THRESHOLD SELECTION CRITERIA FOR QUANTIFICATION OF LUMBOSACRAL CEREBROSPINAL FLUID AND ROOT VOLUMES FROM MRI

ABSTRACT

BACKGROUND AND PURPOSE. Previous studies quantified lumbar CSFvolumes from MR images without detailing criteria for threshold selection. Here, criteria for selecting maximal and minimal lumbosacral CSF and root thresholds through anatomical identification were defined, quantifying the resulting volume variability. MATERIALS AND METHODS. MR images (T2, 16 bits, voxel size=0.65 mm³, n=7 cases) saved on DICOM files were analyzed using 3D software. Thresholds were applied in standardized blocks of 50 slices of the dural sac ending caudally at the L5-S1 intervertebral space for caudal blocks and in middle L3 for rostral blocks. Maximal CSF thresholds avoided unlabeled voxels in secure CSF area. Minimal root thresholds selected secure cauda equina root area but not adjacent gray voxels in the CSF-root interface. RESULTS. Threshold value localization within the grayscale histogram curve of the dural sac content was not consistent enough among cases in the same anatomical zone. Significant differences were found between caudal and rostral CSF and root thresholds, respectively. No significant differences were found between expert and non-expert observers. Average max/min CSF/root threshold values were around 1.30 but average max/min estimated CSF volumes were around 1.15. Great interindividual CSF volume variability was detected among cases (max/min volumes 1.6-2.7). CONCLUSIONS. The selection of maximal-minimal thresholds leads to a range in CSF volume estimates that likely contains the real CSF volume value. High interindividual variability addresses the need to calculate CSF lumbosacral volumes prior to certain intrathecal procedures.

ABBREVIATIONS

3D=Three-dimensional

KEYWORDS

MRI, threshold, cerebrospinal fluid, lumbosacral region

1. INTRODUCTION

Lumbosacral cerebrospinal fluid (CSF) measurements are relevant for several clinical purposes. Previous studies based on MRI have shown high variability among subjects^{1,2,3,4,5,6,7,8}, which may partially explain some of the inconsistency in anesthetic effects among patients. Such variability justifies the need to advance in individualized lumbar CSF volume estimation prior to certain intrathecal procedures like oncologic treatments in young patients, for instance, with the aim to reduce possible side effects. Anesthesiologists will need radiologists for such estimations from neuroimaging and anatomical experts must provide the basis for such MRI-based approach.

The required technology is already available: 3D reconstruction software uses to be attached to MRI equipment and semiautomatic 3D reconstruction and volume quantifications are quick after threshold selection^{7,8}. Some MR based approaches are also being proposed for the routine study of neurologic pathologies ⁹ or for systematic 3D reconstructions prior to spinal surgery¹⁰, as examples.

Furthermore, the neuroimaging process itself may also be a source of variability. Among different variables, the partial volume averaging effect must be taken into account. This effect occurs in voxels that share the boundary zone of two adjacent tissues: CSF and cauda equina nerve roots in the lumbosacral spinal canal. Such voxels will show a gray value between the gray values of the two structures. Notice that different teams may show differences of a 10-17% when estimating CSF lumbosacral volumes in the same cases due to different threshold selection, even when phantom volume estimates match in more than 94%⁸. Thus, the decision on whether to assign the voxels to CSF or roots may affect the final volume estimations.

Some previous studies reported a partial volume averaging effect between the CSF and surrounding structures, such as lumbar or cervical spinal cord ^{1,2, 6,8,11}, brain tissue around

ventricles¹², cerebral aqueduct¹³ or cerebral *gyri¹⁴Refer refs llavors*. However, no previous reports have analyzed the partial volume effect in the borderline zones between nerve root and CSF in the lumbosacral spinal canal or the criteria for selecting segmentation thresholds. Thus, we have investigated the definition of concrete anatomical criteria in threshold selection in this zone.

Here, we defined threshold selection criteria according to secure CSF and root area selection by means of visual anatomical identification, and quantified its degree of influence in final volume estimates.

2. MATERIAL AND METHODS

The study was approved by the "Autoreference Clinical Research Ethics Committee" and informed consent was obtained from patients suffering low back pain, with absence of morphological changes in MR neuroradiological reports. Detailed data on patient gender, height and weight and about MR acquisitions and phantom characteristics were presented previously^{7,8}.

