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Assessment of the Cerebral Venous System from the transcondylar ultrasound window using Virtual Navigator Technology and MRI

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***Abstract*— The Chronic Cerebro-Spinal Venous Insufficiency, recently described as a possible role in Multiple Sclerosis pathogenesis, is diagnosed and classified with Echo Color Doppler (ECD) examination of the extra- and intra-cranial veins. As to the intracranial examination, the presence of reflux in the deep cerebral veins (DCVs) or in the dural sinuses is inspected, with a new insonation approach, i.e. the transcondylar window. This work describes a procedure for the co-registration of anatomical Proton Density-weighted Magnetic Resonance Images (MRI) with the intracranial ECD obtained through the transcondylar window. The procedure, preliminarily tested on 10 volunteers, allowed to assess what are the DCVs visible from this new insonation approach and their position relative to the surrounding brain tissues.**

I. Introduction

Chronic Cerebro-Spinal Venous Insufficiency (CCSVI) is a vascular syndrome recently defined by Zamboni et al. [1], who proposed an association with Multiple Sclerosis (MS) [2], with great expectation as to clinical fall-outs, yet requiring confirmation and further investigation. CCSVI consists of deoxygenated blood flow from brain and spinal veins being slowed down or blocked in its way back to the heart. This condition arises mainly from blockage in the internal jugular (IJV) and/or azygous veins [1]. The diagnosis and severity assessment of CCSVI are performed by the use of B-Mode and Echo-Color Doppler (ECD) Ultrasound of neck veins (IJVs and Vertebral Veins – VVs) and intracranial veins (Deep Cerebral Veins – DCVs, Sinuses and Veins draining subcortical gray matter), examined both in sitting and supine position [3].

The DCVs and sinuses can be imaged trough the transcranial echographic ultrasound (US) window at the level of the condyloid process of the mandible (Figure 1) [4]. This newly developed approach for the assessment of the intracranial venous system has gained particular attention within the scientific community due to its novelty and unconventional access [5], compared to the classical temporal and occipital accesses [6]. The technical difficulties in the assessment of intracranial veins through the condylar window concern their morphology and their flow characteristics. Indeed, DCVs and sinuses are located at 6-8 cm from the ultrasound probe, they are thin (diameter about 2-4 mm), and run parallel to the skull [6]. As to flow, it is slow (0.10-0.40 m/s) and strongly affected by respiratory phase (i.e. usually activated during inspiration). Finally, the US beam, constrained to the narrow transcranial window of the mandible condyloid process, is almost orthogonal to flow thus severely limiting ECD sensitivity unless proper beam steering strategies are applied. As to the last issue, the recently developed Directional Multigate Quality Doppler Profiles technology [1] [5]-[11] is increasingly being used in order to highlight the flow direction in real-time.

The major benefit of ECD scanning lies in the real-time characteristics of the image, the easiness of use compared to a magnetic resonance imaging (MRI) scanner and the low cost per image. However, ECD imaging is patient- and operator- dependent, it is limited in its field of view (FOV) and image quality, especially concerning transcranial application. These drawbacks can be better controlled if detailed anatomical reference can be given through a real-time co-registration with a previously acquired MRI, which offers a detailed view of brain and vessels over a much wider field of view in 3D. Conversely, the anatomical image lacks of and is completed by the real-time functional information provided by ECD. The present work describes the use of an MRI and ECD real time fusion technique (Virtual Navigator) and its preliminary assessment over a group of 10 volunteers. Namely, the DCVs insonated from the transcondylar window by a single highly-trained US examiner, with the usual clinical blind procedure (i.e., without the reference MRI), are assessed on the a-posteriori fusion of the clipped frame with the MRI, which had been previously acquired, loaded, and co-registered.

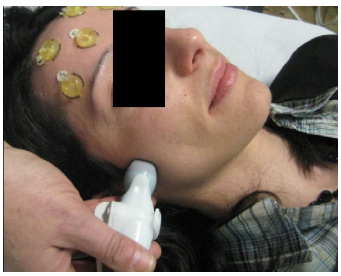

Fig. 1. Probe position at condyloid process of the mandible.

