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FULL PAPER

Automated CT registration tool improves sensitivity to change in ventricular volume in patients with shunts and drains

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Objective: CT is the mainstay imaging modality for assessing change in ventricular volume in patients with ventricular shunts or external ventricular drains (EVDs). We evaluated the performance of a novel fully automated CT registration and subtraction method to improve reader accuracy and confidence compared with standard CT.
Methods: In a retrospective evaluation of 49 ventricular shunt or EVD patients who underwent sequential head CT scans with an automated CT registration tool (CT CoPilot), three readers were assessed on their ability to discern change in ventricular volume between scans using standard axial CT images versus reformats and subtraction images generated by the registration tool. The inter-rater reliability among the readers was calculated using an intraclass correlation coefficient (ICC). Bland–Altman tests were performed to determine reader performance compared to semi-quantitative assessment using the bifrontal horn and third ventricular width. McNemar's test was used to determine whether the use of the registration tool increased the reader's level of confidence.
Results: Inter-rater reliability was higher when using the output of the registration tool (single measure ICC of 0.909 with versus 0.755 without the tool). Agreement between the readers' assessment of ventricular volume change and the quantitative assessment improved with the registration tool (limits of agreement 4.1 *vs* 4.3). Furthermore, the tool improved reader confidence in determining increased or decreased ventricular volume ($p < 0.001$).
Conclusion: Automated CT registration and subtraction improves the reader's ability to detect change in ventricular volume between sequential scans in patients with ventricular shunts or EVDs.
Advances in knowledge: Our automated CT registration and subtraction method may serve as a promising generalizable tool for accurate assessment of change in ventricular volume, which can significantly affect clinical management.

INTRODUCTION

CT is the mainstay imaging modality for assessing change in ventricular volume in patients with a ventricular shunt[1,2] or external ventricular drain (EVD).[3] Patients with ventriculoperitoneal (VP) shunts or other similar shunts often present to the emergency department for headaches or other non-specific symptoms. Rapid and accurate assessment of ventricular volume in this setting is critical for determining stability or change so that management decisions, such as adjusting shunt settings, can be made.

Assessment of ventricular volume change can be complicated by relative differences in head position in the CT gantry between scans, resulting in CT images that are often tilted and incorrectly aligned. The ability to co-register consecutive head CT scans in standard alignment and the creation of subtraction images would allow for more efficient and accurate comparison of the two scans. Rapid and reliable interpretation of ventricular volume based on head CT has significant clinical implications for patients in the Emergency Department, on the Neurosurgery service, and in the ICU. Although in clinical practice measurement tools to estimate ventricular volume would be available to the radiologist, using these tools takes time especially when the scans are not aligned between time points. Furthermore, it is often the emergency department physician, neurosurgeon, or trauma surgeon who is making the assessment of ventricular volume change in real time in order to determine clinical management, and measurement tools may not be readily accessible to these clinicians. Having a tool to quickly assess ventricular volume change could be useful in such circumstances, especially when a radiologist's formal interpretation may not be available in real time.

Several automatic segmentation algorithms for head CT segmentation have been proposed,[4–7] including commercially available software tools that provide automatic registration and matching of volumetric data at different time points.[8] Specifically, a few algorithms for ventricular system segmentation have been proposed[9–12] ; however, none have been applied clinically to assess ventricular volume change in patients with shunts and EVDs. These algorithms typically implement post-processing methods based on anatomic landmarks, thresholding, and regions of interest (ROIs) to provide reproducible assessment of ventricular volume. Limitations of these previously proposed methods include inaccuracies based on variations in anatomic landmarks and partial volume effects, as well as the inability to quantify changes in ventricular volume. Furthermore, none of these methods address the issue of alignment differences between interval scans.

We propose a fully automated CT registration method that corrects for variable head position within the scanner. This allows for standardized and consistent alignment of head CT images, facilitating comparison of sequential scans. Furthermore, this precise alignment allows for the creation of subtraction images, which can highlight subtle differences in ventricular volume between sequential scans.

In this study, we evaluate the performance of a novel fully automated CT registration and subtraction method, CoPilot (HealthLytix, LLC, San Diego, CA), to improve reader accuracy and confidence when assessing ventricular volume change compared with standard-of-care CT.

