



A Randomized Double-Blinded Clinical Study of Early Volumetric Changes After Shunt Surgery and MRI-Resistance of the Codman Certas® Plus Shunt Valve

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OBJECTIVE: Linear radiological measures have low sensitivity to detect changes in ventricular volume in patients with idiopathic normal pressure hydrocephalus. Ventricular volumetry is accurate and sensitive in detecting subtle changes in cerebrospinal fluid volumes. The Codman Certas® Plus is an adjustable shunt valve with 8 settings and resistant to magnetic resonance imaging (MRI)-induced inadvertent adjustments in vitro. The aim of this study was to investigate early volumetric changes in ventricles after ventriculoperitoneal shunting in relation to shunt setting and linear measures. We also wanted to evaluate the MRI-resistance of the Codman Certas® Plus valve in a clinical setting.

METHODS: Forty-five idiopathic normal pressure hydrocephalus patients underwent quantitative MRI, including volumetry before and 36 hours after shunting with Codman Certas® Plus valves set to 4 (20 patients) and 8 (25 patients). Valve setting was blinded to patients and examiners and assessed after each MRI. Patients performed in total 156 MRI examinations during 3 years.

RESULTS: There was significant difference in change of ventricular volume between groups 4 and 8 early after surgery. Patients with setting 4 had a ventricular volume reduction of 16 (standard deviation \pm 9) mL while those

with setting 8 had a reduction of 5 (standard deviation \pm 5) mL. Constriction of subarachnoid cerebrospinal fluid spaces in cerebral high convexity and parafalcine sulci was significantly less in the setting 4 group post-operatively. There were no MRI-induced changes to valve setting after any MRI.

CONCLUSIONS: Ventricular volumetry can detect shunt-induced reduction in ventricle volume early after surgery. The magnitude of reduction is related to shunt valve resistance. The Codman Certas® Plus valve is stable against MRI-induced changes in a clinical setting.

INTRODUCTION

Idiopathic normal pressure hydrocephalus (iNPH) is a treatable cause for balance and gait disturbance and cognitive dysfunction in the elderly. First described by Hakim et al in 1965,¹ the condition has become increasingly common with a reported prevalence of 400/100 000 inhabitants.² Many studies have shown that shunt surgery improves symptoms in 74%–75% of patients³ and is a proven cost-effective treatment, especially as many patients will stay independent longer.⁴ iNPH is the most common indication for shunt surgery in most high-income

Key words

- Codman Certas® plus shunt valve
- Idiopathic normal pressure hydrocephalus
- Quantitative MRI
- Radscale
- Ventriculoperitoneal shunt
- Volumetry
- Tight high convexity

Abbreviations and Acronyms

3D-QALAS: 3D-quantification using an interleaved Look-Locker acquisition sequence with T2 preparation pulse

CA: Callosal angle

CSF: Cerebrospinal fluid

CT: Computational tomography

DESH: Disproportionately enlarged subarachnoid spaces in hydrocephalus

EI: Evan's index

iNPH: Idiopathic normal pressure hydrocephalus

MRI: Magnetic resonance imaging

qMRI: Quantitative MRI

THC: Tight high convexity

VV: Ventricular volume

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countries; however, its prevalence surpasses the amount of shunt surgeries performed annually. In Sweden, this amounts to 1.7 surgeries per 100 000 inhabitants.² The number of patients with iNPH and shunts is anticipated to increase with an aging population.

Follow up of shunted patients consists of both clinical and radiological examinations. Postoperative imaging aims to rule out complications such as subdural hematomas, hygromas, and malpositioned ventricular catheters. However, most traditional linear measures such as frontal horn width and Evans Index (EI) will rarely confirm shunt function in iNPH, as they lack sufficient sensitivity to detect shunt-induced changes in ventricular volume.⁵ The callosal angle (CA), calculated as the angle between the lateral ventricles seen in the coronal plane at the level of the posterior commissure, may be a better measure. CA has been shown to correlate with reduction of ventricular volume 3 months after shunt surgery.⁶ Radscale is a radiological assessment tool specifically designed to evaluate imaging features associated with iNPH.⁷ It provides a quantitative standardized analysis of seven parameters such as EI, CA, and enlargement of hemispherical sulci and more, facilitating consistent diagnosis across different clinical settings and studies. Radscale also includes assessment of the presence of constricted subarachnoid cerebrospinal fluid (CSF)-spaces in cerebral high-convexity and medial parafalcine sulci, in this article called a tight high convexity (THC).⁸ Although Radscale is particularly useful in distinguishing iNPH from other forms of dementia and hydrocephalus, it has yet to be validated as a useful tool for postoperative follow-up and confirmation of shunt function. A common clinical challenge is patients coming back with relapse of iNPH-symptoms, requiring differentiation between shunt failure or disease progression. As current radiological methods rarely suffice to rule out shunt dysfunction, patients are often subjected to invasive procedures such as infusion tests or revision surgeries.

Volumetry is gaining attention as research increasingly highlights its potential in detecting subtle changes in brain structure associated with pathologies like dementia and hydrocephalus.⁹ It provides a more accurate and sensitive measure of ventricular volume changes compared to traditional 2D imaging methods.¹⁰ Reduction in ventricular volume correlates more strongly with clinical improvement after shunt surgery than changes in EI.¹¹ Lidén et al. showed differences in ventricular volume after shunt valve adjustments.¹² As volumetry provides exact measurements of ventricular size, enabling the detection of even subtle changes over time, it is a candidate for noninvasive detection of shunt malfunction. Our group recently showed how an automated ventricle volumetry algorithm can quickly provide accurate and reliable CSF volume measurements from a 6-minute scan using 3D quantitative magnetic resonance imaging (qMRI).¹³ By employing 2D qMRI volumetry, another group has shown that lateral ventricle volume was reduced 30 minutes after lumbar puncture.¹⁴ However, no studies have investigated early changes in ventricular volume after shunt surgery.

