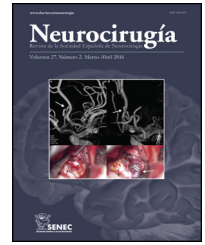




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Clinical Research

Shape-based interpolation method in measuring intracranial volume for pre- and post-operative decompressive craniectomy using open source software



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ARTICLE INFO

Article history:

Received 10 July 2018

Accepted 1 December 2018

Keywords:

Shape-based interpolation method

Computed tomography

Decompressive craniectomy

Intracranial volume

Open source software

ABSTRACT

Introduction: Intracranial volume (ICV) is an important tool in the management of patients undergoing decompressive craniectomy (DC) surgery. The aim of this study was to validate ICV measurement applying the shape-based interpolation (SBI) method using open source software on computed tomography (CT) images.

Methods: The pre- and post-operative CT images of 55 patients undergoing DC surgery were analyzed. The ICV was measured by segmenting every slice of the CT images, and compared with estimated ICV calculated using the 1-in-10 sampling strategy and processed using the SBI method. An independent t test was conducted to compare the ICV measurements between the two different methods. The calculation using this method was repeated three times for reliability analysis using the intraclass correlations coefficient (ICC). The Bland–Altman plot was used to measure agreement between the methods for both pre- and post-operative ICV measurements.

Results: The mean ICV ($\pm$ SD) were 1341.1 ± 122.1 ml (manual) and 1344.11 ± 122.6 ml (SBI) for the preoperative CT data. The mean ICV ($\pm$ SD) were 1396.4 ± 132.4 ml (manual) and 1400.53 ± 132.1 ml (SBI) for the post-operative CT data. No significant difference was found in ICV measurements using the manual and the SBI methods ($p = .983$ for pre-op, and $p = .960$ for post-op). The intrarater ICC showed a significant correlation; ICC = 1.00. The Bland–Altman plot showed good agreement between the manual and the SBI method.

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<http://dx.doi.org/10.1016/j.neucie.2018.12.002>

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Conclusion: The shape-based interpolation method with 1-in-10 sampling strategy gave comparable results in estimating ICV compared to manual segmentation. Thus, this method could be used in clinical settings for rapid, reliable and repeatable ICV estimations.

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Método de interpolación basado en formas para medir el volumen intracraneal en craneotomía descompresiva pre y postoperatoria utilizando un software de código abierto

R E S U M E N

Palabras clave:

Método de interpolación basado en formas
Tomografía computarizada
Craneotomía descompresiva
Volumen intracraneal
Software de código abierto

Introducción: El volumen intracraneal (ICV) constituye una importante herramienta para el tratamiento de los pacientes sometidos a craneotomía descompresiva (CD). El objetivo de este estudio fue validar la medición del ICV aplicando el método de interpolación basado en formas (SBI), utilizando software de código abierto en las imágenes de tomografía computarizada (TC).

Métodos: Se analizaron las imágenes pre- y postoperatorias de TC de 55 pacientes sometidos a CD. Se midió el ICV segmentando cada corte de las imágenes de TC, comparándose con el ICV estimado calculado utilizando la estrategia de muestreo 1 de 10, y procesándose mediante el método SBI. Se realizó una prueba t independiente para comparar las mediciones de ICV entre los 2 métodos. Se repitió 3 veces el cálculo con este método, para realizar el análisis de fiabilidad, utilizando el coeficiente de correlación intra-clase (ICC). Se utilizó el gráfico de Bland-Altman para medir el acuerdo entre ambos métodos, para las mediciones de ICV pre- y postoperatorias.

Resultados: El ICV medio ($\pm$ DE) fue de 1.341,1 ml $\pm$ 122,1 (manual) y 1.344,11 ml $\pm$ 122,6 (SBI) para los datos de la TC preoperatoria. El ICV medio ($\pm$ DE) fue de 1.396,4 ml $\pm$ 132,4 (manual) y 1.400,53 ml $\pm$ 132,1 (SBI) para los datos de la TC postoperatoria. No se encontró diferencia significativa en cuanto a las mediciones de ICV utilizando los métodos manual y SBI ($p=0,983$ para preoperatoria, $p=0,960$ para postoperatoria). El ICC intra-evaluador reflejó una correlación significativa; ICC=1. El gráfico de Bland-Altman reflejó un buen acuerdo entre el método manual y el método SBI.