METHODS AND MATERIALS

Study design

In this retrospective study, in which review of clinical data and imaging was approved by the institutional review board, we examined head CT scans with both standard CT images as well as CT reformats and subtraction images generated by the automated CT registration tool, performed between March 2015 and October 2016. Although the study was retrospective in nature, all of the automated CT registrations and subtractions were performed prospectively at the time of the clinical CT scan and were available in PACS for review. Therefore, no retrospective registration or subtraction was performed. Inclusion criteria were patients with either a ventricular shunt or EVD who had two consecutive head CT scans using the registration tool, resulting in 53 patients. Four patients were excluded from the study due to inaccurate CT reformats due to motion artifact, resulting in a final cohort of 49 patients. For patients with more than two sequential head CTs, the first two consecutive CTs using the automated CT registration tool were selected. Patient age ranged from 21 to 81; 69% were male and 31% were female. Two-thirds of the patients had an EVD, about one-third had a shunt, and one patient had both. The demographic data for this patient population, including age breakdown, are shown in Table 1.

CT registration method

CT reformats and subtraction images were fully automated using CT CoPilot software (HealthLytix, LLC, San Diego, CA), which utilizes the raw thin slice data from the scanner (0.625 mm slice thickness on the GE Discovery HD 750 64 Slice CT Scanner and 0.5 mm slice thickness on the Toshiba Aquilion One 320 Slice CT scanner). On a separate workstation, CT CoPilot registers the thin-slice data to a proprietary atlas using a three-dimensional similarity (7-parameter) transform, with normalized correlation coefficient as the registration metric. The orientation (pitch/roll/yaw) of the patient's head is extracted from the registration matrix. This orientation information allows CT CoPilot to resample the image so that voxel axes are aligned with the anatomy of each patient, facilitating comparison across patients and across time. The slice thickness of the reformatted images is configurable and is typically selected to be 2–2.5 mm in order to increase apparent SNR and to reduce the radiologist's read time.

When a patient receives a follow-up scan, CT CoPilot computes a subtraction image which shows the change in Hounsfield units (HUs) from the prior scan to the follow-up scan. When comparing CT CoPilot-processed images across time, both images have already been registered to the atlas, and are thus already fairly well aligned. CoPilot performs a coregistration to correct for any residual misregistration before performing a voxel-by-voxel subtraction. The coregistration routine is similar to the registration-to-atlas described above, except that it uses a 6-parameter rigid body transform to align images of the same patient across time. The resulting subtraction image is lightly smoothed to correct for the noise enhancing effects of the subtraction operation.

The post-processed images are then automatically sent back to PACS and are available for review in real time, along with the source data from the CT scan. The aligned reformats and subtraction images are available for review on PACS in about 2 min after the completion of the CT scan.

Image review

All imaging studies were visually interpreted in two sessions by three readers: two radiology residents (AS and CL) and a neurosurgery resident (GG). In the first session, each reader individually interpreted two consecutive standard axial head CTs and classified ventricular volume change into five different categories: definite increase (+2), possible increase (+1), no change (0), possible decrease (−1) and definite decrease (−2). In the second session, CT reformats and subtraction images were interpreted and categorized into the same five categories described above. The readers were allowed up to 60 s to interpret change in ventricular volume for each case, in order to simulate clinical reads, by visual inspection. The first and second session interpretations

Table 1. Patient Demographics

Age	Scan interval	Shunt *vs* EVD
61	13d 18 h 49m	EVD
71	3 h 29m	VP shunt
43	1d 14 h 41m	EVD
54	8 h 47m	EVD
25	3d 1 h 4m	EVD
60	1d 21 h 46m	EVD
25	8d 1 h 39m	VP shunt
73	3d 3 h 47m	EVD
33	7d 7 h 25m	R - VP shunt, L - EVD
47	2d 18 h 4m	VP shunt
41	23 h 42m	EVD
65	7d 21 h 28m	EVD
49	15d 21 h 52m	EVD
49	8 h 58m	EVD
74	21 h 8m	VP shunt
26	9 h 31m	EVD
21	1d 1 h 35m	VP shunt
59	3 h 53m	EVD
30	19d 2 h 54m	EVD
39	11 h 15m	EVD
65	1d 7 h 41m	VP shunt
46	2d 00 h 58m	EVD
55	2d 22 h 35m	EVD
81	3d 5 h 27m	EVD
66	6 h 58m	EVD
52	9 h 55m	VP shunt
58	2d 2 h 56m	VP shunt
36	4d 16 h 42m	VP shunt
56	1d 23 h 30m	VP shunt
72	1d 17 h 37m	EVD
27	23 h 56m	VP shunt
62	1d 7 h 49m	EVD
59	2d 17 h 5m	EVD
60	4 h 6m	EVD
23	3 h 13m	EVD
28	29d 4 h 13m	EVD
24	7 h 53m	VP shunt
44	8 h 1m	EVD
76	10 h 21m	VP shunt
25	18 h 22m	EVD