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II. Material and Methods

A. Subject Predisposition

Ten volunteers (5 males and 5 females, mean age = 35, range = 27-49) underwent MR and ECD examinations after a written informed consent. Inclusion criteria of subjects was their capability to take a prolonged inspiration without moving the head. Prior to the examinations, 6 Beekley PinPoint, multi-modality, conical design Fiducial Markers with a 1.27mm diameter center hole, were placed on the forefront of the volunteers. The fiducial markers were positioned avoiding the placement of more than one fiducial Marker on the same plane on the forehead of the subject (the natural curvature of the forehead facilitated the correct positioning of the fiducial markers). For both the examinations, a proper Head Support was used in order to keep the subject's head as steady as possible.

B. Image acquisition

For every subject, a proton density MRI brain volume was acquired using a 1.5 Tesla scanner (Siemens Magnetom Avanto, Erlangen, Germany), with a maximum gradient strength of 33 mT/m and a slew rate of 125 mT/m/ms, using standard 12-channels matrix head coil. The following pulse sequences were acquired from all subjects: 1) scout T1 sequence: three sagittal slices, three coronal slices and one axial slice with low resolution (voxel size=2.2x1.1x6 mm^3). It was used for positioning and orientation of the next sequence; 2) proton density (PD) turbo spin echo, with the following parameters: TR= 3270ms, TE=32 ms; echo train length=5; flip angle=150°, 50 interleaved, 2.5-mm-thick axial slices with a matrix size=256x256, interpolated to 512x512, and a FOV=250x250 mm. The acquisition time was about 7 minutes. The central slice of the slab was positioned to run parallel to a line that joins the most inferior-anterior and inferior-posterior parts of the corpus callosum [12], visible on the sagittal scout T1. This standard guarantee the reproducibility of the acquisition protocol and the covering of all the brain, with particular attention to the inclusion of the 6 fiducial markers inside the FOV.

Then, an Esaote MyLabTwice ultrasound system (Esaote S.p.A., Genova – Italy), equipped with the Virtual Navigation option [13], allowed real-time image fusion of ECD and PD weighted MRI, previously transferred to the ECD system. This system consists of an US scanner connected to the Navigation units. As to the US scanner, an Esaote PA240 Phased Array Probe (Operating Bandwidth: 1 – 4 MHz; B-Modes Frequencies: 2.0 – 2.5 - 3.3 MHz; CFM-PW Frequencies: 1.6 – 2.0 – 2.5 MHz) with a 639-039 CIVCO Reusable Tracking Bracket with sensor mount, has been used. The acoustic lens which covers the borders of the probe forms a soft envelop, in order to enhance the patient comfort during the transcranial examination, which could have a slightly long duration for a correct and complete view of the cerebral hemodynamic situation. The Virtual Navigator procedures were allowed by an electromagnetic tracking system, composed by a transmitter and a small receiver, mounted on the US probe. The transmitter position, which is considered the origin of the reference system, was fixed through a support, and the receiver provides the position and orientation of the US probe in relation to the transmitter.

C. Registration Procedures

The registration procedure of the MRI volume and the real-time ultrasonographic scan consists of two phases: an initial marker based rigid registration of corresponding Fiducial Markers was subsequently refined with the image registration of anatomical features. As to the first step, a registration pen (equipped with a transmitter unit) was used to point the 6 Fiducial Markers on the patient skin. The corresponding external markers visible on the 3D rendering of PD MRI data were selected and the registration matrix was computed. The registration procedure was considered successful if the root mean square error between the points selected with the registration pen and the points in the space as a result of the registration matrix was <0.5 cm. The second level of registration consisted on the B-mode visualization of the third ventricle and mid-brain from the classic transtemporal transcranial window (Figure 2, a), or of some easy-to-recognize bone structures (i.e. the petrous apex and the sphenoid bone from the ultrasound transcranial window at the level of the condyloid process of the mandible (Figure 2, b). After the registration, for any probe position and for any ultrasonographic image, the system gives the related reference modality slice obtained by virtually cutting the volume according to the probe spatial coordinates. Prior to start the patient veins examination through the ECD modality, the system accuracy was tested: the same point coordinates were measured twice, by the use of the registration pen with two different spatial orientations. An accuracy lower than 0.2 cm was considered acceptable.

