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ORIGINAL COMMUNICATION

Comparison of Four Methods for the Estimation of Intracranial Volume: A Gold Standard Study

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Investigators can infer how much reduction in volume has occurred since brain volume was at its peak, by combining measures of brain volume with measures of intracranial volume (ICV). Several methodologies have been proposed to asses the ICV. However, we have not seen a gold-standard study evaluating the results of the methodologies for the assessment of ICV. In the present study, the actual intracranial volume of 20 dry skulls was measured using the water-filling method, using this as a gold standard. Anthropometry, cephalometry, point-counting, and planimetry techniques were applied to the same skulls to estimate the ICV. Anthropometric and cephalometric measurements were carried out directly on skulls and roentgenograms, respectively. Consecutive computed tomography sections at a thickness of 10 mm were used to estimate the ICV of the skulls by means of the point-counting and planimetry methods. The mean (±SD) of the actual ICV measured by the water-filling method was 1,262.0 ± 160.4 cm^3 (1,389.5 ± 96.5 cm^3 for males and 1,134.5 ± 94.3 cm^3 for females, respectively). Our results showed that the estimated values obtained by all four methods differed from the actual volumes of the skulls ($P < 0.05$). The data obtained by anthropometry resulted in overestimation. However, cephalometry, point-counting, and planimetry methods produced underestimation. After calibration, there were no significant differences between the actual volumes and the results of the four methods ($P > 0.05$). While the anthropometric method is easy and quick to apply, its result may deviate from the actual values. The optimized stereological techniques of point-counting and planimetry methods may provide unbiased ICV results since they take the third dimension of the structures into account. Clin. Anat. 20:766–773, 2007.

Key words: intracranial volume; water-filling; cephalometry; point-counting; planimetry; stereology

INTRODUCTION

Brain growth drives skull growth during childhood (Sgouros et al., 1999; Knutson et al., 2001). At about 20 years of age, the volume of the brain starts to decrease, while it is presumed that the intracranial volume (ICV) remains constant (Rushton and Ankney, 1995; Wolf et al., 2003). Thus, the ICV is generally considered to be a more accurate indicator of mature brain volume than head size (Wolf et al., 2003). By

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combining measures of brain volume with measures of ICV, investigators can infer how much reduction in volume has occurred since brain volume was at its peak (Jenkins et al., 2000; Knutson et al., 2001). Hence, ICV provides a more stable and accurate normalization factor for estimating volumetric changes at the onset of a disease (Eritaia et al., 2000).

Several methods have been proposed for the assessment of ICV. The packing/filling method is the most accurate in vitro method for the measurement of ICV (Manjunath, 2002a). The others are the linear measurement and cephalometry methods predicting the ICV using the measures of length, width, and height of the skull directly over the bony structure or lateral and anteroposterior roentgenograms (Manjunath, 2002a).

Unbiased estimation of organs or structures can be made using the Cavalieri principle of stereological approaches (Roberts et al., 1993; Cruz-Orive, 1997). The requirement for the application of this method is an entire set of two-dimensional slices through the object, provided they are parallel, separated by a known distance, and begin randomly within the object, criteria that are met by standard sectional radiological imaging techniques (Roberts et al., 2000; Sahin and Ergur, 2006). Planimetry and point-counting are two methods for estimating volume based on the Cavalieri principle (Gong et al., 1999; Sahin and Ergur, 2006). There are some studies reporting that the application of stereological techniques to computed tomography (CT) scans may provide an unbiased estimation of ICV (Mazonakis et al., 2004; Acer et al., 2007). Their studies are mainly conducted to estimate efficiency of the applied method. However, none of them are gold-standard studies which compare the known ICV with the results of stereological estimations.

In this gold standard study, we aimed to compare the accuracy and the reliability of anthropometry, cephalometry, point-counting, and planimetry methods for the estimation of ICV. We also propose an easy way to calibrate underestimation effects of sectioning on the estimation of ICV on routine CT images.

MATERIALS AND METHODS

This study was performed on 20 adult skulls (10 males and 10 females) obtained from the collection of the Department of Anatomy, Medical Faculty, Adnan Menderes University, Aydın, Turkey.

The ICV of the skull was determined by filling the skulls with water and subsequently measuring the quantity of water using a cylindrical measuring glass. For this purpose, ordinary balloons were introduced into the cranial cavity via the foramen magnum and filled with water under the pressure from the tap. Following the filling process, the water was poured into a measuring cylinder and the volume taken as a measure of the total ICV. The measured ICV values were used as the gold standard of the present study.

The linear dimension measurements were obtained from all dry skulls included, using standard anthropometric methods and measuring gadgets described in the literature. Cephalometric measurements were made on standard lateral and anteroposterior cephalograms of the skulls. An iron bar was placed next to the skull to calibrate the measurements on the roentgenograms.

CT scanning of the skulls was performed on a conventional scanner (Philips Tomoscan LX). Consecutive images were acquired with the use of 320 × 320 field of view, 120 kV, and 100 mAS for all CT scans. All subjects were scanned in coronal plane and the slice thickness was 10 mm without interval. Total ICV was estimated using the Cavalieri principle. The point-counting method and the planimetry technique were applied for the estimation of sections cut surface area. The same sections were used for both volume estimation methods.