(Continued)

Table 1. (Continued)

Age	Scan interval	Shunt *vs* EVD
67	12 h 27m	EVD
53	2d 00 h 53m	EVD
52	17 h 25m	EVD
46	14 h 17m	EVD
71	3d 11 h 26m	3 VP shunts
50	1d 21 h 36m	EVD
52	21 h 47m	EVD
31	6 h 16m	VP shunt
45	1d 7 h 26m	EVD

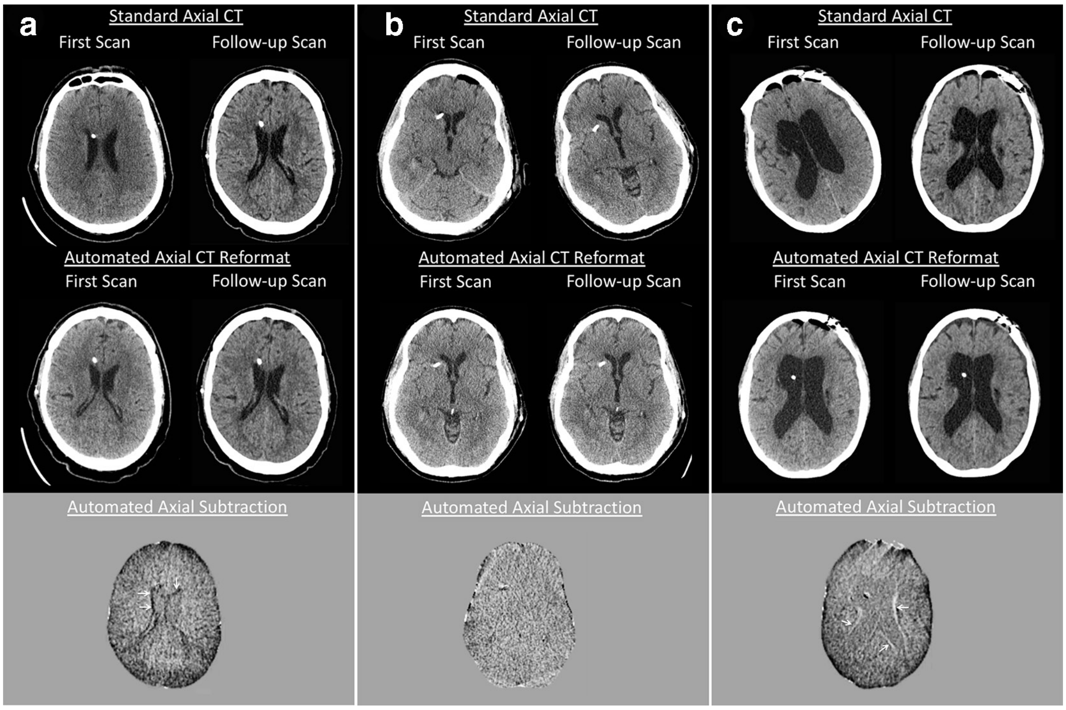
EVD, extraventricular drain; L, Left; R, Right; VP, ventriculoperitoneal.

were scheduled approximately one week apart and the scans were presented in a randomized fashion in order to avoid bias based on the first interpretation. Figure 1 demonstrates examples of sequential standard axial head CT images and the corresponding axial reformats and subtraction images generated by the automated CT registration tool for cases of increased, unchanged, and decreased ventricular volume. As a semi-quantitative measure of ventricular volume, the widths of the bilateral frontal horns and the third ventricle were measured on the standard axial CT images, and these measurements were used to determine if ventricular volume had increased, decreased, or was stable between the sequential scans. These measurements were verified by a board-certified neuroradiologist (NF) with more than eight years of experience in Neuroradiology. Patients with an increase in ventricular volume had a mean increase of 28 mm in bifrontal horn diameter and a mean increase of 14 mm in third ventricular width. Patients with a decrease in ventricular volume had a mean decrease of 31 mm in bifrontal horn diameter and a mean decrease of 24 mm in third ventricular width.