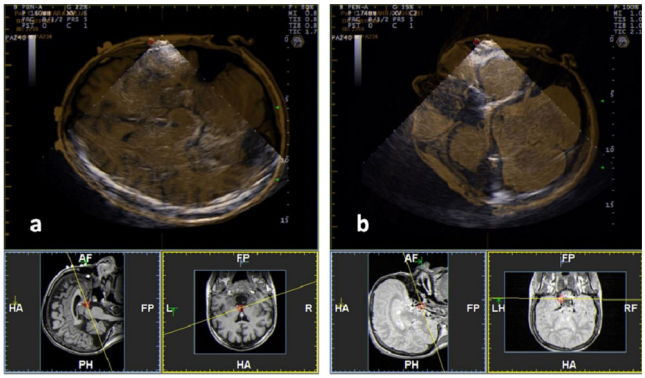

Fig. 2. Second level of registration through the temporal window (a) and the condylar window (b). The III ventricle (a) and the petrous apex and the sphenoid bone (b) are visible with B-mode and the anatomical PD MRI is superimposed.

D. Transcranial ECD examination and Navigation procedures

Examinations were carried out by a radiologist trained for the venous intracranial evaluations with ECD from temporal and condylar windows. Every volunteer was examined supine on an horizontal bed (i.e., 0° tilt) with the ultrasound system through the transcranial window at the level of the

condyloid process of the mandible. MRI frame was switched off during DCV targeting and examination. This phase took place after the above described co-registration procedure; nonetheless, the latter never implied viewing the DCV region of interest, in order to prevent any bias of the former, which had to simulate the normal ECD without MRI guidance. The B-mode with Color Doppler modality was used to select the addressed veins. This approach (though blind to MRI volume information) explores well established reference points, based on neural, arterial and anatomical structures, in order to identify the specific veins to be assessed, as better described by [5].

Lastly, selected vessels, targeting quality, and view direction (Figure 3) where checked by means of the fusion between the PD MRI and the ECD.

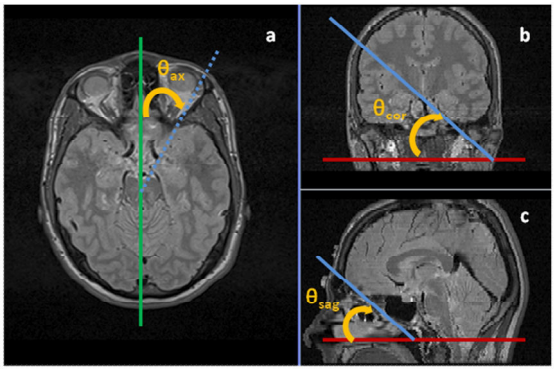

Fig. 3. Axial (a), coronal (b) and sagittal (c) PD MRI slices for the representation of θ_{ax}, θ_{sag} and θ_{cor}. Legend: θ_{sag}=Angle between the ultrasound insonation plane (blue) and the axial plane (red), measured on the sagittal plane. θ_{cor}=Angle between the ultrasound insonation plane (blue) and the axial plane (red), measured on the coronal plane. θ_{ax}=Angle between the transducer axis (dotted blue) and the sagittal plane (green), projected to the axial plane.

III. Results

For all the 10 examinations, the registration error obtained by the corresponding Fiducial Markers procedure was below 0.5 cm. The system accuracy measured with the Registration Pen was always under 0.1 cm.

In all the patients, the transcranial window at the level of the condyloid process of the mandible gave satisfactory image quality and the Doppler signal was always detectable.

The cerebral veins assessed through the transcranial US window at the level of the condyloid process of the mandible were: the Basilar Plexus (BP), the Cavernous Sinus (CS), the Superior Petrosal Sinus (SPS), the Inferior Petrosal Sinus (IPS) and the first segment of the Rosenthal Vein (RV). The Superior and Inferior Petrosal Sinuses (at least ipsilateral to the probe) in some of the examined subjects (6/10) were imaged within the same insonation plane.

Due to normal though sensible anatomical differences, different subsets of intracranial veins were targeted within the selected insonation plane (Figures 4, 5); nonetheless, selections were considered satisfying for a quantification of flow in the deep brain venous compartment. Table I reports the different cases as well as ranges of the relative position of probe and insonation plane with respect to the three brain axes, with the angle convention explained in Figure 3.