Briefly, axial sequence acquisitions were grouped into two aligned adjacent blocks of 130 mm, a caudal and a rostral MR block, extending from the lowest end of the dural sac to the lower thoracic vertebrae (T_{11} or T_{10}), depending on the height of patients. MR images were acquired at 16 bits and exported in DICOM format. Files were analyzed using Amira v5.2 3D software (Mercury Co, Boston, USA), installed in a Dell Precision graphic station. Volume estimates of the two phantoms matched in 98.97% and 101.51% after volume estimation by manual delimitation of cauda equina and dural sac structures⁷. The T1 Fast Field Echo sequence allowed a 3D reconstruction of the dural sac volume of interest (VOI). The T2 weighted sequence was used for CSF and nerve root volume estimations within that pre delineated VOI.

2.1. Studied regions

In order to homogenize threshold selection and volume comparisons within the lumbosacral zone, two blocks of 50 slices -3.25 cm height- were selected in each patient. The caudal block ended caudally at the level of the L5-S1 intervertebral disk while the second block ended caudally at the level of the middle L3 vertebra.

In caudal and rostral blocks, cauda equina roots had a different distribution within the dural sac: in the caudal block, roots are located in the lateral parts (Fig. 1A), while in the rostral block roots are located dorsally (Fig. 1E).

The variability in the vertebral level of the conus medullaris end did not allow to prepare homogenized blocks of the conus region. However, thresholds were also tested in that zone.

2.2. Histogram of the grayscale range

The histogram of the dural sac blocks was generated (Fig 2) to determine the grayscale range and their frequency distribution. Grayscale range was approximately 0–2300 in cases 3-7 and 0-500 in cases 1 and 2, which were arithmetically rescaled by the 3D software to homogenize thresholds among cases. Data window was adjusted in all cases to the maximal gray value prior to threshold selection.

2.3. Thresholds

Decision-making criteria were predefined prior to CSF or nerve root-conus medullaris threshold selection.

-'Maximal CSF threshold': the 'white' voxels are selected in a slice in the middle of the block. The threshold value is dynamically increased until at least one voxel inside a secure CSF area, anatomically identified, is not selected (Fig. 1 B, F). Then, a threshold just below that rate is initially selected. All the slices of the block are then visualized and threshold value is adjusted until no secure CSF area remains unselected in any of the slices (Fig. 1, C, H). The resulting threshold value will finally be chosen to be applied to the whole block.

-'Minimal root threshold': the slice in the middle of the block is initially visualized and the cauda equina root area is selected but not gray voxels in the boundary zone with CSF (Fig. 1, D, I). All the slices of the block are then visualized to ensure that the selected area is consistent among slices and that no secure CSF area is selected in any of them. Threshold value is dynamically adjusted if necessary. The final threshold value will be applied to the whole block.

A second observer, not familiarized with anatomy nor neuroimage analysis, quantified also the CSF thresholds, with the only indication to choose threshold values below those selecting secure incorrect area along the different block slices, and also root thresholds, with the indication of selecting root area but not adjacent gray voxels –less than five minutes training-.

2.4. Volumes

The application of the selected threshold to the dural sac VOI allows CSF and root tissue volume calculations.

Given a CSV volume estimation from applying the 'maximal CSF threshold', indirect root volumes = Sac volume - CSF volume.

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6

2.5. Statistical analysis.

SPSS.21 (IBM, NY, USA) was used for statistical analysis. After confirming normality using either Kolmogorov and Saphiro-Wilk test for small samples, Paired t-test was used for threshold and volume comparisons. Data were also analyzed with the non-parametric Wilcoxon W test. The Pearson correlation coefficient was used for interobserver threshold comparisons. A max/min rate was calculated for threshold values and the resulting CSF and nerve root volumes estimates after applying each criterion and for each case (Tables 3).

3. RESULTS

Detailed segmentation thresholds are summarized in Table 1 and resulting volumes in table 2. Fig. 2 shows examples of histograms of the grayscale values within the dural sac in caudal and rostral blocks, including the selected CSF and cauda equine root thresholds.

3.1. Histogram of the dural sac content

The histogram of gray values within the dural sac showed a range of grayscale range values between 0 and 2300. A peak curve around 1500-2000 was present in both caudal and rostral blocks, while rostral blocks showed another peak curve around 500.

In caudal blocks, maximal CSF thresholds tended to be located at the beginning of the peak curve, while minimal cauda equine root thresholds had a less consistent distribution in the adjacent flattered shape area of the histogram.

In the rostral blocks, maximal CSF thresholds tended to be located in the middle zone between peaks while minimal cauda equine root thresholds tended to be located at the end of the first peak curve.

