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

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RUNNING TITTLE: lumbosacral CSF and root threshold selection.

KEYWORDS:

MRI, threshold, cerebrospinal fluid, lumbosacral region

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ABSTRACT

BACKGROUND AND PURPOSE. The high variability of CSF volumes partly explains the inconsistency of anaesthetic effects, but may also be due to image analysis itself. In this study, criteria for threshold selection are anatomically defined. METHODS. T2 MR images (n=7 cases) were analyzed using 3D software. Maximal–minimal thresholds were selected in standardized blocks of 50 slices of the dural sac ending caudally at the L5-S1 intervertebral space (caudal blocks) and middle L3 (rostral blocks). Maximal CSF thresholds: threshold value was increased until at least one voxel in a CSF area appeared unlabeled and decreased until that voxel was labeled again: this final threshold was selected. Minimal root thresholds: thresholds values that selected cauda equina root area but not adjacent gray voxels in the CSF–root interface were chosen. RESULTS. Significant differences were found between caudal and rostral thresholds. No significant differences were found between expert and non-expert observers. Average max/min thresholds were around 1.30 but max/min CSF volumes were around 1.15. Great interindividual CSF volume variability was detected (max/min volumes 1.6-2.7). CONCLUSIONS. The estimation of a close range of CSF volumes which probably contains the real CSF volume value can be standardized and calculated prior to certain intrathecal procedures.

BACKGROUND AND PURPOSE

Lumbosacral cerebrospinal fluid (CSF) measurements based on MRI have shown high variability among subjects [1,2,3,4,5,6,7,8], which may partially explain 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. MRI scanners equipped with 3D reconstruction software allow quick semiautomatic 3D reconstruction and volume quantifications [7]. For example, MR-based spinal cord segmentation approaches have been proposed for the routine study of multiple sclerosis [9] or for systematic 3D reconstructions prior to spinal surgery [10].

The neuroimaging process itself may be a source of variability. Among different variables, the partial volume averaging effect must be taken into account: voxels that share the boundary zone of two adjacent tissues will show a gray value between the gray values of the two structures, here CSF and cauda equina nerve roots within the lumbosacral dural sac. The decision on whether to assign the voxels to CSF or roots may affect the final volume estimations. Studies reporting a partial volume averaging effect between the CSF and surrounding structures [1,2,6,11] do not describe the criteria for selecting segmentation thresholds.

We have investigated the definition of specific anatomical criteria in threshold selection in the lumbosacral zone and have studied their influence on volume estimations in order to improve the comparability of the results of research studies and to provide a basis for easy CSF volume estimation prior to intrathecal procedures.

METHODS

The study was approved by the “Clinical Research Ethics Committee”. MR from patients suffering low back pain, with absence of morphological changes in MR neuroradiological reports were studied (n=7). Detailed data on patient gender, height and weight and MR acquisitions and phantom characteristics (matching 98.97% and 101.51%) have been were presented previously. The T2 weighted sequence was used for CSF and nerve root volume estimations within the pre delineated dural sac volume of interest (VOI) [7,8].

1.Studied regions

In order to homogenize the conditions for comparisons of thresholds and volumes within the lumbosacral zone, two blocks of the same size, 50 slices (3.25 cm height), were selected in each patient. The inferior level of the caudal block ended at the L5-S1 intervertebral disk while the inferior level of the rostral block ended at the middle L3 vertebra. In the caudal block, roots are located in the lateral parts (Fig.1A), while in the rostral block roots are located dorsally (Fig.1E).

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.

3. Thresholds and volumes

Data window was adjusted in all cases to the maximal gray value prior to threshold selection. Threshold selection criteria were defined according to unambiguous CSF and root area selection by means of visual anatomical identification. 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 CSF area, anatomically identified, is not selected (Fig. 1 B, F). The threshold is then dynamically reduced until the voxel in the CSF area again appears as labeled. This final threshold is then selected. All the slices of the block are visualized. If any CSF area appears unselected in any of the slices, the threshold value is further increased until full CSF selection (Fig. 1, C, H). This final threshold value will 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 CSF area is selected in any of them. If any CSF area appears selected, the threshold value is further decreased until no CSF area appears labeled anywhere in the block. The final threshold value obtained will be applied to the whole block for automatic volume quantification.

