Purpose: Intracranial and intraspinal compliance are parameters of interest in the diagnosis and prediction of treatment outcome in patients with normal pressure hydrocephalus and other forms of communicating hydrocephalus. A noninvasive method to estimate the spinal cerebrospinal fluid (CSF) pulse wave velocity (PWV) as a measure of compliance was developed using a multiband cine phase-contrast MRI sequence and a foot-to-foot algorithm.

Methods: We used computational simulations to estimate the accuracy of the MRI acquisition and transit-time algorithm. In vitro measurements were performed to investigate the reproducibility and accuracy of the measurements under controlled conditions. In vivo measurements in 20 healthy subjects and 2 patients with normal pressure hydrocephalus were acquired to show the technical feasibility in a clinical setting.

Results: Simulations showed a mean deviation of the calculated CSF PWV of 3.41% ± 2.68%. In vitro results were in line with theory, showing a square-root relation between PWV and transmural pressure and a good reproducibility with SDs of repeated measurements below 5%. Mean CSF PWV over all healthy subjects was 5.83 ± 3.36 m/s. The CSF PWV measurements in the patients with normal pressure hydrocephalus were distinctly higher before CSF shunt surgery (33.80 ± 6.75 m/s and 31.31 ± 7.82 m/s), with a decrease 5 days after CSF shunt surgery (15.69 ± 3.37 m/s).

Conclusion: This study evaluates the feasibility of CSF PWV measurements using a multiband cine phase-contrast MRI sequence. In vitro and in vivo measurements showed that this method is a potential tool for the noninvasive estimation of intraspinal compliance.
1 | INTRODUCTION

The intracranial and intraspinal compliance are physiological parameters associated with CSF dynamics and neurological diseases (eg, normal pressure hydrocephalus [NPH] and Chiari malformation). The compliance of a vessel is defined as the ratio of volume change to corresponding transmural pressure change. It has a large impact on prevalent, pulsatile hydrodynamics and is dependent on the transmural pressure. The compliance cannot be measured directly; therefore, advanced methods are necessary to estimate the intracranial or intraspinal compliance.

At present, pressure measurements and spinal-tap tests by invasive lumbar punctures are clinically performed for the diagnosis of NPH. With symptom relief after drainage of 30 to 50 mL CSF, the implementation of a CSF shunt is advised. However, the diagnosis of NPH and the outcome after CSF shunt surgery based on spinal-tap tests are still uncertain and hard to predict.

For a more advanced diagnosis of neurological diseases, such as NPH and other forms of communicating hydrocephalus, different approaches were developed to measure the intracranial or intraspinal compliance. The resistance to outflow of CSF was estimated as an index of the compliance using bolus or continuous injection or drainage of a defined amount of fluid into the subarachnoid space during constant pressure measurement. Studies by Boon et al showed a good prediction of CSF shunt response in patients with NPH by estimating the resistance to outflow as an index of cranio-spinal compliance. Disadvantages of these methods are the invasive character and change of conditions by putting additional strain on a possibly increased pressure in the subarachnoid space. An alternative noninvasive method for estimating the intrathecal compliance was presented by Alperin et al using phase-contrast MRI (PCMRI) velocity measurements. Two separate PCMRI velocity measurements are necessary to estimate the net flow volume defined by arterial, venous and CSF flow, and to calculate the pressure gradient using the Navier-Stokes relationship. However, due to the invasiveness of the former and the complexity of the latter, both methods are rarely integrated into clinical routine.

Therefore, different noninvasive approaches have been suggested to measure the spinal CSF pulse wave velocity (PWV). The global or local PWV serves as a marker for compliance in accordance with the Moens-Korteweg and the Bramwell-Hill equation. The PWV is defined by a distance divided by the transit time that the pressure wave requires to traverse that distance. The transit time can be derived from velocity profiles of the fluid measured by Doppler ultrasound or PCMRI and an algorithm that finds certain reference time points for the arrival of the pressure wave. Kalata et al estimated spinal CSF PWV using sagittal PCMRI measurements in 3 patients. Sass et al performed spinal CSF PWV measurements in 10 healthy subjects and 8 patients with amyotrophic lateral sclerosis by acquiring six axial planes between the Foramen Magnum and vertebra L4 and interpolating over the maximum systolic flow. These methods have not been evaluated in large study cohorts of healthy subjects or patients so far and are therefore not integrated in the clinical routine.