The Codman Certas® Plus shunt valve (Integra LifeSciences Corporation, Plainsboro, NJ, USA) was introduced in 2015. It is an adjustable differential pressure valve with 8 settings ranging from 15 mm H₂O (setting 1) to >400 mm H₂O (setting 8). Setting 8 is also referred to as “virtual off,” as it is designed to simulate shunt

closure in a noninvasive manner, avoiding the need for invasive ligation and opening of the shunt tube. The valve was investigated for its hydrodynamic properties by Czosnyka¹⁵ and Eklund et al.¹⁶ and initial clinical experiences were described by Watt et al.¹⁷ However, surprisingly few studies have evaluated the shunt system in a clinical setting. The Certas® Plus valve is constructed to be MRI-safe and resistant to MRI-induced inadvertent setting adjustments in vitro (a.k.a. MRI-resistant).^{15,18} However, this has yet to be proven in a clinical setting. Despite the valve’s MRI-resistance, it is still recommended by the manufacturer to include mandatory valve setting check after MRI exams. This limits the feasibility to perform MRI examinations at centers lacking the necessary competence and equipment for valve verification. What also remains to be proven is whether “virtual off” truly eliminates CSF-flow through the shunt, considering gravitational effects and shunt physiology. In theory, a shunt system that is turned off should not cause any reduction in ventricular volume.

The aim of this study was to investigate early postoperative changes in ventricular volume after shunting in relation to shunt setting and to compare the sensitivity of volume reductions with linear radiographic 2D-measures. We also wanted to evaluate the MRI-resistance of the Codman Certas® Plus valve in clinical practice and whether valves turned to virtual off caused any reduction of ventricular volume. Finally, we opted to evaluate the reliability and efficacy of an updated qMRI-based automatic volumetric segmentation software (SyMR v 0.62.20).

METHODS

Study Population

Patients referred to our department for possible iNPH were assessed according to international clinical and radiological guidelines.¹⁹ Those who were accepted for shunt surgery between January 2021 and July 2022 were consecutively asked for study participation. Exclusion criteria were as follows: lumbar intrathecal pressure above 18 cm H₂O, lumbar CSF biomarkers showing another more likely cause for symptoms, patients operated with MRI-incompatible implants such as pacemakers, short life expectancy, patients with severe cognitive deficits deemed not fit to comply with study participation and unable to give informed consent. The national Swedish Ethical Review Authority (ref no 2020–00719) approved the recruitment process and data collection and all participants provided written informed consent upon enrolment. The sample size of this cohort was determined based on earlier similar study cohorts.^{10,12,20} The study was registered with [ClinicalTrials.gov \(NCT04785560\)](https://clinicaltrials.gov/ct2/show/study/NCT04785560).

Clinical Assessment and Shunt surgery

The day before surgery, clinical examinations by a physiotherapist and occupational therapist were performed according to the Hellstrom iNPH-scale.²¹ A preoperative MRI was performed to obtain baseline ventricular volumetry and Radscale score.

All patients were operated with a right sided Codman Certas® Plus shunt system. With a planned sample size of 50 patients, block randomization in blocks of 10 was performed using a sealed envelope technique. Envelopes were numbered 1–50. Patients were either assigned to valve setting 4 (=110 mm H₂O) or 8 (>400 mm H₂O—“virtual off”) in a ratio of 1:1. Directly before surgery

an independent neurosurgeon outside the study group set the valve according to randomization information in the consecutive envelope, which was then resealed and kept with the patient for security reasons. Valve setting was thus blinded for surgeons, patient, radiologist, and other staff. Surgery was performed by one or two out of three experienced neurosurgeons in the study group, often with a junior assistant. After sedation directly before surgery all patients were sampled for 10 mL of lumbar CSF using an 18-gauge spinal needle (BD® Quincke Spinal Needle 18 G × 3 1/2 in) for the purpose of another study. Also, during surgery another 10 mL of CSF was sampled from the ventricular catheter. Postoperative immobilization was 6 hours after surgery, the patients could then sit, stand and walk at will.

The patients underwent a second MRI with the same protocol within 24–48 hours postoperatively. Within an hour of the postoperative MRI examination, an independent blinded neurosurgeon outside the study group assessed the patient for valve setting. All valves set to 8 were then adjusted to 4 and hence all patients were discharged with valve setting 4.

MRI imaging was subsequently performed at 3, 12, and 36 months postoperatively. Within an hour of the MRI examination, patients were reassessed for valve settings. Any valve adjustments made from postoperative discharge onward were noted, ensuring that the intended valve setting was known to the examiner before each examination.

Radiological Method. Preoperative, 3, 12, and 36 months postoperative MRI scans were conducted using a 3T Siemens Prisma scanner, while the 24–48 hours postoperative scans were performed on a 3T Siemens Skyra scanner, both equipped with a 20-channel head coil. The imaging protocol included T₁-weighted and T₂-weighted sequences, along with a 3D qMRI sequence, 3D-QALAS (3D-quantification using an interleaved Look-Locker acquisition sequence with T₂ preparation pulse). The 3D-QALAS protocol comprises 5 parallel, segmented 3D TFE gradient echo acquisitions, interleaved with T₂ preparation and inversion pulses, to measure T₁ and T₂ relaxation times and proton density.^{20,22} Utilizing these maps, the partial volume of cerebrospinal fluid (CSF) per voxel was automatically determined using the image analysis software SyMRI v0.62.20 (SyntheticMR AB, Sweden).²³ A full coverage with an isotropic resolution of 1.20 × 1.23 × 1.23 mm³ was achieved in a scanning duration of 6 minutes. Volumetric assessments of the preoperative and postoperative 24–48 hours examinations were performed using 3D-QALAS on synthetic T₁-or T₂-weighted images generated via the SyMRI software. Automatic segmentation of the ventricular system was executed based on the CSF maps using SyMRI v0.62.20, which is an updated version of SyMRI v0.45.36, previously validated by our group.¹³ The refined automated algorithm had gone through further development addressing initial problems segmenting all the CSF in the temporal horns. A neurosurgeon (R. H.) reviewed the automatic segmentations and manually corrected any inaccuracies regarding the inclusion or exclusion of intraventricular CSF (reviewed segmentation). The time taken for each examination's revision was documented. A neuroradiologist (C.G.) assessed all preoperative and early postoperative MRI scans for Radscale score, using conventional T₁ and T₂

sequences. All MRI images were anonymized and assigned a study identification code for research purposes.