Anthropometry

The measurements were calculated in centimeters and made by the same author with the subject in the Frankfurt horizontal plane. The following linear dimensions of the head were recorded by craniometry:

1. Maximum head length (glabella-inion length: *L*).
2. Maximum head width (measured between parietal eminences: *W*).
3. Auricular height (external acoustic meatus to the highest point of the vertex: *H*), using an auricular head spanner.

The ICV was calculated using the following formula given by Williams et al. (1989).

$$\text{Males: } 0.337 \times L \times W \times H + 406.01 \text{ cm}^3 \quad (1)$$

$$\text{Females: } 0.400 \times L \times W \times H + 206.60 \text{ cm}^3 \quad (2)$$

Cephalometry on Roentgenograms

For this purpose, internal length (*L*), internal height (*H*), diameter from bregma to posterior cranial fossa (*B*), and length of width (*W*) of the skulls on roentgenograms were measured (Fig. 1). The ICV was calculated using the formula proposed by Bergerhoff as interpreted below (Manjunath, 2002a).

$$V = (L/2) \times (H + B/4) \times (W/2) \times 0.51 \times 8 \text{ cm}^3 \quad (3)$$

Point-Counting Method

The CT images of a section series at thicknesses of 10 mm were used to estimate ICV. The images were printed on films. A square grid test system with $d = 0.4$ cm between test points was used to estimate the sectioned surface area of the slices. To estimate ICV, the modified formula used for volume estimations of radiological images was applied (Akbas et al., 2004; Bilgic et al., 2005; Sahin and Ergur, 2006):

$$V = t \times \left[\frac{\text{SU} \times d}{\text{SL}}\right]^2 \times \sum P \quad (4)$$

where t is the section thickness of consecutive sections (1 cm), SU is the scale unit of the printed film, d is the distance between the test points of the grid (0.4 cm), SL is the measured length of the scale printed on the film, and ΣP is the total number of points hitting the sectioned cut surface areas of intracranial space.

The films were placed on a negatoscope and the transparent square grid test system was superimposed, randomly covering the entire image frame (Fig. 2a). The points hitting the intracranial sectioned surface area were counted

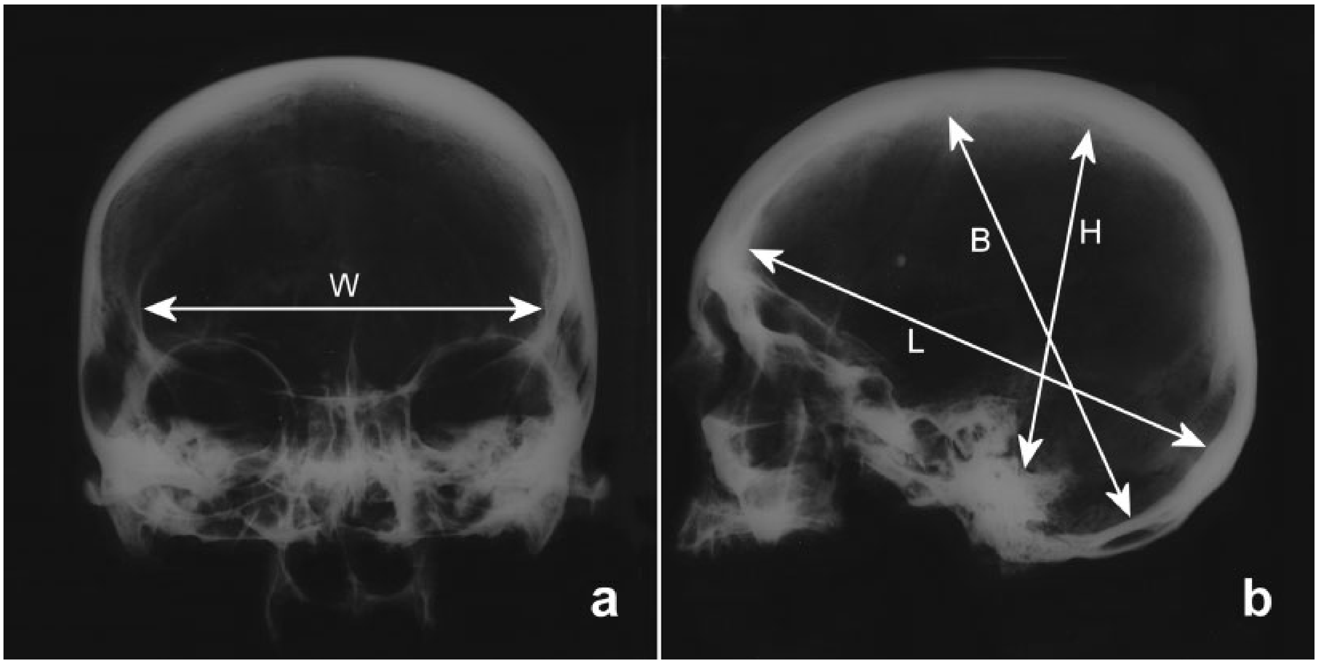

Fig. 1. Two standard anteroposterior (**a**) and lateral (**b**) cephalograms of a skull. Internal length (*L*), internal height (*H*), diameter from bregma to posterior cranial fossa (*B*), and diameter of width (*W*).