Measurements of vessel stiffness or compliance are more common in cardiovascular diagnostics, such as in the diagnosis of aortic atherosclerosis. In cardiovascular applications, one of the most established transit-time algorithms is the foot-to-foot algorithm. The PWV can be derived over the aortic arch by a single PCMRI measurement covering both the ascending and descending aorta at the level of the pulmonary artery. Due to the anatomy of the spinal canal, CSF PWV cannot be derived by a single transversal slice. Additionally, recent studies using real-time MRI acquisitions showed that CSF flow is influenced by respiration. Therefore, the acquisition of consecutive axial cine PCMRI slices of the spinal CSF may be biased by differences in respiration or heart rate.

Acquisition methods such as multiband imaging allow the simultaneous acquisition of two or more slices using a modified RF excitation in combination with image unfolding by spatial coil sensitivity or phase shifts.

In this work, we developed a new method that enables PWV measurements of the CSF along the spinal cord within one measurement using multiband cine PCMRI. The method allows for a very high temporal resolution of 5.5 ms in combination with simultaneous acquisition of both necessary imaging slices along the spinal cord. Therefore, differences between both velocity profiles of the CSF, which may be caused by physiological variations during separate measurements, are minimized (eg, changes in heart rate or respiration). The aim of the presented study was the technical evaluation of this method by simulations and in vitro and in vivo measurements of healthy subjects. Additionally, the technical feasibility in a clinical setting was shown in 2 patients with NPH.

2 | METHODS

To evaluate the influence of respiration-induced CSF flow on cine PCMRI measurements and the error of the PWV...
algorithm at a given temporal resolution, computational simulations were performed. In vitro measurements were acquired to evaluate the method under controlled conditions, and in vivo measurements were performed in healthy subjects and 2 patients with NPH to show feasibility in a clinical scenario.

2.1 Estimation of spinal CSF PWV using multiband cine PCMRI

The compliance of a vessel (C) is defined as the ratio between volume changes (ΔV) and the corresponding transmural pressure changes (ΔP) in a vessel, as follows:

$$ C = \frac{\Delta V}{\Delta P} \quad (1) $$

The propagation speed of a pressure wave in a pulsatile flow can be used as an indirect measure of compliance in accordance with the Bramwell-Hill equation:

$$ PWV = \sqrt{\frac{\Delta P}{\rho \Delta V}} \propto \sqrt{\frac{1}{C}} \quad (2) $$

where $\rho$ is the fluid density and $V$ is the volume. The PWV can be defined as the spatial distance between two observed points (Δd) divided by the time the pulse wave needs to cover this distance, called transit time (Δt):

$$ PWV = \frac{\Delta d}{\Delta t} \quad (3) $$

Thus, the PWV of the CSF can be measured by evaluating the CSF pulse wave at two locations within the spine with a known distance (Figure 1A).

To this end, CSF-PWV measurements were performed using simultaneous PCMRI velocity measurements of two separate slices along the spine (Figure 1B). The PWV was estimated using a foot-to-foot transit-time algorithm. This algorithm calculates the temporal delay of the “feet” of two velocity profiles. The foot is defined as the intersection between a tangent on the point of the maximum gradient during systolic, caudal flow and a horizontal projection through the local minimum (Figure 1C).

2.2 Computational simulations

2.2.1 Influence of respiration-induced CSF flow to cine PCMRI measurements

Numerical simulations were performed to evaluate the influence of respiration-induced variations of CSF flow on cine PCMRI measurements. Therefore, two flow profiles were simulated: a purely cardiac driven flow and a combination of cardiac-driven and respiratory-driven flow. The cardiac-driven flow had a waveform similar to observed in vivo data with a frequency of 1 Hz and an amplitude of 5 cm/s. The respiratory waveform was generated by natural in vivo respiration waveforms, with a frequency of about 0.4 Hz and normalized to a maximum amplitude of 7 cm/s (Figure 2A). These two flow waveforms, cardiac and cardiac + respiration, were transferred to magnitude and phase images of a transversal plane with a simplified model of the spinal anatomy with a laminar flow profile inside the subarachnoid space (Figure 2B). Noise was added to provide more realistic images. The images were sampled in a cartesian cine PCMRI scheme, similar to the MRI sequence of the proposed method with a temporal resolution of 5.5 ms. The velocity was evaluated by averaging over a region of interest (ROI) comprising the spinal canal.