After each postoperative MRI, the on-call neuroradiologist at our radiology department assessed whether ventricular size had decreased compared to the preoperative one using any preferred 2D-measures, providing a binary response (yes/no).

Statistical Analysis. The Shapiro Wilks test was used to assess normal distribution. Differences before and after surgery in ventricular CSF-volumes and Radscale parameters were tested with paired samples t-test. Differences between groups were tested with independent samples t-test. Sex distribution between groups was tested with Chi square test. Correlation between change in ventricular volume and change in CA and Radscale score was investigated with Pearson's correlation analysis, assuming linear correlation. A level of $P < 0.05$ was considered statistically significant. To compare the automatic and reviewed segmentations of ventricular volume, the Dice overlap coefficient was used, defined as twice the sum of all overlapping voxels (O) divided by the sum of all manually included voxels (M) plus the sum of all automatically included voxels (A); $2O/(M+A)$, ranging from 0 for no overlap to 1 for perfect overlap. Inter-rater agreement between automated and corrected segmentation was calculated with intraclass correlation coefficient (ICC) for continuous data using SPSS. Model used was a 2-way mixed effects, absolute agreement, multiple raters/measurements (ICC, 3, k) for inter rater reliability.²⁴ Statistical analyses were carried out using IBM SPSS Statistics for Windows version 29.

RESULTS

During the study period 169 patients were assessed clinically for iNPH by our neurology team and 74 patients were deemed suitable for shunt surgery, met the inclusion criteria, had no exclusion criteria and were offered study participation. The first 50 consecutive patients to accept study participation were included in the study. Study workflow is presented in **Figure 1**. Demographic, clinical, and radiographic data of patients are presented in **Table 1**. There were 23 women in the whole group and evenly distributed sex and age between patients in the valve setting groups.

Forty-nine patients were examined preoperatively and 45 completed the postoperative MRI-examination on average 36 hours after the end of surgery. One patient did not fit in the MRI scanner and had to be excluded before the preoperative MRI-examination. One patient discontinued study participation after the preoperative MRI, one was examined in an MRI scanner lacking 3D-QALAS software postoperatively and two patients did not complete postoperative MRI within the 24–48-hour time frame due to NICU care. Study dropouts affected only the group with valve setting 4, rendering 20 patients in this group and 25 with setting 8.

A total of 94 qMRI-exams were performed pre- and directly postoperatively. Mean difference between the automated ventricular volume provided by the software and the volume after the neurosurgeons revision was 0.6 mL in preoperative and 0.7 mL in the postoperative exams. This equals 0.5% difference in ventricles with a mean total volume of 136 and 126 mL, respectively. Dice-score was 99.5 and ICC for inter-observer reliability was 1.000.

