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Three-dimensional reconstruction and volumetry of intracranial haemorrhage and its mass effect

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Abstract Intracerebral haemorrhage still causes considerable disability and mortality. The studies on conservative and operative management are inconclusive, probably due to inexact volumetry of the haemorrhage. We investigated whether three-dimensional (3-D), voxel-based volumetry of the haemorrhage and its mass effect is feasible with routine computed tomography (CT) scans. The volumes of the haemorrhage, ventricles, midline shift, the intracranial volume and ventricular compression in CT scans of 12 patients with basal ganglia haemorrhage were determined with the 3-D slicer software. Indices of haemorrhage and intracranial or ventricular volume were calculated and correlated with the clinical data. The intended measures could be

determined with an acceptable intra-individual variability. The 3-D volumetric data tended to correlate better with the clinical course than the conventionally assessed distance of midline shift and volume of haemorrhage. 3-D volumetry of intracranial haemorrhage and its mass effect is feasible with routine CT examination. Prospective studies should assess its value for clinical studies on intracranial space-occupying diseases.

Keywords Intracranial haemorrhage · Volumetry · Three-dimensional reconstruction · Prognosis

Introduction

Intracranial, intraparenchymal haemorrhage accounts for 10%–15% of all strokes, with an overall incidence of 1/100,000–2/100,000 in Caucasians [1]. In spite of considerable advances in intensive care medicine and neurosurgery, morbidity and mortality remain high: one-third to almost one-half of the patients admitted with supratentorial haemorrhage die within 30 days [2, 3]. Half of the surviving patients remain permanently disabled [4].

The best management of patients with intraparenchymal haemorrhage is still under debate. Only few randomized studies compared medical and operative therapy directly. Their results are inconclusive with

respect to morbidity and mortality (reviewed in [5]). One reason for the conflicting results may be inexact volumetry of the haemorrhage and its mass effect.

The most important prognostic sign is the volume of the haemorrhage [2, 6, 7]. It is usually measured by the ABC method, which considers the largest diameter, its vertical diameter, and the number and thickness of slices illustrating the bleeding [8]. This method is easy to apply, even in emergency situations, but inaccurate measurements have to be expected with irregularly shaped structures. Moreover, the absolute volume may not be sufficient to predict its space-occupying effect, because the volumes of intracranial space, brain and cerebrospinal fluid (CSF) space are variable and their relations influence the effect of a rapidly evolving mass. The shift

of midline structures is an indirect sign of the supratentorial mass effect and also considered to be an important prognostic sign [9–11]. Its extent is usually measured as the maximum deviation from the expected midline.

To our knowledge, only one study has measured the volumes of intracranial haemorrhages by three-dimensional (3-D) reconstruction [12]. Other signs of intracranial mass effect have not yet been examined, and 3-D reconstruction and volumetry have not been applied.

The 3D Slicer is an open-source program developed at the Surgical Planning Laboratory (SPL) of the Brigham & Women's Hospital, Harvard Medical School, Boston, USA [13], for visualization of medical 3-D volume data sets as well as for a voxel-based 3-D reconstruction and volumetry of magnetic resonance imaging (MRI)-based data. We tested here whether emergency computed tomography (CT) examinations of intracranial haemorrhage (ICH) could be analysed with the 3D Slicer. For a better consideration of the individual space-occupying effect, we intended to assess not only the volume of the haemorrhage but also the volumes of intracranial space, brain, ventricles and midline shift. In order to consider the size of the haemorrhage relative to the patient's individual

intracranial space and cerebral volume, we also calculated the relation of haemorrhage and intracranial space or ventricular volume. The data acquired were then correlated with the clinical data.

Materials and methods

Twelve patients were included in the retrospective study, eight men and four women, with an average age of 68 years (Table 1). The average observation time was 17 days. Four patients died during primary hospital treatment, three of them from secondary haemorrhage [patient identification (PID) 4], additional cerebral infarction (PID 11) or secondary complications with sepsis (PID 7), respectively. Only one patient died from the primary haemorrhage itself (PID 12).