3.2. Thresholds in anatomical regions.

In the caudal lumbar region, significant differences were found between maximal CSF thresholds (range 1160-1599) and root thresholds (range 911-1120, *P*=0.002).

In the rostral lumbar region, significant differences were found between maximal CSF thresholds (range 885-1426) and root thresholds (range 814-971, P=0.008).

Significant differences are found between thresholds in the caudal and rostral blocks, for either CSF (p=0.005) and root thresholds (P=0.014) (table 2). Wilcoxon test also showed significant differences for all those comparisons (p=0,018)

Average max/min thresholds for single cases in the caudal block were 1.38 ± 0.19 and 1.27 ± 0.18 in the rostral block.

Correlation of Pearson coefficient between expert and non-expert observers was of 0.78-0.87 for maximal rostral and caudal CSF thresholds, respectively and 0.28-0.34 for minimal caudal and rostral cauda equina root thresholds, respectively. No significant differences were found between CSF and root thresholds between expert and non-expert observers in caudal or rostral blocks (P=0.20-0.99, respectively).

3.3 Volume variability applying different thresholds in standardized blocks.

A high interindividual CSF volume variability was detected among cases: within the same criterion, the max/min volume rate among cases ranged between 2.2-2.7 in caudal blocks, depending on the threshold criterion, and 1.6-2.1 in rostral blocks (Table 2).

In the caudal standardized blocks, CSF volumes resulting of applying maximal CSF thresholds (range 2.6-7.1 cm³) showed significant differences (P=0.002) regarding those obtained after application of minimal root thresholds (range 3.3-7.5 cm³) (table 3). Similar differences were found in the rostral standardized block (P=0.006), when comparing CSF volumes obtained from CSF thresholds (range 2.9-6,1 cm³) and those from root thresholds (range 3.7-6,2 cm³).

Root volumes in the caudal block were in a the range of 1.3-1.5 cm³ when using root thresholds and 1.6-2.3 cm³ when using CSF thresholds, while volumes in the rostral block were in the range 1.9-2.8 when using root thresholds and in a range of 1.9-3.4 cm³ when using CSF thresholds. Comparisons among root volumes showed the same *P* values as comparisons among CSF volumes.

4. DISCUSSION

It's important to analyze to what extent the image analysis itself may contribute to variability in CSF or root volume estimates. In this study we assessed to which extent the partial volume effect affects such estimations. Voxels that include the borderline zone of two adjacent structures will show a gray value between the gray values of both structures. It will be possible to enhance the precision of the estimations when higher resolution MR images are available. Meanwhile, assumptions and calculations for different threshold criteria can be made to interpret the voxels with intermediate gray values. Significant differences using parametric tests were consistent with significant differences found when using non-parametric tests. Since n>5 and a normal variable is required to use parametric tests and significant differences were already found with the cases available with both methods, the study had the enough power to detect statistical differences and was focused in the patients of which we already had previous detailed anatomical knowledge from tough manual delineation⁸

Here, the distance between slices (0.65 mm) is less than in previous reports on CSF volume estimation: 0.7 mm^6 , 1 mm^5 , $5 \text{ mm}^{1,4}$ and 8 mm^2 . Furthermore, images acquired at 16 bits allow a wide gray scale range (0–4300) which is also higher than those previously used -8 bits, range: 0–255 ⁵. Thus, it is expected that final volume estimates could be more precise. Furthermore, it is the first study where criteria for selecting thresholds are described.

4.1. Histograms vs. visual observation

Threshold segmentation is usually based on decision algorithms from histogram analysis of the gray scale frequency distribution (see ^{15,16,17,18} as examples). Here, threshold selection was complemented with anatomical criteria and visual observation: when studying CSF, the absence of selected voxels outside the CSF anatomical area was required and vice versa when selecting roots, combined with reduced selection of grey voxels in the CSF-root borderline (Figure 1). When drawing the resulting thresholds in the corresponding histogram curves figures, a consistent but not precise distribution of CSF maximal threshold values was seen. Such imprecision was more diffuse in root thresholds. Thus, combining histogram visualization itself with right visual anatomical selection, separating the analysis in caudal and rostral lumbar zones, would lead to more reliable estimations.