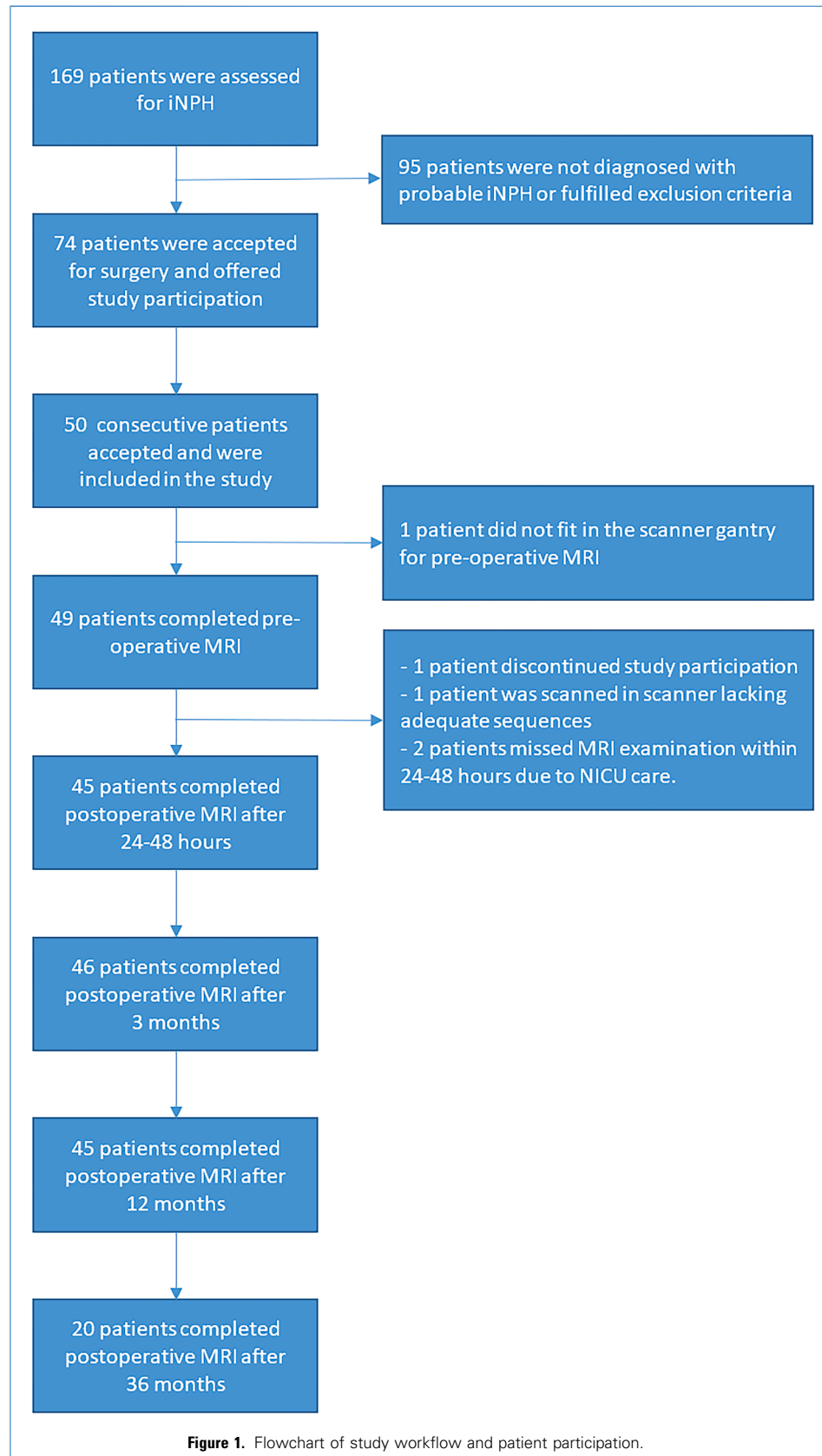


Table 1. Demographic and Radiographic Data of Whole Sample and Groups With Valve Settings 4 and 8

	Whole Sample	Valve Set to 4	Valve Set to 8	P-Value
Demographic parameters				
Group size (original size)	45 (50)	20 (25)	25 (25)	
Female/male	23/22	10/10	13/12	
Age (years) (SD; range)	77 (5; 68–85)	76 (5; 69–83)	78 (4; 68–85)	0.1
Pre-operative Hellstrom iNPH-scale score (0–100)	51 (13)	51 (13)	50 (13)	0.9
Time between surgery and post op MRI (hours)	36 (11)	38 (13)	35 (9)	0.3
Ventricular volumetry				
Ventricular volume (mL)				
Pre op	136 (35)	139 (28)	134 (40)	0.6
Post op	126 (34)	123 (28)	128 (38)	0.6
Δ Ventricular volume pre- versus postoperative MRI (mL) (SD; range)	–10 (9; 0.05–45)	–16 (9; 6–45)	–5 (5; 0.05–18)	<0.001
Fraction postop \div preop ventricular volume (%)	92 (0.06)	88 (0.07)	96 (0.03)	<0.001
Absolute reduction of ventricular volume (%)	8	12	4	
Linear radiographic parameters				
Evan's index				
Pre op	0.36 (0.035)	0.365 (0.036)	0.365 (0.035)	0.98
Post op	0.36 (0.033)	0.357 (0.035)	0.360 (0.033)	0.80
Δ Evan's index pre- versus post op	–0.0065 (0.012)	–0.0078 (0.0092)	–0.0054 (0.014)	0.51
Callosal angle				
Pre op	68 (15)	66 (13)	70 (17)	0.39
Post op	70 (16)	70 (14)	70 (18)	0.94
Δ Callosal angle pre- versus post op	2.4 (11)	4.8 (10)	0.44 (11)	0.15
Total Radscale score (0–12)				
Pre op	8.2 (1.7)	8.5 (1.6)	8.0 (1.7)	0.15
Post op	8.2 (1.5)	8.0 (1.5)	8.4 (1.6)	0.25
Evan's index (0–2)				
Pre op	1.9 (0.25)	1.9 (0.22)	1.9 (0.28)	0.35
Post op	1.9 (0.25)	1.9 (0.22)	1.9 (0.28)	0.35
Tight high convexity (0–2)				
Pre op	0.4 (0.62)	0.4 (0.60)	0.4 (0.65)	0.42
Post op	0.3 (0.46)	0.1 (0.31)	0.4 (0.51)	0.006
Sylvian fissure (0–1)				
Pre op	0.8 (0.40)	0.8 (0.41)	0.8 (0.41)	0.50
Post op	0.9 (0.25)	0.9 (0.31)	0.9 (0.20)	0.22
Focally enlarged sulci (0–1)				
Pre op	0.7 (0.47)	0.7 (0.47)	0.7 (0.48)	0.44
Post op	0.6 (0.48)	0.6 (0.50)	0.7 (0.48)	0.22

Values are presented as mean (SD) unless stated otherwise. Differences in ventricular CSF-volumes and Radscale parameters between groups were tested with independent samples t-test.

Differences before and after surgery within groups were tested with paired samples t-test.

Bolded *P* values indicate statistical significance ($P < 0.05$).

Continues

Table 1. Continued

	Whole Sample	Valve Set to 4	Valve Set to 8	P-Value
Temporal horns (0–2)				
Pre op	1.5 (0.66)	1.6 (0.68)	1.5 (0.65)	0.20
Post op	1.4 (0.69)	1.5 (0.69)	1.4 (0.70)	0.28
Callosal angle (0–2)				
Pre op	1.2 (0.68)	1.3 (0.59)	1.2 (0.75)	0.18
Post op	1.2 (0.63)	1.2 (0.52)	1.2 (0.72)	0.42
Periventricular hypodensities (0–2)				
Pre op	1.6 (0.65)	1.7 (0.64)	1.5 (0.65)	0.086
Post op	1.8 (0.52)	1.8 (0.52)	1.8 (0.52)	0.4
Δ Total Radscale score pre- versus post op	0.02 (1.3)	−0.45 (1.3)	0.40 (1.3)	0.025

Values are presented as mean (SD) unless stated otherwise. Differences in ventricular CSF-volumes and Radscale parameters between groups were tested with independent samples t-test. Differences before and after surgery within groups were tested with paired samples t-test. Bolded P values indicate statistical significance ($P < 0.05$).

Mean time spent by the neurosurgeon reviewing each examination was 115 seconds. There was a small systematic error with the software underestimating ventricular volume mainly in the temporal horns. Data from the evaluation of the automated volumetry in SyMR v 0.62.20 is presented in Table 2 and Figure 2.

