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Dose reduction in dynamic perfusion CT of the brain: effects of the scan frequency on measurements of cerebral blood flow, cerebral blood volume, and mean transit time

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Abstract The influence of the frequency of computed tomography (CT) image acquistion on the diagnostic quality of dynamic perfusion CT (PCT) studies of the brain was investigated. Eight patients with clinically suspected acute ischemia of one hemisphere underwent PCT, performed on average 3.4 h after the onset of symptoms. Sixty consecutive images per slice were obtained with individual CT images obtained at a temporal resolution of two images per second. Eight additional data sets were reconstructed with temporal resolutions ranging from one image per second to one image per 5 s. Cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) measurements were performed in identical regions of interest. Two neuroradiologists evaluated the PCT images visually to identify areas of abnormal perfusion. Perfusion images created up to a temporal resolution of one image per 3 s were rated to be diagnostically equal to the original data. Even at one image per 4 s, all areas of infarction were identified. Quantitative differences of CBF, CBV and MTT measurements were ≤10% up to one image per 3 s. For PCT of the brain, temporal resolution can be reduced to one image per 3 s without significant compromise in image quality. This significantly reduces the radiation dose of the patient.

Keywords Computed tomography · Perfusion imaging · Perfusion CT · Stroke · Cerebrovascular disorders

Introduction

Measurement of cerebral haemodynamics has been shown to be helpful in the management of patients with cerebrovascular diseases and intracranial neoplasms [1–3]. Various imaging techniques have been used for brain perfusion measurement including positron emission tomography (PET), single photon emission tomography (SPECT), magnetic resonance imaging (MRI), computed tomography (CT), and even ultrasound [3, 4].

Perfusion CT (PCT) allows accurate quantitative assessment of brain tissue perfusion, is well tolerated and not time-consuming. Advantages of PCT compared with MRI are that PCT studies can be performed easily and rapidly in the emergency setting as part of the admission imaging protocol, and that CT machines are readily accessible. Since most hospitals do not have MRI units available round the clock, 7 days a week, PCT constitutes a valuable addition to the diagnostic neuroradiological tools [5]. Standard CT systems can be used and no extra

materials are needed, except for dedicated post-processing software. Different PCT types have been proposed, of which dynamic PCT allows the best assessment of cerebral hemodynamics. For dynamic PCT, sequential CT slices are acquired in cine mode during the intravenous administration of iodinated contrast medium. For each pixel, time-density profiles of contrast enhancement are obtained using dedicated post-processing software. From these curves, several perfusion-related parameters are calculated and displayed as colour-coded parameter maps. The perfusion parameters most commonly used include cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT).

With technical improvement of spiral CT and the introduction of multi-slice CT machines, the number of images obtained per dynamic PCT study has increased steadily, and may be expected to increase further in the future. Therefore, it is critical to limit the radiation exposure to the patient. Reducing the tube voltage and using highly concentrated contrast media have been recommended to increase signal-to-noise and reduce radiation exposure [6–8]. Recent PCT protocols use data acquisition frequencies of one to two images per second. From a mathematical perspective, increasing the temporal resolution should improve the quality of the time-density curves, and thus increase the accuracy of perfusion measurements. On the other hand, there is a linear relationship between the number of acquisitions at a given anatomical site and radiation dose. Two other authors have studied whether the temporal resolution may be reduced in PCT but came to different conclusions [9, 10].

In this study, we investigated whether the temporal resolution, and thus the radiation exposure to the patient, can be reduced in dynamic PCT of the brain without losing diagnostic accuracy. Therefore, we studied the influence of the temporal resolution on the quantitative results of PCT measurements in stroke patients. For calculation of PCT measurements we used a mathematical algorithm not yet studied for its interaction with temporal resolution [11].

Materials and methods

Eight patients (age range 59–89 years) with clinically suspected acute ischemia of one hemisphere and no infarct demarcation on plain cerebral CT underwent dynamic PCT, performed on average 3.4 h (range, 1.3-10.9 h) after the onset of symptoms.