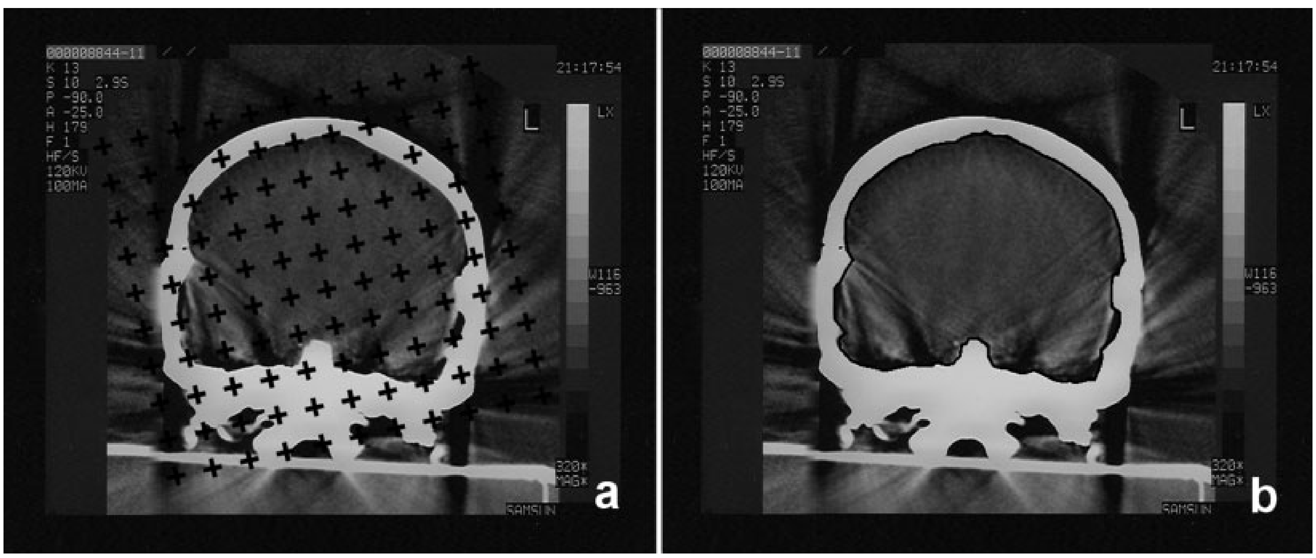

Fig. 2. A computed tomography scan in coronal section. A transparent square grid test system was superimposed, randomly covering the entire image frame to estimate the section cut surface area (**a**). Inner boundaries of the skulls were manually traced on images to calculate the section cut surface area in planimetry method (**b**).

for each section and the volume of the ICV was estimated using the fourth formula. The mean time for the volume estimations was also provided. The coefficient of error (CE) of the point-counting method was calculated using the formula described in previous studies (Sahin et al., 2001; Sahin et al., 2003b). Calculation of ICV, CE of estimates, and other related data were obtained as a spreadsheet using Microsoft Excel. After initial setup and preparation of the formula, the point counts and other data were entered for each scan and the final data were obtained automatically.

Planimetry Method

The cross-sectional surface area of intracranial space was measured by means of the planimetry method using software, namely, DICOMWORKS (version 1.3.5). For the planimetry measurements the same scans were used. Pictures were taken from the CT images, which use a millimetric scale for the calibration. Each scale measurement was carried out at least three times to the nearest millimeter using the tools of software, and the average was considered for calculation. Inner boundaries of the skull were manually traced on each CT image using the computer's mouse. The software automatically calculated the number of pixels enclosed by the traced skull contours on each section and provided the cross-sectional area of the skull on a slice-by-slice basis (Fig. 2b). The sum of the areas multiplied by the section thickness provided the ICV. The planimetric volume estimation formula can be written as follows:

$$V = t \times \sum A \quad (5)$$

where t is the section thickness of consecutive sections (1 cm) and ΣA is the total sectional area of the consecutive sections.

The CE of planimetric volume estimations was calculated using the formula described in the literature (Mazonakis et al., 2002; Sahin et al., 2003a; Sahin and Ergur 2006). The mean time for the volume estimations was also provided. Calculation of ICV, CE of estimates, and other related data were obtained as a spreadsheet using Microsoft Excel as the given point-counting method.

Statistical Analysis

The differences in the estimated volumes obtained by four different approaches were compared using Bland and Altman (1995) statistical test to check the methodological differences. Pearson correlation test was also applied to assess the relation agreements between the results of four different approaches and the actual values. A "P" value lower than 0.05 was accepted as being statistically significant.

RESULTS

The volume values obtained by means of the water-filling method were used as the gold-standard data of the present study. The ICV estimation results of the other four methods were obtained and compared with the results of the water-filling method. The estimated ICV values were calibrated regarding the actual volume of skulls. The calibrated results showed neither a difference from the actual volume of the skulls nor from the other prediction methods ($P > 0.05$). The agreements between four methods were evaluated using Bland and Altman statistical test. All three methods correlated well with each other and with the actual ICV data. The statistical analysis also showed that the point-counting and the planimetry methods have the highest correlation with the actual ICV of skulls. The details of the measured or estimated ICV values are shown in Table 1. The results of statistical comparisons between the methodologies and between the actual volume and the results of estimation methodologies and their correlation analyses are presented in Table 2.

Water-Filling Method

The mean (±SD) of the ICV measured by water-filling method was 1,262.0 ± 160.4 cm^3. It was 1,389.5 ± 96.5 cm^3, and 1,134.5 ± 94.3 cm^3 for males and females, respectively.

