature based registration parameters. a) Moving image b) Bones feature c) Distance map.

The Intensity vs feature methods are useful and fast but, these are not robust.

### 4.1.4 Transformation models

The transformation approach introduced in the computer vision field in 1995 that used the geometric transformations to match the floating image with the template image. The transformation can be the rigid, non-rigid, affine, projective, curved form, etc. These transformations can be applied in local part of image (local mode) or in whole image (global mode).

There are two main groups of transformation, rigid and non-rigid. The rigid transformations are a linear transformation that are based on the rotation and translation, these transformations preserve the distances between two points (pixels). There are several important linear transformations such as: the affine, that tries to map a parallel line onto parallel lines, projective that tries to map each line to line. However, these transformations have a simple process, they are not effective in medical applications. Then, generally the non-rigid transformation techniques are used in medical applications such as: soft-tissue deformation during imaging or surgery, images registration, etc. The non-rigid transformations are not linear transformations, that are based on the shape change and warping [8]. These transformations use deformed forces and deforming the moving image to match it on the template image. The deformed forces can be based on the elastic, fluid and diffusion models. The Figure 4.3 shows some transformations.


Figure 4.3: Transformations: a) translation, b) rotation, c) scaling, d) shear, e) affine and f) nonlinear.

## Chapter 5

## The proposed method

As mentioned in the chapter 4, the intra cranial midline area, posterior fossa midline area and cerebellum midline area segmentations are necessary to the Chiari diagnostic. Currently, the manuals approaches are utilized to segment these regions, but one important disadvantage of manuals approaches, are their user dependency. Clearly, some difference in the masks that are segmented by two different users, can be directly effect on diagnostic and increasing the clinical risk.

Then, the manuals approaches do not have enough robustness and it is recommended the automatic approaches, where the segmentation has predictive behaviour and avoiding the clinical risk. Also, the precise segmentation can be a part of the large algorithms that recognizing the type of Chiari through extraction of some region segmented features and classified. In this study, we focus on the segmentation algorithm and extracting some factures that may be useful for creating the classification in future.

### 5.1 Introduction

The segmentation algorithm is based on some general and Atlas-Based segmentation methods. Then, the algorithm is divided in three main parts: pre-processing, processing and post processing (Flowchart 5.1).


Figure 5.1: The proposed algorithm flowchart

The pre-processing algorithm step tries to adjust the images intensity distribution, in order to achieve the most similarity intensity distribution between the reference and moving image. This step is necessary to reduce the errors in processing algorithm. The processing algorithm step uses the Atlas-Based Segmentation to segment the interest regions. Finally, the post processing tries to control the segmented regions to correct their errors.

### 5.2 Pre-processing Approaches

In this section, is introduced several pre-processing approaches that was tested on the images to find the efficient pre-processing approaches which are
most similarity between the reference and moving image and consequently the accurate segmentation in the processing step. The pre-processing approaches can be consisted of the intensity enhancement, filtering, reduce the background and bias effects in the images and general segmentation method.

### 5.2.1 Extract the Image Background

For improving the processing results, the pre-processing tries to eliminate the effect of some pixels that do not have useful information. We know that the segmentation focus on brain pixels. Then, the pixels that are out of the skull can be considered as to background and creating the same background intensity in template and moving images. This can be effected on the precision registration results and reducing their errors. The Figure 5.2 shows the background effect.


Figure 5.2: Extract the Image Background: a) input image, b) image without background effect.

### 5.2.2 Level Set segmentation with bias correction

The image contrast is one important quality factors in the processing algorithm. The level set is one approach that is able to create more contrast in brain image and reduce errors that due to inhomogeneous intensity images[13]. Therefore, level Set segmentation with bias correction function can be used to segment the reference and moving images, in the three regions for simplifying the registration algorithm work.

The Level Set segmentation with bias correction as input, can be written:

$$
\begin{equation*}
I=b J+n \tag{5.1}
\end{equation*}
$$

where $I, b, J$ and $n$ are the image intensity, true signal to be restored, the bias field and addictive noise respectively.

To reduce the bias effect in image and segmented it. It used the local classification and piecewise constant approaches [21] [41]. Therefore, the $n$ is assumed as the Gaussian noise with mean zero and variance. The $J$ is assumed as the piecewise constant:

$$
\begin{equation*}
J(x)=c_{i}, \quad x \epsilon \Omega_{i} \tag{5.2}
\end{equation*}
$$

where $i=1,2, . ., n$. Assumed the cluster center $m_{i} \sim b(x) c_{i}$. The level set energy formulation changes:

$$
\begin{equation*}
F(\phi, b, c) \triangleq \int\left(\sum_{i=1}^{N} \int k(x-y)\left|I(y)-b(x) c_{i}\right|^{2} M_{i}(\phi(y)) d y\right) d x+\sum_{i=1}^{n} R\left(\phi_{i}\right) \tag{5.3}
\end{equation*}
$$

where $F$ and $\phi$ are energy function and level set function respectively. The $k$ is the weighting function that defined by Gaussian kernel:

$$
K(u)= \begin{cases}\frac{1}{a} e^{\frac{-|u|^{2}}{2 \delta^{2}}} & \text { for }|u|<\phi  \tag{5.4}\\ 0 & \text { otherwise }\end{cases}
$$

where $a$ is the constant value. $R$ is the regulation term that is defined:

$$
\begin{equation*}
R(\phi) \triangleq v \int|\nabla H(\phi)| d x+\mu \int(|\nabla \phi|-1)^{2} d x \tag{5.5}
\end{equation*}
$$

$H$ is Heaviside function. $\mu$ and $v$ are the constant. $M_{i}$ is the function of $\phi$ when $\sum_{i=1}^{n} M_{i}(\phi)=1$. Also, if is defined the $M_{i}$ in three phase where $N=3$ and the $\phi$ is seted in two level: $\phi_{1}$ and $\phi_{2}$. The $M_{i}$ can be written:

$$
\begin{gather*}
M_{1}\left(\phi_{1}, \phi_{2}\right)=H\left(\phi_{1}\right) H\left(\phi_{2}\right) \\
M_{2}\left(\phi_{1}, \phi_{2}\right)=H\left(\phi_{1}\right)\left(1-H\left(\phi_{2}\right)\right) \\
M_{3}\left(\phi_{1}, \phi_{2}\right)=\left(1-H\left(\phi_{1}\right)\right) \tag{5.6}
\end{gather*}
$$

Minimized $F$ and discrete in time, can be calculated through a numerical approach gradient descent, therefore, fixed the $b$ and $c$ :

$$
\begin{equation*}
\frac{\partial \phi}{\partial t}=-\frac{\partial F}{\partial \phi} \tag{5.7}
\end{equation*}
$$

and replacing the $b$ and $c$ :

$$
\begin{equation*}
b=\frac{\left(I J^{(1)}\right) * K}{J^{(2)} * K} \tag{5.8}
\end{equation*}
$$

The $*$ represent the convolution operation. The $J^{(1)}$ and $J^{(2)}$ is defined:

$$
\begin{align*}
J^{(1)} & =\sum_{i=1}^{N} c_{i} M_{i}(\phi)  \tag{5.9}\\
J^{(2)} & =\sum_{i=1}^{N} c_{i}^{2} M_{i}(\phi) \tag{5.10}
\end{align*}
$$

The $c=\left(c_{i}, \ldots, c_{N}\right)$ finds to fix the $\phi$ and $b$ when minimized $F(\phi, c, b)$ :

$$
\begin{equation*}
c_{i}=\frac{(b * K) I M_{i}(\phi) d x}{\left(b^{2} * K\right) M_{i}(\phi) d x} \tag{5.11}
\end{equation*}
$$

The Figures 5.3 and 5.4 show the level set effect on reference and moving images.