Time between end of surgery and postoperative MRI was on average 36 hours. Both groups were equal regarding Radscale score including individual parameters before surgery. Total Radscale score was equal between groups also postoperatively. The only individual Radscale parameter that was significantly different between Groups 4 and 8 after surgery was THC ($P = 0.01$). Change in total Radscale score from baseline to postoperatively was different between Groups 4 and 8 ($P = 0.025$) while change in CA and EI was equal.

Pre- and postoperative ventricular volumes went down from 139 (SD ± 28) to 123 mL (SD ± 28) in setting 4 and from 134 (SD ± 40) to 128 (SD ± 38) mL in setting 8. There was no statistical difference between groups regarding total postoperative ventricular volumes. There was, however, a significant reduction in ventricular volume in both the setting 4 (16 ± 9 mL) and setting 8 (5 ± 5 mL) group compared to baseline and between the groups on the $P < 0.01$ level. Absolute reduction of preoperative ventricular volume in groups was 12% and 4%, respectively. Postoperative increase of CA showed a negative Pearson correlation with reduction of total ventricular volume ($r = -0.47$, $P < 0.01$). The correlation between reduction of ventricular volume and reduction in total Radscale score was 0.3 ($P = 0.05$). There was overlap in the volumes drained in patients with different settings: ranges in setting 4 were 5.7–45 mL and in setting 8 0.05–18 mL. In all, 80% of the patients with setting 4 had more than 9 mL reduction, while 80% of the patients with setting 8 had less than 9 mL reduction. Radiological outcome data are presented in Table 1 and Figure 3.

All patient ventricle volumes were reduced regardless of shunt setting. Ten out of 45 patients were reported to have smaller ventricles according to the neuroradiologist report after assessing

traditional 2D-measures (Figure 4). The mean volume reduction in this group was 20 (SD ± 12) mL or 15% of preoperative ventricular volume. Corresponding numbers in the group of 35 patients who had unchanged linear measures were 7 (SD ± 6) mL or 5% of preoperative volume. One outlier reduced ventricles by 45 mL in 46 hours contributing to this difference, which was statistically significant on the $P < 0.001$ level.

Including the follow-up examinations done after 3 months ($n = 46$), 12 months ($n = 45$), and 36 months ($n = 20$), a total of 156 postoperative 3T MRI examinations were done. All valves were checked after all MRI examinations, and there was no inadvertent valve change. Valve checks after the 45 early postoperative MRI examinations were blinded and all valve settings were according to randomization (Table 3).

DISCUSSION

This study demonstrates a significant reduction of ventricular volume in shunted iNPH-patients early after surgery, even when imperceptible to most traditional linear radiographical measures. Additionally, there is a clear difference in ventricular volume reduction in relation to shunt setting after 36 hours. Furthermore, the Codman Certas® Plus valve construct was proven to be MRI-resistant according to manufacturer specifications also in a clinical setting. The SyMRI v 0.62.20 software showed further improved time expenditure and precision in the qMRI-based automatic ventricle segmentation algorithm.

Neither total Radscale score, EI, CA nor total ventricle volume was different between setting 4 and 8 groups early after shunt surgery. The only parameter that showed difference between groups postoperatively was THC, a 2D-measure first described by Sasaki et al.²⁶ It is also part of DESH (disproportionately enlarged subarachnoid spaces in hydrocephalus), a neuroimaging phenotype of iNPH central to diagnostics in The Japanese Society of Normal Pressure Hydrocephalus guidelines.²⁷ Both the total Radscale score and the THC parameter have demonstrated good inter- and intrarater reproducibility.²⁸ However, it is important to

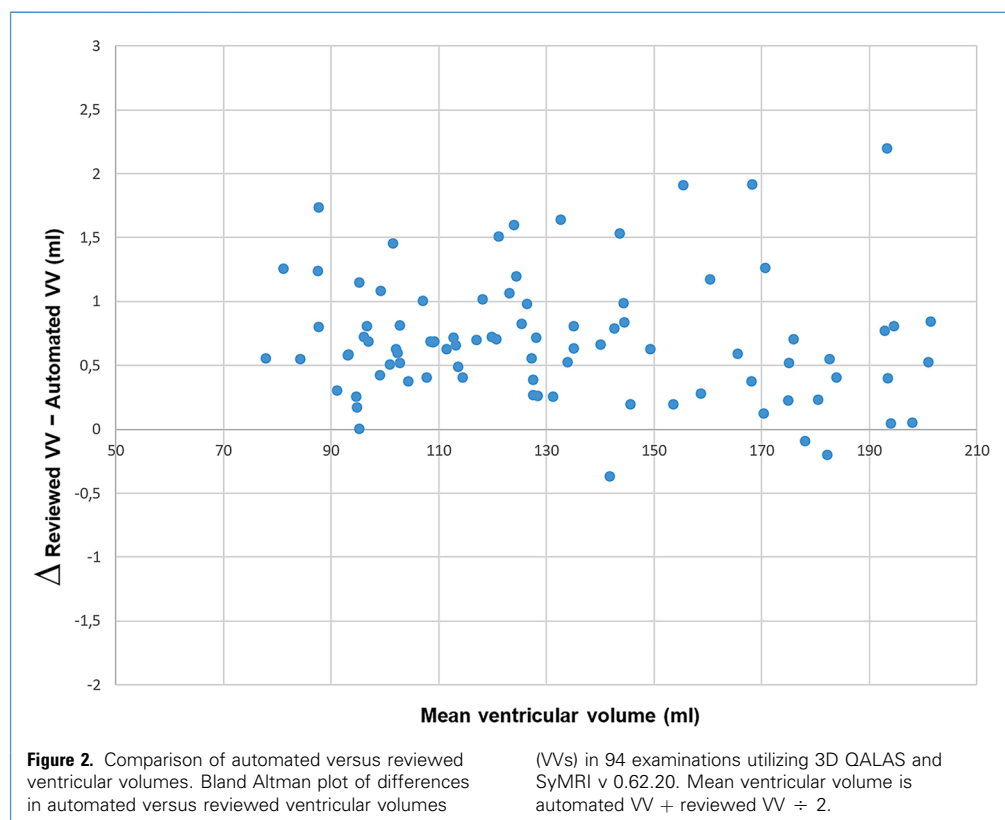
Table 2. Evaluation of Automated ventricular volumetry in SyMRI v 0.62