Statistical analysis

Statistical analyses were performed using MedCalc for Windows, v. 17.2 (MedCalc Software, Ostend, Belgium; available at: https://www.medcalc.org) and the lmer function in the lme4 package for R.[13] Inter-rater reliability (IRR) among the three readers was assessed using two-way random intraclass correlation coefficients (ICCs).[14] Significant differences between ICCs were determined by examining the confidence intervals for both single and average measures. Bland–Altman analysis was performed to evaluate the agreement between the readers and the bifrontal and third ventricular width measurements when using standard axial CT images versus when using the output of the CT registration tool, and the limits of agreement (LOA) were calculated.[15–17] Figure 2 demonstrates an example standard axial head CT with bifrontal horn and third ventricular width measurements. McNemar's test was performed to evaluate whether the use of the CT registration tool increased the readers' confidence in their rating. A reader rating of +1 (possible increase) or −1 (possible decrease) was subjectively categorized as "less confident", while a reader rating of +2 (definitely increased), −2 (definitely decreased), and

Figure 1. Comparison of standard axial CT and the corresponding axial reformats and subtraction images generated by the automated CT registration tool showing increased (a), unchanged (b), and decreased (c) ventricular volume. On the subtraction images, the arrows highlight areas of decreased (a) and increased (c) attenuation along the borders of the ventricles, compatible with increased (a) and decreased (c) ventricular volume, respectively. For (a), note the difference in the orientation of the head between the initial and follow up scans, with the frontal sinuses seen on the initial scan but not on the follow-up scan, confounding the assessment of change in ventricular size.

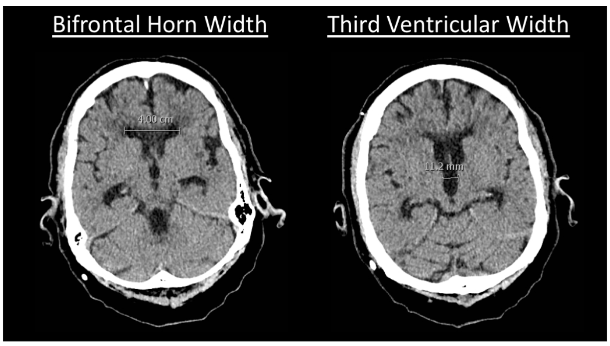


0 (no change) was categorized as "confident." The data were then plotted using SigmaPlot 12.5 (Systat Software Inc.).

RESULTS

Of the 49 cases, ventricular volume was increased in 16, decreased in 17, and unchanged in 16 based on the quantitative bifrontal horn and third ventricular width measurements. Analysis of variance (ANOVA) demonstrated that there was no significant difference among the three groups in terms of age [$F(2, 46)=0.51$, $p = 0.61$]. For patients with either increased or decreased ventricular volume, Reader #1 categorized 29/33 patients correctly for both sessions.. Reader #2 categorized 27/33 patients correctly for Session 1 and 29/33 patients correctly for Session 2. Reader #3 categorized 27/33 patients correctly for Session 1 and 29/33 patients correctly for Session 2.