PCT measurements were conducted for clinical purposes on a multi-slice CT system (Aquilion, Toshiba Medical Systems Europe, Zoetermeer, Netherlands) using four slices with a scan volume of 4×8 mm. The detector of the the CT system consists of 34 rows covering a scan width of 32 mm. Its four central rows have a thickness of 0.5 mm, whereas the other 30 rows have a thickness of 1.0 mm. The area of the patient to be examined by CT was centered at the level of the Foramina of Monro with the orientation of the volume parallel to the native CT. Forty millilitres of non-ionic iodinated contrast agent (Ultravist 370, Schering, Berlin, Germany) were injected intravenously with a flow rate of 5 ml per second. Five seconds after injection of the contrast agent, 60 consecutive images per slice were obtained with a temporal resolution of two images per second. CT parameter were as follows: 120 kV, 150 mAs, rotation time 0.5 s, field of view 240 mm, matrix 512×512, low contrast filter (FC 22). The study protocol was approved by the local ethics committee, and informed consent was obtained from each patient or their relatives before the PCT was performed.

After clinical evaluation of the PCT, one typical section through the basal ganglia per PCT study was selected for further analysis. These 60 images per study were transferred to a work station (Anet, Toshiba Medical Systems Europe, Zoetermeer, Netherlands). Full data sets were acquired at at a temporal resolution of 500 ms (two images per second). Then, eight additional data sets were synthesized by using only every other, every third, fourth, fifth, sixth, seventh, eighth, and every tenth sample, resulting in temporal resolutions between 1 and 5 s. Simulated data sets are listed in Table 1 and illustrated in Fig. 1. A dedicated software package (CBP-study, Toshiba Medical Systems Europe, Zoetermeer, Netherlands) based on a parametric deconvolution algorithm was used for quantitation of PCT parameters [11].

Colour-coded parameter maps for CBF, CBV, and MTT were calculated for all data sets and presented together to two neuroradiologists. Maps of each case and data set were presented independently in random order. The evaluators stated whether they could identify areas of abnormal perfusion and noted their location. For quantitative analysis, 12 regions of interest (ROIs) were drawn on the original data sets of the subjects (scan frequency of two images per second) and then copied to all data sets of this

Table 1 Perfusion CT data were acquired at a temporal resolution of 500 ms. Then, eight additional data sets were synthesized by using only every other, every third, every fourth, etc sample up to a sampling rate of 5 s. Note that the last image of the original data sets (data set 1) was taken as last image for data sets 8 and 9

Data sets	Simulated temporal resolution of CT data sets	No. of images used for analysis
1	One image/0.5 s	60
2	One image/1 s	30
3	One image/1.5 s	20
4	One image/2 s	15
5	One image/2.5 s	12
6	One image/3 s	10
7	One image/3.5 s	8
8	One image/4 s	7
9	One image/5 s	6

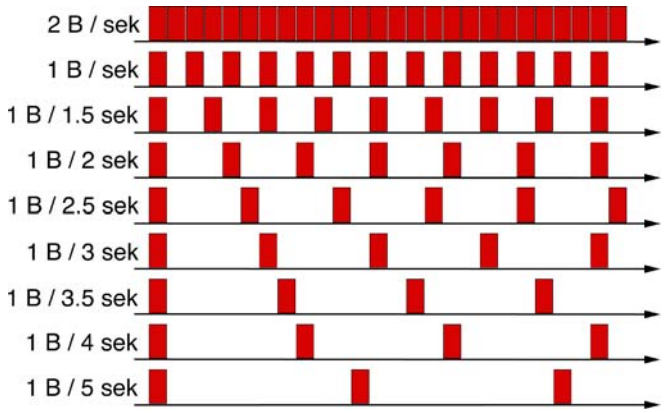

Fig. 1 Schematic representation of the method used to obtain eight additional data sets for perfusion analysis simulating different temporal resolutions. PCT data were acquired at a temporal resolution of 500 ms. Then, eight additional data sets were synthesized by using only every other, every third, every fourth, etc. sample up to a sampling rate of 5 s

subject. In both hemispheres, ROIs were drawn on cortical grey matter (frontal cortex, temporal cortex, occipital cortex), white matter (frontal lobe), and basal ganglia (lentiform nucleus, thalamus). ROIs were not placed in areas of suspected abnormal perfusion. CBF, CBV, and MTT values of these ROIs were compared across data sets using statistical analysis. Measurements from the original data sets were considered as the "gold standard" and compared with measurements obtained from data sets with reduced scan frequencies. All results are given as mean ± standard deviation unless stated otherwise. To describe the compromised precision of CBF, CBV, and MTT measurements caused by reducing the temporal resolution, we calculated the *absolute mean imprecision*. To obtain this value, the integers of all differences between the ROI measurements for a given temporal resolution to the gold standard (i.e. minus values are converted to plus) are averaged. As an arbitrary measure, we considered an imprecision of 10% as acceptable. The statistical analysis was performed using the SPSS 12.0 package (SPSS, Chicago, Ill., USA). The significance of differences between groups was examined using the Wilcoxon test. Correlations between variables were calculated using the Spearman rank order correlation coefficient.

