Quantification of posterior fossa structures in fetal brain MR images

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\textbf{Abstract} – This paper describes results for an ongoing research on the segmentation of the posterior fossa and the structures it contains in fetal brain MR images. A semi-automatic segmentation algorithm based on Dijkstra’s algorithm and a fast marching level set method is suggested. The algorithm has been tested on a small number of images and compared to manual segmentations done by experts. It shows reasonable results, but a more elaborate study with more data is needed to statistically evaluate the proposed algorithm.

\textbf{Index terms} – Fetal brain, MRI, segmentation, Dijkstra’s algorithm, fast marching method.

\section{I. INTRODUCTION}

The main imaging modality to perform routine visualizations of the fetus during pregnancy is ultrasonography. Fetal MRI can be an accurate additional method, because of better soft-tissue contrast, especially for the structures in the posterior fossa (PF) \cite{1}. Furthermore, fetal MRI has a larger field of view than ultrasound, but the spatial resolution is lower \cite{2}.

Fetal MRI is performed when irregularities are seen in the sonogram or in results of any other prenatal diagnostic technique. Another case in which MRI can be performed in addition to ultrasound is when the sonogram seems normal but there is a family history of a disease which can be overlooked by ultrasound \cite{2}. The frequency of MRI usage for these purposes depends heavily on the hospital (and country) \cite{2}. In Shengjing hospital, Shenyang, China, every year around 300 fetal MRI exams are performed. This makes the analysis of the images a relevant problem.

In clinical practice, the analysis of fetal MR images is mostly based on the experience of the radiologist. Shape and size of the structures relative to each other are observed to study the development of the fetus. Quantitative data would therefore be a welcome addition to help doctors make a diagnosis. To get quantitative data, segmentation can be done manually by doctors for every image separately, but this would be time consuming and would show high inter- and intra-observer variations. Hence automatic or semi-automatic segmentation can be very helpful to produce more valid and better comparable results.

In this paper the segmentation of mid line structures in the PF is discussed. The PF contains the brain stem and the cerebellum. In the central sagittal slice, the following structures are visible inside the PF: the brain stem, the vermis (part of the cerebellum), the cisterna magna and the fourth ventricle (Fig. 1). This project is focused on the segmentation of the brain stem and the vermis. To be able to calculate the relative size of these structures, also the segmentation of the PF as a whole is investigated.

There are several diagnoses that involve abnormalities in these structures. An example of such a diagnosis is the Dandy Walker malformation. The three basic criteria for this malformation are \cite{3}:

– Complete or partial vermian agenesis or hypoplasia, or in other words, the vermis is smaller, or – in very rare cases – completely missing.
– Dilation of the fourth ventricle.
– Enlargement of the PF itself.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig1.png}
\caption{Central slice of a fetal brain with a gestational age of 38 weeks with: a) the brain stem, b) the vermis, c) the fourth ventricle and d) the cisterna magna.}
\end{figure}

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\end{figure}
More diagnoses that have abnormalities in the structures of the PF include, among others: Isolated cerebellar hypoplasia, isolated vermian agenesis, rhombencephalosynapsis and arachnoid cyst [3].

To study the relative development of the PF structures the following ratios can be calculated [4]:

\[
R_1 = \frac{A_{\text{vs}} + A_{\text{bs}}}{A_{\text{pf}}} \\
R_2 = \frac{A_{\text{vs}}}{A_{\text{pf}}} \\
R_3 = \frac{A_{\text{bs}}}{A_{\text{pf}}} \\
R_4 = \frac{A_{\text{vs}}}{A_{\text{vs}} + A_{\text{bs}}} \\
R_5 = \frac{A_{\text{vs}}}{A_{\text{vs}} + A_{\text{pf}}} 
\]

Where \(A_{\text{vs}}, A_{\text{bs}}\) and \(A_{\text{pf}}\) are the areas of respectively: the vermis, the brain stem and the posterior fossa. Note that \(R_1 = R_3 + R_5\) and \(R_4 = 1 - R_5\). Previous research [4] showed ratio \(R_4\) (and therefore also \(R_5\)) to be the most interesting for clinical diagnosis, because it is independent of the size of the PF.