Figure 5.3: Applying the level set: a) reference image, b) level set image.

a


Figure 5.4: Applying the level set: a) moving image, b) level set image

### 5.2.3 Contrast Enhancement

The contrast limited adaptive histogram equalization (CLAHE) is one powerful contrast approach in medical images [17]. This method applies the histogram equalization on each region of the image to enhancement the contrast and prevents the over amplification of noise, that adaptive histogram equalization can give rise[29] [34],[43]. The Figure 5.5 shows the adaptive histogram equalization effect:


Figure 5.5: a) reference image, b) CLAHE on reference image, c) moving image, d) CLAHE on moving image.

### 5.2.4 Filtering

The Filters are used to smoothing the images. Then, choose the Gaussian or median filters [31].

The Gaussian filter is result of the Gaussian kernel 5.12 convolution and image.

$$
\begin{equation*}
G(x, y)=\frac{1}{2 \pi \sigma^{2}} \exp -\frac{x^{2}+y^{2}}{2 \sigma^{2}} \tag{5.12}
\end{equation*}
$$

The $G$ is the 2D Gaussian kernel. $x, y$ are image coordinates and $\sigma$ is the standard deviation of the distribution [33].

The median filter replaces each pixel with the median of the neighborhood [15], [16]. These Filters are demonstrated in the Figures 5.7 and 5.6.


Figure 5.6: a) reference image, b) Gaussian filter result.


Figure 5.7: a) reference image, b) Median filter result.

Choice the best pre-processing among the all of approaches above, is very important because it can increase or decrease the segmentation errors. The best pre-processing can be defined that the methods have same behaviour in all images, do not need much time and do not have errors which can be propagated in the processing algorithm.

### 5.3 The processing algorithm

The processing algorithm uses the registration method to achieve the segmentation regions, through the minimization of the similarity function between reference and moving images. Therefore, in the current section, introduced the Demons and multi-image Demons algorithms registration.

### 5.3.1 Demons Registration

The Demons is a non-ridged registration method, that first time proposed by Thirion in 1998 [19]. There are several Demons algorithms with different calculation in deformed forces, but all of them are based on the optical flow estimation to optimize the energy function [24], [40], [22].

### 5.3.2 Optical Flow

The optical flow was proposed by American psychologist James J. Gibson in the 1940 [12]. He described the visual stimulus provided to animals moving through the world. The method uses several applications such as robotics, control of navigation, object segmentation and etc [2]. It can use the partial derivatives with respect to the spatial and temporal coordinates, in order to calculated the motion between two image frames in time. The method estimations that the real point intensity is constant in time. Therefore, the intensity $I$ in an image sequence can be written:

$$
\begin{equation*}
I(x(t), y(t), t)=I\left(x\left(t_{o}\right), y\left(t_{o}\right), t_{o}\right)=C \tag{5.13}
\end{equation*}
$$

the $I, t$ and $c$ are intensity, time and constant respectively. Consequently, the time derivative in equation 5.14 can be obtained:

$$
\begin{equation*}
\frac{\partial I(x(t), y(t), t)}{\partial t}=\frac{\partial I}{\partial x} \frac{d x}{d t}+\frac{\partial I}{\partial y} \frac{d I}{d y}+\frac{\partial I}{\partial t}=0 \tag{5.14}
\end{equation*}
$$

Defined the point velocity:

$$
\begin{equation*}
v=\left(\frac{d x}{d t}, \frac{d y}{d t}\right) \tag{5.15}
\end{equation*}
$$

The equation 5.14 can be separated in two parts: image gradient and point velocity:

$$
\begin{equation*}
\nabla I . v=-\frac{\partial I}{\partial t} \tag{5.16}
\end{equation*}
$$

Therefore, the motion is estimated by the spatial gradient and the temporal derivative of the image intensity.

### 5.3.3 Demons Pushing Force

In order to find the intensity similarity, The Demons uses the optical flow method. The $f$ and $m$ were considered the two frames of a motion sequence. Calculated the motion vector $v$ to find the $m$ more similar to $f$. Therefore, the motion intensity point can be written:

$$
\begin{equation*}
\frac{\partial I}{\partial x} \frac{\partial x}{\partial t}+\frac{\partial I}{\partial y} \frac{\partial y}{\partial t}+\frac{\partial I}{\partial z} \frac{\partial z}{\partial t}=-\frac{\partial I}{\partial t} \tag{5.17}
\end{equation*}
$$

Considered:

$$
\begin{equation*}
\frac{\partial I}{\partial t}=f-m \tag{5.18}
\end{equation*}
$$

And the motion vector that is the instantaneous velocity from $m$ to $f$ defines:

$$
\begin{equation*}
v=\left(\frac{\partial x}{\partial t}, \frac{\partial y}{\partial t}, \frac{\partial z}{\partial t}\right) \tag{5.19}
\end{equation*}
$$

Therefore, the equation 5.17 can be written:

$$
\begin{equation*}
v . \nabla f=m-f \tag{5.20}
\end{equation*}
$$

The Demons pushing force can be defined with the motion vector:

$$
\begin{equation*}
v_{p}=\frac{(f-m) \nabla f}{|\nabla f|^{2}+(g-f)^{2}} \tag{5.21}
\end{equation*}
$$

The $v_{p}$ is the motion vector that control the pushing force. It means that when $v_{p}$ is positive, the motion vector pushes inward. when $v_{p}$ is negative, the motion vector pushes outward.