A second observer, not familiarized with anatomy or neuroimage analysis, also quantified the CSF thresholds, with a brief indication to choose high threshold values, below the appearance of unlabeled voxels in the CSF area (incorrect thresholds), along the different block slices, and also root thresholds, selecting the middle zone of the root area but not adjacent gray voxels in the borderline zone with the CSF.

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

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.

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, including selected thresholds.

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

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 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 between 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 showed significant differences compared with those obtained after application of minimal root thresholds (*p*=0.002) (table 3), with an average max/min ratio of 1.17. Similar differences were found in the rostral standardized block when comparing CSF volumes obtained from CSF thresholds and those from root thresholds (*p*=0.006) with an average max/min ratio of 1.14. Comparisons between root volumes showed the same *p* values as comparisons between CSF volumes.

DISCUSSION

The image analysis itself may contribute to variability in CSF or root volume estimates. This is the first study where criteria for selecting thresholds are described.

Here, the distance between slices (0.65 mm) is less than in previous reports on CSF volume estimation: 0.7 mm [6], 1mm [5], 5 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.

Significant differences were found between threshold values and estimated volumes using both parametric and 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 [12] from tough manual delineation [8].

1. Histograms vs. visual observation

Threshold segmentation is usually based on decision algorithms from histogram analysis of the gray scale frequency distribution (see [13,14,15,16] as examples). Here, threshold selection was complemented with anatomical criteria and visual observation. When drawing the resulting thresholds in the corresponding histogram curves figures, a consistent but not precise distribution of threshold values was seen. 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.

2. Thresholds

Previous studies of spinal cord area and volume quantification involved automatic spinal cord delimitation by edge detection [12] assuming a straight cord position, with its long axis perpendicular to the axial plane. Those conditions were not reproduced by the oblique trajectory of the multiple lumbosacral cauda equina roots leaving the spinal canal.

Maximal CSF threshold values probably underestimate CSF volumes, since voxels surrounding roots, that probably contain a certain amount of CSF, are not included. But an unambiguous value of the minimal volume of the CSF present is obtained. Considering its variability, with a ratio of 2.2 between maximal and minimal estimates among cases, and its implications in the dilution volume of intrathecal drugs, the estimation of a minimal CSF volume is of special interest. In minimal root threshold values, the root structure is selected and all the surrounding gray voxels are assigned to CSF, thus possibly underestimating root volumes and overestimating CSF volumes. However, in upper lumbar levels the minimal root threshold may select most of the dorsal area of the dural sac, including some less intense gray voxels where a certain amount of CSF probably exists. Nevertheless, the number of these voxels is inferior to the number of grey voxels in the CSF-root interface, and thus, it has been considered that it would still represent a probable minimal value of root volume. Since one is based on an underestimation of CSF and the other on a possible overestimation, the real volume values are expected to be between the range obtained after applying maximal CSF and minimal root threshold criteria.

CSF and root threshold comparisons in the same zone showed significant differences, with max CSF/min root rates of up to 1.58, which also lead to different estimated volumes. 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.

No significant differences were found between expert and non-expert observers when selecting thresholds. 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.

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 [8,17], that zone was excluded of the homogenized comparisons.

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. Our previous reported CSF and root volumes per vertebral level from T12 to the lower sacral levels [8] are within the highly variable range of CSF volumes of previous estimations using MRI [2]. However, our average root volume estimates in MRI of living humans [8] are slightly higher than those of a previous study based on nerve root measurements in 8 hours dead subjects [18] ($10.7 \pm 0.8 cm^3$ vs $7.1 \pm 0.3 cm^3$, respectively), about $0.5 cm^3$ per vertebral segment -similar to the homogenized block size-. The differences between the two studies (58 vs 36.5 years of the subjects, volumetric analysis from 3D reconstructions vs inference of volume from average cross-sectional area, dead vs living subjects, etc.) could explain the slight difference in the absolute measure of such a variable structure.

Since our estimations are based on a range of thresholds that are chosen above or below incorrect minimal and maximal wrong thresholds, the difference between the maximal–minimal volumes is an indirect measure of the precision of the estimation.