Conclusión: El método de interpolación basado en formas con estrategia de muestreo 1 de 10 proporcionó resultados comparables a la hora de calcular el ICV, en comparación con la segmentación manual. Por tanto, este método podría utilizarse en el entorno clínico para realizar estimaciones del ICV rápidas, fidedignas y repetibles.

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Introduction

Intracranial volume (ICV) is defined as the volume within the cranium, including the brain, meninges, and cerebrospinal fluid. It increases from birth throughout childhood and reaches its final size at the age of 16–20 years. The volume of the brain starts decreasing when a person is about 20 years old¹; however, it is presumed that ICV remains constant even after the brain atrophies as it is replaced with cerebrospinal fluid. Thus, the ICV is generally considered as an accurate indicator of a mature brain volume.^{2,3}

In a living human being, ICV is indirectly measured via computed tomography (CT) scans. ICV measurements using CT scans have been reported in the literatures.^{1,4} Most commonly, the manual method was carried out to determine the ICV. The manual method is considered the gold standard in

measuring ICV.^{3–8} It is used as the reference method in comparison with any new measurement methods. The manual method is regarded the most accurate method to measure ICV as it assesses every slice of the image. The ICV is the sum of the area of all slices multiplied by its slice thickness. The area of each slice could be measured by manually tracing the intracranial cavity or using the segmentation procedure. Manual tracing is performed by using the computer's mouse to trace the boundary of the intracranial region on each slice. Although this manual method is precise and accurate, its major limitation remains in the fact that it is tedious, time consuming, and requires experience.^{9,10}

As manually tracing the boundary of each slice is tedious, other techniques to segment the intracranial region were introduced. One of them is the semi-automatic segmentation using region growing.^{11,12} This method is also known as

pixel-based image segmentation as it involves an initial seed point. Starting with a pixel or a group of pixels as the seed point, the neighbouring pixels are examined. If a neighbouring pixel meets certain criteria (for example, they have similar pixel value), it is added to the group and if it does not, it will not be included as part of the region. This process is continued until no neighbouring pixels can be added to the group. Thus, a region is defined.

The aim of the region growing method is to group pixels of similar value into a defined region according to some assigned criteria. Although the region growing method is faster than manually tracing the boundaries, it would not help much to save time in 1-mm CT scan slices as the process has to be repeated about 200 times. This process is tedious and time consuming. To overcome this problem, we investigated shape-based interpolation method¹³ with 1-in-10 sampling strategy to rapidly estimate ICV for use in clinical setting.

One of the significant applications of the ICV measurement is in the management of patients undergoing decompressive craniectomy (DC). A DC surgery is a lifesaving procedure that removes a section of the skull to relieve intracranial pressure (ICP) secondary to trauma, stroke, and subarachnoid haemorrhage.^{14,15} Following DC, the brain expands through the skull defect created by DC, resulting in transcalvarial herniation. Thus, a few studies were conducted in volumetric comparisons of ICVs,¹⁶⁻¹⁸ or herniation volume,¹⁹ in addition to ICPs to manage patients with DC surgery.

Materials and methods

Traumatic and non-traumatic cases requiring decompressive craniectomy were evaluated in this study. Non-traumatic cases commonly seen in practice for which the procedure is readily employed as part of treatment are cerebrovascular cases such as malignant middle cerebral artery territory infarcts and haemorrhagic strokes. A sample population from May 2009 until December 2012 was obtained from the Neurosurgery Department, Hospital Universiti Sains Malaysia (USM), Kubang Kerian, Kelantan. All patients were scanned twice pre- and post-operative DC surgery using the Siemens Somatom Definition AS+128-slice (Siemens, Erlangen, Germany) housed at the Radiology Department, Hospital USM. Data was

collected from archived images of patients from the Picture Archiving and Communication System (PACS) server. Ethical application was approved by the Ethics and Research Committee USM, reference number USM/KK/PPP/JEPeM (246.3[13]) dated 9th January 2013. The inclusion criterion of this study was CT images of 1-mm slice thickness with a matrix of 512×512 pixels. An exclusion criterion was CT images with incomplete brain images. A total of 67 CT head scans of patients aged between 15 and 86 years old were retrieved from the Picture Archiving and Communication System (PACS) server housed at the Radiology Department, Hospital USM. Twelve patients were excluded because the images did not satisfy the criteria. Thus, 55 patients (41 males, 14 females) were included in this study.

