Quantitative cerebral water content changes after CSF removal in idiopathic normal pressure hydrocephalus: a preliminary analysis using MRI at 3 T

Zaheer Abbas[1], Kathrin Reetz[1,2], Ana Sofia Costa[2], Vincent Gras[1], Shahram Mirzazade[1,2], Johannes Schiefer[2], Georg Neuloh[3], Jörg Bernhard Schulz[2,4], and N Jon Shah[1,2]

[1]INM-4, Research Centre Jülich GmbH, Jülich, Germany, [2]Department of Neurology, RWTH Aachen University, Aachen, Germany, [3]Department of Neurosurgery, RWTH Aachen University Hospital, Aachen, Germany, [4]Translational Brain Medicine, Jülich Aachen Research Alliance (JARA), Jülich and Aachen, Germany

TARGET AUDIENCE: This work primarily will concern MRI scientist interested in applications of quantitative imaging for studying changes in the human brain.

PURPOSE: The **quantitative** and **non-invasive** measurement of **tissue water content** using magnetic resonance imaging aids the monitoring and interpretation of the disease-related integrity of brain tissue[1]. This method has already allowed for a better characterization of several different neurological pathologies in which local or global disturbances in the water distribution and content were identified[2, 3]. It may also help to clarify the still unclear **pathophysiology of idiopathic normal pressure hydrocephalus (iNPH)** – an adult chronic and generally, in its early stages, reversible disorder, characterized by the gradual onset of a triad of gait impairment, cognitive dysfunction, and urinary incontinence. The aim was to verify the hypothesis of cerebrospinal fluid (CSF) exudation into, in particular, periventricular white matter, and to investigate if the clinical improvement after CSF removal is regulated by changes of the cerebral water content and spatial water distribution.

METHODS: A quantitative cerebral water content MRI protocol was implemented in five iNPH patients on a 3 T Siemens (Erlangen, Germany) TIM TRIO system, using the 32-channel head coil for signal reception. Each patient underwent the examination twice, once before and once after diagnostic CSF removal by lumbar puncture (LP). The measurement protocol was based on a 2D multi-echo multi-slice spoiled gradient echo sequence with subsequent correction of the influence of T_1, T_2^* and RF non-uniformities[4]. To accurately correct the receive profile of the head coil, a T_1-based residual non-uniformity correction technique was employed which exploits the measured correlation between PD and T_1 in a WM-GM transition region, i.e. characterized by $50 < T_2^* < 60$ ms[2]. The PD maps were finally calibrated to the ventricular CSF signal, which was assumed to have the same PD as pure water. For each subject, both measurements were co-registered (FSL-FLIRT, rigid-body transformation), and water content changes were reported in region of interests (ROIs) placed in such as the frontal, parietal, occipital, temporal and cerebellar cortices as well as globally in the cortical WM and the cortical GM. On the other hand morphologic changes were assessed using FSL-SIENA (*http://fsl.fmrib.ox.ac.uk/fsl*) and ventricular changes were assessed using FSL-VIENA[5].

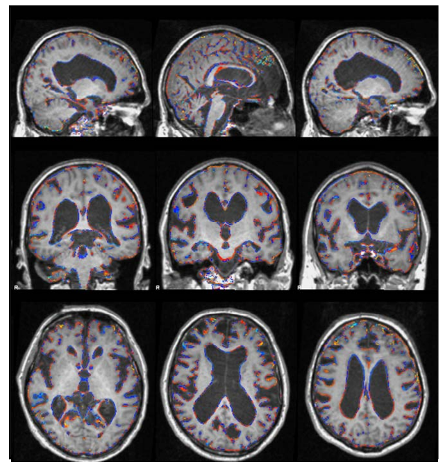

Fig. 1. *Volumetric changes of grey matter in one iNPH patient after LP (red loss, blue growth). The pathognomonic enlarged ventricle size is clearly visible.*

RESULTS: Besides the expected **enlarged ventricle size**, longitudinal brain change analysis using FSL-Siena from a patient is exemplarily shown in Figure 1. The estimated cortical percentage brain volume changes (PBVC) reveals a **volumetric loss of brain volume** (between 0.2 to 2.8 %) after CSF removal. The water content distribution in the brain of iNPH patients showed a globally **increased water content** (approximately up to 3%) in the **white matter**, including **periventricular** structures. **Water content decreased after LP.** No significant changes in the grey matter mean values were found. Figure 2 shows the quantitative water content before and after LP. Water content mean differences (mean and standard deviations) per global region of interest (ROI) are shown in Figure 3.

DISCUSSION: These preliminary results are encouraging by allowing the quantification of **changes in water content** which may help to better understand the pathophysiological basis of iNPH and identify predictors for reversibility of clinical symptoms, e.g. due to recurrent water content after CSF removal in disease-relevant structures such as periventricular regions. Further steps, including a larger sample size, comparison to age- and gender-matched healthy controls, comprise additional analyses including association with clinical variables (e.g. change in measures of gait and cognition after LP) and identified structural changes (e.g., cortical atrophy, ventricular size) are indicated by the current results.

CONCLUSION: Water content measurements performed at 3 T provided higher SNR. These preliminary results are the first of their kind obtained in iNPH patients and are encouraging and enhance our understanding about clinical improvement and controlled CSF exudation effects.

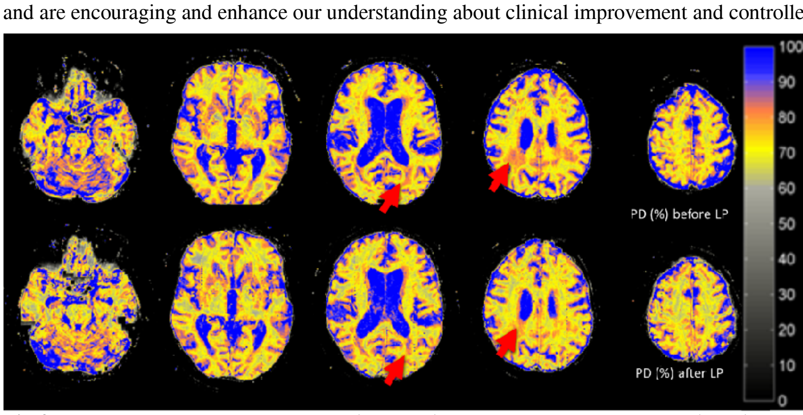

Fig. 2. *Quantitative water content (in percent) before and after LP in one iNPH patient. Analysis shows reduction of W (up to 3 %) after LP especially in white matter tissue.*

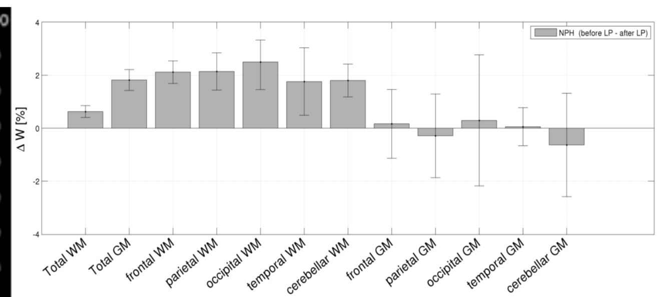

Fig. 3. *ROI based analysis averaged over five iNPH show mainly reduction of water content in white matter (WM) and less in gray matter (GM) after CSF removal.*

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