Here, CSF or root thresholds lead to different estimated volumes in the same cases: the mean max/min rate of CSF volumes per case 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.

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].

Here, CSF and root thresholds were applied in semiautomatic manually predelineated dural sac VOIs [8]. An approximate way of routinely estimating the lumbosacral CSF volume range during clinical assessment could be to use the maximal CSF criterion for selecting its specific threshold in T2, individualized in caudal and rostral lumbar regions, and to cautiously apply an empiric reduction of around 15% in the final estimated volume. Future studies are needed to assess volumes under different physiological and clinical 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. Predefined criteria may allow easy and reproducible threshold selection ranges from MRI and volume estimations in the lumbar region, thus facilitating the comparability of results from future studies of CSF and root lumbosacral volumes.

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

	Caudal homogenized block			Rostral homogenized block		
	Thresholds			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	

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.

Table 2. CSF and root volumes (in cm^3).

	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			Lumbosacral 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	

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.

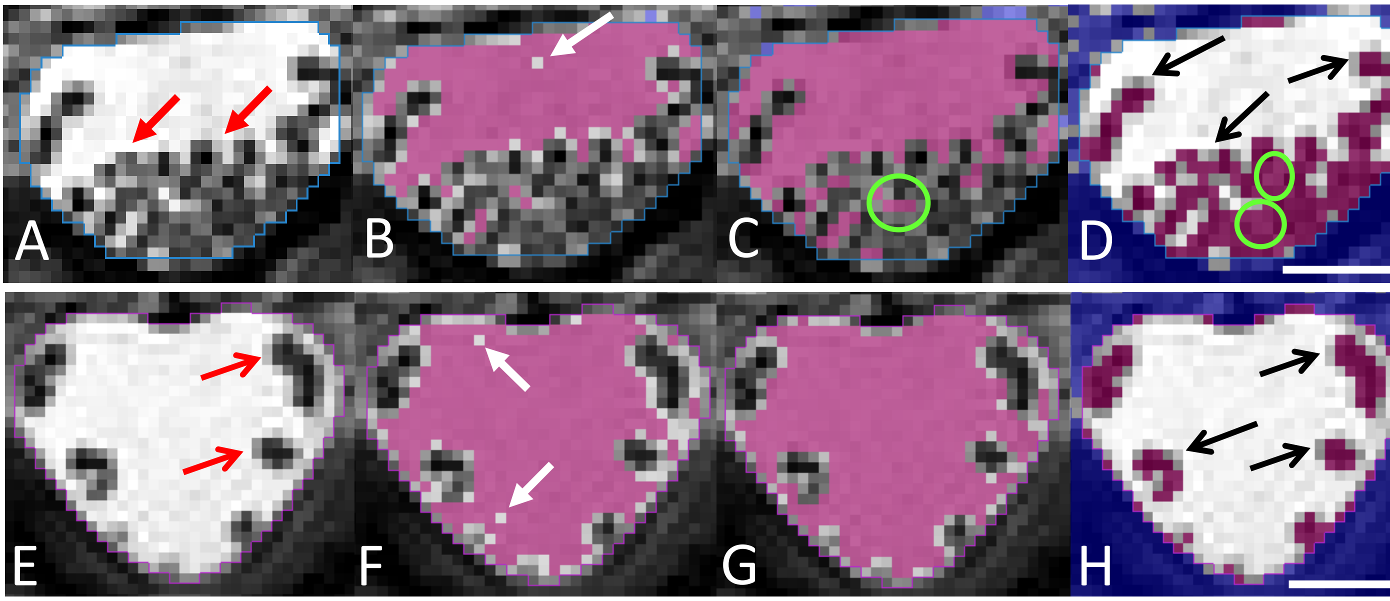

Figure 1. Anatomical regions and area selected – magenta - with wrong (B,F) and right CSF (C,G) and root (D,H) thresholds. Cauda equina roots (red arrows) are located dorsally in the rostral lumbar region (A) and laterally within the dural sac in caudal lumbar region (E). Maximal CSF threshold selection: the threshold is dynamically increased until a voxel in a CSF area, anatomically identified, becomes unlabeled (white arrows, B, F) and then decreased until the voxel is labeled again (C,G). This final threshold value is chosen; the rest of the slices of the block are checked to ensure that there are no unselected CSF voxels, even if the root-CSF interface is slightly occupied in some slices (C, green circle). Minimal root threshold: the selection includes voxels within the root area, but not adjacent grey voxels in the root-CSF interface (black arrows, D,H). Although a few voxels are included in which a certain amount of CSF probably exists (D, green circles), they are less numerous than the grey voxels in the root-CSF interface. Scale bar: 1cm.