CT images were retrieved from the PACS Server to a Dell Precision T7500 workstation in Digital Imaging and Communications in Medicine (DICOM) format. All measurements were performed using open source MITK 3M3 image analysis framework.^{20,21} In this study, the ICV was defined as the volume of the intracranial cavity from the vertex to the foramen magnum.^{3,22}

Manual method

The DICOM data was loaded into MITK 3M3 image analysis framework. The level window was adjusted to Level=50 and Window=120 for best contrast as recommended by Strik et al.²³ The intracranial areas on the CT scans were delineated in each slice using a semi-automatic region growing method.^{12,21} This method consists of selecting a pixel inside the volume to be segmented, which is called a seed, by pointing and clicking a mouse in the intracranial region. The algorithm then automatically connects all the neighbouring pixels of the initial seed with similar intensity. Manual editing was performed on some of the slices to correct leakage or over-segmentation (Fig. 1), which could lead to over estimation of ICV.

The process was repeated in each axial slice, from the vertex to the foramen magnum, until the entire region of the intracranial area was segmented (Fig. 2). For each CT data, there were about 200 axial slices on average.

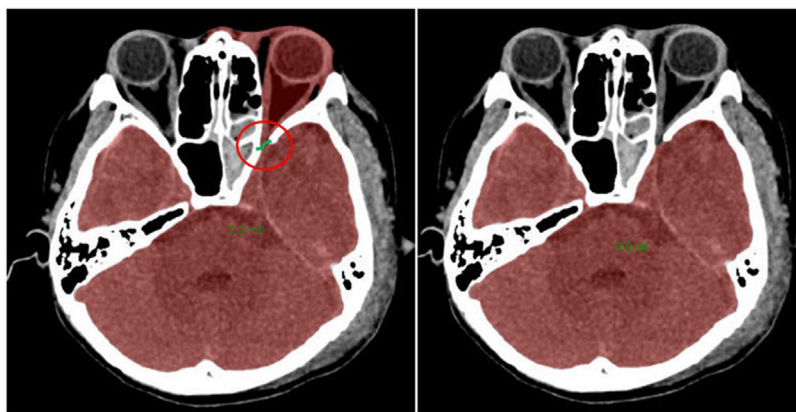


Fig. 1 – The red circle shows the leakage due to the opening on the orbit (left), the intracranial area was corrected by a correction tool (green line in a red circle) and the corrected intracranial area is produced (right).

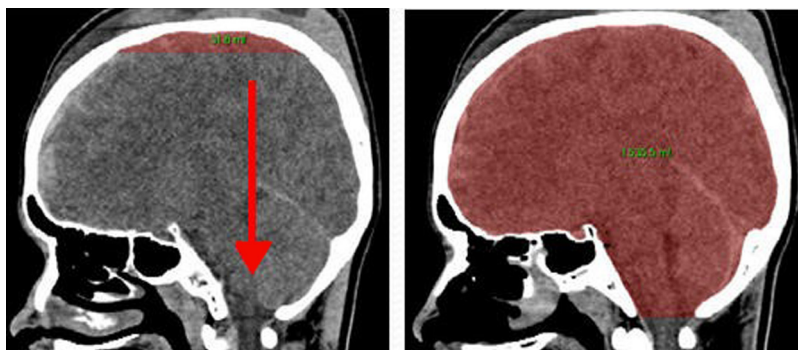


Fig. 2 – The process of segmentation was done slice by slice from the vertex (left) to the foramen magnum (final slice). The segmentation was then completed and the ICV was obtained (right).