	No of Examinations (n)	Ventricular Volume Automated by SyMRI 0.62 (ml)	Ventricular Volume after review of Neurosurgeon (ml)	Δ Automated versus Reviewed Ventricular Volume (ml)	Δ Automated versus Reviewed Ventricular Volume (%)	Time Spent per Exam Reviewing Automated Volumetry (seconds)
Preoperative MRI examinations	49	135.5 (35)	136.1 (35)	0.6 (0.5)	0.4	123 (37)
Postoperative MRI examinations after 24–48 hours	45	125.3 (34)	126.0 (34)	0.7 (1.1)	0.5	108 (30)
All MRI examinations	94	129.8 (34)	130.4 (34)	0.6 (0.8)	0.5	115 (34)
Intra-class correlation automated versus reviewed ventricular volume		1.000 (0.999–1.000)				
Dice-score automated versus reviewed ventricular volume		99.5				

Values are means (SD). Intra-class correlation value presented is based on average measures and their 95% confident intervals (lower bound-upper bound). Model used is two-way mixed effects, absolute agreement, multiple raters/measurements (ICC, 3, k) for inter rater reliability.²⁵

note that this remains a relatively subjective measure, relying solely on visual inspection. In our study, the assessment of postoperative MRI scans was not fully blinded, as artifacts from the shunt valve were visible. This potential bias, however, should have had a similar effect on all nonquantifiable parameters of Radscale.

The magnitude of change in ventricular volume and total Radscale score differed between settings 4 and 8 from baseline to postoperative scans, whereas no significant differences were observed in CA and EI. The positive correlation between change in CA and ventricular volume was weaker than but in accordance with the study by Virhammar et al.⁶ The main methodological



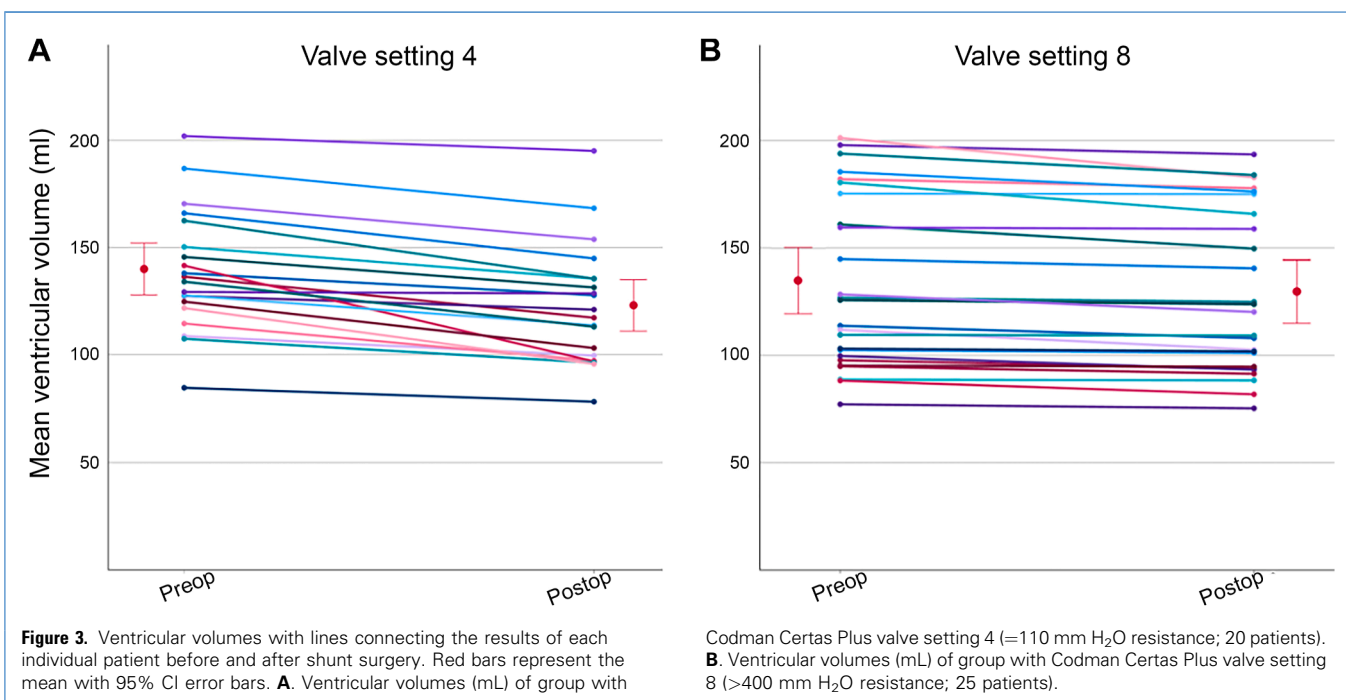
difference is that this study compared CA with total ventricular volume reduction, whereas Virhammar et al. compared CA with the volume reduction of one lateral ventricle and used an older 2D qMRI-sequence. We find ventricular volumetry to be a more precise measure, as CA measurements are inevitably user-dependent and prone to error depending on how they are obtained.²⁹ The exact location of measurement along the anterior commissure-posterior commissure line and the angulation of the coronal plane play a decisive role in what the CA will be. The automated ventricular volumetry algorithm presented in this study is an objective tool that circumvents errors caused by intra- and inter-examiner variability. Moreover, it provides a ventricular volume measurement in milliliters, allowing for direct comparisons across earlier and later examinations in a more nuanced manner than the ordinal scale grading used by Radscale and its parameters. Our results highlight the limitations of 2D linear measures in the follow up of shunted iNPH-patients and further emphasize that ventricular volumetry could be a valuable tool for objectively evaluating and optimizing shunt function.