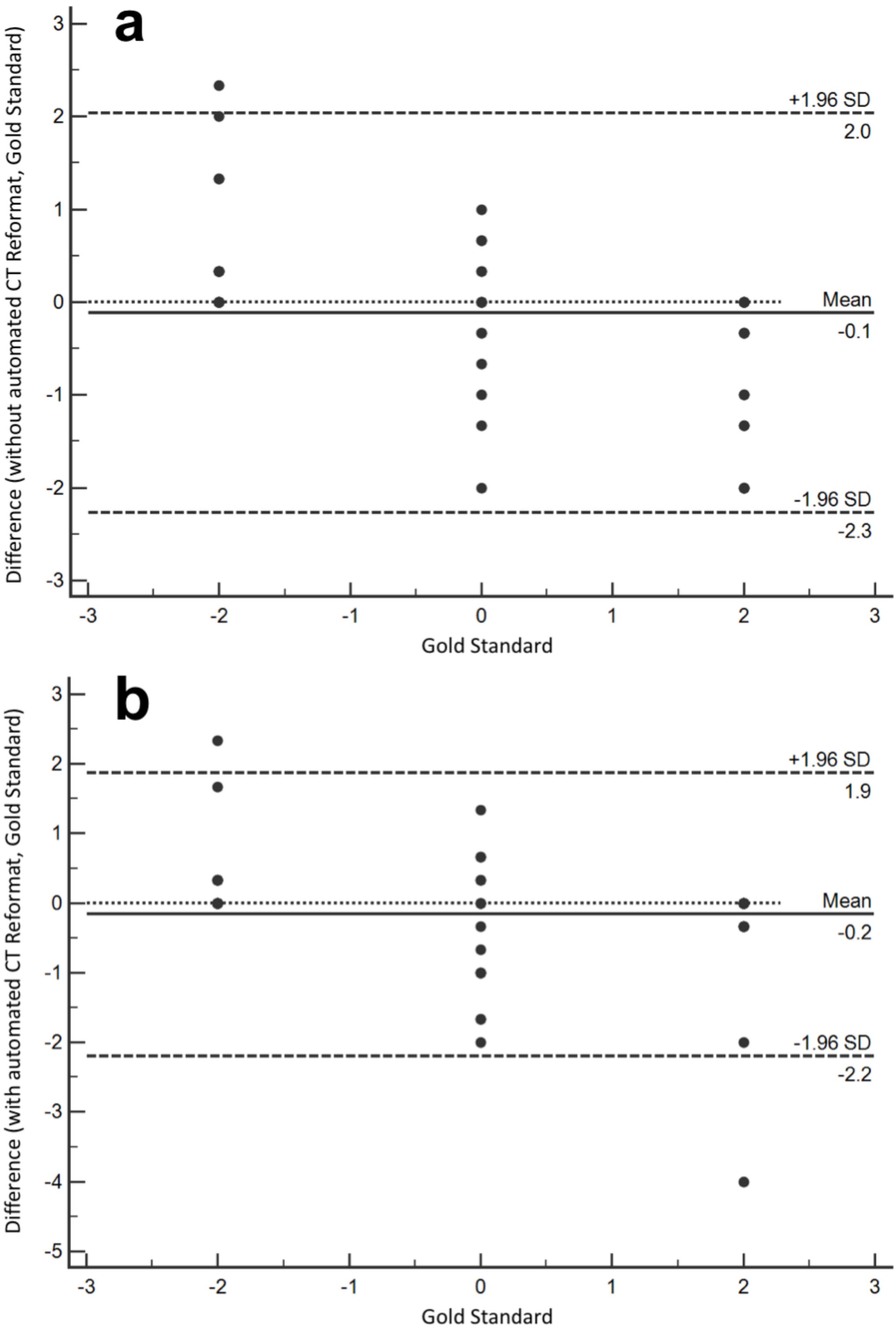
Figure 2. Standard axial head CT demonstrating how the bifrontal horn and third ventricular width measurements were performed.



Among the three readers, IRR was significantly higher when using the CT registration tool [single measure ICC = .909; 95% CI (.859, .944) and average measure ICC = .968; 95% CI (.948, .981)] versus when using the standard axial CT images [single measure ICC = .755; 95% CI (.643, .843) and average measure ICC = .903; 95% CI (0.844, .942)].

Bland–Altman analysis was used to assess agreement between the readers' rating of ventricular volume change and the actual ventricular volume change (based on the bifrontal horn and third ventricular width), using standard axial CT versus the output of the CT registration tool (Figure 3). The LOA was larger (*i.e.* lower agreement with the bifrontal horn/third ventricular width) when the rating was based on standard axial CT (LOA = 4.3) compared to when the rating was based on the output of the CT registration tool (LOA = 4.1). Specifically, the results of the logistic linear mixed effects models showed that the CT registration tool improved the readers' ability to detect change (increase or decrease) in ventricular volume (GLMER: $Z = 4.09$, $p < 0.001$), while the ability to detect unchanged ventricular volume did not improve (GLMER: $Z = -1.83$, $p = 0.07$).