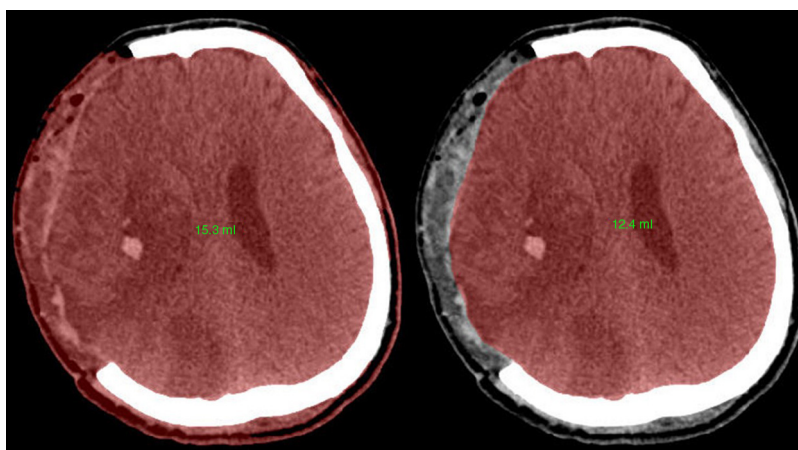


Fig. 3 – The post-operative CT data after segmentation (left), and after correction of the over-segmentation (right).

The segmentation for the post-operative CT data followed the same principle for the pre-operative CT data. The only difference was that the amount of over-segmentation was bigger, thus taking a lot more time for manual editing. For a normal skull with no defects, only a few slices were needed for the manual editing. However, for the post-operative CT data, a lot more time was consumed to delineate the intracranial area by manually drawing the line (correction tool) along the dura mater (Fig. 3).

The segmentation process was repeated on all axial slices. This process was periodically assessed for over-segmentation by comparing the segmented images in the coronal view (Fig. 4).

Shape-based interpolation method

The 1-in-10 sampling strategy was used to obtain an estimate of the ICV before applying the shape-based interpolation method. Manual segmentation was conducted on every 10th slice in the axial plane for the 1-in-10 sampling strategy. For this sampling strategy, the number of slices to be processed was reduced considerably from about 200 slices using manual method to about 20 slices as shown in Fig. 5. The ICV was obtained when all slices were segmented after the

interpolation process. For the post-operative CT data using shape-based interpolation method, the process was similar to the pre-operative CT data (Fig. 6).

Statistical analyses

The IBM SPSS Statistics version 20 was used for statistical analyses. Descriptive statistics were described in mean and standard deviation. Measurement of the 55 ICV for each CT data was carried out by one observer (JYA) and validated by our co-authors (AGM & ZAR). The ICV was measured by segmenting every slice of the CT images, and compared with estimated ICV calculated using shape-based interpolation method. An independent t test was conducted to compare ICV measurements between two different methods. The calculation using shape-based interpolation method was repeated three times for reliability analysis using two-way mixed effect intraclass correlations coefficient (ICC). Bland-Altman plot was used to measure agreement between the methods for both pre- and post-operative ICV measurements. Each measurement of the same CT scan image was carried out at different times (about one month apart) and blind to each measurement. For confidentiality, scans were not identified by the patient's name.

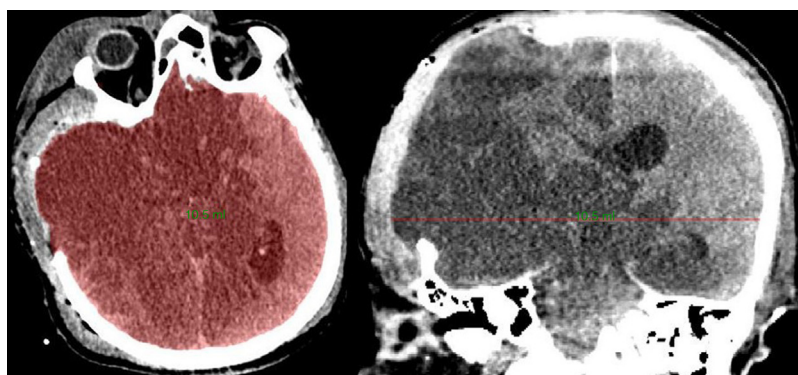


Fig. 4 – An axial slice of the post-operative CT data with skull defect after segmentation (left). The coronal view was viewed to assess for over-segmentation (right).