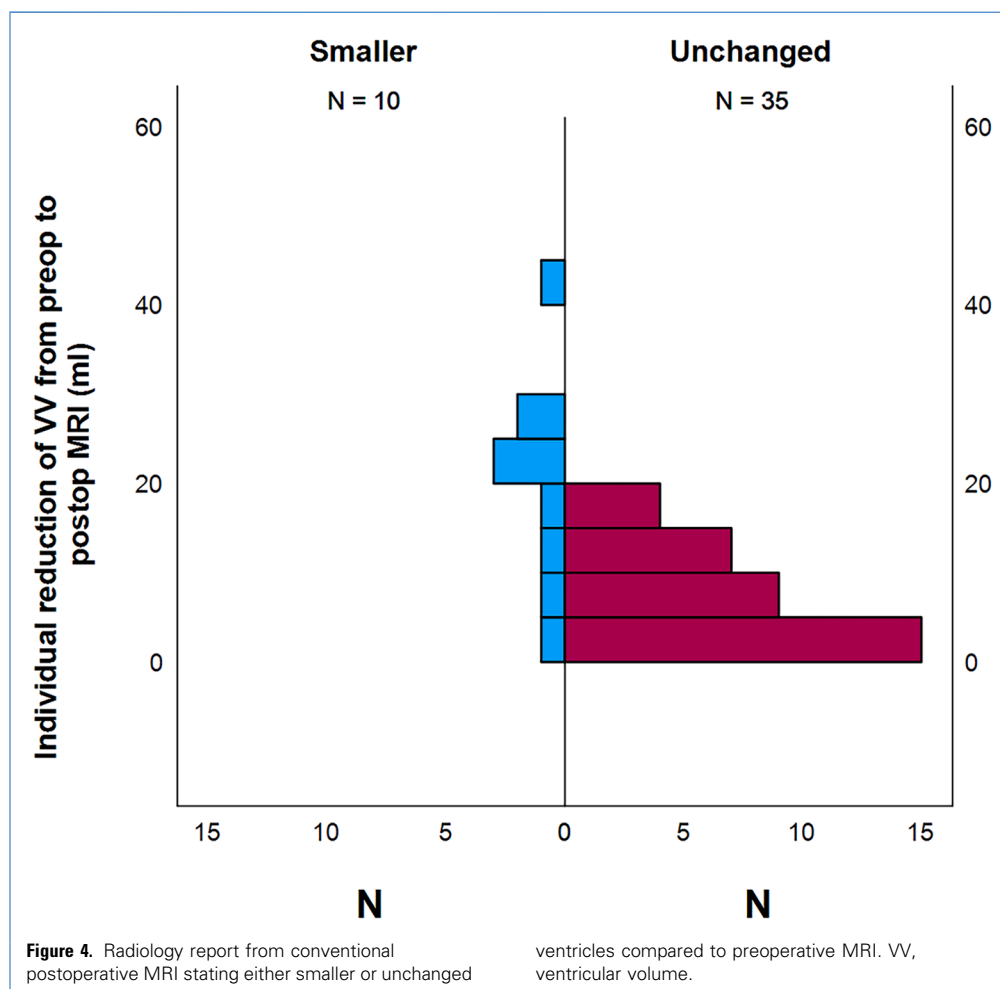
Every single patient's ventricle volume was reduced regardless of shunt setting but only 10 out of 45 patients had smaller ventricles according to the radiologists' answer after assessment of conventional MRI images. The mean volume reduction that seemed necessary for radiologists to perceive reduced ventricles was 20 mL or at least 15% reduction of initial ventricular volume. However, neuroradiologists also confirmed reduced ventricles when patients had reduced volumes by 5 mL or less and negated change in patients with volume reductions of 15–20 mL. This part of the study has methodological weaknesses, as several radiologists made the assessment only once and their response was binary (yes/no) regardless of what measures they chose to use. However, this highlights the challenges faced in authentic clinical

settings to confirm shunt function, and hence shunt blockage, in traditional 2D images. The substantial under-detection of CSF decompression when relying on 2D measures alone supports using automated volumetry as a sensitive adjunct in the post-operative period. Reporting could include both absolute change (mL), percent change from the preoperative baseline and trend across time points. This would assure both the clinician and patient that the shunt is functional, especially if symptoms of iNPH persist postoperatively.

We were surprised to find considerable variation in the early reduction of ventricular volume in patients with the same setting. Patients with setting 4 had an initial reduction ranging between 5.7 and 47 mL and in the "virtual off" setting 8 the same figure was 0.05 and 20 mL. This illustrates a significant inter-individual variability, possibly caused by heterogeneity in brain compliance, atrophy, and CSF dynamics among patients. It also highlights how a one-off measurement can have limited value in clinical decision-making and the need for repeated longitudinal monitoring to capture the individual trajectory of a patient's ventricular volume. However, if substantial volumetric reduction is observed early postoperatively, the clinician could consider cautiously increasing the valve resistance in order to avoid over-drainage symptoms and complications.