Retrospectively, we reviewed CT scans of patients treated between 2001 and 2003 at the neurological intensive care unit of the University Hospital of Göttingen for basal ganglia or thalamic haemorrhage. Patients with complete CT scans of sufficient quality performed at the department of neuroradiology and with sufficient documentation of clinical data were included. CT scans were recorded with a third-generation

Table 1 Clinical and volumetric data (*I/co* died from complications, *DNF* data not in file, *PD* patient died, parameter not applicable)

Parameter	Patient ID											
	No. 01	No. 02	No. 03	No. 04	No. 05	No. 06	No. 07	No. 08	No. 09	No. 10	No. 11	No. 12
Age (years)	82	69	69	82	61	79	62	74	44	79	46	77
Glasgow Coma Score	10	15	10	14	DNF	DNF	DNF	15	13	8	14	6
Babinski sign	Extensor	Flexor	Extensor	Flexor	Extensor	Extensor	Flexor	Extensor	Flexor	Extensor	Extensor	Flexor
Hemiparesis (grade 0–5)	0	5	0	2	0	2	0	0	DNF	0	1	DNF
Operation	–	–	–	–	+	–	–	–	+	–	–	–
Respiration therapy (days)	11	0	36	PD	20	0	PD	0	26	15	PD	PD
Intensive care unit (days)	27	0	52	PD	31	13	PD	6	28	20	PD	PD
Arterial hypertension	+	+	+	+	+	+	–	+	+	+	+	–
Glasgow Outcome Scale	2	5	3	(1/co)	3	3	(1/co)	DNF	2	3	(1/co)	1
Hemiparesis discharge (0–5)	0	5	0	PD	0	2	PD	2	0	3	PD	PD
Haemorrhage (ml)	36	11	16	18	53	28	7	11	33	13	12	99
Intracranial space (ml)	1,491	1,696	1,680	1,409	1,586	1,327	1,604	1,500	1,295	1,315	1,117	X
Volume left ventricle (ml)	23	21	30	26	6	17	14	42	12	14	6	4
Haemorrhage left ventricle (ml)	0.7		3.0	0.6								
Volume right ventricle (ml)	5	8	4	54	11	10	17	24	4	11	2	18
Haemorrhage right ventricle (ml)	11	1	10									
Volume third ventricle (ml)	2	5	2	8	2	4	5	6	2	3	0.3	0.3
Haemorrhage third + fourth ventricles (ml)	0.4		2									
Ventricular volume (ml)	42	35	52	89	19	31	36	72	18	27	8	22
Midline shift (ml)	11	2	5	7	8	2	4	0	14	0	9	52
Haemorrhage/intracranial space (%)	2	0.7	1	1	3	2	0.4	0.7	3	1	1	
Haemorrhage/ventricles (%)	85	33	32	21	277	93	19	16	183	49	148	450
Ventricular compression (%)	32	59	57	51	43	39	16	44	65	25	73	80

spiral CT scanner (Xpress/GX, Toshiba). The slice series had a matrix of 512×512 pixels each. The distance between the slices was 5 mm at a slice thickness of 2 mm in the basal parts (cerebellum) and 10 mm at a thickness of 10 mm in the supratentorial parts.

Initial Glasgow Coma Score, hemiparesis, Babinski's sign, pupil status, duration of respiration therapy and intensive care treatment, survival, hemiparesis and Glasgow Outcome Score at discharge were recorded (Table 1). Data accrued from the CT scanner were DICOM files of the CT scans. Post-processing included segmentation of the intracranial space, haemorrhage, ventricles, and midline shift as described below.

Examinations of patients with ventricular shunts, incomplete examinations (more than three 5-mm-slices lacking) or individuals with incomplete clinical data were excluded.