2.2.2 Accuracy of PWV measurements using a foot-to-foot algorithm

Velocity data were extracted from 1 subject with a temporal resolution of 5.5 ms. Processing steps similar to that used by Dorniak et al. were applied, and the velocity data were interpolated to a temporal resolution of 0.1 ms. Temporal shifts were added for a given distance of $d = 190$ mm and PWV of 2-50 m/s in steps of 1 m/s, resulting in pulse-wave transit times of 95.0-3.8 ms. Afterward, both resulting velocity curves, the original and the shifted, were down-sampled to the original temporal resolution of 5.5 ms, and the foot-to-foot algorithm was applied to calculate the PWV. Differences between the true and the calculated PWV were estimated and evaluated for all simulated PWV. To minimize the rounding error due to the discrete shift based on a temporal resolution of 0.1 ms, the true PWV was defined by the actual, discrete shift.

2.3 In vitro study

To evaluate the measurement and algorithm accuracy under ideal conditions, a distensible silicon tube was connected in a tube system with rigid tubes and a programmable flow pump (CardioFlow 5000; Shelley Medical, London, Canada) (Figure 3). The phantom had a length of 50 cm, an outer diameter of 27 mm, and an inner diameter of 23 mm. A pulsatile flow with a frequency of 0.97 Hz was adjusted, corresponding to a heart rate of 58 beats per minute. Two axial images along the tube were acquired simultaneously using a multiband cine PCMRI sequence. The measurement was repeated five times. The study was repeated six times with
increased pressure levels in steps of 5 cm H2O relative to the initial pressure by increasing the water level of the reservoir. The FOV was placed in the center of the phantom tube to avoid disturbances from the flow inlet or outlet.

2.4 | In vivo study

All subjects were examined with the permission of the institutional ethics committee, and informed consent was obtained before the study. The study cohort consisted of 22 healthy subjects (9 female, 13 male, mean age 29.1 ± 7.4 [21, 45] years), and 2 male patients suffering from NPH (76-year-old and 70-year-old). The patient data were acquired 1 day before CSF shunt surgery and 5 days after surgery. The cranial slice was positioned between vertebrae C1 and C2, and the caudal slice was positioned 180 mm caudal to the cranial slice (Figure 1A). Based on an initial multiband 2D phase-contrast gradient-echo image, to determine the maximum velocity, the encoding velocity was increased in individual subjects from 10 cm/s to 15 cm/s, if necessary, to avoid phase wraps. The imaging sequence was repeated 10 times in healthy subjects within two sessions, with five acquisitions in each session. The subjects were repositioned between the two sessions. The break between sessions was about 5 minutes. Patient measurements were acquired three times per imaging session, without repositioning.

2.5 | Magnetic resonance imaging sequence

Images were acquired on a 3T MRI system (Ingenia; Philips Medical Systems, Best, the Netherlands). For in vitro
FIGURE 2  Simulation of influence of respiration-induced flow on CSF velocity measurements using cine PCMRI. A, Exemplary 10 seconds of cardiac (black) and cardiac + respiration (gray) velocity waveforms that were used for the input of the simulation. Amplitude of respiratory flow was 40% greater than cardiac-driven flow. B, Simulated anatomy of an axial plane. The geometry is similar to the human chest with a simulated subarachnoid space at the posterior side. C, Results of a simulated cine PCMRI acquisition of cardiac (solid), cardiac + respiratory (dashed), and cardiac ground truth (dotted)—driven flow averaged over a region of interest comprising the simulated subarachnoid space.

FIGURE 3  Schematic drawing of the phantom setup. The reservoir and the tube system with the phantom tube were arranged on the MRI table. A flow pump introduced a pulsatile flow from the reservoir into the tube system. Two transversal image planes covering the phantom tube were acquired. The pressure of the system was increased by increasing the water level of the reservoir.
measurements, a 28-channel anterior and posterior coil array was used. For in vivo measurements, no anterior coil was used, and the 12-channel posterior coil array was combined with a 16-channel head coil array. Beforehand, a sagittal $T_2$-weighted 3D image volume was acquired for planning. The trigger signal of the flow pump and a wireless pulse oximeter were used for retrospective triggering of the cine acquisitions for the in vitro and in vivo measurements, respectively. Two transversal image planes were acquired simultaneously using a multiband cine PCMRI sequence with imaging parameters listed in Table 1. Due to the velocity encoding and the large slice distance of 180 mm, no FOV shift between the two excited slices was applied. Instead of typical phase-contrast imaging, consisting of an alternated acquisition of velocity-encoded and velocity-compensated images, only velocity-encoded images were acquired for the PWV measurements, resulting in a high temporal resolution of one TR.