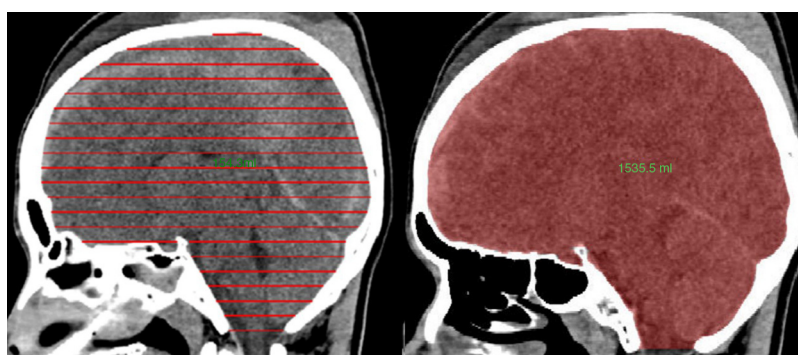


Fig. 5 – The 1-in-10 (left) sampling strategy for shape-based interpolation method which involves about 20 axial slices, and after the interpolation process (right) which covers 200 slices. The ICV was calculated automatically by summing all the intracranial areas.

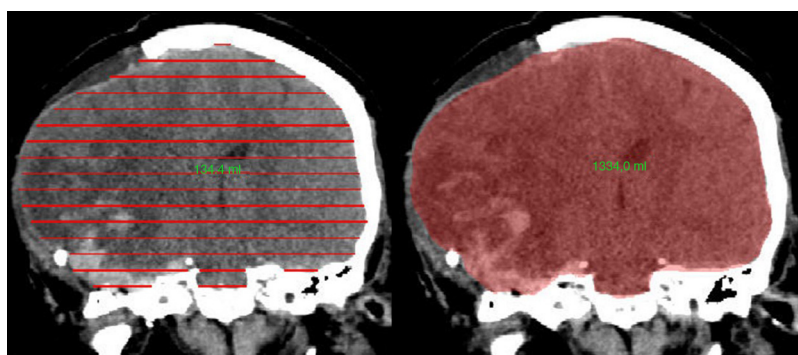


Fig. 6 – The coronal view of the post-operative CT data before running the shape-based interpolation algorithm (left) and after interpolation (right).

Results

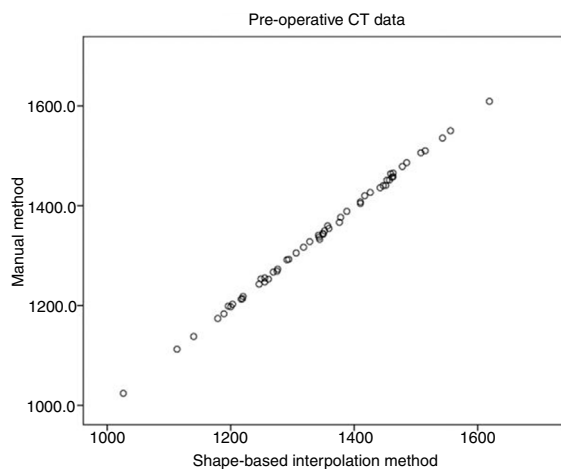
Table 1 presents the results of ICV measurements using the two different methods, the manual and shape-based interpolation method. An independent *t* test was conducted to compare the ICV measurements using different methods. The mean ICV ($\pm$ SD) were 1341.1 ± 122.1 ml (manual method) and 1344.11 ± 122.6 ml (shape-based interpolation method) for preoperative CT data. The mean ICV ($\pm$ SD) were 1396.4 ± 132.4 ml (manual method) and 1400.53 ± 132.1 ml

Table 1 – Results of ICV measurements using the two different methods.

Variable		ICV measurement (ml)			
		n	Manual Mean (SD)	Shape-based interpolation Mean (SD)	p
Methods					
Pre-op CT data	55		1341.1 (122.1)	1344.1 (122.6)	.983
Post-op CT data	55		1396.4 (132.4)	1400.5 (132.1)	.960

Table 2 – Intrarater correlation of ICV measurements using ICC (n = 55).