The calculations were carried out on a Microsoft Windows 2000-based standard PC with a Duron 700 MHz processor and 384 MB memory. The data sets were analysed and processed with two software programs: the Hipax Dicom Viewer from Steinhart Medizinsysteme [14], to obtain information from the DICOM header, and the 3D Slicer software package [13], for visualization, semi-automatic segmentation and volumetry.

The 3D Slicer is an open-source software for free academic use. It provides program modules for visualization, segmentation, distance and volume quantification and overlay (=rigid registration) of 3-D medical volume data sets [13]. Developed in 1996 for magnetic resonance (MR) and CT volume data sets, it is now able to visualize any kind of slice series including 3-D ultrasound and single-photon emission computed tomography (SPECT) data sets. 3D Slicer is used to combine functional and morphological information of medical imaging techniques, especially in neurosurgical interventions. The actual software is version 2.0. Because the same algorithms for segmentation and volumetry are used and the previous version 1.3 uses much fewer hardware resources, we decided to use the 3D Slicer version 1.3.

3D Slicer code is based on modules written in VTK for imaging [15], TCL/TK for scripting and C++ for data processing. The description of any processed data (models, original CT data sets and label-maps) is stored in a "scene", including paths, resolution, orientation, etc. in an XML document using an open source MRML-based format [16]. For our purposes the 3D Slicer modules "Editor", "ModelMaker" and "Measure" were used. The label-map created with the segmentation was the base for modelling and volumetry. The 3D surface models were calculated with the Marching Cubes algorithm [17]. To decrease the physical size on the hard disk and the processing time for visualization, we smoothed (minimization algorithm to flatten the forming of edges and angles) and decimated (minimization algorithm to

increase the number of polygons displayed) the models. This had no effect on the volumetry, which was calculated directly from the voxels included in the label-map. All data (models, original CT data sets and label-maps) were stored in MRML-formatted scenes as XML files.

The total intracranial volume, the haemorrhages and the ventricles were segmented semi-automatically using standard thresholding as described [16] and manual editing for finishing. Intraventricular blood was assigned to the ventricular volume because it exerted no direct mass effect to the brain parenchyma. The best contrasts were achieved for all CT data sets with the values Window = 120 and Level = 50. The intra-individual variability was tested by repeated segmentation and volumetry in one single CT examination. Haemorrhage, intracranial space, ventricles and midline shift were assessed four times in patient 5 at a distance of 5 or more days.

To evaluate the size of the haemorrhage and its mass effect on the brain, we intended to measure the following volumes: haemorrhage, intracranial space, lateral, third and fourth ventricles separately, external CSF space and midline shift. As expected, the external CSF space could not be evaluated with sufficient accuracy due to the relatively low resolution of the CT scans.

For further assessment of the impact of the bleeding on the brain and intracranial mass effect, indices were established: haemorrhage to intracranial volume, and ventricular compression (volume of ipsilateral ventricle as percentage of contralateral ventricle). Because the number of examinations was too low, the results were analysed by descriptive evaluation.