The aim of this project is to find a 2D segmentation method which can segment the three above described areas in central sagittal slices as automatically as possible.

II. MATERIALS & METHODS

A. Images

The images used for this research are made in Shengjing hospital of Shenyang, China, by a Philips (Best, The Netherlands) Gyroscan Intera 1.5 T MRI scanner in the period of January-April 2009. In this paper six images are used; three of them are diagnosed normal, the other three are diagnosed abnormal. These images are named N1, N2, N3, AN1, AN2 and AN3, where N stands for normal and AN for abnormal. The gestational age of the fetuses in these images is between 32 and 38 weeks.

B. Manual interaction

Because this paper focuses on mid line structures, the first necessary manual interaction is to select the central sagittal slice from an image series.

As described by Claude et al. [4], to come to an accurate estimation of the size of the PF it is necessary to manually limit its segmentation. This is done by selecting five anatomically defined points to limit the upper and lower parts of the segmentation by straight lines between these points.

The positioning of these points is as follows, see Fig. 2:

A: at the beginning of the great vein of Galen.
B: at the mamillary body.
C: at the clivus.
D: at the anterior point of the spinal cord.
E: at the posterior point of the spinal cord.
F: is introduced to assist the segmentation method and will be discussed in the next part.

Straight lines can then be drawn from point A via B to C to form the upper limit of the PF. The lower limit is formed by a line normal to the brain stem at point E, thus reaching point D. A better description for point E is the corner of the triangle formed by the cisterna magna and the spinal canal.

C. Dijkstra's algorithm and Bresenham line algorithm

For a complete segmentation of the PF, point C should be connected with D following the edge of the PF. The same holds for points A and E. This can be done using Dijkstra's algorithm, which is a solution to the shortest path problem [5].

Dijkstra's algorithm can be used on images to search for a lowest-cost path connecting two pixels. Because the path that the algorithm is supposed to follow should be along the edges of the PF, the cost-function can be based on the negative image gradient. The cost-function that is used here is:

\[
(-|\nabla I(i, j)| + \max(|\nabla I|)) \cdot n + w \cdot \text{step} \quad (6)
\]

Where \(|\nabla I(i, j)|\) is the length of the image gradient at pixel \(i,j\); \(\max(|\nabla I|)\) is the maximum length of the image gradient in the whole image. This maximum is added to the negative gradient to make all costs nonnegative, which is a requirement for Dijkstra's algorithm. \(n\) is a parameter to give more weight...
to the gradient. \textit{step} is a parameter to give more weight to the number of steps that is used to reach the current pixel from the starting point. \( w \) is 1 if the neighbouring pixel is horizontally or vertically connected to the current pixel and \( \sqrt{2} \) if it is diagonally connected.

The gradient needed for this method is calculated using a Gaussian derivative with scale \( \sigma \).

Because the lowest cost path between point A and point E tends to be along an edge of the vermis or brain stem an extra manual point F is added at the posterior corner of the PF. Now Dijkstra’s algorithm is used to connect points A and E via point F.

To get the in-between locations of pixels belonging to the straight lines that connect the other manual points the Bresenham line algorithm [6] is used. This algorithm estimates the pixels that best form a line between points using:

\[
y = \frac{y_1 - y_0}{x_1 - x_0} (x - x_0) + y_0
\]  

(7)

For lines with a slope less than 1, if \( x_0 < x_1 \), \( x \) should be increased by steps of 1, otherwise it should be decreased by steps of 1. For lines with a slope bigger than 1, the \( y \)-coordinates are estimated while taking steps of 1 or -1 in the \( y \)-direction.