Results

Four patients suffered from territorial infarction of the middle cerebral artery. One patient suffered from territorial infarctions of the middle as well as the posterior cerebral artery. The remaining three patients suffered from transient ischemic attacks, and ischemic areas were not found on initial or follow-up scans.

In the five cases with infarctions, areas of abnormal perfusion were clearly demonstrated on the original PCT images, whereas no perfusion abnormalities were found in the other three cases. The regions of abnormal perfusion were correctly identified by both evaluators on the original data sets as well as on all data sets with reduced temporal resolution except in one of the five cases, in which the data set with a temporal resolution of 5 s was compromised by artefacts

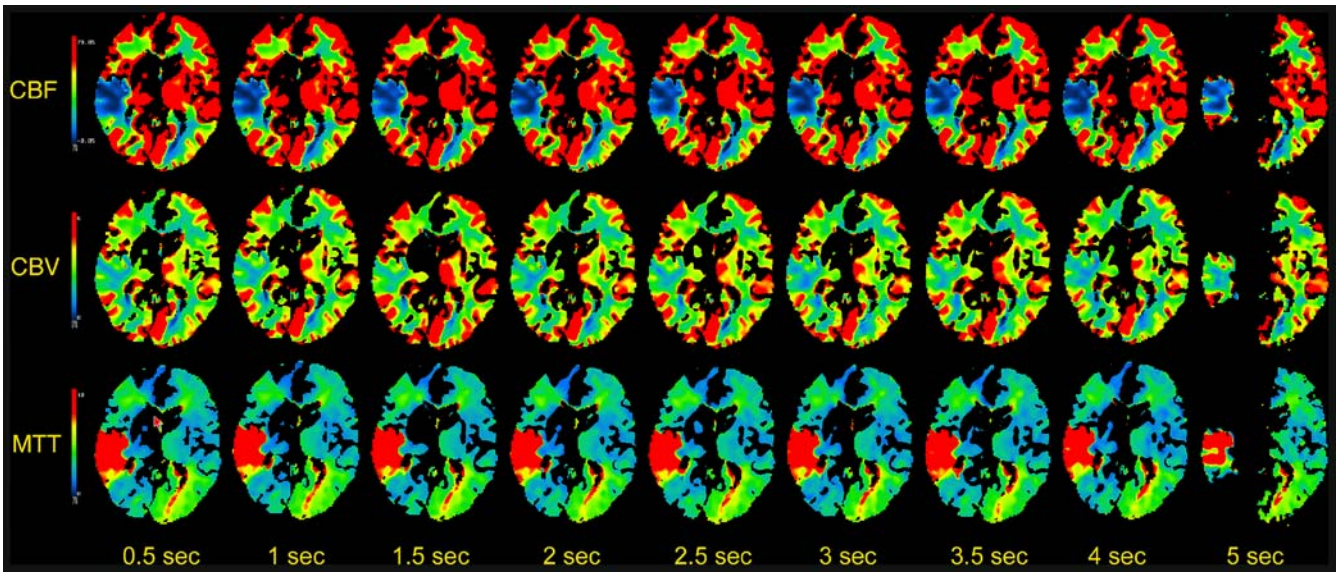

Fig. 2 Sample perfusion CT data sets in one patient with an ischemic lesion in the territory of the right middle cerebral artery. The ischemic lesion is characterised as an area of decreased blood flow (CBF, *upper row*), decreased blood volume (CBV, *middle row*), and increased transit time (MTT, *lower row*). The lesion is clearly visualised on the original data sets (0.5 s) as well as on the simulated data sets with reduced scan frequency (1–4 s) except on the data set with a CT acqisition rate of one image/5 s, which was compromised by artefacts

