ABSTRACT. We describe a hybrid approach to the volumetry of intracerebral and entire intracranial CSF spaces, combining two imaging techniques. Ultra-fast and reproducible quantification of intracranial liquor volumes is carried out based on T2-weighted MR images. Isotropic T1-weighted data is used as a basis for robust semi-automatic three-dimensional segmentation procedures. Variability of the proposed method, including image acquisition, is evaluated on volunteers and phantoms to be well below 2%. The total time required for image analysis including interaction is below 5 minutes.

KEYWORDS: Neuroimaging, MRI, Volumetry, CSF, Cerebral Ventricles

1. INTRODUCTION

Since the seminal work of Galen of Pergamum (AD 129–216), cerebral liquor dynamics have been object to concentrated medical research [1]. Early estimates of the cerebrospinal fluid (CSF) volumes, derived from post-mortem anatomical cast studies, have been reported fifty years ago [2]. By 1970, various linear measures have been used, however these often did not correlate well with changes in volume [3, 4]. Modern volumetric methods based on computed tomography emerged with a series of publications in 1978 [5–7]. At the same time, mathematical models of the cerebrospinal fluid system have been developed to study intracranial liquor kinetics [8]. In the late 1980s, first quantitative studies based on magnetic resonance imaging (MRI) were published. An elegant method to derive separate measures for intracranial and ventricular CSF volumes from two sagittal MR projection images was proposed by Grant et al. [2, 9]. While overall volumes can be reliably estimated by such a method, systematic errors occur for the ventricular CSF spaces due to anatomical misinterpretation of periventricular CSF spaces. Furthermore, contra-lateral differences can not be derived. More recent approaches use semi-automatic image processing algorithms for the analysis of MRI data containing a larger number of slices [10–13]. However, most approaches require time consuming user interaction induced by slice-based image processing. Therefore, the number of slices is kept low, increasing the slice thickness to several millimeters. This
results in an imprecise anatomical representation of thin structures in addition to important volumetric inaccuracy caused by partial voluming [5].

The purpose of the presented project is to reproducibly measure the volumes of intra- and extracerebral liquor spaces based on MRI. Further goals are to efficiently segment and visualize the intracerebral liquor spaces.

In order to be applicable in a clinical environment, the developed methods should be [14]:
- Fast – to require less than 10 minutes for image analysis,
- Flexible – to work robustly for normal and abnormal anatomy, and
- Reproducible – to show less than 5% relative variation.

No suitable method for routine clinical use has been available so far, due to the anatomical complexity of the intracranial liquor spaces and the lack of fast and reliable segmentation procedures. Clinical indications for volumetry of intracranial CSF spaces include congenital abnormalities, normal pressure hydrocephalus (NPH), postoperative hydrocephalus, or cerebral atrophy. Quantification of atrophy due to neurodegenerative diseases, demyelinating diseases, cognitive dysfunction, psychiatric diseases, and after severe head injury is possible, thus allowing therapy-monitoring.

2. METHODS

Independent measurements are performed for intracranial and intracerebral liquor spaces. A hybrid approach has been designed to combine the advantages of different acquisition protocols. Figure 1 shows a systematic overview. All image data has been acquired on a Siemens Magnetom Vision Plus at 1.5 T.

![Figure 1. Dual image processing and analysis pipeline. Two independent datasets are acquired. Post processing is performed in three successive steps: 1. pre processing to reduce the amount of data and to account for background noise, 2. interactive segmentation to accurately define the anatomical structures of interest, and 3. automatic histogram analysis.](image-url)
Figure 2. Healthy volunteer (35 yo woman). left: 3 orthogonal views of isotropic T1-weighted MRI data, slice thickness 1mm. right: Hybrid rendering of ventricular segmentation result fused with brain segmentation and clipped original data.

Figure 3. Typical marker positions for segmentation of all four ventricles. Five different markers are available for ventricle labeling (R, L, 3, and 4) and region exclusion (dots). The images represent a VOI interactively selected from the data depicted in Figure 2.