TABLE 1. The Details of the Measured or Estimated ICV Values

Method	Minimum	Maximum	Mean	SD
Actuel	1,010.0	1,550.0	1,262.0	160.4
Anthropometry	1,246.8	1,681.3	1,495.1	132.4
Cephalometry	757.3	1,590.9	1,161.5	226.1
Point counting	925.9	1,450.6	1,135.5	134.6
Planimetry	961.0	1,395.0	1,153.6	126.8
CAnthropometry	1,046.5	1,474.6	1,262.7	145.8
CCephalometry	1,096.8	1,487.8	1,276.1	146.8
CPointCounting	1,018.5	1,595.7	1,249.0	148.0
CPlanimetry	1,105.2	1,604.3	1,326.7	145.8

C, Calibrated; SD, standard deviation.

Anthropometry

The mean (±SD) of the ICV estimated by means of the regression formula, based on the anthropometric measurements, was 1,495.1 ± 132.4 cm^3. It was 1,581.7 ± 79.9 cm^3 and 1,408.5 ± 118.1 cm^3 for the males and females, respectively. The estimated volume results were statistically significantly different from the actual volumes of the skulls ($P < 0.05$). In spite of an overestimation of anthropometric data by 18.5%, the results correlated well with the actual volume of the skulls ($r = 0.839$, $P < 0.001$). The final analysis shows that the anthropometric results systematically deviate from the actual volume of the skulls. The estimated ICV values were not statistically different from the other three volume estimation methods ($P > 0.05$). Hence, we propose new regression formulae for the prediction of ICV using anthropometric measurements for both genders as follows:

$$\text{Predicted volume for males} = 392.306 + (0.286 \times L \times W \times H)\ \text{cm}^3 \quad (6)$$

$$\text{Predicted volume for females} = 474.33 + (0.220 \times L \times W \times H)\ \text{cm}^3 \quad (7)$$

The mean (±SD) of the ICV estimated by means of the new prediction formula, based on the anthropometric measurements was 1,262.7 ± 145.8 cm^3. It was 1,390.1 ± 67.8 cm^3, and 1,135.4 ± 56.0 cm^3 for males and females, respectively. The estimated ICV results did not show a statistically significant difference from the actual volumes of the skulls ($P > 0.05$).

Cephalometry

The mean (±SD) of the ICV estimated by means of the regression formula, based on the cephalometric measurements, was 1,161.5 ± 226.1 cm^3. It was 1,312.5 ±153.1 cm^3, and 1,010.5 ± 184.0 cm^3 for males and females, respectively. The estimated volume results were statistically significantly different from the actual volumes of the skulls ($P < 0.05$). In spite of an underestimation of 8% by cephalometric data, the results correlated with the actual volume of the skulls ($r = 0.639$, $P < 0.001$). The final analysis shows that the cephalometric results systematically

TABLE 2. The Results of Bland and Altman (B and A Test) Statistical Analysis Between the Methodologies, Actual Volume, and Their Correlation Analyses

	B and A test		Correlations	
Pairs	Proportional bias	*P*	*r*	*P*
Actual–Anthropometry	233.1	0.001	0.839	0.001
Actual–Cephalometry	−100.5	0.701	0.639	0.002
Actual–PointCounting	−126.6	0.005	0.944	0.001
Actual–Planimetry	−108.4	0.001	0.940	0.001
Actual–Canthropometry	0.7	0.067	0.909	0.001
Actual–Ccephalometry	14.1	0.065	0.838	0.001
Actual–CpointCounting	−12.9	0.089	0.944	0.001
Actual–Cplanimetry	64.6	0.062	0.940	0.001
Anthropometry–Cephalometry	−333.6	0.986	0.589	0.006
Anthropometry–PointCounting	−359.6	0.274	0.839	0.001
Anthropometry–Planimetry	−341.5	0.072	0.742	0.001
Cephalometry–PointCounting	−26.0	0.001	0.690	0.001
Cephalometry–Planimetry	−7.9	0.001	0.674	0.001
PointCounting–Planimetry	18.1	0.143	0.918	0.001
CAnthropometry–CCephalometry	13.4	0.450	0.922	0.001
CAnthropometry–CPointCounting	−13.7	0.352	0.876	0.001
CAnthropometry–CPlanimetry	63.9	0.257	0.857	0.001
CCephalometry–CPointCounting	27.1	0.140	0.781	0.001
CCephalometry–CPlanimetry	27.1	0.222	0.824	0.001
CPointCounting–CPlanimetry	77.6	0.313	0.918	0.001
Anthropometry–CAnthropometry	−232.4	0.874	0.923	0.001
Cephalometry–CCephalometry	114.6	0.001	0.700	0.001
PointCounting–CPointCounting	113.6	0.001	1.000	0.001
Planimetry–Cplanimetry	173.0	0.001	1.000	0.001

C indicates Calibrated.

deviate from the actual volume of the skulls. The estimated ICV values also were statistically significantly different from the other three volume estimation methods ($P < 0.05$). Hence, we propose a new regression formula for the prediction of ICV using cephalometric measurements as follows:

$$\text{Predicted volume for males} = 1169 + (0.008 \times L \times H \times B \times W)\ \text{cm}^3 \quad (8)$$

$$\text{Predicted volume for females} = 1199 + (-0.003 \times L \times H \times B \times W)\ \text{cm}^3 \quad (9)$$

The mean (±SD) of the ICV estimated by means of the new prediction formula, based on the cephalometric measurements, was 1,276.1 ± 146.8 cm^3. It was 1,415.6 ± 41.9 cm^3 and 1,136.7 ± 23.6 cm^3 for the males and females, respectively. The estimated ICV results did not differ statistically significantly from the actual volumes of the skulls ($P > 0.05$).