### 2.6 Data analysis

All images were reconstructed online at the scanner. Further image processing of in vitro and in vivo data was performed in MATLAB (2019a; The MathWorks, Natick, MA). The background phase was removed by subtraction of the first dynamic from all subsequent dynamics. Contours were manually drawn in the image with the most apparent flow and copied to all time points. Velocity data were extracted by averaging over the contours (Figure 1B). The resulting velocity data were interpolated to a temporal resolution of 0.1 ms using a spline interpolation. System imperfections of the phantom setup induced a high frequency flow with a relatively small amplitude, which is superimposed to the adjusted approximate 1-Hz flow. To avoid errors of the PWV algorithm due to this high frequency, a low-pass filter was applied. The foot-to-foot algorithm (Figure 1C) was applied, and the resulting reference time points were checked manually. If the algorithm failed to find the significant systolic upslope due to noise, the interval for searching the maximum gradient was restricted manually to the section of the relevant slope during systolic flow. The distance between both transversal slices was measured manually along the travel distance based on the previously acquired sagittal image (Figure 1A).

### 2.7 Statistical analysis

In vitro results are presented as mean ± SD. In vivo results are log-normal distributed, as no negative values are physiologically expected and occurring outliers may be determined primarily by increased values. Therefore, in vivo results are represented as expected value ± SD based on calculations for log-normal distributions and were analyzed using a Wilcoxon Mann–Whitney U test to compare the averaged expected values of sessions 1 and 2 with a significance level of $\alpha = 0.05$. For in vitro data, the minimal difference that can be detected as a true difference, called the critical difference $d_{crit}$, was calculated as shown in Eq. 4 with the mean PWV ($PWV_{mean,l}$), the SD ($SD_l$) averaged over each pressure level $n_l$, the maximum PWV of all measurements ($PWV_{max}$), and a significance level of $\alpha = 0.05^{29}$:

$$d_{crit} = 2.77 \cdot PWV_{max} \cdot \frac{1}{n_l} \sum_{l=1}^{n_l} \frac{SD_l}{PWV_{mean,l}}$$

### 3 RESULTS

#### 3.1 Computational simulations

The resulting velocity waveforms were plotted for the cardiac driven flow, the cardiac + respiration driven flow, and the cardiac ground truth (Figure 2C). The mean absolute difference between the waveforms proved to be $0.10 \pm 0.08$ cm/s, the maximum absolute difference 0.28 cm/s, and the difference of the peak velocity 0.12 cm/s.

Calculated PWV from simulated transit times using a foot-to-foot algorithm ranged from 2.01 to 45.80 m/s (Figure 4A), with absolute errors compared with true PWV ranging up to 8.41% (Figure 4B), an average absolute PWV error of $3.41\% \pm 2.68\%$, and a median of 2.92%. Pearson correlation calculations showed a correlation coefficient of $R = 0.995$ ($p < .0001$) between the calculated and true PWV. The deviation from the ideal linear relationship and the absolute PWV
error followed an alternating form, with an increasing amplitude by increasing PWV.

3.2 | In vitro study

The resulting velocity wave forms and PWV of in vitro measurements are shown in Figures 5 and 6, respectively. The minimum and maximum measured PWV were 2.45 and 3.78 m/s, respectively. The SDs for five repeated measurements at the same pressure level reached from 2.36% to 3.24%. Pearson correlation coefficient between relative pressure levels and PWV$^2$ averaged over repeated measurements was $R = 0.93$ ($p = .008$). The critical difference was calculated as $d_{crit} = 0.30$ m/s.

3.3 | In vivo study

Two of the 22 healthy subjects were excluded due to low, insufficient CSF flow, possibly induced by motion or varying heart rate, and due to unreasonable, nonphysiological results of the PWV algorithm, respectively. In 1 subject, only four repeated measurements in the second session were possible,
resulting in 199 evaluated PWV measurements in 20 healthy subjects.

The measurement after surgery in the 70-year-old patient and the last repetition in the 76-year-old patient after surgery failed due to low signal of the peripheral pulse trigger, resulting in three measurements before surgery in both patients and two measurements after surgery in patient 1.

The average deviation of the slice distances along the spine between sessions 1 and 2 was 1.36 ± 1.81 mm, according to 0.70% ± 0.93% of the slice distance in session 1. The mean PWV over all healthy subjects was 5.83 ± 3.36 m/s.