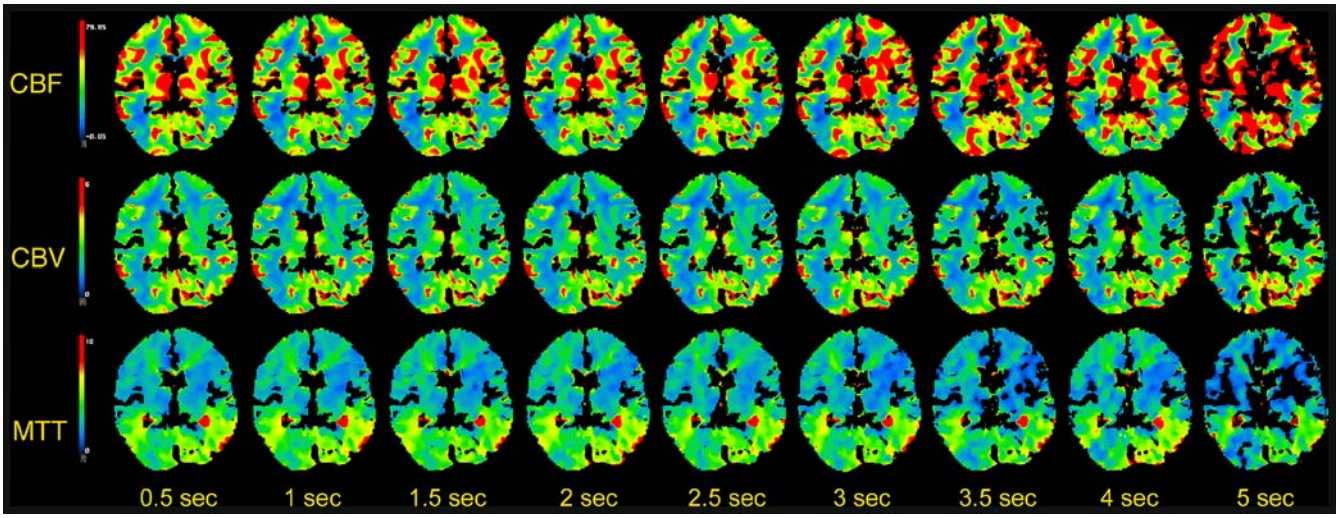

Fig. 3 Sample perfusion CT data sets in one patient with a transient ischemic attack. Normal perfusion measurements are found in both hemispheres using the original data sets (temporal resolution, 0.5 s) as well as the simulated data sets with reduced temporal resolution. However, some degradation of image quality is seen at lower temporal resolutions (3.5–5 s)

(Fig. 2). In the three cases with transient ischemic attacks, false-positive findings were noted neither on the original data sets nor on the data sets with reduced temporal resolution (Fig. 3). However, the evaluators noted that reducing the temporal resolution led to some degradation of the image quality of the perfusion maps. This effect was clearly seen at frequencies of one image/3.5 s or above (Fig. 3).

As expected, the temporal resolution had some influence on the accuracy of the derived arterial input and venous output functions as illustrated in Fig. 4.

In the original data sets we found mean CBF values of 54.4±17.9 μg/100 ml/min for cortex, 19.3±8.1 μg/100 ml/min for white matter, and 61.4±20.6 μg/100 ml/min for basal ganglia. CBV measurements were 3.3±1.3% for