Point-Counting

The mean (±SD) volume of the ICV estimated using the point-counting method was 1,135.5 ± 134.6 cm^3. It was 1,230.1 ± 116.5 cm^3, and 1,040.9 ± 69.0 cm^3 for the males and females, respectively. The estimated volume results were statistically significantly different from the actual volumes of the skulls ($P < 0.05$). There was no statistically significant difference between the results of point-counting and planimetry methods ($P > 0.05$). However, the estimated ICV values were statistically significantly different from anthropometric and cephalometric results ($P < 0.05$). Analysis of ICV estimates using the point counting showed that the section thickness has an underprojection effect on the obtained section scan images. In spite of a 10.0% underestimation, the results correlated well with the actual volume of the skulls ($r = 0.944$, $P < 0.001$). The final analysis shows that the results of the point-counting method systematically deviate from the actual volume of the skulls.

We simply calibrated the data obtained using the point-counting method by multiplying them by the coefficient 1.10. The mean (±SD) calibrated ICV based on the point counting method was 1,249.0 ± 148.0 cm^3. It was 1,353.1 ± 128.1 cm^3 and 1,144.9 ± 75.9 cm^3 for the males and females, respectively. The estimated ICV results did not differ statistically significantly from the actual volumes of the skulls ($P > 0.05$).

The mean time needed for the point counting was 7 and 24 min (minimum 4, 29 and maximum 9 min). The mean CE was 1.12% (minimum 0.6% and maximum 1.16%).

Planimetry

The mean (±SD) volume of the ICV estimated using the planimetry method was 1,153.6 ± 126.8 cm^3. It was 12,557 ± 80.6 cm^3 and 1,051.5 ± 65.6 cm^3 for the males and females, respectively. The estimated volume results were statistically significantly different from the actual volumes of the skulls ($P < 0.05$). There was no statistically significant difference between the results of planimetry and point-counting and methods ($P > 0.05$). However, the estimated ICV values were statistically significantly different from anthropometric and cephalometric methods ($P < 0.05$). Analysis of ICV estimates using the planimetry showed that the section thickness has an underprojection effect on the obtained section scan images. In spite of 8.6% underestimation, the results correlated well with the actual volume of the skulls ($r = 0.940$, $P < 0.001$). The final analysis shows that the results of the planimetry method also deviate systematically from the actual volume of the skulls.

We simply calibrated the data obtained by the planimetry method by multiplying them by the coefficient 1.086. The mean (±SD) calibrated ICV based on the planimetry method was 1,252.8 ± 137.7 cm^3. They were 1,363.7 ± 87.4 cm^3 and 1,141.9 ± 71.3 cm^3 for the males and females, respectively. However, the calibrated ICV results did show a statistically significant difference from the actual volumes of the skulls (Proportional bias: −16.1; $P < 0.05$). In the light of Bland and Altman analysis, we assessed 1.15 as the new coefficient. The mean (±SD) calibrated ICV based on the planimetry method was 1,326.7 ± 145.8 cm^3. They were 1,444.1 ± 92.6 cm^3 and 1,209.3 ± 75.5 cm^3 for the males and females, respectively. The results of last calibration coefficient to obtain ICV did not show a statistically significant difference from the actual volumes of the skulls ($P > 0.05$).

The mean time needed for the planimetric delineation was 15 and 30 min (minimum 12, 10 and maximum 20, 25 min). The mean CE was 0.2% (minimum 0.1% and maximum 0.3%).

DISCUSSION

The human brain varies widely in size (Knutson et al., 2001). There are several factors that contribute to this variation. Factors related to brain growth, such as gender and physical size, are thought to influence the maximal size of an individual's brain (Raz et al., 1998; Sgouros et al., 1999). Many studies have shown that the ICV increases with age from birth throughout childhood. Most growth is achieved in the first 5 years (Piatt and Arguelles, 1991; Sgouros et al., 1999). At the age of 16–20, the ICV reaches its final size and it is thought that it does not change its size thereafter (Knutson et al., 2001; Wolf et al., 2003). Reported experience has suggested that the ICV remains stable even after brain atrophy. Large variability in brain size related to age, sex, and body size makes it difficult to compare the degree of brain atrophy or swelling among individuals, or correlate histopathological findings with the degree of brain atrophy or swelling. To calibrate these variations, the volume ratio between the brain and the intracranial cavity should be evaluated (Yamada et al., 1999; Whitwell et al., 2001; Mazonakis et al., 2004). Alternatively, ICV measurements may provide reliable indications of the premorbid brain size in neurodegenerative diseases (Jenkins et al., 2000). For this reason many studies are focused on the assessment of ICV.

Several investigators have estimated the ICV, mostly in dry skulls using linear dimensions, packing methods, or occasionally radiological methods (Manjunath, 2002a,b). The packing/filling method involves packing the interior of the skull with filling materials and then measuring it. This is the most accurate in vitro method for measuring ICV, but since it could not provide a volume measurement for living subjects, some approaches have been suggested for predicting the volume using anthropometric measurements. The linear measurement and cephalometry methods are the most common approaches predicting the ICV using measures of length, width, and height of skull directly over the bony structure or lateral and anteroposterior roentgenograms (Manjunath, 2002a).