Intrarater	Pre-op		Post-op	
	Correlation	Significance	Correlation	Significance
1 and 2	0.999	<.001	0.998	<.001
1 and 3	1.000	<.001	0.999	<.001
2 and 3	1.000	<.001	0.999	<.001

**Fig. 7 – Scatter plot of manual versus shape-based interpolation methods for pre-operative CT data.**

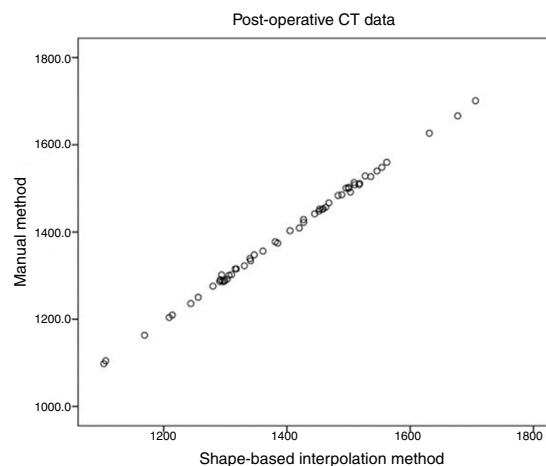
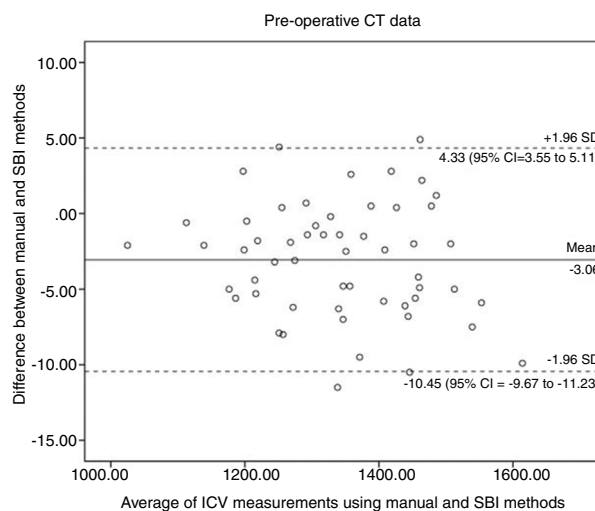
(shape-based interpolation method) for post-operative CT data. No significant difference was found in ICV measurement using the manual and the shape-based interpolation methods ($p = .983$ for pre-op, and $p = .960$ for post-op).

The Intrarater correlation coefficients (ICC) are shown in Table 2. The three observation measurements were highly correlated within-subjects for pre-operative and post-operative CT data.

The correlation coefficients are shown in Table 3. There were highly significant correlations between the manual and shape-based interpolation methods for both pre-operative and post-operative CT data. This means the shape-based interpolation method is comparable with the manual method if used to measure ICV for either pre- or post-operative CT data of DC patients.

Fig. 7 shows the scatter plot between the ICV measurements of manual method and shape-based interpolation method for pre-operative CT data. The two methods appear to be well correlated with a coefficient of correlation that is highly significant ($r = 1.000$, $p < .001$).

Fig. 8 shows the scatter plot between the ICV measurements of manual method and shape-based interpolation method for post-operative CT data. The two methods appear

**Fig. 8 – Scatter plot of manual versus shape-based interpolation methods for post-operative CT data.****Fig. 9 – A Bland-Altman plot analysis of the pre-op ICV measurements using the manual versus shape-based interpolation methods.**

to be well correlated with a coefficient of correlation that is highly significant ($r = 0.999$, $p < .001$).

The agreements between the two methods for pre-operative ICV measurements were evaluated using Bland-Altman plot as shown in Fig. 9.

For each DC patient data, the mean of the ICV measurements using manual and shape-based interpolation methods is plotted on the x-axis, against the difference between the measurement methods on the y-axis. The output of the One-sample t-test analysis provides all the relevant data to draw a Bland-Altman plot.

Table 3 – Measurement of ICV with two different methods using ICC (n = 55).

Method	Pre-op		Post-op	
	Correlation	Significance	Correlation	Significance
Manual and shape-based interpolation	1.000	<.001	0.999	<.001

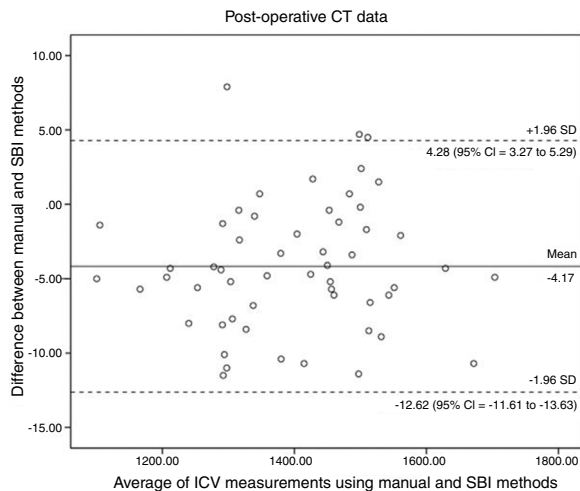


Fig. 10 – A Bland–Altman plot analysis of the post-op ICV measurements using the manual versus shape-based interpolation methods.