Figure 3. Bland–Altman analysis comparing standard axial CT (a) and the automated CT registration tool (b). SD, standard deviation.



To determine whether the CT registration tool improved reader confidence relative to standard axial CT, McNemar's test was used to evaluate the difference between paired nominal data. McNemar's test showed that the CT registration tool improved reader confidence (*i.e.,* more + 2,–2, and 0 ratings and less +1 and −1 ratings) compared to standard axial CT [$p = 0.004$, odds ratio = 6.5 with 95% CI (1.47, 28.8)].

DISCUSSION

We demonstrate that an automated CT registration tool improves reader accuracy and confidence in detecting change in ventricular volume between sequential scans in patients with ventricular shunts and EVDs. Although a few automated segmentation algorithms have been developed for detection of ventricular volume change,[9–12] to our knowledge this is the first method to be successfully applied clinically.

Accurate assessment of change in ventricular volume is critical as detection of subtle changes may have significant clinical impact. For instance, detection of small changes in ventricular volume is relevant in critical care patients with suspected ventriculostomy catheter obstruction that can occur secondary to hemorrhage, debris, or mechanical failure.[18] In the pediatric population, detecting subtle change in ventricular volume is imperative in suspected VP shunt failure, where impaired ventricular compliance from rising intracranial pressure manifests as a small increase in ventricular volume that may be difficult to assess subjectively.[19–22] Furthermore, in the setting of normal-pressure hydrocephalus, a subtle decrease in ventricular volume following VP shunting has been shown to correlate with clinical improvement.[23] However, it is important to note that small changes in ventricular volume can occur on a physiologic basis; therefore, subtle changes detected on the subtraction images should be interpreted within the appropriate clinical context.[24,25]

In addition to improving detection of change in ventricular volume, another advantage of this registration tool is the generation of automated, aligned, orthogonal reformats of head CT images. Misaligned head CTs due to head tilt and rotation and neck flexion/extension can confound the interpretation of head CTs. Although the CT technologist can manually generate aligned orthogonal reformats on the CT scanner, this takes time and the output will be inconsistent. This automated CT registration tool standardizes the process by generating consistently accurate reformats, saves time, and therefore may increase CT throughput.

Radiology and neurosurgery residents were selected to perform the initial interpretation in order to emphasize the added value/benefit of this automated CT registration and subtraction tool. Although interobserver agreement would likely have been higher among experienced board-certified radiologists, the reason this group was not selected as initial readers was based on the principle that challenges posed by non-aligned images would have been more easily overcome on a visual basis by more experienced radiologists. Our aim was to assess the value of this tool in more inexperienced trainees who are often on the frontlines of emergent image interpretation, especially at academic institutions.

Limitations of this study include the small sample size and the retrospective nature of the study. Furthermore, although the two rating sessions were separated by 1 week and the cases were presented in a different order during each session to limit recall bias, the readers may have had greater certainty during the second session if they remembered their ratings from the first session. Additionally, since the readers were aware of which type of CT they were reviewing during each session (standard *vs* registered), this could also introduce bias with inherently increased confidence during the second session. Moreover, intraobserver variability was not assessed as the readers did not perform multiple ratings with and without the automated registration and subtraction tool.

Further potential advantages of this automated CT registration tool include improved efficiency with increased speed of interpretation relative to standard CT, which will be the subject of future investigations. Future directions also include automatic ventricular segmentation with acquisition of volumetric data. Incorporating ventricular segmentation into the automated CT registration algorithm such that ventricular volumes would be generated for each patient will not only improve assessment of patients with communicating and non-communicating hydrocephalus, but can also be utilized as a surrogate of parenchymal volume loss to diagnose and monitor patients with dementia and cognitive impairment.

CONCLUSION

A novel fully automated CT registration and subtraction method improves the ability to reliably detect change in ventricular volume between sequential scans in patients with ventricular shunts or EVDs, and therefore may serve as a tool for accurate assessment of change in ventricular volume, which can significantly affect clinical management.

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ETHICAL APPROVAL

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT

Since this was a retrospective imaging review that did not alter official interpretations of the studies or the clinical management, informed consent was not obtained.

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