Published studies use different formulae for the estimation of ICV on roentgenograms, the most commonly used being the ellipsoid formula and MacKinnon's formula or its variations (Sgouros et al., 1999). MacKinnon (1955) was the first to demonstrate a method to estimate the cranial capacity using the cranial length measured on lateral roentgenograms. MacKinnon et al. (1956) in their further studies derived a reliable method for estimating cranial capacity from roentgenograms. The internal lengths, height, and some other data were measured and a prediction formula proposed. This formula had been advanced and a new prediction formula based on the resemblance of the cranial cavity to an ellipsoid had been proposed (Manjunath, 2002a).

In addition to the MacKinnon's formula and its variations, several formulae have also been constructed to indicate cranial capacity from length, width, and height of the cranium. However, such volume determinations may be considered to be inaccurate due to their dependence on linear measurements and due to the limited cephalometric landmark validity characterizing the skull radiographs. Various corrections do not entirely remove this inaccuracy (Williams et al., 1989; Sgouros et al., 1999; Mazonakis et al., 2004).

Kragskov et al. (1997) compared the reliability of anatomic landmarks based on lateral and frontal cephalometric radiographs and 3D CT scans. The authors found that lateral cephalogram measurements were more reliable than the 3D CT ones, with interobserver variations of less than 1 mm for most points compared with about 2 mm for 3D CT. Lateral cephalometry also showed significantly fewer interobserver variations for six variables. This was, however, less obvious when 3D CT was compared with frontal cephalograms. The authors concluded that according to their results, there was no evidence that 3D CT is more reliable than conventional cephalometry in normal skulls.

Our results showed that the volume prediction results obtained by anthropometry and cephalometry were statistically significantly different from the actual volume of skulls obtained by the water-filling method. However, the results of these two methods correlated well with the actual volume of skulls. The volume prediction formulae may result in differences due to the racial, regional, and gender differences, a problem which may be solved by proposing new formulae for different societies or nations. No one can, however, give the assurance that the calibrated results are accurate, since, the last two methods obtain data from two-dimensional linear measurements. As the third dimension is lacking, the method always fails to provide accurate information about the third dimensional value, the volume.

Sectional imaging modalities have provided an opportunity for volumetric quantification of the intracranial cavity. Both CT and magnetic resonance (MR) imaging may produce reliable measurements of ICV. MR imaging offers optimal soft tissue contrast resolution and multiplanar capability without the use of ionizing radiation. However, CT imaging is still a powerful modality for central nervous system imaging and for subsequent routine ICV measurements because of the reduced scanning duration, the availability and the detailed depiction of bony structures (Sugouros et al., 1999; Mazonakis et al., 2004).

Most of the studies adopting the point-counting technique for organ volume estimations have mentioned that this volumetric approach is superior to the technique of planimetry (Roberts et al., 1993; Mazonakis et al., 2002). There are limited studies performing measurements to compare the two volumetric techniques. Gong et al (1999) reported that the planimetry technique should be preferred approach for the measuring tumor volume. However, Mazonakis et al. report that the point-counting method is the most efficient way for the estimation of liver volume (Mazonakis et al., 2002).

ICV measurements using CT scans have already been reported in the literature (Abbott et al., 2000; Wolf et al., 2003; Mazonakis et al., 2004). Most of the above attempts to determine ICV were carried out using the technique of manual planimetry (Lyden et al., 1994; Abbott et al., 2000; Mazonakis et al., 2004). The studies reported that operator intervention was necessary to manually trace the intracranial cavity borders on CT sections. However, manual delineation of the intracranial cavity boundaries is a tedious and labor intensive process. Point-counting estimations are based on the process of point-counting and not on the user's skill in delineating the boundaries of the structure of interest (Mazonakis et al., 2004).

In the present study, we used point-counting and planimetry techniques to estimate ICV on a series of CT sections. The results obtained with these two methods are compared with each other and also with the results of other methods. Finally, the results of stereological estimates were compared with the actual volume of skulls to check the accuracy. Our findings revealed that there was no difference between the results of the point-counting and planimetry methods. The results of both stereological methods were, however, statistically significantly different from the actual volume of the skulls. Correlation analysis revealed that the results of point-counting and planimetry not only correlated well with each other but also with the actual volume of the skulls. The systematic deviation from the actual volume for the point-counting and planimetry methods resulted in underestimation. Since the deviation degree was fluctuating between certain percentages we calibrated the estimated results simply by multiplying the estimated result by the underestimation degree in percentages. Calibrated results of point-counting and planimetry did not show a difference from the actual volumes.

The underestimation problem of the stereological methods probably originated from the effect of section thickness on the printed two-dimensional images. There are restricted studies evaluating the effects of section thickness on the estimated volume of structures using CT and MR images (Emirzeoglu et al., 2005; Sahin and Ergur, 2006). In the present study, however, we did not evaluate the effect of section thickness on the estimated ICV. Decreasing the slice thickness to less than 10 mm may decrease the underprojection effect of sectioned structures which may result in a smaller degree of underestimation (Emirzeoglu et al., 2005; Sahin and Ergur, 2006). In the present study, the thickness of the CT scans was 10 mm since it is routinely used for brain studies in most radiological departments. Smaller slice thicknesses are rarely used for specific clinical purposes.