Figure 6 shows the average PWV for each session and subject. The mean absolute difference in healthy subjects between the average PWV of sessions 1 and 2 was found not to be significant using Wilcoxon Mann–Whitney U test ($p = .4903$). Figure 8 shows a histogram of all PWVs measured in healthy subjects. The mean PWVs of the 76-year-old patient before and after surgery were 33.80 ± 6.75 m/s and 15.69 ± 3.37 m/s, respectively. The mean PWV of the 70-year-old patient was 31.31 ± 7.82 m/s. Individual PWVs of the patient measurements are shown in Figure 7.

4  |  DISCUSSION

A new method for noninvasive CSF PWV measurements combining the use of multiband cine PCMRI velocity measurements with very high temporal resolution of 5.5 ms was developed and evaluated in numerical simulations and in vitro and in vivo measurements. Simulations were performed to evaluate the influence in respiratory-driven CSF flow and the accuracy of the CSF-PWV calculation at a certain temporal resolution. In vitro and in vivo measurements were performed to estimate the reproducibility under controlled and physiological conditions, respectively. Two patients with NPH were acquired to show the technical feasibility in a clinical setting.

The comparison between cardiac-driven velocity waveforms and cardiac + respiration-driven velocity waveforms showed that the influence of respiratory-driven flow is marginal in cine PCMRI measurements. Therefore, cine PCMRI measurements are justified for the purpose of time-averaged spinal CSF-PWV measurements. These results are in line with previous studies in phantom and in vivo measurements.
Studies by Yildiz et al and Spijkerman et al showed that real-time PCMRI measurements provide more accurate quantifications of peak velocity, net flow, and stroke volume. However, the difference of the velocity waveforms between cardiac and cardiac + respiratory-driven flow (Yildiz et al, Figure 3) as well as respiratory-gated and nonrespiratory-gated acquisitions (Spijkerman et al, Figure 2) are marginal.\(^8,9\) Therefore, the proposed multiband cine PCMRI acquisitions provide time-averaged and respiratory-averaged spinal CSF-PWV measurements, which are comparable to previously applied invasive methods to estimate the spinal compliance or other CSF-PWV methods.\(^{10-12}\)

Simulations with CSF PWV and the application of the foot-to-foot algorithm showed an increasing error with increasing PWV, expectably due to lower transit times and the limited temporal resolution. The mean and the median error of simulated PWV were within an acceptable range of under 5%. The results are in line with the findings of Gaddum et al\(^{30}\), for PWV of about 5 m/s simulated in the aorta using the foot-to-foot algorithm, an error of under 5% was found. They showed that this algorithm is suitable for blood flow with temporal resolutions under 10 ms and noise less than 10%. Based on the computational simulations performed in this study, the foot-to-foot algorithm is also suitable for CSF flow. However, PWV larger than 25 m/s, and therefore shorter transit times, may suffer from lower accuracy due to the limited temporal resolution. The alternating form of the error versus true PWV plot arises from interpolation during the simulation. The interpolation on the different shifted velocity data may hit prominent points required for the foot-to-foot algorithm with varying accuracy. However, the data can be interpreted as a simulation of a worst-case-scenario, according to the minima and maxima. As the same data were used for both the original and the shifted velocity data, the results showed the error caused by the foot-to-foot algorithm and the temporal resolution, regardless of image quality, physiological variation, or modulated velocity waveform along the spinal canal.

Due to the PCMRI acquisition of only velocity-encoded images and the subtraction of the first dynamic, a global offset may be introduced to the velocity data. However, this does not influence the PWV measurements, as the foot-to-foot algorithm defines the transit time only based on internal reference points and is therefore independent of offsets.

The variations of the phantom study were larger than given by simulations for PWV of 2-4 m/s, which may be due to MRI acquisition, system imperfections of the flow pump, or different velocity shapes between the slices, and therefore reduced accuracy in the determination of reference time points. However, the phantom study showed good agreement of velocity waveforms in repeated measurements and good reproducibility with SDs under 5% for the corresponding PWV measurements. The increasing PWV with increasing pressure followed a square-root function, in line with the Bramwell-Hill equation,\(^{12}\) and confirmed by the excellent linear correlation between pressure and PWV\(^2\) averaged over repeated measurements. The lower the initial pressure, the larger the difference in the resulting PWV at a certain pressure increase. Differences in the average PWV between the lowest two pressure levels and the following increased pressure levels were higher than the critical difference, and thus statistically significant. Due to the square-root relation, pressure levels from \(\Delta p \geq 10\) cm H\(_2\)O result in increased PWV, but were below the critical difference. However, all results are still in agreement with the theory of a square-root relation. The chosen interval of transmural pressures covers part of the physiologic range. However, the phantom measurements do not represent physiologic conditions.