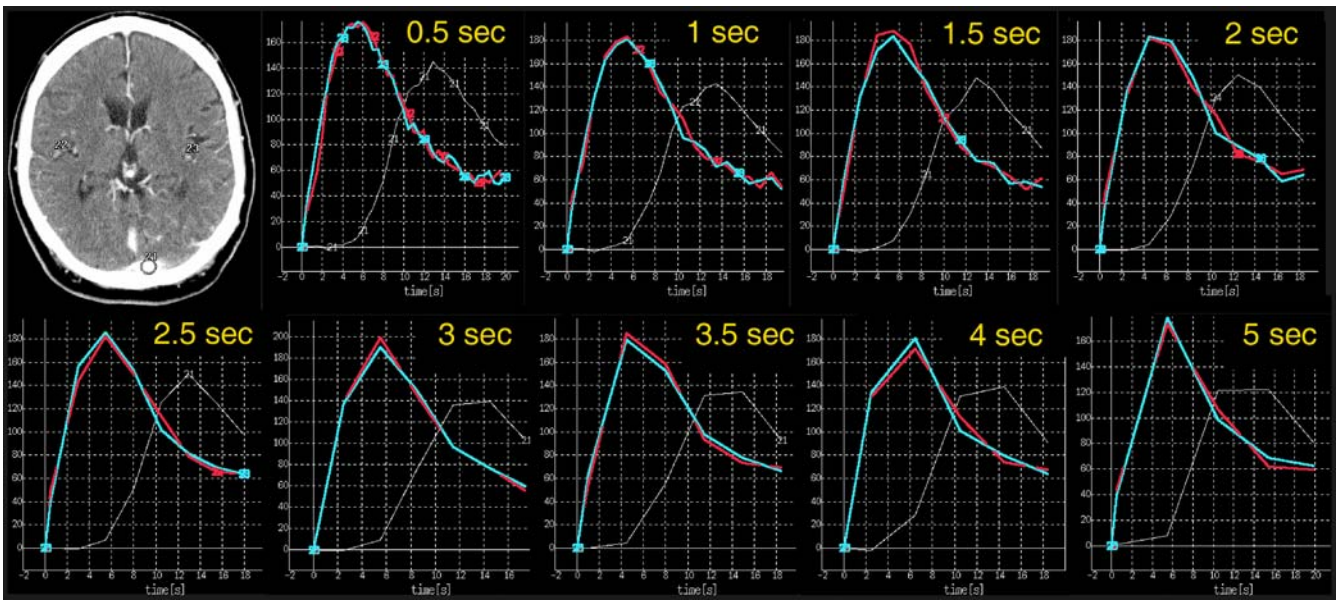

Fig. 4 Influence of the temporal resolution on time-density curves used for definition of arterial input and venous output functions. Shown are typical measurements of one patient. Time-density curves were obtained from the left middle cerebral artery (shown in *red*), right middle cerebral artery (*blue*), and superior sagittal sinus (*white*). With decreasing temporal resolution, the difference between the shape of the curves obtained from the original data set (0.5 s) and the derived data sets increases. The shape of arterial input and venous output functions influences the precision of calculated CBF, CBV, and MTT values

Table 2 Effects of the temporal resolution on CBF, CBV, and MTT measurements in PCT. In eight patients, ROI measurements were taken from cortex (six ROIs each), white matter (two ROIs each), and basal ganglia (four ROIs each). Values are shown as mean ± standard deviation

Simulated temporal resolution	CBF (ml/100 ml/min)			CBV (%)			MTT (s)		
	Cortex	White matter	Basal ganglia	Cortex	White matter	Basal ganglia	Cortex	White matter	Basal ganglia
One ima/0.5 s	54.4±17.9	19.3±8.1	61.4±20.6	3.3±1.3	1.6±0.5	3.1±1.2	3.9±1.4	5.7±2.3	3.4±1.5
One ima/1 s	52.0±16.1	19.0±9.0	58.5±19.7	3.1±1.1	1.6±0.5	3.0±0.9	3.9±1.3	5.8±2.5	3.4±1.6
One ima/1.5 s	53.0±20.1	19.2±10.1	59.7±21.0	3.1±1.1	1.6±0.5	3.0±1.0	3.9±1.4	5.8±2.3	3.3±1.4
One ima/2 s	53.7±18.5	19.1±8.3	61.2±20.3	3.1±1.1	1.5±0.5	3.0±1.0	3.8±1.3	5.6±2.4	3.3±1.4
One ima/2.5 s	54.6±17.9	19.0±8.5	60.9±19.7	3.1±1.2	1.6±0.6	3.0±1.1	3.7±1.2	5.7±2.3	3.3±1.4
One ima/3 s	54.1±19.9	19.5±8.3	63.6±20.5	3.2±1.3	1.6±0.5	3.1±1.2	3.8±1.2	5.7±2.2	3.2±1.4
One ima/3.5 s	57.1±19.5	20.2±8.2	67.3±23.1	3.3±1.4	1.7±0.6	3.2±1.2	3.8±1.4	5.7±2.4	3.2±1.5
One ima/4 s	53.2±20.3	19.5±7.9	65.9±20.2	3.3±1.4	1.6±0.6	3.2±1.2	4.1±1.3	5.7±2.3	3.2±1.3
One ima/5 s	59.0±23.3	20.0±7.6	66.8±23.4	3.1±1.3	1.5±0.5	3.1±1.3	3.7±1.3	5.5±2.5	3.1±1.5

cortex, 1.6±0.5% for white matter, and 3.1±1.2% for basal ganglia. MTT values were 3.9±1.4 s for cortex, 5.7±2.3 s for white matter, and 3.4±1.5 s for basal ganglia. The effects of reducing the temporal resolution on these measurements are summarised in Table 2. Average values of CBF, CBV, and MTT measurements over all ROIs and effects of reducing the temporal resolution are summarised in Table 3. In general, the quantitative changes in CBF, CBV, and MTT measurements were rather small.