2.1. Intracerebral Liquor Spaces

The volumetry of cerebral ventricles is based on a three-step approach: data acquisition, image segmentation, and computation of volume. Isotropic 3d data is acquired (Figure 2): flash 3D, T1-weighted, TR 9.7 ms, TE 4.0 ms, flip angle 20 deg, sagittal, FOV 256 mm, matrix $256 \times 256$, 160 slices, slice thickness 1.0 mm, acquisition time about 8 min.

This standard MR technique is combined with new image postprocessing and quantification methods. The thin slices provide the basis for fast 3d segmentation procedures and for minimizing partial volume effects. A 3d semi-automatic modified watershed algorithm has proven to be useful for removing extracerebral tissue from T1-weighted cranial MRI data [15]. For ventricular segmentation, the algorithm has been enhanced by an unrestricted number of point markers that can be interactively located to accurately define the ventricular anatomy (Figure 3). A few markers each defined by a single mouse click, serve as initial information for the segmentation algorithm that automatically traces the borders of all four ventricles in 3d. Processing times are less than 1 second on a standard PC for a typical region of
interest (1 million voxels). A 2d color overlay and an interactive 3d volume rendering are used to verify the segmentation result. The complete segmentation procedure including user interactions takes 2 min on the average for all 160 slices.

The volume of the segmented ventricles can be directly computed from the corresponding regional image histograms. In a fully automatic manner, those are estimated simultaneously within a few seconds. Noise, image non-uniformity, and partial volume effects are taken into account. The expected measurement error is calculated based on the image quality.

2.2. Intracranial Liquor Spaces

For volumetry of entire intracranial CSF volumes one projection dataset is acquired: RARE, heavily T2-weighted, TR inf., TE 1100 ms, flip angle 150 deg, bandwidth 156 MHz, sagittal, FOV 230 mm, matrix 256×240, 1 acquisition, slice thickness 160.0 mm, standard head coil, acquisition time 2.8 sec. Line and point markers are used to interactively define the ROI (Figure 4a, b). After automatic background subtraction, the gray value is supposed to be directly proportional to the liquor volume represented by a certain image element. Additional noise and contributions from other tissues can be neglected due to its much shorter T2 values.

Table 1. Cerebral ventricular volumetry: Evaluation of total reproducibility on one volunteer (38 yo man) that independently underwent MRI 5 times (acquisition A₁–A₅), different head positions, 30 min rest between acquisitions, volumes in ml.

<table>
<thead>
<tr>
<th></th>
<th>A₁</th>
<th>A₂</th>
<th>A₃</th>
<th>A₄</th>
<th>A₅</th>
<th>Mean (SD)</th>
<th>SD / mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>17.96</td>
<td>17.83</td>
<td>17.73</td>
<td>18.01</td>
<td>17.83</td>
<td>17.87 (0.11)</td>
<td>0.63 %</td>
</tr>
<tr>
<td>Left</td>
<td>14.37</td>
<td>14.26</td>
<td>14.06</td>
<td>14.37</td>
<td>14.23</td>
<td>14.26 (0.13)</td>
<td>0.88 %</td>
</tr>
<tr>
<td>3ʳᵈ</td>
<td>2.22</td>
<td>1.99</td>
<td>2.07</td>
<td>2.17</td>
<td>2.00</td>
<td>2.09 (0.10)</td>
<td>4.80 %</td>
</tr>
<tr>
<td>4ᵗʰ</td>
<td>2.64</td>
<td>2.75</td>
<td>2.60</td>
<td>2.74</td>
<td>2.78</td>
<td>2.70 (0.08)</td>
<td>2.82 %</td>
</tr>
<tr>
<td>Total</td>
<td>37.16</td>
<td>36.95</td>
<td>36.42</td>
<td>37.25</td>
<td>36.98</td>
<td>36.95 (0.32)</td>
<td>0.87 %</td>
</tr>
<tr>
<td>Lateral</td>
<td>32.33</td>
<td>32.12</td>
<td>31.79</td>
<td>32.39</td>
<td>32.12</td>
<td>32.15 (0.24)</td>
<td>0.74 %</td>
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</table>