The in vivo data showed no significant differences between the averages of two sessions with five repeated PWV measurements. The mean PWV over all subjects was within the range of PWV found in previous studies. Jackson et al obtained a PWV of 13.5 m/s using invasive pressure measurements in a patient with an unspecified disease, and evaluated the results as an overestimation.\(^{31}\) Kalata et al estimated PWV using sagittal PCMRI measurements in 3 patients with pathologies that are typically not accompanied by increased intracranial or intraspinal pressure or compliance. They obtained a mean PWV of 4.6 ± 1.7 m/s over all 3 patients during systolic acceleration.\(^{16}\) Martin et al obtained PWV in an in vitro syringomyelia model of about 25 m/s over the cardiac cycle.\(^{32}\) Sass et al found a spinal CSF PWV of 3.47 m/s averaged over 10 healthy subjects by the consecutive acquisition of six axial PCMRI planes.\(^{17}\)

The SD of in vivo PWV measurements is determined by two effects. The PWV is determined by the difference between two measurements, the determination of the foot of two wave forms that is accompanied with uncertainties. The error of the difference of the measurement (transit time) is given by the sum of the absolute errors of the measurements. As high PWV are induced by low transit times, these are accompanied with increasing relative errors. Therefore, a correlation between mean PWV and relative SD can be
observed ($R = 0.553$, $p > .001$). Additionally, the PWV is not normal-distributed but right-skewed, log-normal distributed. Negative values do not exist, and outliers are determined by high values. Therefore, outliers induce not only increased SDs but also increased mean PWV. This affects a correlation between mean PWV and absolute SD ($R = 0.857$, $p > .001$), which is increased with decreasing measurements per session, as outliers are weighted more.

The phantom study also showed lower SDs than the in vivo study. Therefore, the intrasubject variations may be attributed primarily to physiological variations instead of algorithm inaccuracy or measurement error. Intrasubject and intersubject variations of the PWV have been reported in cardiovascular examinations. Parikh et al showed large correlations with age and small correlations with heart rate. These parameters may also influence CSF PWV and may explain variations between repeated measurements. As the patients were distinctly older than the healthy subjects in this study, the increased PWV in the patients may also be attributed to the increased age. However, as the PWV is greatly decreased after CSF shunt surgery, the age-related effect is likely to be small compared with the pathological effect of NPH. At present, previous studies on CSF PWV are limited, making further studies necessary to determine whether age or heart rate–specific reference values are required for the CSF PWV. For the evaluation of reference values, regarding the intraspinal compliance or pressure, a large study cohort is required based on a sagittal 2D plane were below 10 mm. In this study, a slice distance of 180 mm was used, which conforms to deviations under 5.5% with uncertainties below 10 mm. Although differences between the average of both sessions of the in vivo measurements were not significant and deviations of slice distances between session 1 and 2 were low, automatic distance measurements, such as using 3D centerline extraction, may further improve the accuracy of CSF-PWV measurements.

The distance of the slices was chosen under consideration of different aspects. An increased slice distance is accompanied by increased transit times, and therefore provides higher temporal accuracy. However, the image quality increases with decreasing slice distances, as the magnetic field homogeneity increases near the isocenter, which also improves the accuracy of the multiband RF pulse. Further studies are warranted to investigate the influence of the slice distance.

The influence of intra-observer and interobserver variations was found to be low in other studies of CSF flow measurements. Therefore, we expect the influence of the region-of-interest selection to be small. In addition, the mean velocity inside an ROI was quantified, which, unlike flow, is not dependent on the ROI size. Ten measurements were acquired at the same location in each subject in two sessions. The deviation of the repeated measurements is also determined by the uncertainty of the ROI selection. However, the influence of the ROI selection on PWV measurements needs to be evaluated in further studies.
Although the influence of respiration-dependent CSF flow in cine PCMRI was shown to be small, a dedicated technique that enables respiration-dependent flow acquisitions might provide more accurate, respiration-resolved spinal CSF-PWV measurements. However, further developments are necessary to overcome challenges of temporal and spatial resolutions, such as in real-time acquisitions. Patient studies will show whether these provide a clinical benefit compared with respiration-averaged CSF-PWV measurements.