From these values, we calculated the absolute mean imprecision as described above. Results are presented in Fig. 5. For CBF measurements, the absolute mean imprecision was found to be about 10% up to a temporal resolution of 3 s. At a temporal resolution of 5 s the imprecision increased to 21.7% ($p<0.0001$). The absolute mean imprecision of CBV measurements was found to be below 10% at all temporal resolutions used. The imprecision of MTT measurements was found to be below or about 10% up to a temporal resolution of 3 s. The imprecision amounted to 10.2% ($p=0.003$) at a temporal resolution of 3 s, 11.4% ($p<0.0001$) at 3.5 s, 20.1% ($p=0.001$) at 4 s, and 19.0% ($p<0.0001$) at 5 s.

Discussion

Various parameters involved in the performance of PCT affect the accuracy of perfusion values and the associated radiation dose. In this study, we investigated whether the temporal resolution, and thus the radiation exposure to the patient, can be reduced in dynamic PCT of the brain without losing diagnostic accuracy. Our findings suggest that it is possible to reduce the temporal resolution to a value as low as one image every 3 s.

Two other reports on the optimal temporal resolution for PCT have been published. In accordance to our findings, Wintermark et al. [9] also advocated a temporal resolution of 3 s for a contrast bolus of 40 ml as used in our study. By

Table 3 Effects of the temporal resolution on CBF, CBV, and MTT measurements in PCT. In eight patients, ROI measurements were taken from cortex (six ROIs each), white matter (two ROIs each), and basal ganglia (four ROIs each). Values are shown as mean ± standard deviation. Measurements from simulated data sets were tested for statistical difference to the values obtained from the original data set (one image/0.5 s) using the Wilcoxon test. *P* values are given *in parentheses*, *n.s.* not significant

Simulated temporal resolution	CBF (ml/100 ml/min)		CBV (%)		MTT (s)	
One image/0.5 s	49.8±21.7		2.9±1.3		4.0±1.8	
One image/1 s	47.8±20.2	($p=0.036$)	2.8±1.1	($p=0.003$)	4.1±1.8	(n.s.)
One image/1.5 s	48.5±22.4	($p=0.015$)	2.8±1.1	($p=0.001$)	4.0±1.8	(n.s.)
One image/2 s	49.3±21.7	(n.s.)	2.8±1.1	($p<0.001$)	3.9±1.7	($p=0.001$)
One image/2.5 s	49.7±21.4	(n.s.)	2.8±1.2	(n.s.)	3.9±1.7	($p=0.003$)
One image/3 s	50.5±22.6	(n.s.)	2.9±1.3	($p<0.001$)	3.9±1.7	($p=0.001$)
One image/3.5 s	53.0±23.7	($p<0.001$)	3.0±1.4	(n.s.)	3.9±1.8	($p=0.001$)
One image/4 s	50.7±22.9	(n.s.)	2.9±1.3	(n.s.)	4.1±1.7	(n.s.)
One image/5 s	53.4±25.3	($p<0.001$)	2.9±1.3	(n.s.)	3.8±1.8	($p<0.001$)