Figure 4. Volumetry of intracranial liquor volume. a: T2-weighted projection data with spherical phantom. Point and line markers are interactively used to define the ROI. b: ROI after background subtraction. c: Detail of b. d: Evaluation of temperature influence.
Table 2. Total intracranial CSF volumes: Evaluation of total reproducibility on one volunteer (28 yo man) that independently underwent MRI 9 times (acquisition A1–A9), different head positions, 20 sec rest between acquisitions, volumes in ml, compare Figure 4 a.

<table>
<thead>
<tr>
<th>A1</th>
<th>A2</th>
<th>A3</th>
<th>A4</th>
<th>A5</th>
<th>A6</th>
<th>A7</th>
<th>A8</th>
<th>A9</th>
<th>Mean (SD)</th>
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<tbody>
<tr>
<td>146.4</td>
<td>147.5</td>
<td>146.9</td>
<td>148.0</td>
<td>145.2</td>
<td>143.8</td>
<td>146.6</td>
<td>144.3</td>
<td>145.5</td>
<td>146.0 (1.4)</td>
<td>0.97%</td>
</tr>
</tbody>
</table>

3. RESULTS AND DISCUSSION

Accurate measurements of cerebral ventricular volumes can even be achieved with standard T1-weighted isotropic datasets. The need for interaction and thus the occurrence of user-induced errors are minimized by using isotropic data acquisition and automated marker-based 3d segmentation methods. The reproducibility is high (Table 1). The volume of the lateral ventricles can be measured with a variability well below 2%. The expected accuracy, that has been calculated based on the image quality, corresponds well to the standard deviation from repeated independent measurements. The complete volumetry procedure can be performed in less than 5 minutes within the clinical workflow.

The sagittal T2-weighted projection dataset provides the required information to reliably quantify intracranial CSF volumes and can be acquired within a few seconds. Reproducibility for intra- and extracerebral liquor volumes has been evaluated by repeated independent measurements on the same patients and volunteers (Table 2). Image postprocessing has been performed by two independent expert radiologists. No significant difference of measured cerebral liquor volume could be observed for different head positions. Absolute calibration has been performed by water phantoms (compare Figure 4 a). To our knowledge, water and CSF bear almost identical T1 relaxation times at identical temperatures (~ 3000 ms).

Previous results for the measurement of T1, as a means of temperature monitoring, have demonstrated a linear behavior with a coefficient of approximately 1.5% per °C [16, 17]. Similarly, T2 relaxation time will increase with temperature, besides other parameters connected with temperature, e.g., chemical shift effects. In order to estimate the degree of influence, a series of 50 ml syringes filled with pure water at different temperatures has been examined using the protocol described above. Resulting images demonstrated a significant increase of the signal by roughly 0.4% per °C at body temperature (Figure 4 d). Further studies are intended to accurately quantify this behavior in the range of 35 to 45 °C. Including calibration inaccuracy and flow artifacts, entire CSF volumes are quantified with variations of less than 4%.

4. CONCLUSION

We present a new 3d semi-automatic approach resulting in a speed-up of image acquisition and image analysis, besides improving the reproducibility compared to manual or semi-automatic slice-based evaluation. Interaction times drop from more than one hour to a few minutes. The method thus can be applied in the clinical routine. By independently measuring
intracranial and intracerebral CSF volumes, accurate estimates for extracerebral CSF volumes can be derived. A first clinical installation of postprocessing and analysis tools has been realized in November 2000 for beta testing and methodological evaluation. Clinical validation will comprise posttraumatic disorders and NPH patients.

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