In the classical Demons registration proposed by Thirion, the motion vector corresponds to the inverse of instantaneous displacement $d$ (5.22) and in the diffeomorphisms Demons (log Demons) registration, that is proposed by Mauna Kea Technologies [28], the exponential of motion vector corresponds the inverse of instantaneous displacement (5.23).

$$
\begin{gather*}
v_{p}=-d  \tag{5.22}\\
\exp \left(v_{p}\right)=-d \tag{5.23}
\end{gather*}
$$

### 5.3.4 Demons energy

The algorithm aim is optimizing the energy functional, where there is most similarity between the moving and reference image. Therefore, the energy functional is defined:

$$
\begin{equation*}
E(c, d)=\operatorname{sim}(F, M o c)+\left(\frac{\sigma_{i}}{\sigma_{x}}\right)^{2} \operatorname{Reg}(d) \tag{5.24}
\end{equation*}
$$

The $\operatorname{sim}(F, M o c)$ corresponds to the energy term, that represents the similarity relationship between two images. $\operatorname{Reg}(d)$ corresponds to the regularization term, that tries to prevent an ill-posed problem with unstable and non-smooth solutions. The $d$ is the instantaneous displacement or the displacement field. The $c$ represents the $d o \exp \left(v_{p}\right)$. The $F$ and $M$ are the reference and moving images. The $\sigma_{i}$ and $\sigma_{x}$ are the intensity and transformation constant uncertainty. Finally, the o represents the image transformation.

### 5.3.5 Demons Algorithm

In order to reach the efficient and robust registration. The algorithm uses the iterative solution. The algorithm chooses the initial displacement filed based on the equation 5.22 or 5.24 . calculating the pushing force to update the displacement filed and minimizing the energy function. This process continues until to convergence. The Flowchart 5.8 shows the Demons Algorithm.


Figure 5.8: Demons Flowchart

### 5.3.6 Demons multi-image Algorithm

The multi-image algorithm uses more than one images which create from the reference and moving images, to find the best displacement filed in Demons, and improving the processing results. The multi-image algorithm inputs can be created with several approaches such as gradient, the Laplacian, entropy operation, etc. The approaches are applied in two different modalities:

### 5.3.7 First Modality

In the first modality is created more images from reference and moving image by Laplacian, gradient, local range filter, adaptive histogram equalization and k means classification.
The k-means classification tries to put the images pixels value in three classes.

### 5.3.8 Second Modality

In the second modality is created more images extraction features and local entropy approaches, adaptive histogram equalization and k- means classification.

In sum up, applied all modalities, we can have more than one reference and moving images, that arrived from the Demons inputs. This process shows in Flowchart 5.9.


Figure 5.9: Demons multi-image Flowchart

The figures 5.10 show the Demons multi-image Algorithm results. The parameters applied with $\sigma_{i}=1, \sigma_{x}=1$ and iteration number $=600$ parameters:


Figure 5.10: Demons multi-image Algorithm results and the MB (blue), MC (red) and MPF (green) segmented: a) reference image, b) moving image, c) warped on reference image, d) warped on moving image.

The figure 5.11 shows the Demons multi-image energy and difference between registered and reference image:



Figure 5.11: The figure shows the difference between reference image and registered image. The graphic shows the energy function in each iteration. The Demons are applied with $\sigma_{i}=1, \sigma_{x}=1$ and iteration number $=600$.

The figure 5.12 shows the displacement and transformation Fields:


Figure 5.12: The figure shows the displacement and transformation Fields: a) moving image displacement, b) moving image transformation, c) reference image displacement, d) reference image transformation.

The figures 5.13 and 5.14 compare the Demons and multi image Demons algorithm.


Figure 5.13: The MC and MPF segmented in first patient with both algorithm. The red masks show the Demons algorithm results, and the green masks show the multi image results. The algorithms parameters are: $\sigma_{i}=1, \sigma_{x}=1$ and iteration number $=600$.


Figure 5.14: The MC and MPF segmented in second patient with both algorithm. The red masks show the Demons Algorithm results and the green masks show the multi image results. The algorithms parameters are $\sigma_{i}=1, \sigma_{x}=1$ and iteration number $=600$.

### 5.4 The post processing algorithm

The post processing algorithm controls the segmented masks and trying to minimize their errors.

### 5.4.1 Region growing

The Region growing is a simple iterative segmentation method. This method consists of a specific threshold and initial seed point. The segmentation starts of the initial seed point, that growing by comparing all unallocated neighbourhood pixels to the region. Therefore, the process starts to calculate the difference between a pixel intensity value and the regions mean until its difference is smaller than specific threshold [30], [6].

### 5.4.2 Active contour

Active contour or snakes were introduced by Kass, Witkin and Terzopoulos in 1987 [18]. It is the typically segmentation method that uses to detection the weight boundary or edge in medical images[16] . The snake is based on the energy minimization that is controlled by the internal, external and image force [42]. The snake $v$ is defined parametrically:

$$
\begin{equation*}
v(s)=[x(s), y(s)], s \epsilon[0,1] \tag{5.25}
\end{equation*}
$$

where $x, y$ are the image coordinates and $s$ is the arc-length. The energy function defines:

$$
\begin{equation*}
E=\int_{0}^{1} E_{\text {int }}(v(s))+E_{\text {image }}(v(s))+E_{\text {con }}(v(s)) d s \tag{5.26}
\end{equation*}
$$

where $E_{\text {int }}, E_{\text {image }}$ and $E_{\text {con }}$ are the internal, external and the image energy respectively.

The internal energy consists of elastic and bending energy. It can be defined:

$$
\begin{equation*}
E_{\text {int }}=\frac{1}{2}\left(\alpha\left|v(s)^{\prime}\right|^{2}+\beta\left|v(s)^{\prime \prime}\right|^{2}\right) \tag{5.27}
\end{equation*}
$$

where $v(s)^{\prime}$ is the tangential direction at the point that calculates the elastic force snake and $\alpha$ is the weighting parameter that controls snake $s$ elasticity.The $v(s)^{\prime \prime}$ is the curvature at the point that calculates the bending force snake and $\beta$ is weighting parameter that controls snakes bending [7].

The image energy is based on the some image feature function to push the snake toward. Therefore, it can be written:

$$
\begin{equation*}
E_{\text {image }}=w_{\text {line }} E_{\text {line }}+w_{\text {edge }} E_{\text {edge }}+w_{\text {term }} E_{\text {term }} \tag{5.28}
\end{equation*}
$$

The $w_{\text {line }}, w_{\text {edge }}$ and $w_{\text {term }}$ are weights of these features. The $E_{\text {line }}, E_{\text {edge }}$ and $E_{\text {term }}$ represent the lines that defined by image intensity, the edge image is defined by image gradient and the curvature of level lines respectively.

### 5.4.3 The post processing MC algorithm

The MC segmented mask can have some errors, especially to segment the tonsillar herniation (5.15). These errors can be result of some morphology difference between the reference and moving image. Therefore, it is necessary to correct the errors from post processing step.


Figure 5.15: Patient with tonsillar herniation

This algorithm segments the brainstem, to analyse the cerebellum left limitation where the cerebellum is separated of others anatomy parts and possibility of tonsillar herniation. If the tonsillar herniation exists, the algorithm must try to detect it and create the correct cerebellum boundary.

The algorithm uses the region growing and level set approaches to segment the spinal cord, and finding the joint point between the spinal cord and cerebellum. Then, the algorithm tries to detect the brainstem by the line that passes from the joint point between the spinal cord and initial part of cerebellum mask. This step helps us finding the tonsillar herniation and creating correct cerebellum boundary. Finally, according to the new boundary and applying the active contour, the algorithm can be correct the processing errors and segment the cerebellum. This process demonstrated in Flowchart 5.16.