As all patients with virtual off still had a mean of 5 mL reduction of ventricular volume at 36 hours, we find there still is a possibility that shunting occurs even at setting 8. According to basic shunt physiology models,²⁵ there is still a possibility of CSF-flow through a differential pressure valve with a resistance slightly above 400 H₂O, especially if the patient is in the upright position and if there is no antisiphoning device in the shunt system. In this study protocol, there are methodological shortcomings that prevent us to confidently verify or exclude shunt patency with the





virtual off setting 8. Patients were 36 hours earlier sampled for 20 mL of CSF from ventricles and the lumbar cistern during surgery. The effects on volumetric ventricular reduction due to the withdrawal of CSF should according to an earlier study be normalized after 24 hours.³⁰ However, the recent lumbar puncture and shunt surgery can possibly cause leakage of CSF both to the lumbar paravertebral muscles and soft tissues as well as to the subcutaneous tissues around the burr hole. What effect such a leakage has had on the reduced volume in patients with setting 8 cannot be estimated and this is a confounding factor. The reason we chose the 24–48-hour time frame for the first postoperative MRI were logistical, as patients were bound for discharge from the hospital and while being often frail, patients would have problems to come back shortly after discharge. We also wanted to focus on early volumetric effects of shunt surgery, hence the trade-off. We have used the Codman Certas® Plus valve in our department since 2017 and our experience from the virtual off function is that it has been useful in assessing shunt dependency and treating postoperative subdural hematomas and hygromas conservatively. This clinical usefulness is seen regardless of whether there is no or minimal shunting through the valve.

However, to study the impact on ventricular volumetry of “virtual off,” there would need to be a longer interval from surgery or adjustment to setting 8, such as in the PENS (Placebo-Controlled Efficacy in INPH Shunting) trial.³¹

The results of both blinded and non-blinded readings of valve resistance confirmed our clinical experience of the Codman Certas® Plus valve being trustworthy as for MRI-resistance.¹⁸ There were no MRI-induced valve changes after more than 150 3T MRIs. In our department, we discontinued routine valve setting check-ups in Certas® Plus shunt valves after MRI in 2019 and this applies for the rest of our catchment area in Southeast Sweden with 9 referring hospital and 1.1 million inhabitants. It is difficult to estimate the extent of economic and climate related savings of patient and health care staff time expenditure, transport emissions across our region, radiation for shunt valve checks and education on valve setting check-up technique in each hospital with an MRI examining patients with shunts. We are, however, confident our routine is patient safe based on our clinical experience and the results from this and earlier studies.¹⁸

A variety of segmentation software tools are available for volumetric post-processing of standard 3D MRI images, most of

Table 3. MRI-resistance in Codman Certas® Plus Valves After 3T MRI

	No of 3T MRI Examinations (n)	Correct Valve Readings after 3T MRI (n)	Percentage of Correct Readings (%)
Postoperative MRI—24–48 hours	45	45	100
Setting 4	20	20	
Setting 8	25	25	
Postoperative MRI—3 months	46	46	100
Postoperative MRI—12 months	45	45	100
Postoperative MRI—36 months	20	20	100
Total	156	156	100

Valve readings after 24–48 hours were blinded to the examiner and patient.

which use isotropic T1-weighted sequences.^{32,33} Several of these tools include automated segmentations of brain structures, including the ventricles. Despite its potential, the integration of ventricular volumetry into clinical practice faces several challenges. These include the complexity of the software required for analysis, the time required for manual segmentation and MRI availability. The development of automated and AI-based methods for measuring ventricular volume has enhanced the efficiency and accuracy of this technique,^{34,35} but widespread adoption will likely depend on further simplification of these technologies and demonstration of clear clinical benefits. Regarding the efficacy and precision of the 3D-QALAS qMRI automated volumetry, this study confirms our earlier published results, demonstrating that this method is both fast and reliable.¹³ The time required to correct the output of the automated algorithm is less than 2 minutes. Furthermore, the short scan time of 6 minutes was, in our experience, well tolerated even by elderly patients with cognitive decline.

The results from this study support moving toward volumetry-guided postoperative management in iNPH. By highlighting the limitations of 2D measures and providing a more sensitive, objective readout of early shunt effects automated volumetry offers a more nuanced approach to valve management and follow-up imaging. We believe automated ventricular volumetry could be integrated into postoperative workflows to confirm shunt patency when questioned and assess possible over- or underdrainage.

There are limitations to the generalizability of this automated algorithm beyond iNPH-patients. It was developed and validated using data from iNPH-patients and age matched healthy subjects. Patients with obstructive hydrocephalus, pediatric patients and other hydrocephalus forms are yet to be studied before the SyMRI automated ventricle volumetry software can be applied to these groups. Future studies should include long-term follow-up of volumetry in shunted iNPH-patients in relation to traditional radiological parameters, clinical outcome and overdrainage complications. The goal would be linking volumetric changes with long-term clinical outcomes to establish evidence-based decision thresholds. Investigations into how ventricular volume changes with shunt setting adjustments need to be done in

multicenter cohorts to assess generalizability and reliability of automated volumetry across scanners and centers. A study exploring if preoperative CSF dynamics or measures of brain compliance such as MR elastography can predict the postoperative volumetric response could elucidate the inter-individual variation in postoperative drainage volumes. Also, the use of ventricular volume and assessment of THC as noninvasive means of diagnosing shunt failure in iNPH need to be explored.

CONCLUSIONS

In conclusion, this study demonstrates that ventricular volumetry using a qMRI-based sequence and automated ventricle segmentation algorithm can confirm early ventricular reduction after shunt surgery. The magnitude of volume reduction is clearly related to shunt setting. Decompression of tight high-convexity and medial parafalcine sulci emerges as a potential early indicator of shunt function in iNPH-patients. Moreover, our findings show that the Codman Certas® Plus valve is resistant to MRI-induced changes also in a clinical setting. Future work should emphasize exploring whether volumetry can be used to rule out shunt failure, integration of volumetry into clinical decision-support tools and determine if volumetry-guided shunt valve resistance optimization could improve long-term symptom relief in iNPH-patients.

CRedit AUTHORSHIP CONTRIBUTION STATEMENT

Rafael T. Holmgren: Writing – original draft, Visualization, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.
Martin Nilsson: Investigation.
Charalampos Georgiopoulos: Writing – review & editing, Formal analysis, Conceptualization.
Peter Zsigmond: Writing – review & editing, Supervision, Investigation, Conceptualization.

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