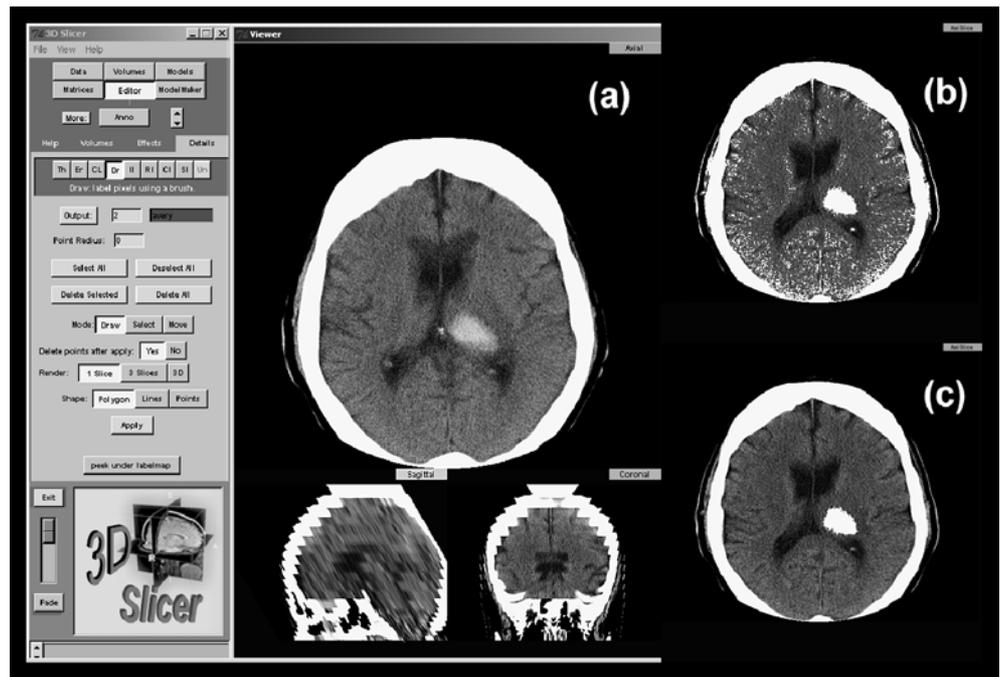
The process to identify the bleeding is shown in Fig. 1. For thresholding, the lower level was set to 40–44 and the upper level was set to 100–140 for all data sets, depending on the signal-to-noise ratio of the single data set. As a result, a label-map was created, which is shown in Fig. 1b. The areas marked as unnecessary could be removed by the 3D Slicer option "save island" (Fig. 1c) for each slice separately. From the label-maps, the volumes were calculated in millilitres by the module "MeasureVol" according to the following formula:

$$V = \frac{A \cdot B \cdot N \cdot Z}{1,000}$$

where V is the volume (in millilitres), A the width of pixel (in millimetres), B the height of the pixel (in millimetres), N the number of voxels in the label-map with the same number and Z the slice thickness + interslice gap (in millimetres). ABZ is the volume of a single voxel.

For visualization, models were created from the label-maps. In order to overcome the volume effect from the CT scanner due to the slice thickness, and to obtain a more realistic model, we created the models using a smoothing factor (smooth = 5) with lowest decimation (decimate = 1). This is shown in Fig. 2.

Fig. 1 The process to identify the bleeding



Segmentation, volumetry and model generation were done for the haemorrhage, the intracranial volume, the ventricles (sub-divided into left and right, third and fourth). In cases of intraventricular bleeding, the haemorrhage was sub-divided by the same procedure. According to the inclusion criteria, examinations with up to three slices lacking either in the basal or in the apical part to illustrate the intracranial volume completely were included in the study. The missing slices were reconstructed manually. The reconstructed volume accounted for less than 3% of the total volume.

In patients with a shift of the midline structures, the deviation was segmented as an additional parameter,

taking into account the difference between the anatomical and the individual centre line. An example image is shown in Fig. 3. The midline structures were marked manually, segmenting the deviation from a line connecting the frontal insertion of the falx cerebri with its contact with the tentorium. The volume inside the midline shift was determined by 3-D reconstruction.

In order to compare our 3-D reconstruction-based volumetry with the conventional methods, we measured the distances of the midline shifts, calculated the volumes of the haemorrhages with the ABC method from the DICOM data and compared the coefficients r^2 for the correlation with the clinical parameters.