Figure 5.16: The MC correction flowchart.

The Figures 5.17 and 5.18 show the correction algorithm results of the two patients.


Figure 5.17: Compared the MC segmented before and after correction algorithm of the first patient. The red masks show the results before the correction and green masks show the results after the correction.


Figure 5.18: Compared the MC segmented before and after correction algorithm of the second patient. The red masks show the results before correction and green masks show the results after correction.

### 5.4.4 The post processing algorithm for MPF

The MPF segmentation can have any error in the principle boundaries. These errors have directly effect in correct posterior fossa area, this segmentation can be excluded or included of correct posterior fossa area.

For the segmentation correction firstly, is necessary to divide the MPF segmented in two vertical parts. The right part is corrected by the cerebellum edge precedent segmented in the algorithm. The figure 5.19 demonstrates the segmentation error, referent edge and correct segmentation.


Figure 5.19: Confrontation between the MPF segmented before and after correction algorithm. The red masks show the results before correction with vertical errors and green masks show the results after correction.

The MPF left part is corrected by medulla precedent segmented, the medulla edge works as a MPF boundary. Where the MPF edge is more than boundary, the edge is decreased and vice versa.


Figure 5.20: Compared the MPF segmented before and after correction algorithm. The red masks show the results before correction with vertical errors and green masks show the results after correction.

In second step, for the top and bottom part segmentation, the MPF is divided in two horizontal parts. The top part is corrected by two reference points. The first point and second point get from the medulla and cerebellum last pixel segmented respectively. Finally, these points are connected through a line. The figure 5.21 shows the respective edges.


Figure 5.21: Compared the MPF segmented before and after correction algorithm. The red masks show the results before correction with up parts errors and green masks show the results after correction.

The bottom part is corrected through MB boundary that is segmented with processing algorithm. It shows in figure 5.22.


Figure 5.22: Compared the MPF segmented before and after correction algorithm. The red masks show the results before correction with bottom parts errors and green masks show the results after correction.

## Chapter 6

## Results Analysis

To reach the best results and choice the most effective pre-processing and processing algorithm, we did several analyses that will be described in this chapter.

We created 30 tests with different pre-processing and processing algorithms, valuated their results to find the algorithm with lowest error. Each algorithm applied on the 15 sagittal MRI subjects. The result of each test was valuated with 5 indicators that compare the segmentation mask with reference mask that was drawn by the neurosurgeon.

### 6.1 Performance Indices

In order to validate the segmentation masks, it was used some indictors that compare the segmentation with a reference mask which is drawn by the neurosurgeon. In this section, we focus on each indictor function.

### 6.1.1 Different Mask Areas

This indicator calculates the different areas percentile between the segmentation and reference mask [39]. Therefore, if this value is high, there are a high error in the segmentation:

$$
\begin{equation*}
\text { area }=\frac{\left(\sum_{x=1}^{N} \sum_{y=1}^{M}\left|\operatorname{Mask}_{\text {seg }}(x, y)-\operatorname{Mask}_{\text {ref }}(x, y)\right|\right)}{\left(\sum_{x=1}^{N} \sum_{y=1}^{M} \operatorname{Mask}_{\text {seg }}(x, y)\right)} * 100 \tag{6.1}
\end{equation*}
$$

where $\operatorname{Mask}_{\text {seg }}(x, y)$ and $\operatorname{Mask}_{\text {ref }}(x, y)$ are the segmentation and reference mask respectively. $x$ and $y$ are the image coordinates. $M, N$ are the image dimensions

### 6.1.2 Difference Mask

The different Mask indicator uses the equation 6.2 to calculate the difference between two masks:

$$
\begin{equation*}
\text { Difference }=\frac{\left(\sum_{x=1}^{N} \sum_{y=1}^{M}\left|\operatorname{Mask}_{\text {seg }}(x, y)-\operatorname{Mask}_{r e f}(x, y)\right|\right)}{N M} \tag{6.2}
\end{equation*}
$$

where $M a s k_{s e g}(x, y)$ and $M a s k_{r e f}(x, y)$ are the segmentation and the reference mask respectively. $x$ and $y$ are the image coordinates. $M, N$ are the image dimensions.

### 6.1.3 The Mean Square Error

The Mean Square Error(MSE) indicator uses the equation 6.3 to calculate the segmentation error:

$$
\begin{equation*}
M S E=\frac{\left(\sum_{x=1}^{N} \sum_{y=1}^{M}\left(\operatorname{Mask}_{\text {seg }}(x, y)-\operatorname{Mask}_{r e f}(x, y)\right)\right)^{2}}{N M} \tag{6.3}
\end{equation*}
$$

where $\operatorname{Mask}_{\text {seg }}(x, y)$ and $\operatorname{Mask}_{\text {ref }}(x, y)$ are the segmentation and reference mask respectively. $x$ and $y$ are the image coordinates. $M, N$ are the image dimensions.

### 6.1.4 Difference Centroid Masks

This indicator calculates the difference between the segmentation and the reference centroid masks:

$$
\begin{equation*}
\text { Difference }_{\text {Center }}=\sqrt{\left(x c_{\text {seg }}-x c_{r e f}\right)^{2}+\left(y c_{s e g}-y c_{r e f}\right)^{2}} \tag{6.4}
\end{equation*}
$$

where $x c_{\text {seg }}$ and $x c_{\text {ref }}$ are the horizontal center coordinate of segmentation and reference mask. $y c_{s e g}$ and $y c_{r e f}$ are the vertical center coordinate of segmentation and reference mask .

### 6.1.5 Difference Orientation Masks

This indicator calculates the difference orientation between two masks.

$$
\begin{equation*}
\text { Difference }_{\text {orientation }}=\left|\left(O_{\text {seg }}-O_{\text {ref }}\right)\right| \tag{6.5}
\end{equation*}
$$

where $O_{\text {seg }}$ and $O_{r e f}$ are the orientation of segmentation and reference mask.

### 6.1.6 Similarity Shape

This indicator calculates the similarity ratio between two masks:

$$
\begin{equation*}
\text { similarityratio }=\frac{\left(\sum_{x=1}^{N} \sum_{y=1}^{M}\left(\operatorname{Mask}_{\text {seg }}(x, y)-\operatorname{Mask}_{r e f}(x, y)\right)^{2}\right)}{\left(\sum_{x=1}^{N} \sum_{y=1}^{M} \operatorname{Mask}_{\text {seg }}(x, y)\right)^{2}} \tag{6.6}
\end{equation*}
$$

where $\operatorname{Mask}_{\text {seg }}(x, y)$ and $\operatorname{Mask}_{r e f}(x, y)$ are the segmentation and reference masks respectively. The $x$ and $y$ are the image coordinates. The $M$, $N$ are the image dimensions.