The dashed line $+1.96SD$ represent the mean systematic difference between manual and shape-based interpolation methods, which amount to -3.06 (95% CI: 3.55–5.11). It appears that there was no statistically significant difference in mean. The two-dotted line above and below the mean line represent the limits of the agreement, and these are drawn at $\text{mean} \pm 1.96 \times SD$. We can interpret mean (-3.06) as the systematic error and $1.96 \times SD$ as the random error. If the ICV measurements using manual and shape-based interpolation method differ a lot, the SD of the differences will be large and the lines will be further away from the mean line. The limits of agreement here are -10.45 to 4.33 ml. As these are expressed in the units of measurement, we have a direct indication of the size of the measurement error. Fig. 9 shows that good agreement is obtained between manual versus shape-based interpolation methods for pre-operative CT data, according to the Bland–Altman plot.

The agreements between the two methods for post-operative ICV measurements were evaluated using Bland–Altman plot as shown in Fig. 10.

The Bland–Altman plot showed that 95% of differences of ICV measurements using manual and shape-based interpolation methods were between -12.62 and 4.28 ml. Fig. 10 shows that good agreement is obtained between manual versus shape-based interpolation methods using 1-in-10 sampling strategy for post-operative CT data.

Discussions

Intracranial volume is one of the measures to evaluate brain size; it is particularly useful in the management of patients undergoing DC where there will be changes in the shape and size of the brain. Several methods were used to measure ICV and in this study we aimed to measure the pre- and post-operative ICV of DC patients using a rapid and reliable method. The pre- and post-operative ICV of DC patients were first measured using the manual method as the gold standard, and

then compared with the shape-based interpolation method using 1-in-10 sampling strategy.

The manual method is considered the gold standard in measuring ICV.^{3–8} It is used as the reference method in comparison with any new measurement methods. Most of these studies^{3,5–7,24} measured ICV on MRI compared to CT.^{2,4,25} The automatic method to measure ICV is only suitable for MRI data,^{3,5,24} and studies to automatically measure ICV on defected skull of CT data is scarce.

ICV measurements using CT scans have been reported in the literatures.^{1,4} Most commonly, the manual method was carried out to determine the ICV. Several studies manually trace the borders to delineate the intracranial cavity^{3,6,7,25}; this method is more time consuming. In our study, instead of manually tracing the borders of the intracranial area, region growing method was used to segment the intracranial area on every slice. The process was semi-automatic where the user just point the mouse to the region of interest and the intracranial area would be segmented automatically. The benefit of this method compared to manually tracing the borders is the process is faster with only one click. The amount of time needed to segment each slice was also less compared to manually tracing the borders as it is semi-automatic. Furthermore, based on our results, this method provides a good ICV measurement.

On the other hand, according to Adamson et al.,²⁶ region-growing methods are prone to “leaking”, where the segmentation boundary penetrates into back-ground voxels or into the brainstem, or both. Therefore, manual editing was necessary to correct segmentation leakage which was tedious and time consuming for large datasets, particularly for DC data with cranial defects. To overcome this problem, is to segment the images on every n th slice. The loss of precision when segmenting every n th slice has been evaluated by Eritaia et al.,⁷ where it was shown that it is possible to get reasonable accurate ICV measurements without segmenting every slice. They reported that there was a positive relationship between the number of slices used to estimate ICV and the accuracy of that measurement. As the number of slices sampled decreased, ICV between the estimated ICV and the actual ICV also decreased. In addition, the variance of the estimated ICVs increased. They also stated that the ICV can be confidently estimated using every 10th slices without significant loss of accuracy, which should significantly save time. Our results showed that these techniques are comparable to the manual method. Indeed, the time spent to measure ICV using the 1-in-10 sampling strategy was reduced significantly. Using the manual method, about 200 slices were assessed, compared to just 20 slices in the 1-in 10 sampling strategy.