Fig. 2 Models created using a smoothing factor

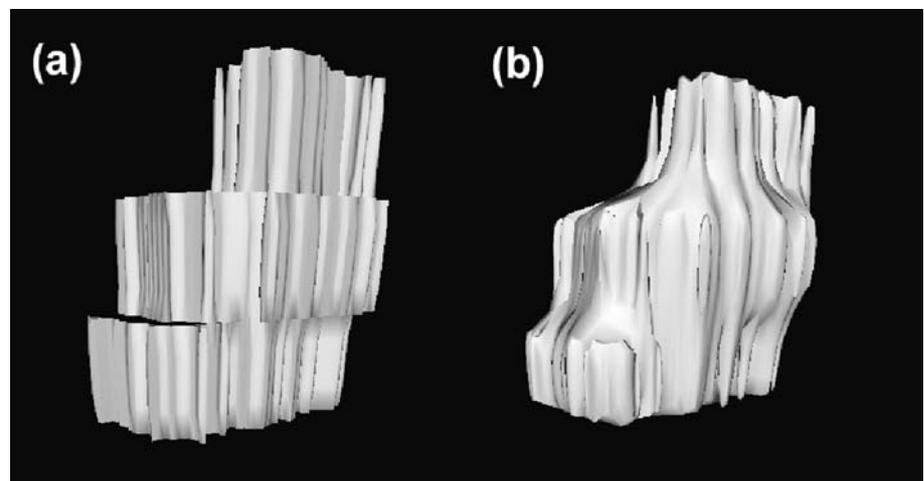
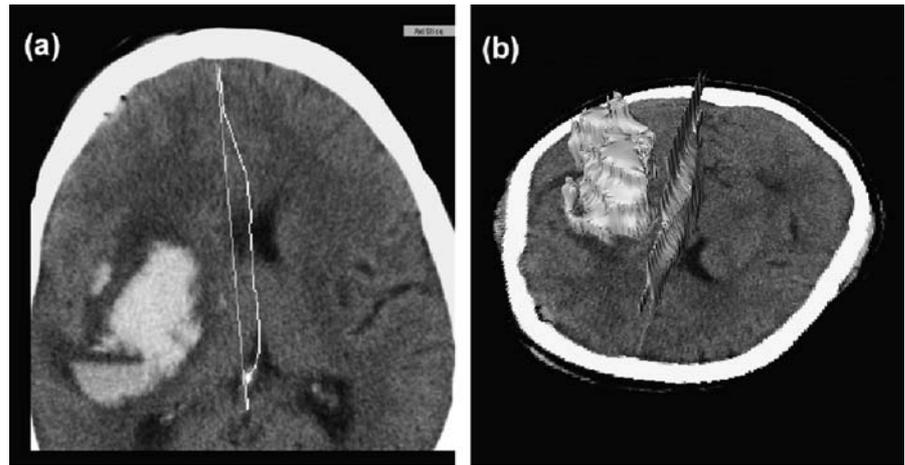


Fig. 3 An example image



Results

The volumes of intracranial space, haemorrhage, ventricles and midline shift could be assessed in all complete examinations. The variability of four repeated segmentations and volumetries was smallest for the intracranial volume (1582.1 ± 3.2 ml, average and SD) and highest for the third and fourth ventricles (2.2 ± 0.3 ml, Table 2). With the model maker, 3-D models of all reconstructed structures could be created and the haemorrhage and its effect on intracranial structures visualized.

Measured volumes

Intracranial volumes were, on average, $1,305 \pm 153$ ml in the women and $1,543 \pm 138$ ml in the men. Repeated measurements in the same patient (PID 4) varied between 1,579 ml and 1,586 ml (1582.1×3.2 ml). The measured volumes of the haemorrhages ranged from 7 ml to 99 ml in all patients. The variability in one patient was 51–54 ml (52.7 ± 1.5 ml). Total ventricular volume in all patients ranged between 8 ml and 89 ml. The intrapersonal variability ranged from 19 ml to 24 ml (20.6 ± 2.1 ml). The maximum midline shift was 52 ml in patient 12. The variability of measurements in

one patient (patient 4) ranged from 8.1 ml to 9.4 ml (8.9 ± 0.6 ml).

Correlation between volumes and indices of volumes

In order to evaluate the size of the haemorrhage relative to the size of the patient's skull and brain, we related the measured parameters to the intracranial space or ventricular volume with indices. The volume of the haemorrhage was calculated as a percentage of the total intracranial volume or of the ventricular volume. The compression of the ipsilateral ventricle was assessed as a percentage of the contralateral ventricle.