6 CONCLUSIONS

Multiband cine PCMRI velocity measurements allow the estimation of the spinal CSF PWV. This method enables non-invasive, respiration-averaged measurements of PWV as a marker of intraspinal pressure or compliance within a single, 2-minute MRI acquisition and limited processing steps. In vivo and preliminary measurements in 2 patients with NPH show the technical feasibility of the presented technique in a clinical setting. However, further studies in larger cohorts are warranted to investigate the dependency of CSF PWV on physiological parameters and to investigate the clinical benefit of this novel technique.

CONFLICT OF INTEREST

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REFERENCES

1. Bothwell SW, Janigro D, Patabendige A. Cerebrospinal fluid dynamics and intracranial pressure elevation in neurological diseases. Fluids Barriers CNS. 2019;16:9.
2. Mase M, Miyati T, Yamada K, Kasai H, Hara M, Shibamoto Y. Non-invasive measurement of intracranial compliance using cine MRI in normal pressure hydrocephalus. Acta Neurochir Suppl. 2005;95:303-306.
3. Alperin N, Sivaramakrishnan A, Lichtor T. Magnetic resonance imaging-based measurements of cerebrospinal fluid and blood flow as indicators of intracranial compliance in patients with Chiari malformation. J Neurosurg. 2005;103:46-52.
4. Damasceno BP, Carelli EF, Honorato DC, Facure JJ. The predictive value of cerebrospinal fluid tap-test in normal pressure hydrocephalus. Arq Neuropsiquiatr. 1997;55:179-185.
5. Hebb AO, Cusimano MD. Idiopathic normal pressure hydrocephalus: a systematic review of diagnosis and outcome. Neurosurgery. 2001;49:1166-1184; discussion 1184-1166.
6. Marmarou A, Shulman K, LaMorgese J. Compartamental analysis of compliance and outflow resistance of the cerebrospinal fluid system. J Neurosurg. 1975;43:523-534.
7. Cardoso ER, Rowan JO, Galbraith S. Analysis of the cerebrospinal fluid pulse wave in intracranial pressure. J Neurosurg. 1983;59:817-821.
8. Boon AJW, Tans TJ, Delwel EJ, et al. Dutch normal-pressure hydrocephalus study: prediction of outcome after shunting by resistance to outflow of cerebrospinal fluid. J Neurosurg. 1997;87:687-693.
9. Alperin NJ, Lee SH, Loth F, Raksin PB, Lichtor T. MR-intracranial pressure (ICP): a method to measure intracranial elastance and pressure noninvasively by means of MR imaging: baboon and human study. Radiology. 2000;217:877-885.
10. Isebree MA. Die Pulscurve. Leiden, the Netherlands: E.J. Brill; 1878.
11. Korteweg DJ. Uber die Fortpflanzungsgeschwindigkeit des Schalles in elastischen Röhrnen. Ann Phys. 1878;241:525-542.
12. Bramwell JC, Hill AV. The velocity of the pulse wave in man. Proc Royal Soc B. 1922;93:298-306.
13. Lehmann ED, Gosling RG, Fatemi-Langroudi B, Taylor MG. Non-invasive Doppler ultrasound technique for the in vivo assessment of aortic compliance. J Biomed Eng. 1992;14:250-256.
14. Forbat SM, Mohiaddin RH, Yang GZ, Firmin DN, Underwood SR. Measurement of regional aortic compliance by MR imaging: a study of reproducibility. J Magn Reson Imaging. 1995;5:635-639.
15. Laffon E, Marthan R, Montaudon M, Latrabe V, Laurent F, Ducassou D. Feasibility of aortic pulse pressure and pressure wave velocity MRI measurement in young adults. J Magn Reson Imaging. 2005;21:53-58.
16. Kalata W, Martin BA, Oshinski JN, Jerosch-Herold M, Royston TJ, Loth F. MR measurement of cerebrospinal fluid velocity wave speed in the spinal canal. IEEE Trans Biomed Eng. 2009;56:1765-1768.
17. Sass LR, Khani M, Romm J, et al. Non-invasive MRI quantification of cerebrospinal fluid dynamics in amyotrophic lateral sclerosis patients. Fluids Barriers CNS. 2020;17:4.
18. Latham RD, Westerhof N, Sipkema P, Rubal BJ, Reuderink P, Murgio JP. Regional wave travel and reflections along the human aorta: a study with six simultaneous micromanometric pressures. Circulation. 1985;72:1257-1269.
19. Voges I, Jerosch-Herold M, Hedderich J, et al. Normal values of aortic dimensions, distensibility, and pulse wave velocity in children and young adults: a cross-sectional study. J Cardiovasc Magn Reson. 2012;14:77.
20. Drehu-Kulaczewski S, Joseph AA, Merboldt KD, Ludwig HC, Gartner J, Frahm J. Inspiration is the major regulator of human aortic compliance. J Biomed Eng. 2012;34:393-400.
21. Tschachler P, de Susse SH, Niederer PA, et al. Non-invasive Doppler ultrasound technique for the in vivo assessment of aortic dimensions, distensibility, and pulse wave velocity in children and young adults: a cross-sectional study. J Cardiovasc Magn Reson. 2012;14:77.
22. Chen L, Beckett A, Verma A, Feinberg DA. Dynamics of respiratory and cardiac CSF motion revealed with real-time simultaneous multi-slice EPI velocity phase contrast imaging. NeuroImage. 2015;122:281-287.
23. Yildiz S, Thyagaraj S, Jin N, et al. Quantifying the influence of respiration and cardiac pulsations on cerebrospinal fluid...
dynamics using real-time phase-contrast MRI. *J Magn Reson Imaging*. 2017;46:431-439.