ICV measurement of CT images are normally performed using either commercial software such as BrainLAB iPlan software^{27,28} or in-house software.^{29,30} While the in-house software are only limited to users from that particular institution, the commercial software is very expensive. For instance, Kenning et al.²⁷ used commercial BrainLAB iPlan software for volumetric analysis of DC patients; this software is rather expensive and cannot be afforded by this institution. Thus, in this study, MITK 3M3 was used for the ICV estimation using both manual and shape-based interpolation methods. This software is an open source medical image processing

framework that fulfils a specific and pressing need of cranio-facial imaging research by providing a combination of manual and semi-automatic tools for extracting structures of interest.

A few studies to estimate the ICV on CT scans applying open source software have been conducted.^{2,23,31} They measured ICV of 30 normal subjects,² 5 dry skulls³¹ and 12 subjects with intracranial haemorrhage.²³ However, only normal skulls were measured in these studies, unlike the present study where we included the measurement of patients after DC surgery where part of the skull is removed. Our study is more challenging as loss of some parts of the bony structures of the skull makes the segmentation of the intracranial areas difficult.

As in Ricard et al.³² study, open source ITK-SNAP was used to measure ICV. ITK-SNAP uses active contour segmentation and offers automatic segmentation of the ICV. The active contour initialization was performed by placing a sphere in the intracranial cavity. Each boundary point of this sphere was moved iteratively until the cranial cavity was full and the algorithm stopped when the entire boundary was reconstructed. User had to eliminate the excess of the active contour through the foramina of skull base using cutting planes. However, this segmentation could only work with the normal skull or pre-operative DC patients. It was impossible to eliminate the excess of the ICV from the skull defect in post-operative DC patients using the same cutting planes. Therefore, this method is appropriate to measure the ICV of normal patients with no skull defects but not for the post-operative DC patients.

There are several studies which involved measuring ICV of the defect skulls such as craniosynostosis. Ritvanen et al.²⁸ proposed the use of mesh-based method to measure ICV in patients with craniosynostosis from CT images. The software they used to measure ICV was the commercial Amira software. In other similar study, Hill et al.³³ used another commercial software, Analyze, to measure ICV of unicoronal craniosynostosis patients from MRI images while Fischer et al.,³⁴ Maltese et al.,³⁵ and Wikberg et al.²² used Matlab to measure total intracranial volume and frontal volume of sagittal synostosis, craniosynostosis and metopic synostosis patients from CT images, respectively. Similarly, Anderson et al.²⁹ measured ICV of sagittal craniosynostosis patients using their in-house Persona Software. The studies mentioned above all used either commercial or in-house software to measure ICV in patients with skull defect. As they are not available for our use, we opted for MITK 3M3, which is an open source software capable of measuring ICV in defective skull.

The shape-based interpolation method in this study applied semi-automatic segmentation with manual editing which was observer-dependent. This finding could be further improved via an implementation of inter-observer agreement to validate this method. Therefore, both intra- and inter-observer agreements should be considered in future studies.

Conclusion

In this study, the amount of slices used for ICV estimation were reduced from about 200 to 20 slices using the 1-in-10 sampling strategy on CT images with 1-mm slice thickness.

Further investigation could be done using lesser slices such as 1-in-20 sampling strategy which could reduce the number of slices to 10 slices, or a few other sampling strategies to find the optimum amount of slices that could accurately estimate ICV based on the shape-based interpolation method.

In conclusion, the results of this study confirmed that the shape-based interpolation method with 1-in-10 sampling strategy gave comparable results in estimating ICV compared to the manual gold standard. Thus, this method could be used in clinical settings for a rapid and reliable ICV estimation of DC patients.

Ethical standards and patient consent

We declare that all human and animal studies have been approved by the Ethics and Research Committee USM, reference number USMKK/PPP/JEPeM (246.3[13]) dated 9th January 2013 and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. We declare that all patients gave informed consent prior to inclusion in this study.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgements

This study was made possible with financial assistance via USM Research University Team grant no: 1001/PPSG/852004.

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