The volume of the haemorrhage correlated well with the midline shift ($r^2 = 0.82$), while no correlation was observed between the ventricular compression and the volume of the midline shift ($r^2 = 0.23$) or with the volume of the haemorrhage ($r^2 = 0.14$).

Correlation with clinical parameters

Although a number of clinical parameters were documented by non-metric scores, the correlation coefficient r^2 was calculated to compare the value of the parameters in our descriptive analysis.

Table 2 Intra-individual variability of volumetry (four repeated segmentations)

Parameter	Average (ml)	Maximum (ml)	Minimum (ml)	Standard deviation (ml)	Standard deviation (% of average)
Haemorrhage	52.7	53.7	50.5	1.5	2.8
Intracranial volume	1,582.1	1,586.2	1,579.2	3.2	0.2
Right lat. ventricle	11.7	13.4	10.9	1.1	9.7
Left lat. ventricle	6.7	7.7	6.2	0.7	10.4
Third + fourth ventricles	2.2	2.7	1.8	0.3	15.3
Total ventricular volume	20.6	23.8	19.3	2.1	10.3
Midline shift	8.9	9.4	8.1	0.6	6.6

Good correlations (Table 3) were found between the survival of the patient and the volumes of the midline shift ($r^2=0.91$) and of the haemorrhage ($r^2=0.75$). The correlation of both parameters with the Glasgow Outcome Scale and with the hemiparesis at discharge was worse (Table 3). All other parameters were not correlated with the volume of the haemorrhage. No correlations were found between ventricular compression and any clinical parameter. In addition, the relation of the haemorrhage with the intracranial volume or with the ventricular volume was not correlated with any clinical data.

In order to compare the value of the measured parameters with the conventional assessment of the volume of the haemorrhage and the deviation of midline structures, we determined both parameters with the ABC method and by direct 1-D measurement of the distance of the midline shift, respectively. The correlation coefficients for most of the clinical parameters tended to be better with the 3-D based volumetry than with the measures determined conventionally (Table 3).

Discussion

The results of the study presented here show two facts: (a) 3-D reconstruction and volumetry is feasible in routine CT scans and (b) 3-D reconstruction could be used as an alternative to the well-known ABC formula, especially in clinical studies.

As a suitable disease to assess the feasibility of the method we chose basal ganglia haemorrhage for its relatively well-demarcated margins that are usually distant from other hyperintense structures of the cranial vault and its contents. In all chosen CT scans, segmentation and 3-D reconstruction of intracranial space, haemorrhage, ventricles and midline shift could be performed. The total intracranial volumes measured with our CT-based method (men $1,543 \pm 138$ ml, women $1,305 \pm 153$ ml) were comparable with the volumes assessed in an MRI-based study (men $1,558 \pm 97$ ml, $1,352 \pm 115$ ml) [18]. The accuracy of the method in four repeated measures was acceptable, with a standard deviation of 0.2% of the average for the intracranial space—a large structure with well-demarcated margins. The maximum standard deviation of 15.3% of the average was achieved in small, less-clearly demarcated structures (third and fourth ventricles). The resolution of the CT scans was not sufficient for a segmentation of the external CSF space. Therefore, also the volume of the brain could not be evaluated.