24. Breuer FA, Blaimer M, Heidemann RM, Mueller MF, Griswold MA, Jakob PM. Controlled aliasing in parallel imaging results in higher acceleration (CAIPIRINHA) for multi-slice imaging. *Magn Reson Med*. 2005;53:684-691.

25. Breuer FA, Blaimer M, Mueller MF, et al. Controlled aliasing in volumetric parallel imaging (2D CAIPIRINHA). *Magn Reson Med*. 2006;55:549-556.

26. Barth M, Breuer F, Koopmans PJ, Norris DG, Poser BA. Simultaneous multislice (SMS) imaging techniques. *Magn Reson Med*. 2016;75:63-81.

27. Sonnabend K, Brinker G, Maintz D, Bunck A, Weiss K. Cerebrospinal fluid pulse wave velocity measurements using multiband CINE phase-contrast MRI. In: *ISMRM & SMRT Virtual Conference & Exhibition*, 650. 2020.

28. and Chiari malformation Dorniak K, Heiberg E, Hellmann M, et al. Required temporal resolution for accurate thoracic aortic pulse wave velocity measurements by phase-contrast magnetic resonance imaging and comparison with clinical standard applanation tonometry. *BMC Cardiovasc Disord*. 2016;16:110.

29. Smellie WS. What is a significant difference between sequential laboratory results? *J Clin Pathol*. 2008;61:419-425.

30. Gaddum NR, Alastruey J, Beerbaum P, Chowienczyk P, Schaeffter T. A technical assessment of pulse wave velocity algorithms applied to non-invasive arterial waveforms. *Ann Biomed Eng*. 2013;41:2617-2629.

31. Jackson JR, Williams B. Errors in velocity measurement by the Pitot principle in fluids with slowly propagated pressure waves. *J Biomed Eng*. 1979;1:50-54.

32. Martin BA, Kalata W, Loth F, Royston TJ, Oshinski JN. Syringomyelia hydrodynamics: an in vitro study based on in vivo measurements. *J Biomech Eng*. 2005;127:1110-1120.

33. Parikh JD, Hollingsworth KG, Kunadian V, Blamire A, MacGowan GA. Measurement of pulse wave velocity in normal ageing: comparison of Vicorder and magnetic resonance phase contrast imaging. *BMC Cardiovasc Disord*. 2016;16:50.

34. Miyati T, Mase M, Kasai H, et al. Noninvasive MRI assessment of intracranial compliance in idiopathic normal pressure hydrocephalus. *J Magn Reson Imaging*. 2007;26:274-278.

35. van Engelen A, Silva Vieira M, Rafiq I, et al. Aortic length measurements for pulse wave velocity calculation: manual 2D vs automated 3D centreline extraction. *J Cardiovasc Magn Reson*. 2017;19:32.

36. Sakhare AR, Barisano G, Pa J. Assessing test-retest reliability of phase contrast MRI for measuring cerebrospinal fluid and cerebral blood flow dynamics. *Magn Reson Med*. 2019;82:658-670.

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