### 6.1.7 Difference Perimeter Masks

This indicator calculates the difference perimeter between two masks. The Perimeter is calculating by using the distance around the boundary of the region.

$$
\begin{equation*}
\text { Difference }_{\text {Perimeter }}=\left|\left(P_{\text {seg }}-P_{\text {ref }}\right)\right| \tag{6.7}
\end{equation*}
$$

where $P_{\text {seg }}$ and $P_{\text {ref }}$ are the Perimeter of segmentation and the reference.

### 6.2 Processing Algorithm Valuation

For selecting the best processing algorithm and its parameters, we compared the mean and variance indicators, that was calculated between the algorithm segment and reference masks segmented in15 subjects.

Therefore, in the first step, we had several tests to find the efficient parameters and try to valuate indictors between demons and multi-image method. According to these tests, we choice the multi-image algorithm for processing with global transformation, $\sigma_{i}=1, \sigma_{x}=1$ and iteration number $=600$. The tables 6.1 and 6.1 show the indicators results in two difference tests.

| Evaluation Indicators extracted from all images (200 Iterations) |  |  |  |
| :--- | :---: | :---: | :---: |
|  | MPF | MB | MC |
| Different Mask Areas ( pixels mean) | 13.4004 | 7.2307 | 17.9940 |
| Different Mask Areas (pixels variance) | 28.8854 | 24.3073 | 85.3675 |
| Difference Mask (pixels mean) | 0.0054 | 0.0146 | 0.0042 |
| Difference Mask (pixels variance) | $4.3021 \mathrm{e}-06$ | $6.1800 \mathrm{e}-05$ | $3.0397 \mathrm{e}-06$ |
| The Mean Square Error (pixels mean) | 0.0051 | 0.0146 | 0.0042 |
| The Mean Square Error (pixels variance) | $4.0927 \mathrm{e}-06$ | $6.1800 \mathrm{e}-05$ | $3.0397 \mathrm{e}-06$ |
| Difference Center Masks (pixels mean) | 2.0321 | 2.3982 | 2.1271 |
| Difference Center Masks (pixels variance) | 1.0063 | 3.7466 | 2.4970 |
| Difference Orientation Masks (degrees mean) | 5.6767 | 2.5351 | 46.8488 |
| Difference Orientation Masks (degrees variance) | 37.7299 | 2.5068 | $3.9565 \mathrm{e}+03$ |
| Similarity Shape (mean) | 0.0088 | 0.0039 | 0.0101 |
| Similarity Shape (variance) | $4.8630 \mathrm{e}-06$ | $1.2726 \mathrm{e}-06$ | $1.1818 \mathrm{e}-05$ |
| Difference Perimeter Masks ( pixels mean) | 8.7885 | 11.0391 | 12.6805 |
| Difference Perimeter Masks (pixels variance) | 73.2685 | 119.5983 | 104.9044 |

Table 6.1: Evaluation Indicators extracted from all images (200 Iterations)
The test applied on Demons Algorithm with: $\sigma_{i}=1, \sigma_{x}=1$.

| Evaluation Indicators extracted from all images (600 Iterations) |  |  |  |
| :--- | :---: | :---: | :---: |
|  | MPF | MB | MC |
| Different Mask Areas (pixels mean) | 12.3856 | 6.8947 | 15.8970 |
| Different Mask Areas (pixels variance) | 21.2243 | 11.3247 | 44.9643 |
| Difference Mask (pixels mean) | 0.0050 | 0.0126 | 0.0038 |
| Difference Mask (pixels variance) | $4.2168 \mathrm{e}-06$ | $3.0602 \mathrm{e}-05$ | $2.1650 \mathrm{e}-06$ |
| Mean Square Error (pixels mean) | 0.0050 | 0.0126 | 0.0038 |
| Mean Square Error (pixels variance) | $4.2168 \mathrm{e}-06$ | $3.0602 \mathrm{e}-05$ | $2.1650 \mathrm{e}-06$ |
| Difference Center Masks (pixels mean) | 1.8551 | 2.0617 | 1.8112 |
| Difference Center Masks (pixels variance) | 1.0028 | 2.0285 | 1.2024 |
| Difference Orientation Masks (degrees mean) | 5.6283 | 2.1958 | 42.6120 |
| Difference Orientation Masks (degrees variance) | 40.3787 | 2.1765 | $3.6977 \mathrm{e}+03$ |
| Similarity Shape (mean) | 0.0085 | 0.0038 | 0.0098 |
| Similarity Shape (variance) | $3.4195 \mathrm{e}-06$ | $1.2258 \mathrm{e}-06$ | $1.0267 \mathrm{e}-05$ |
| Difference Perimeter Masks (pixels mean) | 6.8757 | 10.1570 | 11.5971 |
| Difference Perimeter Masks (pixels variance) | 49.3263 | 60.4104 | 68.6171 |

Table 6.2: Evaluation Indicators extracted from all images (600 Iterations)
The test applied Demons Algorithm with: $\sigma_{i}=1, \sigma_{x}=1$

### 6.3 Preprocessing Valuation

After the valuation of the processing algorithm, applied different preprocessing method and valuated the indicators results to find the efficient pre-processing algorithm. These algorithms use the level set, Gaussian, median filters and histogram equation to create more similarity contrast and intensity between the moving and reference images. Finally, the results show that the median filter has been more efficiently respect the others. The table 6.3 show one pre-processing test indicators results that was applied the Level set and CLAHE on moving and reference images.

| Evaluation Indicators extracted from all images with preprocessing |  |  |  |
| :--- | :---: | :---: | :---: |
|  | MPF | MB | MC |
| Different Mask Areas (pixels mean) | 13.4976 | 6.6325 | 17.2465 |
| Different Mask Areas (pixels variance) | 16.9310 | 7.7229 | 43.9124 |
| Difference Mask (pixels mean) | 0.0055 | 0.0123 | 0.0042 |
| Difference Mask (pixels variance) | $3.6304 \mathrm{e}-06$ | $2.5817 \mathrm{e}-05$ | $2.2939 \mathrm{e}-06$ |
| Mean Square Error (pixels mean) | 0.0055 | 0.0123 | 0.0042 |
| Mean Square Error (pixels variance) | $3.6304 \mathrm{e}-06$ | $2.5817 \mathrm{e}-05$ | $2.2939 \mathrm{e}-06$ |
| Difference Center Masks (pixels mean) | 2.1265 | 1.9077 | 2.0396 |
| Difference Center Masks (pixels variance) | 1.3320 | 1.8362 | 1.3507 |
| Difference Orientation Masks (degrees mean) | 7.3697 | 2.1338 | 67.0878 |
| Difference Orientation Masks (degrees variance) | 53.9270 | 4.7212 | $5.9983 \mathrm{e}+03$ |
| Similarity Shape (mean) | 0.0086 | 0.0039 | 0.0103 |
| Similarity Shape (variance) | $1.9958 \mathrm{e}-06$ | $6.1515 \mathrm{e}-07$ | $4.5446 \mathrm{e}-06$ |
| Difference Perimeter Masks (pixels mean) | 7.4909 | 8.5235 | 12.5106 |
| Difference Perimeter Masks (pixels variance) | 46.0611 | 38.7546 | 70.6977 |

Table 6.3: Evaluation Indicators extracted from all images with preprocessing
The test applied preprocessing and Demons Algorithm with: $\sigma_{i}=1, \sigma_{x}=1$ and iteration number $=600$

### 6.4 Evaluation Method Description

In this section is demonstrated the final algorithm, the algorithm is described in Flowchart 6.1 and tables show the indicators results in 3 different subjects and all of subjects.