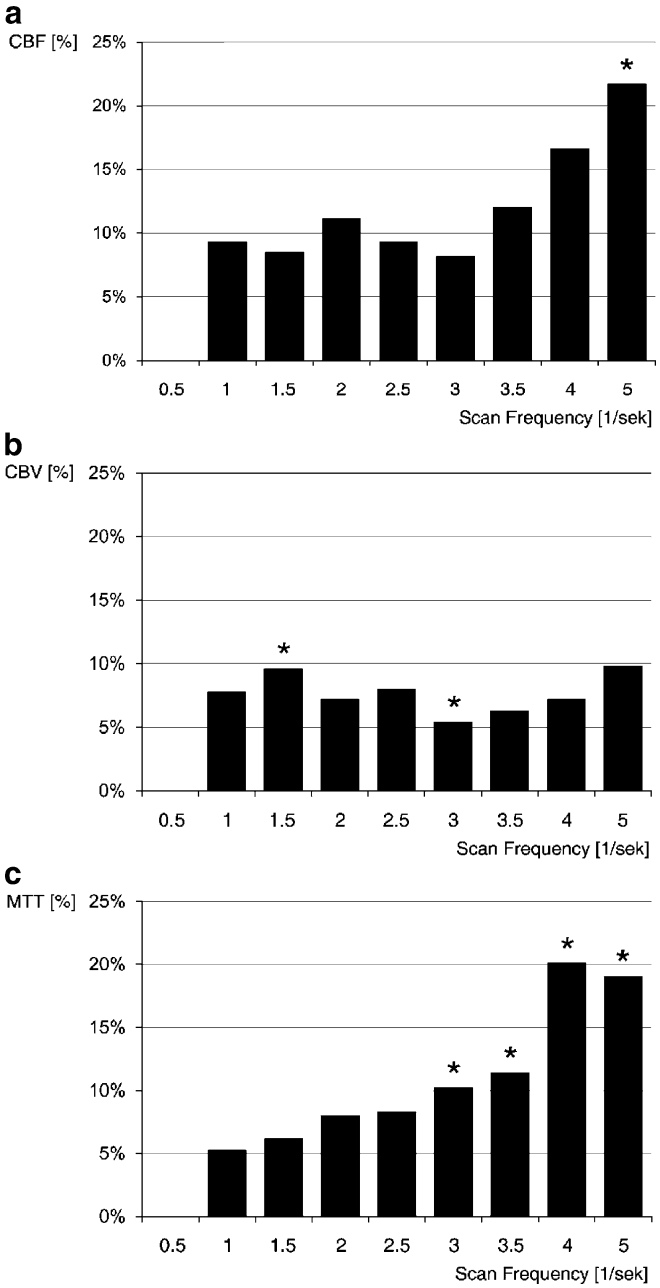

Fig. 5 **a** Influence of the temporal resolution on the precision of CBF values generated from healthy brain tissue. CBF measurements were performed in 12 ROIs per subject. ROIs were placed in both hemispheres in cortical grey matter (frontal cortex, temporal cortex, occipital cortex), white matter (frontal lobe), and basal ganglia (lentiform nucleus, thalamus). ROIs were not placed in areas of suspected abnormal perfusion. CBF values were averaged across ROIs and subjects. Measurements from the original data sets were considered as the gold standard and compared with measurements obtained from data sets with reduced temporal resolutions. To describe the compromised precision of measurements caused by reducing the temporal resolution, the absolute mean imprecision was calculated. To obtain this value, the integers of all differences between the ROI measurements of a given temporal resolution to the gold standard (i.e. minus values are converted to plus) were averaged. The absolute mean imprecision was found to be about 10% up to a temporal resolution of one image/3 s. At a temporal resolution of one image/5 s, the imprecision increased to 21.7% ($p<0.0001$). **b** Influence of the temporal resolution on the precision of CBV values generated from healthy brain tissue. The absolute mean imprecision of CBV measurements was found to be below 10% at all temporal resolutions used. At a temporal resolution of one image/1.5 s, the imprecision amounted to 9.6% ($p=0.02$). **c** Influence of the temporal resolution on the precision of MTT values generated from healthy brain tissue. The absolute mean imprecision of MTT measurements was found to be below or about 10% up to a temporal resolution of one image/3 s. The imprecision amounted to 10.2% ($p=0.003$) at a temporal resolution of one image/3 s, 11.4% ($p<0.0001$) at one image/3.5 s, 20.1% ($p=0.001$) at one image/4 s, and 19.0% ($p<0.0001$) at one image/5 s

comparison, the study of Kämena et al. [10], using temporal resolutions with sampling intervals longer than 1 s, found a significantly poorer depiction of ischemic areas although they used similar CT parameters. The authors even recommended to keep the temporal resolution at two images per second to achieve the best detection and depiction of ischemic areas. Most probably, the divergence of findings of these two studies can be explained by the method used for calculation of perfusion parameters.