D. Seed area selection

Now that the area of the PF is known, it is reasonable to assume that pixels belonging to the brain stem or vermis generally have a lower intensity value. There is no clear histogram separation however, so a global threshold cannot be used as a complete segmentation method, but the results of such a (conservative) threshold can be used as starting areas for a more advanced segmentation algorithm, such as a level set method. For the threshold a certain percentage of the total histogram width of the PF area can be used, this percentage should be kept as low as possible because the results are only used as seed areas.

To remove very small areas – caused by noise or at the edges of the PF area – that do not belong to the vermis or brain stem from the seed area selection, a binary opening operation is performed on the threshold segmentation using 4-connectedivity. This means first erosion and then dilation, which makes small areas that consist of just one pixel or a few pixels disappear.

E. Fast marching level set method

The fast marching method is a special case of the level set segmentation method [7]. The level set method is a method of describing curve propagating as a partial differential equation without the need to parameterize the curve. The fast marching method is based on the assumption that the curve will always propagate either outwards or inwards.

The boundary value formulation for this method is of the form [7]:

\[
|\nabla T(i, j)| F(i, j) = 1
\]  

(8)

Where \( T(i,j) \) is the arrival time for the curve at a point \((i,j)\) of the image and \( F(i,j) \) is the speed function based on the image. The speed function is known for every point in the image so the time value can be calculated by solving this equation. A discrete approximation based on the Hamilton-Jacobi equation is given by [8]:

\[
\begin{align*}
\max(T(i, j) - T(i - 1, j), T(i, j) - T(i + 1, j)) &
\leq \max(T(i, j) - T(i, j - 1), T(i, j) - T(i, j + 1)) \\
&
+ \frac{1}{F^2(i, j)} \\
= & 1
\end{align*}
\]  

(9)

Using this approximation, \( T(i,j) \) can be estimated using the neighbouring time-values and the speed-function. Pixels that have not been reached yet are set to a time-value of \( \infty \) and pixels that are inside of the seed area are set to a value of 0.

The speed function used here is:

\[
F(i, j) = e^{-\alpha |\nabla T(i,j)|}
\]  

(10)

Where \( \alpha \) is a parameter to change the shape of the speed function. As described before, the speed function is used to estimate the arrival time of the curve to a point in the image. When the curve is on an edge, the movement should be minimal, so the speed should be small. The gradient is approximated using the Sobel operator. Sobel is used in this case instead of a Gaussian derivative to simulate a smaller scale.

The curve propagates following the time values from low to high. For the stopping criterion the mean of the time values of the pixels that are currently on the curve is used. If this will get lower than a set value the algorithm will stop.

The advantage of using a level set method for this problem instead of e.g. an active contours method is that the regions can merge. Because an automatic seed point selection method is used, it is possible that the algorithm starts with more seed areas inside of the same region, which would not be a problem when merging is possible.

F. Distinguishing the two different areas from each other

The results of the fast marching method are two 4-connected areas, one representing the brain stem, the other representing the vermis. Because the area of the brain stem has a more stretched-out shape than the vermis, these areas can be distinguished from each other. For this the statistical method of principle component analysis (PCA) [9] can be used on the coordinates of the pixels belonging to the areas. PCA tries to find the principle component for a set of points, so in this case the direction of the object. For this purpose the scatter matrix is calculated for both areas:

\[
S = \sum_{i=1}^{N} (x_i - m)(x_i - m)^T
\]  

(11)
Where: $x_k$ is the coordinates for pixel $k$ of the area, $m$ is the centroid of the area and $n$ is the number of points in the area. The largest eigenvector of $S$ then represents the major direction of the object. Therefore, $\lambda_1/\lambda_2$ (where $\lambda_1 > \lambda_2$), will give an indication of the shape. For a perfect circle this ratio will be 1, for a more stretched-out structure, the ratio will be larger than 1.