Figure 6.1: Final algorithm Flowchart.

The tables below show the final algorithm indicators results for three different patents.

| Evaluation Indicators extracted by final algorithm from Subject 1 |  |  |  |  |
| :--- | :---: | :---: | :---: | :---: |
|  | MPF | MB | MC |  |
| Different Mask Areas (pixels) | 11.93 | 6.33 | 15.83 |  |
| Difference Mask (pixels) | 0.0046 | 0.0118 | 0.0045 |  |
| The Mean Square Error (pixels) | 0.0046 | 0.011 | 0.0045 |  |
| Difference Center Masks (pixels) | 1.47 | 0.80 | 0.80 |  |
| Difference Orientation Masks (degrees) | 3.56 | 1.39 | 3.18 |  |
| Similarity Shape | 0.0096 | 0.0038 | 0.0097 |  |
| Difference Perimeter Masks (pixels) | 5.15 | 8.95 | 14.15 |  |

Table 6.4: Indicators calculated for the subject 1 image Subject 1 Indicators.

| Evaluation Indicators extracted by final algorithm from Subject 2 |  |  |  |  |
| :--- | :---: | :---: | :---: | :---: |
|  | MPF | MB | MC |  |
| Different Mask Areas (pixels) | 15.99 | 6.06 | 10.80 |  |
| Difference Mask (pixels) | 0.0069 | 0.0123 | 0.0028 |  |
| The Mean Square Error (pixels) | 0.0063 | 0.011 | 0.0023 |  |
| Difference Center Masks (pixels) | 1.47 | 2.77 | 0.89 |  |
| Difference Orientation Masks (degrees) | 14.26 | 3.07 | 2.13 |  |
| Similarity Shape (pixels) | 0.0092 | 0.0038 | 0.0091 |  |
| Difference Perimeter Masks (pixels) | 17.52 | 18.56 | 14.62 |  |

Table 6.5: Indicators calculated for the subject 2 image Subject 2 Indicators.

| Evaluation Indicators extracted by final algorithm from Subject 3 |  |  |  |  |
| :--- | :---: | :---: | :---: | :---: |
|  | MPF | MB | MC |  |
| Different Mask Areas (pixels) | 17.71 | 4.72 | 16.76 |  |
| Difference Mask (pixels) | 0.0073 | 0.0090 | 0.0047 |  |
| The Mean Square Error (pixels) | 0.0068 | 0.0079 | 0.0042 |  |
| Difference Center Masks (pixels) | 2.76 | 2.25 | 1.87 |  |
| Difference Orientation Masks (degrees) | 1.42 | 1.179 | 4.706 |  |
| Similarity Shape | 0.010 | 0.0038 | 0.010 |  |
| Difference Perimeter Masks (pixels) | 12.34 | 0.33 | 9.18 |  |

Table 6.6: Indicators calculated for the subject 3 image Subject 3 Indicators.

The table 6.7 shows the final algorithm indicators results for all images:

| Evaluation Indicators extracted by final algorithm from all images |  |  |  |
| :--- | :---: | :---: | :---: |
|  | MPF | MB | MC |
| Different Mask Areas (pixels mean) | 14.1948 | 5.2537 | 14.4075 |
| Different Mask Areas (pixels variance ) | 9.2279 | 2.7454 | 21.0766 |
| Difference Mask (pixels mean) | 0.0058 | 0.0098 | 0.0035 |
| Difference Mask (pixels variance ) | $2.5574 \mathrm{e}-06$ | $9.6606 \mathrm{e}-06$ | $1.3071 \mathrm{e}-06$ |
| Mean Square Error (pixels mean) | 0.0053 | 0.0087 | 0.0031 |
| Mean Square Error (pixels variance ) | $2.3904 \mathrm{e}-06$ | $1.0127 \mathrm{e}-05$ | $1.3781 \mathrm{e}-06$ |
| Difference Center Masks (pixels mean) | 1.8211 | 1.4477 | 1.4691 |
| Difference Center Masks (pixels variance ) | 0.4932 | 0.6787 | 0.4731 |
| Difference Orientation Masks (degrees mean) | 5.4998 | 1.9270 | 27.7219 |
| Difference Orientation Masks (degrees variance ) | 27.3333 | 3.6634 | $3.2530 \mathrm{e}+03$ |
| Similarity Shape (mean) | 0.0095 | 0.0038 | 0.0106 |
| Similarity Shape (variance ) | $1.2049 \mathrm{e}-06$ | $6.2504 \mathrm{e}-07$ | $2.8334 \mathrm{e}-06$ |
| Difference Perimeter Masks (pixels mean) | 11.0961 | 13.3828 | 12.5161 |
| Difference Perimeter Masks (pixels variance ) | 36.7400 | 82.2154 | 49.4336 |

Table 6.7: Evaluation Indicators extracted by final algorithm from all images The test applied for method described.

The Figures below show the final algorithm results for five different patients:


Figure 6.2: Valuation of the final algorithm results, with reference masks that are drawn by the neurosurgeon. The red masks show the final algorithm results and the green masks show the reference masks of the first patient: a) MC Masks, b) MPF Masks and c) MB Masks.


Figure 6.3: Valuation of the final algorithm results, with reference masks that are drawn by the neurosurgeon. The red masks show the final algorithm results and the green masks show the reference masks of the second patient: a) MC Masks, b) MPF Masks and c) MB Masks.


Figure 6.4: Valuation of the final algorithm results, with reference masks that are drawn by the neurosurgeon. The red masks show the final algorithm results and the green masks show the reference masks of the third patient: a) MC Masks, b) MPF Masks and c) MB Masks.


Figure 6.5: Valuation of the final algorithm results, with reference masks that are drawn by the neurosurgeon. The red masks show the final algorithm results and the green masks show the reference masks of the fourth patient: a) MC Masks, b) MPF Masks and c) MB Masks.


Figure 6.6: Valuation of the final algorithm results, with reference masks that are drawn by the neurosurgeon. The red masks show the final algorithm results and the green masks show the reference masks of the fifth patient: a) MC Masks, b) MPF Masks and c) MB Masks.

## Chapter 7

## Extraction and Analysis of Features

Extracting the important characteristics of an image, shows the differences and similarities between the forms to be classified.