Two major mathematical approaches are used to calculate colour-coded parameter maps. Deconvolution algorithms, which are currently used, for example, by General Electric and Toshiba, generally yield quantitatively more accurate results at low injection rates. On the other hand, calculation takes longer and an arterial input function has to be determined. The maximum-slope model, which is currently used, for example, by Siemens and Vitrea, is easier to calculate and less prone to motion artefacts, but is also considered mathematically less precise. Both approaches have been shown to yield reliable results in the clinical setting of acute stroke [2, 12] but differ considerably in their demand on temporal resolution. For maximum-slope models, the depiction of the point of maximum steepness of the upslope of time-density curves is critical. As indicated by our own data (not published), reducing the temporal resolution often leads to missing the point of maximum steepness. This will, for example, result in a significant reduction of calculated CBF values. Reducing the temporal resolution can, therefore, not be recommended for PCT systems using maximum-slope models.

Deconvolution algorithms may generally be expected to be more robust at reduced temporal resolutions. But although the various mathematical approaches proposed for deconvolution of PCT data are all based on the central volume principle, they differ considerably in the numerous steps involved; e.g. in correcting for motion and reducing noise, the fitting to obtain mathematic descriptions of the time-density curves, and the method of deconvolution. It is, therefore, well conceivable that some deconvolution algorithms are more sensitive for reduced temporal resolutions than others. This may explain the difference

between the findings of this study and the reports of Wintermark et al. [9] and Kämena et al. [10].

Possible limitations of our study include the fact that the intrinsic MTT of brain tissue has an influence on the appropriate sampling rate. The shorter the MTT, the higher the sampling rate needs to be. Therefore, our results need to be confirmed by quantitative analyses of infarcted tissue. This will be the subject of further studies recruiting a larger number of patients. However, in our study all infarcts were seen up to a sampling rate of 4 s, and in infarcted tissue the MTT may even be expected to be increased instead of shortened.

It should also be noted that we have performed sampling of perfusion data over an observation time of 30 s. This was sufficient in our group of patients. However, it may be worth considering to increase the observation time to 40 s, for instance, for two reasons. (1) It has been reported that in patients with severe cardiac insufficiency the passage of the contrast bolus may sometimes be severely delayed. (2) In ischaemic regions, the MTT may be considerably increased. Therefore, in some cases the time-density curve in ischaemic regions may not yet have returned to baseline after 30 s. Although regions with abnormal perfusion will still be discernible on the parameter images, the precision of CBV, CBV, and MTT values may then be reduced.

Decreasing the temporal resolution in PCT to 2 s, for instance, can be done in two different ways. The data can either be sampled over a 2-s interval (e.g. shuttle mode) or over 0.5 s with a subsequent 1.5-s wait period. This may influence the results in two ways. (1) Reducing the rotation time to 500 ms, as done in this study, slightly reduces the number of projections of which the images are calculated. This means that the synthesized data sets we used have a lower signal-to-noise ratio than data sets that may be obtained from protocols using rotation times of, for example, 1, 2, or 3 s. Therefore, our calculations are conservative and we are confident that the conclusions we have drawn will also be valid for protocols with longer rotation times. (2) Long rotation times lead to a significant amount of temporal averaging. This means that the peak of the time-density curves may be attenuated. On the other hand, if the data are sub-sampled in 0.5 s, for instance, followed by a wait period, the peak may be missed if it occurs during the wait period. This requires a highly effective fitting algorithm to obtain correct mathematic descriptions of the time-density curves.

It has been demonstrated that PCT can be performed with a cerebral effective dose as low as 1.2 mSv, which is inferior to the reference dose level for a standard cerebral CT examination (2.5 mSv), if optimised parameters are used and only two slices of 10-mm thickness are obtained [13]. On the contrary, significant side effects of radiation exposure have been described after PCT when parameters were not optimised for radiation dose and repetitive measurements were obtained [14].

One major disadvantage of PCT, compared with other methods of perfusion measurement, is that dynamic PCT does not yet allow complete coverage of the brain. Typically, sections between 8 and 40 mm are studied. If necessary, additional PCT measurements can be performed, although this increases the radiation dose of the patient. However, in the future 256-row multi-slice CT systems may allow complete coverage of the brain. This would only aggravate the need to limit the associated radiation dose.

We, therefore, believe that our findings are of significance. In our clinical setting, decreasing the temporal resolution from two images/s to one image every 3 s, as indicated by the results of our study, reduces the radiation dose of the patient by 83%. It should be considered, however, that the feasibility of this approach depends on the PCT post-processing software.

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