G. Expert data
Evaluation of the results of the proposed segmentation algorithm is done by comparison with manual segmentations done by experts in this field. To be able to do this, two doctors of Shengjing hospital and one expert of North Eastern University, Shenyang are asked to give manual segmentations of the three areas for six different images.

H. Comparison
The comparison is done using the overlap fraction [10]. The overlap fraction between two areas $A_1$ and $A_2$ can be defined as the size of intersection divided by the size of union between these areas:

$$O(A_1, A_2) = \frac{|A_1 \cap A_2|}{|A_1 \cup A_2|} \quad (12)$$

To evaluate inter-observer variations, the overlap fractions between all experts are computed for all the areas in all the images. The experts have done the segmentation of the regions only once, so intra-observer variability is not investigated for this paper.

The results of the semi-automatic segmentation algorithm are compared with all experts separately and mean values for the overlap fractions are calculated.

I. Area ratios
For all manual segmentations and for the results of the semi-automatic segmentation algorithm the previously described area ratios are calculated.

III. RESULTS

A. Parameters
There are 3 parameters that influence the result of Dijkstra’s algorithm and consequently the PF segmentation. As described before: $\sigma$, $n$ and step. Because of the low resolution of the images the scale is kept at the low value of $\sigma = 1.5$. A suitable value for $n$ is found to be 2. Adding extra weight for taking a step is not necessary for most of the lines in the images. For 1 of the 6 researched cases the value of step for the line between point A and F has to be set to 500. This is necessary because the vermis almost completely joins with the edge of the PF in that image, so the border between these structures is not obvious at all.

For the segmentation of the brain stem and the vermis, there are also three parameters that influence the result. For the seed area threshold on the PF region, 40% of the total histogram width is found to be suitable for all the studied images. The other two affect the result of the fast marching method and are the $\alpha$ of the speed function and the value used for the stopping criterion. For all images $\alpha = 2$ is used. For the stopping criterion, values between 0.20 and 0.33 are used. The main reason no generally applicable value can be found yet is that the areas of the brain stem and the vermis tend to merge at some point, due to the small distance between these areas – i.e. the size of the fourth ventricle – and the low resolution of the images.

B. Segmentation results
The segmentation results for two images are shown in Fig. 3 and Fig. 4 together with the average segmentations of the experts. If 2 of the 3 experts agree that a pixel should belong to an area, it is included in the average segmentation.

To show the inter-observer variability of the experts, the overlap fractions between the experts are shown in Table I. To evaluate the semi-automatic segmentations, the overlap fractions with the manual segmentations are shown in Table II.

The area ratios for the manual and the semi-automatic segmentations are shown in Table III and Table IV.
Fig. 4: Segmentation results for the PF, brain stem and vermis in image AN1. In the left column the average manual segmentations done by the three experts are shown, in the right column the segmentation results of the algorithm are shown.

### TABLE I
INTER-OBSERVER VARIABILITY SHOWN IN MEAN ($\mu \pm \sigma$) OVERLAP FRACTION BETWEEN THE THREE EXPERTS, WHO PERFORMED SEGMENTATIONS FOR SIX IMAGES.

<table>
<thead>
<tr>
<th></th>
<th>Expert 1 with expert 2</th>
<th>Expert 1 with expert 3</th>
<th>Expert 2 with expert 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>PF</td>
<td>0.835 ± 0.027</td>
<td>0.806 ± 0.057</td>
<td>0.819 ± 0.068</td>
</tr>
<tr>
<td>Brain stem</td>
<td>0.730 ± 0.049</td>
<td>0.784 ± 0.029</td>
<td>0.781 ± 0.065</td>
</tr>
<tr>
<td>Vermis</td>
<td>0.821 ± 0.024</td>
<td>0.845 ± 0.019</td>
<td>0.826 ± 0.053</td>
</tr>
</tbody>
</table>