During the windowing of frames, different levels of settings to obtain best view are chosen. Windowing adjustments are related to the nature of scanned structure and the imaging technique. Moreover, Diederichs et al. (1996) showed that a proper windowing must be chosen to obtain maximum intensity projections. In the living subjects, the skull is filled up with brain, meninges, and cerebrospinal fluid. During the scanning, all those structures absorb or reflect X-ray waves in different degrees. However, in the present study we used dry skulls that only contain air inside it. Therefore, windowing process may produce overprojection of the bony structure on air spaces. Hence, the obtained results may be resulted in underestimation.

Good agreement was found between results obtained with the point-counting and planimetry techniques, the former being 50% faster. As the point-counting method can be applied to any sets of printed CT images, this approach allows one to perform retrospective and prospective studies, and the CT machines and their PC accessories do not have to be engaged. Moreover, the procedure of manually tracing boundaries of the intracranial cavity in all CT sections using planimetry is tedious and requires experience (Mazonakis et al., 2002; Sahin and Ergur, 2006).

In a previous study, we also compared the methodologies proposed for the estimation of ICV on living subjects (Acer et al., 2007). Results showed that there were good agreements between the anthropometric assessments and three dimensional methods, i.e., point-counting and planimetry approaches. It was mainly conducted to check the efficiency of the methods and relation between the estimated results. However, it was not a gold standard study which compares the known ICV with the results of stereological or anthropometric estimations. In the presented study, we were able to compare the estimated results with the actual values.

The stereological technique may be optimized by systematically sampling CT sections and by determining an optimum distance between test points of the grid (Mazonakis et al., 2004). The counting of $\sim$115 points on six to eight systematically sampled CT sections enables the determination of the ICV with a CE below 5% in less than 3 min. The combination of the optimized stereological technique with CT scanning gives the possibility of obtaining acceptable ICV estimations with minimal effort (Mazonakis et al., 2004). Eritaia et al. (2000) reported that there is 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, the ICV between the estimated ICV and the actual ICV also decreased. In addition, the variance of the estimated ICVs increased. They also reported that ICV can be confidently traced using a 1/10 section sampling strategy, which should result in significant time-saving. This sampling strategy produced 5–10% differences between the estimated volumes. However, it reduced the time required for ICV measurement from 120 to 10 min with minimal loss of accuracy or reliability (Eritaia et al., 2000). In the present study, we evaluated all consecutive sections with 1 cm thickness. Decreasing the number of examined slices by using systematic random sampling will decrease the required time period for the point-counting and delineation process.

In the present study, we used different formulas to estimate CE of the point-counting and planimetry methods. In the planimetry method, unbiased estimation of the ICV is obtained by means of manually contouring the boundaries on each section and it is considered to coincide with the exact areas. Therefore, the formula for the CE estimation does not consider the error due to the manually traced boundaries and it gives information about the sufficiency of the number of sections.

In conclusion, the current study evaluates four different techniques for determining the ICV. Our results showed that the results of four methods have differences from each other. While the anthropometric and cephalometric methods are easy and quick to apply, their results may deviate from the actual values. The stereological methods, i.e., point-counting and planimetry can be used to determine ICV on CT images. The optimized stereological techniques may provide unbiased ICV results since they take the third dimension of the structures into account. Finally, estimated ICVs should be calibrated or thin sections should be used to obtain realistic results.

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REFERENCES

Abbott AH, Netherway DJ, Niemann DB, Clark B, Yamamoto M, Cole J, Hanieh A, Moore MH, David DJ. 2000. CT-determined intracranial volume for a normal population. J Craniofac Surg 11:211–223.

Acer N, Sahin B, Bas O, Ertekin T, Usanmaz M. 2007. Comparison of three methods for the estimation of total intracranial volume: Stereological, planimetric, and anthropometric approaches. Ann Plast Surg 58:48–53.

Akbas H, Sahin B, Eroglu L, Odaci E, Bilgic S, Kaplan S, Uzun A, Ergur H, Bek Y. 2004. Estimation of breast prosthesis volume by the Cavalieri principle using magnetic resonance images. Aesthetic Plast Surg 28:275–280.

Bilgic S, Sahin B, Sonmez OF, Odaci E, Colakoglu S, Kaplan S, Ergur H. 2005. A new approach for the estimation of intervertebral disc volume using the Cavalieri principle and computed tomography images. Clin Neurol Neurosurg 107:282–288.

Bland JM, Altman DG. 1995. Comparing methods of measurement: Why plotting difference against standard method is misleading. Lancet 346:1085–1087.

Cruz-Orive LM. 1997. Stereology of single objects. J Microsc 186: 93–107.

Diederichs CG, Keating DP, Glatting G, Oestmann JW. 1996. Blurring of vessels in spiral CT angiography: Effects of collimation width, pitch, viewing plane, and windowing in maximum intensity projection. J Comput Assist Tomogr 20:965–974.

Emirzeoglu M, Sahin B, Selcuk MB, Kaplan S. 2005. The effects of section thickness on the estimation of liver volume by the Cavalieri principle using computed tomography images. Eur J Radiol 56:391–397.