Some characteristics are defined by a visual appearance in the image. Among these features may include the brightness of a particular region or the texture of a region. Another definition is the delimitation of its frontier through the form of objects. Qualitative and quantitative techniques are developed to describe and represent the shape variation of objects, such as circularity, among others. With the establishment of measures of distance, area and perimeter various geometric attributes of objects can be developed.

The indexes to characterize the posterior fossa, cerebrum and cerebellum segmented by the algorithm are:

- Curvature;
- Area: Number of pixels in the region;
- Perimeter, distance around the boundary of the region;
- Centroid: Center of mass of the region;
- Orientation: Angle between the x-axis and the major axis of the ellipse that has the same second moments as the region;
- Smallest convex polygon that can contain the region;
- Eccentricity of the ellipse that has the same second-moments as the region;
- Length (in pixels) of the major axis of the ellipse, that has the same normalized second central moments as the region;
- Length (in pixels) of the minor axis of the ellipse, that has the same normalized second central moments as the region;
- Solidity: Proportion of the pixels in the convex hull that are also in the region.

For the implementation of the algorithm of extraction of the features of form was developed a script in Matlab, where as a result we have a matrix with the value of each feature for each image. In the Table 7.1 we have the indexes calculated for the subject 1 in Figure 7.1


Figure 7.1: MPF, MB, MC extracted masks from subject 1

| Features Extracted from Subject 1 |  |  |  |
| :--- | :---: | :---: | :---: |
|  | MPF | MB | MC |
| Curvature | 97,91 | 227,09 | 86,85 |
| Area ( in pixels) | 257800 | 1215600 | 160600 |
| Centroid | 2,06 | 174,73 | 216,48 |
| Perimeter | 191,08 | 439,47 | 168,77 |
| Orientation | $-51,42$ | $-30,80$ | 75,04 |
| Solidity | 0,95 | 0.93 | 0,93 |
| Eccentricity | 0,50 | 0,66 | 0,80 |
| Smallest convex polygon | 183,49 | 109,95 | 225,92 |
| Length of the major axis (in pixels) | 62,53 | 146,82 | 61,85 |
| Length of the minor axis (in pixels) | 53,79 | 110,02 | 36,68 |

Table 7.1: Indexes calculated for the subject 1 image Subject 1 indexes

### 7.1 Features selection

The high number of available features can impair the accuracy of the generated models for classification, requiring the use of techniques to select the most relevant features to make the models more robust. The selection of features (or index) proposes, by Fisher Ratio, that the analysis should be able to select the most discriminating (i.s less noisy) feature.

Fisher's exact test is a test of statistical significance used for the analysis of contingency tables.It is a method of a class of exact tests, so called because of the significance of the deviation of a null hypothesis (eg, p-value) that can be accurately calculated, rather than depending on an approximation that becomes exact in the limit according to sample size increases to infinity, as in many statistical tests [20]. Although in practice it is employed when sample sizes are small, it is valid for all sample sizes.

To calculate the significance of each feature, the total probability of observing data as extreme if the null hypothesis is true, we have to calculate the values of p .

$$
\begin{equation*}
p=\frac{\left(\bar{x}_{i}-\bar{x}_{i+1}\right)^{2}}{\left(\sigma x_{i}+\sigma x_{i+1}\right)} \tag{7.1}
\end{equation*}
$$

The value of $p$ is computed between each combination of features, with a class relation. Thus, each fisher ratio demonstrates how much each feature from a class is independent from another feature of other classes. The Fisher ratio is shown along with a Boxplot graph, which is useful for visualizing the position of features in the features versus classes space. Below we have two figures (Figure 7.2, 7.3 ), which shows the Fisher's ratio calculated for two features.


Figure 7.2: Boxplot and Fisher ratio - Curvature MC vs Classes


Figure 7.3: Boxplot and Fisher ratio - Eccentricity MPF vs Classes

It is clearly the difference in the significance level between the two features. The Length index of the Curvature MC (Figure 7.2), shows to be separable in each class, with a significant distance between them, that means
that it is good index to carry out the classification in the respective classes. On the other hand the Eccentricity MPF (Figure 7.3) proves to be a not separable index between the classes, thus, generating always an error in the selection of the correct class.

Finally we will have a matrix with Fisher's ratio, where it was calculated for each combination of the 4 classes, among the 30 features. Now for each feature, we select those that will have the highest Fisher's ratio, thus selecting those with more significance. In the Table 7.2 we can see the selected features.

| More Significance Features Extracted |  |
| :--- | :---: |
| Feature | Mean Fisher Ratio |
| Length of the major axis MC / Length of the major axis MPF | 4.08 |
| Length of the major axis MC | 16.13 |
| Area MC / MPF | 4,53 |
| Length of the major axis MC / Length of the minor axis MPF | 6,5 |

Table 7.2: Selected Features with more significance

## Chapter 8

## Conclusion

The aim of this research, was been to find the efficient automatic approach to understand about Chiari malformations and their type thorough identifying the cerebellum (MC), posterior fossa (MPF) and brain (MB). This approach can help to reduce the manual approaches segmentations errors that due to user dependency. Also, it is able to recommend some features to analyse the Chiari types. In order to this purpose, is suggested the multi-image Demons registration method that totally is independent of the user and with using more than one reference and moving images can be more efficiently. In additional, we try to apply pre-processing algorithm to improve the registration functional and post processing to decrease errors where registration is not able to correct them.

In the first step, the algorithm is applied on 15 different patients, and is valuated with 5 indicators to find about it robustness behaviour and its difference with neurosurgeon manual segmentations. The results show that the autumnal segmentation is efficient.

In second step, we try to extract some segmented masks features, in order to be vaulted their relationship with Chiari types. In the features analyses, the algorithm tries to find best features that can be create most separation among classes (Chiari types). The advantage of this analyse is that calculate some proprieties that there is not possibility to calculate with manual approaches and It can be led to efficient diagnostic method. The results of this analyse shows that the Chiari types haves relationship with some features.

In this research can be continent in future, to create a classification Chiari malformations types based on the segmented masks and features that extract of them and studying deeply motivation of the features effect on Chiari identification.