4.2. Thresholds

Previous studies of automatic spinal cord area and volume quantification involved automatic spinal cord delimitation by edge detection¹¹ assuming a straight cord position, with its long axis perpendicular to the axial plane. Those conditions are not followed by the oblique trajectory of lumbosacral cauda equina roots leaving the spinal canal. Furthermore, the multiple 'edges' of multiple cauda equina roots with multiple voxels affected by the partial volume averaging effect makes more difficult such approach. We have finally focused in finding thresholds that select voxels that could belong for sure to either root or CSF, assuming that the difference between the resulting volumes regarding the dural sac volume would be an indirect estimation of voxels affected the partial volume averaging effect.

Although thresholds decision is made by interactive visualization of 2D images, once a concrete threshold is applied to the RM stack of slices, the resulting reconstructed structure operates in the 3D MRI image space with 3D continuity, where the volume calculations are made by the same software.

Minimal root threshold values assure that only the root structure is selected, since all surrounding gray voxels are assigned to CSF, but probably underestimate root volumes and overestimates CSF volumes. In the other hand, maximal CSF threshold values probably underestimate CSF and overestimate root volumes. CSF and root threshold comparisons in the same zone showed significant differences, showing max CSF/min root rates of up to 1.58, which also lead to different estimated volumes. The real volume values are expected to be between the range obtained after applying maximal CSF and minimal root threshold criteria, which lead to a

11

secure range of resulting volumes. If high precision is desired, gray voxels in the roots and anterior dural sac-CSF interfaces should be manually assigned.

Since there are significant differences between the same threshold criteria in the rostral and caudal lumbar zones and also with the conus medullaris zone, semiautomatic quantification of the whole lumbosacral volumes must separate volume estimations in the different anatomical regions if precision is desired. Since no significant differences were found between expert and non-expert observers when selecting thresholds, and considering that one of the observers had no experience in neither anatomy nor neuroimaging analysis, it appears that threshold selection following the proposed criteria is easy and quickly reproducible.

4.3. Volumes.

To allow comparability, the detailed volume calculations were made in two standardized 50 slices-3.25 cm blocks, comparable to the height of a vertebral segment, in either the caudal or rostral lumbar zone. Since the vertebral level of the conus medullaris is not consistent among cases ^{19,8}, that zone was excluded of the homogenized comparisons. However, the finding of different threshold values in that region suggests that volume estimations must be also studied separately.

Different CSF or root thresholds lead to different estimated volumes: the mean max/min rate of CSF volumes applying different criteria was 1.14-1.17 in the rostral and caudal lumbar zones, respectively. However, high interindividual variability was also detected among cases for a single criterion: max/min volume rate among cases reached 2.7 for the 'maximal CSF threshold' in the caudal lumbar region.

The lack of a gold standard technique that allows comparability of the obtained results with the real CSF and root volumes doesn't allow quantifying the exact precision of the technique. However, it is based on a range of 'secure' thresholds, since wrong thresholds are just above and below the selected ones. Thus, the difference between the maximal-minimal volumes is an indirect measure of the precision of the estimation.

Altogether, threshold variability, around 30%, only affects CSF volume variability in about 15%, while true interindividual variability is about ten times higher, reaching up to 170%. Such high interindividual variability in volumes is consistent with previous reports of CSF estimations ^{1,2,3,4,5,6}, even when concrete vertebral segments are studied and it's independent on the patient size ⁸. Furthermore, high intraindividual variability (up to 41% combining hyperventilation and abdominal compression) has already been described in four volunteers ³.

Here, CSF and root thresholds were applied in semiautomatic predelineated dural sac VOIs, which included detailed manual editing. However, while CSF is easily selected in T2, the rest of dural sac structures show a gray scale values similar to the value of the surrounding structures. Thus, during clinical assessment, radiologists will not be able to estimate volumes directly after maximal and minimal thresholds selection, since surrounding structures would result also selected when applying minimal root thresholds. An approximate way of estimating lumbosacral CSF volumes could be to use the maximal CSF criterion for selecting its specific threshold in T2, individualized in caudal and rostral lumbar regions, and applying an empiric reduction of about a 15% in the final estimated volume to get the 'secure' range, considering with caution those results. If further time is available, the reconstruction of the dural sac is mandatory to use the methodology of maximal CSF-minimal root threshold selection.

13

Altogether, this is the first study that includes a description of how thresholds were decided in an easy reproducible way in the lumbosacral region and quantified the resulting volume variability. Future studies are needed to assess volumes under different physiological and clinical conditions and to assess if the use of an averaging value within the secure max-min range could be useful in medical situations, taking in consideration the high intraindividual variability³ in real conditions.