Eritaia J, Wood SJ, Stuart GW, Bridle N, Dudgeon P, Maruff P, Velakoulis D, Pantelis C. 2000. An optimized method for estimating intracranial volume from magnetic resonance images. Magn Reson Med 44:973–977.

Gong QY, Tan LT, Romaniuk CS, Jones B, Brunt JN, Roberts N. 1999. Determination of tumour regression rates during radiotherapy for cervical carcinoma by serial MRI: Comparison of two measurement techniques and examination of intraobserver and interobserver variability. Br J Radiol 72:62–72.

Jenkins R, Fox NC, Rossor AM, Harvey RJ, Rossor MN. 2000. Intracranial volume and Alzheimer disease: Evidence against the cerebral reserve hypothesis. Arch Neurol 57:220–224.

Knutson B, Momenan R, Rawlings RR, Fong GW, Hommer D. 2001. Negative association of neuroticism with brain volume ratio in healthy humans. Biol Psychiatry 50:685–690.

Kragskov J, Bosch C, Gyldensted C, Sindet-Pedersen S. 1997. Comparison of the reliability of craniofacial anatomic landmarks based on cephalometric radiographs and three-dimensional CT scans. Cleft Palate Craniofac J 34:111–116.

Lyden PD, Zweifler R, Mahdavi Z, Lonzo L. 1994. A rapid, reliable, and valid method for measuring infarct and brain compartment volumes from computed tomographic scans. Stroke 25:2421–2428.

MacKinnon IL. 1955. The relation of the capacity of the human skull to its roentgenological length. Am J Roentgenol Radium Ther Nucl Med 74:1026–1029.

Mackinnon IL, Kennedy JA, Davis TV. 1956. The estimation of skull capacity from roentgenologic measurements. Am J Roentgenol Radium Ther Nucl Med 76:303–310.

Manjunath KY. 2002a. Estimation of cranial volume—An overview of methodologies. J Anat Soc India 51:85–91.

Manjunath KY. 2002b. Estimation of cranial volume in dissecting room cadavers. J Anat Soc India 51:168–172.

Mazonakis M, Damilakis J, Maris T, Prassopoulos P, Gourtsoyiannis N. 2002. Comparison of two volumetric techniques for estimating liver volume using magnetic resonance imaging. J Magn Reson Imaging 15:557–563.

Mazonakis M, Karampekios S, Damilakis J, Voloudaki A, Gourtsoyiannis N. 2004. Stereological estimation of total intracranial volume on CT images. Eur Radiol 14:1285–1290.

Piatt JH, Arguelles JH. 1990–1991. Reduction cranioplasty for craniocerebral disproportion in infancy: Indications and technique. Pediatr Neurosurg 16:265–270.

Raz N, Dupuis JH, Briggs SD, McGavran C, Acker JD. 1998. Differential effects of age and sex on the cerebellar hemispheres and the vermis: A prospective MR study. AJNR Am J Neuroradiol 19:65–71.

Roberts N, Cruz-Orive LM, Reid NM, Brodie DA, Bourne M, Edwards RH. 1993. Unbiased estimation of human body composition by the Cavalieri method using magnetic resonance imaging. J Microsc 171:239–253.

Roberts N, Puddephat MJ, McNulty V. 2000. The benefit of stereology for quantitative radiology. Br J Radiol 73:679–697.

Rushton JP, Ankney CD. 1995. Brain size matters: A reply to Peters. Can J Exp Psychol 49:562–569.

Sahin B, Ergur H. 2006. Assessment of the optimum section thickness for the estimation of liver volume using magnetic resonance images: A stereological gold standard study. Eur J Radiol 57:96–101.

Sahin B, Aslan H, Unal B, Canan S, Bilgic S, Kaplan S, Tumkaya L. 2001. Brain volumes of the lamb, rat and bird do not show hemispheric asymmetry: A stereological study. Image Anal Stereol 20:9–13.

Sahin B, Alper T, Kokcu A, Malatyalioglu E, Kosif R. 2003a. Estimation of the amniotic fluid volume using the Cavalieri method on ultrasound images. Int J Gynaecol Obstet 82:25–30.

Sahin B, Emirzeoglu M, Uzun A, Incesu L, Bek Y, Bilgic S, Kaplan S. 2003b. Unbiased estimation of the liver volume by the Cavalieri principle using magnetic resonance images. Eur J Radiol 47:164–170.

Sgouros S, Goldin JH, Hockley AD, Wake MJ, Natarajan K. 1999. Intracranial volume change in childhood. J Neurosurg 91:610–616.

Whitwell JL, Crum WR, Watt HC, Fox NC. 2001. Normalization of cerebral volumes by use of intracranial volume: Implications for longitudinal quantitative MR imaging. AJNR Am J Neuroradiol 22:1483–1489.

Williams PL, Warwick R, Dyson M, Bannister LH. (eds.) 1989. Gray's Anatomy. 37th Ed. Edinburgh: Churchill Livingstone. p 398.

Wolf H, Kruggel F, Hensel A, Wahlund LO, Arendt T, Gertz HJ. 2003. The relationship between head size and intracranial volume in elderly subjects. Brain Res 973:74–80.

Yamada S, Esaki Y, Mizutani T. 1999. Intracranial cavity volume can be accurately estimated from the weights of intracranial contents: Confirmation by the dental plaster casting method. Neuropathol Appl Neurobiol 25:341–344.