## Bibliography

[1] Afshar E., Watkins E.S., Yap J.C.: Stereotactic Atlas of the Human Brainstem and Cerebellar Nuclei. Raven, New York. 1978
[2] Aubert G, Deriche, R, and Kornprobst P.,Computing optical flow via variational techniques. SIAM Journal on Applied Mathematics, v. 60, n. 1, p. 156-182, 1999.
[3] Bindal AK, Dunsker SB, Tew JM., Chiari I malformation: classification and management. Neurosurgery, 1995.
[4] Brodbelt, Andrew Robert. Investigations in post-traumatic syringomyelia. 1977.
[5] Carter R .: The Human Brain Book.New York: Penguin; 2014.
[6] Chang YL, Li X.,Adaptive Image Region-Growing, IEEE Trans. on Image Processing, vol. 3, no. 6, pp. 868-872, 1994.
[7] Cohen L. D., On active Contour Models and Balloons.CVGIP,Image Understanding, vol. 53, pp. 211-218, 1991.
[8] Dawant. B. M., Hartmann S. L, Gadamsetty S. Brain Atlas Deformation in the Presence of Large Space-occupying Tumors. In Medical Image Computing and Computer- Assisted Intervention, 1999.
[9] Eccles JC, Ito M, SzentÃigothai J. The Cerebellum as a Neuronal Machine. Springer-Verlag; 1967.
[10] Elster AD, Chen MY.,Chiari I malformations: clinical and radiologic reappraisal. Radiology, 1992.
[11] Fix J.D.: Atlas of the Human Brain and Spinal Cord. Aspen, Rockville . 1987
[12] Fleet, D, Weiss, Y., Optical flow estimation. In Handbook of mathematical models in computer vision (pp. 237-257). Springer, Boston, MA,2006.
[13] Getreuer P., Chan-vese segmentation. Image Processing On Line, v. 2, p. 214-224, 2012.
[14] Giger, Maryellen L., and Kenji Suzuki. "Computer-Aided Diagnosis." Biomedical information technology. 2008. 359-XXII.
[15] Guohong Liu, Wenming Guo.,Application of improved arthmetic of median filtering denoising. Computer Engineering and Applications, 46 (10) 2010.
[16] Huang C, Zeng L., An active contour model for the segmentation of images with intensity inhomogeneities and bias field estimation. PloS one, v. 10, n. 4, p. e0120399, 2015.
[17] Hummel R. , Image Enhancement by Histogram Transformation. Computer Vision, Graphics and Image Processing, vol. 6, 1977.
[18] Kass M, Witkin A, TerzopoulosD.,Snakes: Active contour models. In: Proc. 1st Int. Conf. on Computer Vision. 1987. p. 268.
[19] Kroon, D. J ,Slump, C. H., MRI modalitiy transformation in demon registration. In Biomedical Imaging: From Nano to Macro. ISBI’09. IEEE International Symposium on (pp. 963-966). IEEE,2009.
[20] Lazar C ., A survey on filter techniques for feature selection in gene expression microarray analysis. IEEE/ACM Transactions on Computational Biology and Bioinformatics (TCBB), v. 9, n. 4, p. 1106-1119, 2012.
[21] LI C., A variational level set approach to segmentation and bias correction of images with intensity inhomogeneity. In: International Conference on Medical Image Computing and Computer-Assisted Intervention. Springer, Berlin, Heidelberg, 2008. p. 1083-1091.
[22] Lombaert H, Grady L, PennecX, Ayache N , Cheriet F., Spectral Demons-image registration via global spectral correspondence. Springer, Berlin, Heidelberg,In Computer Vision-ECCV 2012.
[23] Loukas M, Shayota BJ, Oelhafen K, Miller JH, Chern JJ, Tubbs RS, Oakes WJ. "Associated disorders of Chiari Type I malformations: a review". Neurosurg Focus, 2011.
[24] Lu, H, Cattin, P. C, Reyes, M., A hybrid multimodal non-rigid registration of MR images based on diffeomorphic demons. In Engineering in Medicine and Biology Society (EMBC), 2010 Annual International Conference of the IEEE.
[25] Maria A. Patestas, Leslie P. Gartner: A Textbook of Neuroanatomy, John Wiley \& Sons, 2016..
[26] Marin P., Morphogenesis of experimentally induced Arnold-Chiari malformation. Journal of the neurological sciences, 1981.
[27] Milhorat TH, Chou MW, Trinidad EM et al.: Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. Neurosurgery, 1999.
[28] Peroni M. et al., Stopping Criteria for Log-Domain Diffeomorphic Demons Registration: An Experimental Survey for Radiotherapy Application. Technology in cancer research \& treatment, v. 15, n. 1, p. 77-90, 2016.
[29] Pisano ED, Chandramouli J, Hemminger BM, et al. The effect of intensity windowing as an image processing tool in the detection of simulated masses embedded in digitized mammograms. J Digit Imaging. 1997.
[30] Pohle, R, Toennies, K. D., Segmentation of medical images using adaptive region growing.In Medical Imaging 2001: Image Processing (Vol. 4322, pp. 1337-1347). International Society for Optics and Photonics, 2001.
[31] Polesel A, Ramponi G, Mathews V. J., Image Enhancement via Adaptive Unsharp Masking.IEEE Trans. Image Processing, Vol. 9, No. 3, pp. 505-510, March 2000.
[32] Saleh, Marwan D.; Eswar an, C., An Automated Decision-support System for Non-proliferative Diabetic Retinopathy Disease Based on MAs and HAs Detection. Comput. Methods Prog. Biomed, 2012.
[33] Shapiro, L. G. ,Stockman, G. C., Computer Vision, page 137, 150. Prentice Hall, 2001.
[34] Sharma D. P., Intensity Transformation using Contrast Limited Adaptive Histogram Equalization. International Journal of Engineering Research (ISSN : 2319-6890) Volume No.2, Issue No. 4, pp : 282-285, 2013.
[35] Stovner, Lars Jacob, and Peter Rinck. Syringomyelia in Chiari malformation: relation to extent of cerebellar tissue herniation. Neurosurgery, 1992.
[36] Suzuki, K.; Li, Feng; Sone, S.; Doi, K. Computer-aided diagnostic scheme for distinction between benign and malignant nodules in thoracic low-dose CT by use of massive training artificial neural network. IEEE Transactions on Medical Imaging, 2005 .
[37] Tubbs RS, Elton S, Grabb P, Dockery SE., Analysis of the posterior fossa in children with the Chiari 0 malformation. Neurosurgery, 2001.
[38] Vannemreddy, Prasad; Nourbakhsh, Ali; Willis, Brian; Guthikonda, Bharat. "CongenitalChiari malformations: A review". Neurology India. 2010.
[39] Veltkamp R.C., Shape matching: Similarity measures and algorithms. In: Shape Modeling and Applications, SMI 2001 International Conference on. IEEE, 2001. p. 188-197.
[40] Vercauteren T, Pennec X, Perchant A, AyacheN.,Symmetric log-domain diffeomorphic registration: A demons-based approach. In International conference on medical image computing and computer-assisted intervention (pp. 754-761). Springer, Berlin, Heidelberg, 2008.
[41] Wang X, Li H ,Wang X., A bias correction variational level set image segmentation model combining structure extraction. In: Image, Vision and Computing (ICIVC), 2017 2nd International Conference on. IEEE, 2017. p. 327-331.
[42] Williams D. J, Shah M., A fast algorithm for active contours and curvature estimation. CVGIP: Image Understanding, vol. 55, no. 1, pp. 14-26, 1992.
[43] Zuiderveld K., Contrast Limited Adaptive Histogram Equalization.Chapter VIII.5, Graphics Gems IV. P.S. Heckbert (Eds.), Cambridge, MA, Academic Press, 1994.