### TABLE II
OVERLAP FRACTIONS FOR SIX IMAGES (THREE DIAGNOSED NORMAL (N), THREE DIAGNOSED ABNORMAL (AN)).

<table>
<thead>
<tr>
<th></th>
<th>PF</th>
<th>Brain stem</th>
<th>Vermis</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>0.831 ± 0.0496</td>
<td>0.775 ± 0.0254</td>
<td>0.747 ± 0.0376</td>
</tr>
<tr>
<td>N2</td>
<td>0.842 ± 0.0453</td>
<td>0.814 ± 0.0185</td>
<td>0.683 ± 0.0151</td>
</tr>
<tr>
<td>N3</td>
<td>0.828 ± 0.0530</td>
<td>0.786 ± 0.0246</td>
<td>0.573 ± 0.0319</td>
</tr>
<tr>
<td>AN1</td>
<td>0.774 ± 0.0651</td>
<td>0.663 ± 0.1165</td>
<td>0.356 ± 0.0360</td>
</tr>
<tr>
<td>AN2</td>
<td>0.809 ± 0.0628</td>
<td>0.749 ± 0.0085</td>
<td>0.654 ± 0.0340</td>
</tr>
<tr>
<td>AN3</td>
<td>0.759 ± 0.1213</td>
<td>0.663 ± 0.0225</td>
<td>0.597 ± 0.0129</td>
</tr>
</tbody>
</table>

### TABLE III
AREA RATIOS FOR THE SEGMENTATIONS OF THE SIX IMAGES DONE BY THE EXPERTS ($\mu \pm \sigma$).

<table>
<thead>
<tr>
<th></th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>0.668 ± 0.118</td>
<td>0.333 ± 0.066</td>
<td>0.334 ± 0.055</td>
<td>0.502 ± 0.021</td>
<td>0.498 ± 0.021</td>
</tr>
<tr>
<td>N2</td>
<td>0.633 ± 0.038</td>
<td>0.338 ± 0.028</td>
<td>0.295 ± 0.011</td>
<td>0.467 ± 0.015</td>
<td>0.533 ± 0.015</td>
</tr>
<tr>
<td>N3</td>
<td>0.597 ± 0.032</td>
<td>0.316 ± 0.010</td>
<td>0.281 ± 0.029</td>
<td>0.470 ± 0.026</td>
<td>0.530 ± 0.026</td>
</tr>
<tr>
<td>AN1</td>
<td>0.605 ± 0.064</td>
<td>0.332 ± 0.022</td>
<td>0.272 ± 0.048</td>
<td>0.448 ± 0.037</td>
<td>0.552 ± 0.037</td>
</tr>
<tr>
<td>AN2</td>
<td>0.547 ± 0.039</td>
<td>0.312 ± 0.028</td>
<td>0.235 ± 0.0217</td>
<td>0.430 ± 0.029</td>
<td>0.570 ± 0.029</td>
</tr>
<tr>
<td>AN3</td>
<td>0.638 ± 0.121</td>
<td>0.386 ± 0.070</td>
<td>0.252 ± 0.051</td>
<td>0.394 ± 0.013</td>
<td>0.606 ± 0.013</td>
</tr>
</tbody>
</table>

### TABLE IV
AREA RATIOS FOR THE SEMI-AUTOMATIC SEGMENTATION OF THE SIX IMAGES.

<table>
<thead>
<tr>
<th></th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>0.499</td>
<td>0.270</td>
<td>0.229</td>
<td>0.459</td>
<td>0.541</td>
</tr>
<tr>
<td>N2</td>
<td>0.471</td>
<td>0.280</td>
<td>0.191</td>
<td>0.406</td>
<td>0.594</td>
</tr>
<tr>
<td>N3</td>
<td>0.378</td>
<td>0.234</td>
<td>0.144</td>
<td>0.381</td>
<td>0.619</td>
</tr>
<tr>
<td>AN1</td>
<td>0.326</td>
<td>0.234</td>
<td>0.092</td>
<td>0.283</td>
<td>0.717</td>
</tr>
<tr>
<td>AN2</td>
<td>0.422</td>
<td>0.269</td>
<td>0.153</td>
<td>0.362</td>
<td>0.638</td>
</tr>
<tr>
<td>AN3</td>
<td>0.440</td>
<td>0.310</td>
<td>0.130</td>
<td>0.296</td>
<td>0.704</td>
</tr>
</tbody>
</table>