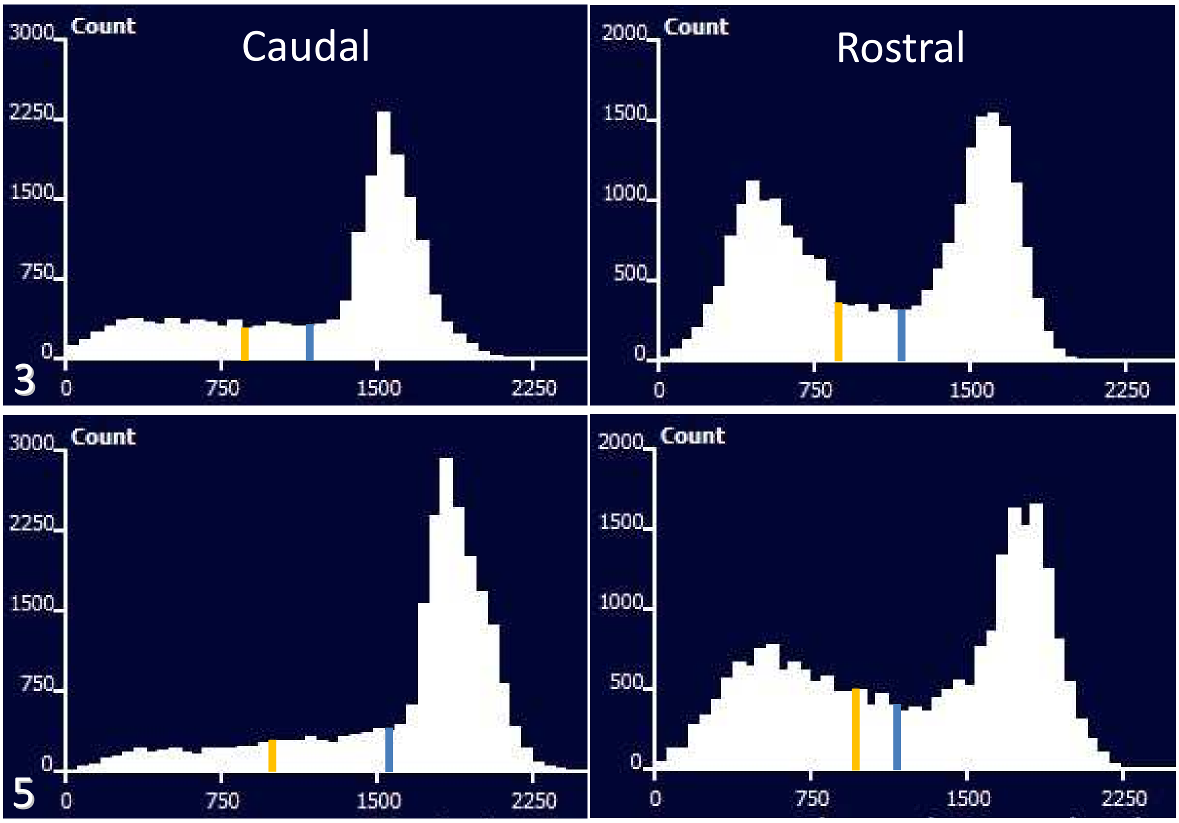

Figure 2. Histogram of the grayscale range of the dural sac content of caudal (left) and rostral (right) homogenized blocks. Cases 3 and 5 were chosen as examples. Orange lines: root thresholds. Blue lines: CSF thresholds. CSF thresholds tend to be located at the beginning of the second peak curve while 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.