5. Conclusions

The high variability in lumbosacral CSF volumes justifies the need to advance in the quantification of volumes from MRI prior to certain intrathecal drug administration procedures to reduce side effects. Technology already allows individualized estimations: predefined criteria may allow easy and reproducible threshold selection and volume estimations in the different lumbar regions. True values will be within the range of volumes that result from using 'maximal-minimal' threshold criteria.

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TABLES

	Caudal homogenized block			Rostral homogenized block			
	Thrhes	holds	Thresholds				
Case	CSF max	Root min	Max/min	CSF max	Root min	Max/min	
1	1160	1102	1.05	911	895	1.01	
2	1232	998	1.23	855	814	1.08	
3	1233	911	1.35	1185	872	1.35	
4	1512	956	1.58	1127	906	1.24	
5	1599	1009	1.58	1194	971	1.22	
6	1580	1120	1.41	1303	874	1.49	
7	1469	1011	1.45	1426	953	1.49	
Mean	1397.8	1015.3	1.38	1147.3	897.8	1.27	
SD	183.9	74.4	0.19	196.0	52.8	0.18	
Max/min	1.37	1.22		1.61	1.19		

Table 1. Threshold values in caudal and rostral lumbar anatomical regions.

Max/min threshold values among cases following the same criterion are given below SD while max/min rate of threshold values for each case are shown at the last right column.

	Caudal homogenized block		Rostral homogenized block				
Thresholds:	CSF max	Root min	Max/min	CSF max	Root min	Max/min	
Case	Lumbosacral CSF volumes						
1	5.2	5.3	1.02	6.1	6.2	1.01	
2	7.1	7.5	1.06	4.9	5.2	1.05	
3	3.5	3.9	1.14	3.2	3.9	1.18	
4	3.5	4.3	1.22	5.0	5.4	1.08	
5	4.8	5.8	1.21	3.9	4.4	1.12	
6	2.6	3.3	1.28	2.9	3.7	1.27	
7	3.2	4.2	1.28	3.3	4.3	1.31	
Mean	4.3	4.9	1.17	4.2	4.7	1.14	
±SD	1.5	1.4	0.10	1.2	0.8	0.11	
Max/min	2.7	2.2		2.1	1.6		
Case		Lumbo	sacral cauda	equina root	volumes		
1	1.6	1.5	1.06	1.9	1.9	1.0	
2	1.8	1.4	1.30	2.7	2.5	1.1	
3	1.9	1,4	1.34	3.4	2.8	1.2	
4	1.9	1.1	1.69	2.6	2.2	1.2	
5	2.0	1.0	2.02	3.1	2.6	1.2	
6	2.0	1.3	1.58	3.0	2.2	1.3	
7	2.3	1.4	1.66	3.1	2.4	1.2	
Mean	1.9	1.3	1.52	2.8	2.4	1.2	
±SD	0.2	0.2	0.31	0.4	0.3	1.1	
Max/min	1.5	1.4		1.7	1.4		

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Table 2	CSF a	nd roc	t volu	nes (in	cm^{3})

Resulting from applying thresholds in the standardized blocks of 50 slices. Caudal block: ending caudally at the L5-S1 intervertebral disk. Rostral block: ending caudally in middle L3 vertebra. Max/min volumes among cases following a concrete criterion are shown below SD, while max/min estimations for each case are calculated in the last right column for each anatomical region.

FIGURE LEGENDS

Figure 1. Anatomical regions and area selected -magenta- with wrong and right CSF and root thresholds. Cauda equina roots (red arrows) are located laterally within the dural sac in caudal lumbar region (A) and dorsally in the rostral lumbar region (E). For maximal CSF threshold selection, threshold is dynamically increased until a secure CSF area, anatomically identified, becomes unlabeled (white arrows, B, F). Then, a threshold value below that one is chosen (C,G); the rest of the slices of the block are verified for consistent CSF selected area and adjusted to avoid any unselected CSF voxels, even if the root-CSF interface results is slightly occupied in some slices (G). For minimal root threshold voxels, selection includes secure root area but not adjacent gray voxels in the boundary root-CSF interface (black arrows, D,H). Scale bar: 1cm.

Figure 2. Histogram of the grayscale range of the dural sac content of caudal (left) and rostral (right) homogenized blocks. Cases 3 and 5 were chosen as examples. Orange lines: root thresholds. Blue lines: CSF thresholds. Notice that CSF thresholds tend to be located at the beginning of the second peak curve while root thresholds tend to localized at the end of the first curve in the rostral block. However, the localizations are not precise enough to allow threshold decision only from histogram examination.