### IV. DISCUSSION
This paper reports results for a project which is still in progress. The aim of this project is to develop a segmentation method which works as automatically as possible. The designed algorithm first needs the user to select the sagittal slice that is most central in the fetal brain. The second manual interaction needed is the selection of the six points.

Selecting the central slice is not always possible, since it might not exist in the dataset. The sequences that are used to make the images should be fast in order to reduce possible motion artifacts caused by the moving fetus. Therefore slice spacing distance is large, which makes the out-of-plane resolution low. The large slice spacing distance also makes the difference in size of the structures between two successive slices large, which makes the segmentation results sensitive to the selection of the most central slice. Furthermore, the sagittal slices do not always have to be perfectly sagittal, which also influences the size of the structures.

For the points that should be selected manually, an anatomical positioning is given. However, this does not mean the exact location can always be found easily. When the choice of the experts for these points is compared, it is obvious that there is no definite agreement among them.

The results for the segmentation of the PF look reasonable
The overlap values with the expert data have fairly high values (Table II), compared to the calculated inter-observer values (Table I). However, it is important to realize that what is compared here is not just the algorithm to the expert data, because the algorithm uses user-defined points as well. Therefore, it is hard to form clear conclusions about the performance of the algorithm based on these results. Moreover, because there are only three experts who all did the segmentations only once, these results are highly sensitive to inter- and intra-observer variability.

The results for the segmentation of the brain stem and the vermis look slightly worse (Fig. 3 and Fig. 4). The segmentation does not always move outwards as much as one would expect based on the expert data, because in some cases the two areas merge before these parts of the structures are reached. This can also be seen from the overlap fractions (Table II) that are calculated with the expert segmentations, especially for the results of the vermis. There is an outlier with a mean overlap fraction for the vermis of just 0.356. The segmentation results for this image are shown in Fig. 4. In this image the problem of the brain stem and vermis being too close together can be seen clearly.

The area ratios $R_1$, $R_2$, and $R_3$ (Table III and Table IV) mostly show a larger value for the segmentation done by the algorithm. This is caused by the fact that in most cases the size of the PF is being overestimated and the sizes of the brain stem and vermis are being underestimated when compared to the expert data. This does not hold for the ratios $R_4$ and $R_5$ because they are independent on the size of the PF. Mostly $R_4$ gets underestimated and therefore $R_5$ gets overestimated. This makes the area ratios not very accurate. With the data available at this stage of the project, the usefulness of these ratios in assisting the diagnosis – which does not have to be related to the accuracy – cannot be determined. Furthermore, if the ratios can be estimated accurately, it is important to realize that one abnormal value at one point during pregnancy does not mean the fetus can be diagnosed with an abnormality. These ratios should be considered as an additional method to study development of the fetus during pregnancy.

Further research should first include a more elaborate study of the suggested algorithm using more data. Based on the data that are used in this paper no real conclusions can be stated about the performance of the algorithm.

Because, unlike the proposed algorithm, doctors have experience in analyzing these images, it will be interesting to investigate the possibilities of a model-based segmentation algorithm.

IV. CONCLUSION

The suggested algorithm shows reasonable results but a study with more data is necessary to evaluate the performance accurately.

ACKNOWLEDGMENT

We would like to thank Dr. Yong Yue and Dr. Hongwei Wang of Shengjing hospital for performing the manual segmentations and discussing the problem with us.

REFERENCES