To our knowledge, only one other study measured the volumes of intracranial haemorrhage by 3-D reconstruction of CT-based data [12]. In this study, 3-D volumetry of intracranial haemorrhage was also considered feasible. Other parameters, such as intracranial

Table 3 Coefficient r^2 for correlations of measured volumes and indices with clinical parameters

Method	Haemorrhage (ml)		Haemorrhage/intracranial space (%), segmentation	Haemorrhage/ventricle volume (%), segmentation	Ventricular compression (%), segmentation	Midline shift	
	Segmentation	ABC-F				Segmentation	Distance
Glasgow Coma Scale	0.47	0.45	0.06 ^a	0.34	0.00	0.38	0.36
Babinski sign	0.03	0.08	0.06 ^a	0.03	0.01	0.15	0.10
Hemiparesis, initial	0.04 ^a	0.01 ^a	0.04 ^a	0.04	0.19	0.05	0.03
Respiration therapy (days) ^b	0.07 ^a	0.06 ^a	0.06 ^a	0.11	0.10	0.29	0.16
Intensive care (days) ^a	0.13 ^a	0.05 ^a	0.10 ^a	0.08	0.01	0.25	0.24
Glasgow Outcome Score	0.53	0.46	0.36 ^a	0.44	0.07	0.54	0.59
Hemiparesis, discharge	0.43 ^a	0.25 ^a	0.43 ^a	0.28	0.00	0.54	0.52
Survival	0.75	0.87	—	0.66	0.45	0.91	0.76

^aValues could not be calculated for all patients. The correlation between survival and the index haemorrhage/intracranial space could not be calculated because the intracranial space could not be determined in the patient who died from the haemorrhage

space and its relation to the volume of the haemorrhage or signs of mass effect, have not been evaluated.

Most haemorrhages treated on our neurological intensive care unit were of moderate size, because patients with less bleeding are admitted to our stroke unit, and those with larger haemorrhages are most often treated in the department of neurosurgery. Therefore, the volumes of the haemorrhages and also the clinical signs differed only moderately. This limited variation may explain, in part, why most of the clinical signs did not correlate closely with the measured parameters. In line with previous studies we found that the size of the haemorrhage [2, 6, 7] and of the midline shift [8] was most important for the patient's prognosis. Both parameters correlated best with the patients' survival, while only moderate correlation was found with the Glasgow Coma and Outcome scales and with the grade of hemiparesis at discharge.

Because of individual differences in the size of skull and brain, we tested if the relation of the haemorrhage to the intracranial space or to the ventricular volume correlated better with the clinical data, or if ventricular compression, as an indirect sign of the intracranial mass effect, could serve as an additional prognostic sign. Neither parameter yielded better results than the volumes of haemorrhage and midline shift. The variation of intracranial and ventricular volumes may be too low to be of importance for the patient's prognosis. Ventricular compression may be of minor importance because the CSF, as a reserve space, may be evacuated without considerable damage to the brain, while much stronger force is needed to cause a deviation of the midline structures. Moreover, contralateral ventricular congestion may lead to conflicting results.

The data achieved by 3-D volumetry tended to correlate better with most of the clinical signs than the distance of the midline shift or the volume of the haemorrhage determined with the ABC method—except for the correlations between haemorrhage and survival and for midline shift and Glasgow Outcome Scale (Table 3). In our hands, semi-automated segmentation and three dimensional reconstruction of the DICOM data took approximately 20 min. This prevents a wide use of this method in the clinical setting, because the conventional ABC method provides volumetric data of acceptable accuracy in less than 1 min [8]. Three dimensional reconstruction, however, may be of interest for scientific purposes, where more time is available for the analysis and more-precise data are needed.

We conclude that 3-D reconstruction and volumetry of haemorrhage and its mass effect is feasible and can be applied to CT techniques. High-resolution CT or MRI examinations and complete illustration of the skull and intracranial structures will probably yield better results and may allow for segmentation of the external CSF space. We presume that direct and indirect signs of mass effects can be evaluated by 3-D reconstruction and volumetry, not only in spontaneous haemorrhage, but also in traumatic haemorrhage or other types of intracranial space-occupying disease. While conventional assessment of midline shift and calculation of the volume of a haemorrhage are quick and feasible for emergency situations, the data achieved in this pilot study indicate that 3-D volumetry of a haemorrhage and its mass effect may yield more-precise results, which may be valuable for scientific analyses. The method and the presented parameters should be assessed in larger, prospective studies.

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