TABLE I

Intracranial veins	θax	θcor	θsag
SPS, IPS (same side of the probe), contralateral IPS and/or SPS	+5°; +20°	+10°; +45°	+10°; +45°
SPS, IPS and initial segment of the RV	-10°; +10°	+40°; +50°	-10°; -30°
CS and partially the IPS and/or SPS	+5°; +20°	+30°; +50°	+10°; +45°

Ranges of the relative position of probe and insonation plane with respect to the three brain axes

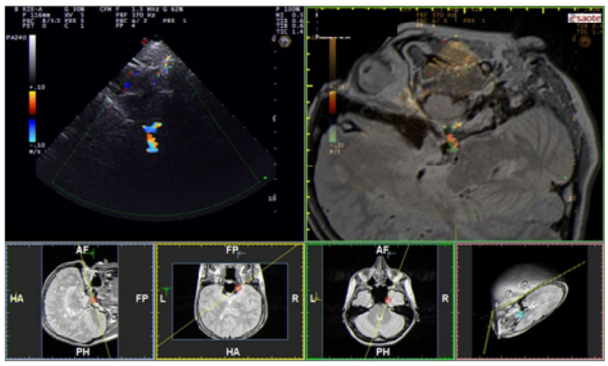

Fig. 4. Superior and Inferior Petrosal Sinuses visualized with ECD. The coregistered DP MRI is superimposed with Virtual Navigator as anatomical confirmation.

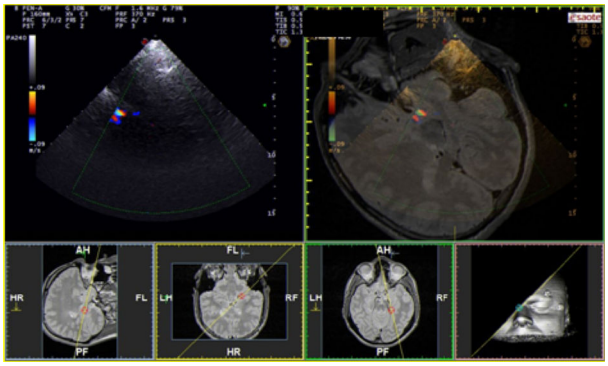

Fig. 5. Visualization of the first segment of the Vein of Rosenthal and the Superior Petrosal Sinus. The coregistered DP MRI is superimposed with Virtual Navigator as anatomical confirmation.

IV. Discussion and Conclusion

This study described and preliminarily validated a procedure to identify what veins are framed by ECD through the condylar window, the relevant pointing parameters, and the inter-subject variability ranges. With this aim, the proper vessels were images by an expert examiner with the only support of B-mode and Colour Doppler US. Subsequently, the ECD snapshot was fused with a high-resolution PD MRI in the Virtual Navigator for an a-posteriori evaluation. A single trained examiner was enrolled in this study, since an interobserver reproducibility with an agreement coefficient of 0.47 for trained *vs* not-trained examiners and a one of 0.80 between two trained examiners are reported in a study [14] regarding a complete CCSVI examination, to be compared with a score of 0.93 for a single trained examiner.

The fusion of the US with MRI data created a complete high-quality picture, permitting to set the insonation plane and the veins targeted by ECD into the detailed anatomical volume of MRI for each subject [13]. The Navigation procedure consisted both on external marker and a further registration refinement based on internal structures. The role of the latter step has to be further investigated. However, the quality of the whole registration permitted an unambiguous recognition of the framed venous structures and a quantitative measurement of the pointing directions. In perspective, the proposed set-up can be proposed both for improving the quality of expert an non-expert examiner performance by means of delivering the fusion view during the vein targeting phase. Alternatively, special sessions on ECD-MRI fusion could better train examiners for the routine clinical ECD exams, where a reference MRI may not be available.

The choice of PD weighted MRI produced many advantages: it allowed to visualize the fiducial markers needed for the registration and contrasted the intracranial veins from the surrounding brain tissue, permitting to validate the ECD results. Since PD MRI is also the optimal sequence for MS lesion localization and segmentation, it is likely to be a good reference frame for ECD even in clinical cases were the relationship of DCVs and the surrounding white matter structures are aimed at. The selected scan would permit precise lesion volume measures due to its high resolution (voxel size =0.49x0.49x1.65 mm).

Finally, the proposed procedure may bridge a connection to vascular (i.e. susceptibility weighted [15]-[21]), hemodynamic (i.e. phase contrast [22],[23]), and microstructural (i.e. diffusion [24]) contrast delivered by other MRI modalities, using PD MRI as main reference for the intra-subject image registration, toward a deeper insight of the correlation between CCSVI and brain damage.

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