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### CT perfusion for acute ischemic stroke: Vendor-specific summary maps, motion correction and application of time invariant CTA

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## **Chapter 3**

### **Head Movement**

### **during CT Brain Perfusion Acquisition of Patients with Suspected Acute Ischemic Stroke**

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## Abstract

**Objective:** Computed Tomography Perfusion (CTP) is a promising tool to support treatment decision for acute ischemic stroke patients. However, head movement during acquisition may limit its applicability. Information of the extent of head motion is currently lacking. Our purpose is to qualitatively and quantitatively assess the extent of head movement during acquisition.

**Methods:** From 103 consecutive patients admitted with suspicion of acute ischemic stroke, head movement in 220 CTP datasets was qualitatively categorized by experts as none, minimal, moderate, or severe. The movement was quantified using 3D registration of CTP volume data with non-contrast CT of the same patient; yielding 6 movement parameters for each time frame. The movement categorization was correlated with National Institutes of Health Stroke Scale (NIHSS) score and baseline characteristic using multinomial logistic regression and student's t-test respectively.

**Results:** Moderate and severe head movement occurred in almost 25% (25/103) of all patients with acute ischemic stroke. The registration technique quantified head movement with mean rotation angle up to  $3.6^{\circ}$  and  $14^{\circ}$ , and mean translation up to 9.1 mm and 22.6 mm for datasets classified as moderate and severe respectively. The rotation was predominantly in the axial plane (yaw) and the main translation was in the scan direction. There was no statistically significant association between movement classification and NIHSS score and baseline characteristics.

**Conclusions:** Moderate or severe head movement during CTP acquisition of acute stroke patients is quite common. The presented registration technique can be used to automatically quantify the movement during acquisition, which can assist identification of CTP datasets with excessive head movement.

**Keywords:** *Computed Tomography, Perfusion, Head Movements, Stroke*

## Introduction

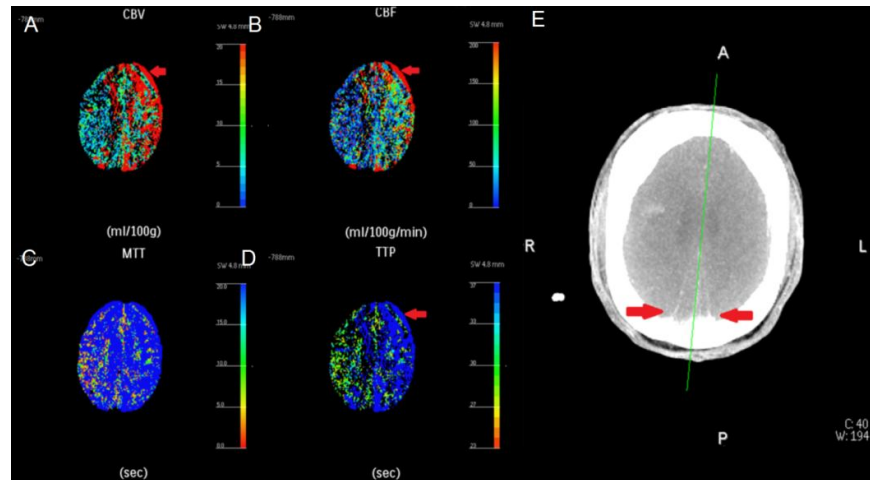
Stroke is the 3<sup>rd</sup> most common cause of death and ranks second after ischemic heart disease as a cause of lost disability-adjusted life-years in the western world<sup>1, 2</sup>. CT Brain Perfusion imaging (CTP) is a promising diagnostic tool for initial evaluation of acute ischemic stroke patients<sup>3-5</sup> and has been validated in some previous study<sup>6-9</sup>. With CTP analysis, areas with brain perfusion defects can be detected after the onset of clinical symptoms, which allows the differentiation between the irreversibly damaged infarct core and the potentially reversibly damaged infarct penumbra<sup>10, 11</sup>. This information is important in choosing the most suitable therapy<sup>12</sup>.

During CTP acquisition, CTP source images are acquired every 1 to 3 seconds for approximately 1 minute. Time-attenuation curves of individual voxels in these images are used to estimate local perfusion parameters such as cerebral blood volume, cerebral blood flow, and mean transit time. Using pre-defined thresholds and contra-lateral comparison, these maps are combined to create a summary map estimating the volume of infarct core and penumbra<sup>3, 13</sup>. In the analysis, it is assumed that a certain position in the CTP source images is associated with a single anatomical position in each time frame. In clinical practice, this assumption may not hold due to the patient's head movement during the image acquisition.

Several approaches for reduction of head movement during image acquisition have been proposed. The most straight-forward method is to use a head restraint. Acceptable methods for use in human studies are foam headrest, molded plastic masks, tapes, orthopedic collars and straps, and vacuum-lock bags<sup>14, 15</sup>. However, such methods are not able to eliminate movement entirely. The more restrictive methods may be uncomfortable, reducing their acceptability by patients and potentially even giving rise to further movement to relieve discomfort<sup>16</sup>. From Positron Emission Tomography (PET) studies it is known that even with headrests sudden or gradual head movements are frequently observed during image acquisition<sup>14, 17</sup>.

Head movement during CTP image acquisition has been recognized as a source of inaccuracy in cerebral blood flow measurements<sup>15, 18</sup>. CTP analysis software packages are usually capable of correcting for small head movements, but in our experience this correction is often not sufficient. Figure 1 shows an example of the impact of head movement on the perfusion parameters generated from a CTP dataset, where the time-

Minimum Intensity Projection (t-MIP) image shows a double falx cerebri and perfusion maps show a frontal left shadow with high Cerebral Blood Volume (CBV) and Cerebral Blood Flow (CBF) values. In current practice, time frames within a CTP dataset with excessive movement are commonly considered unusable and are excluded from analysis. This results in a reduction of information and an increase of uncertainties in the perfusion parameter estimation. The decision to remove these time frames is currently based on subjective interpretation of radiologists or technicians.



**Figure 1.** Examples of a perfusion map disturbed by head movement CBF (a), CBV (b), MTT (c), TTP (d), and Summary Map (e).

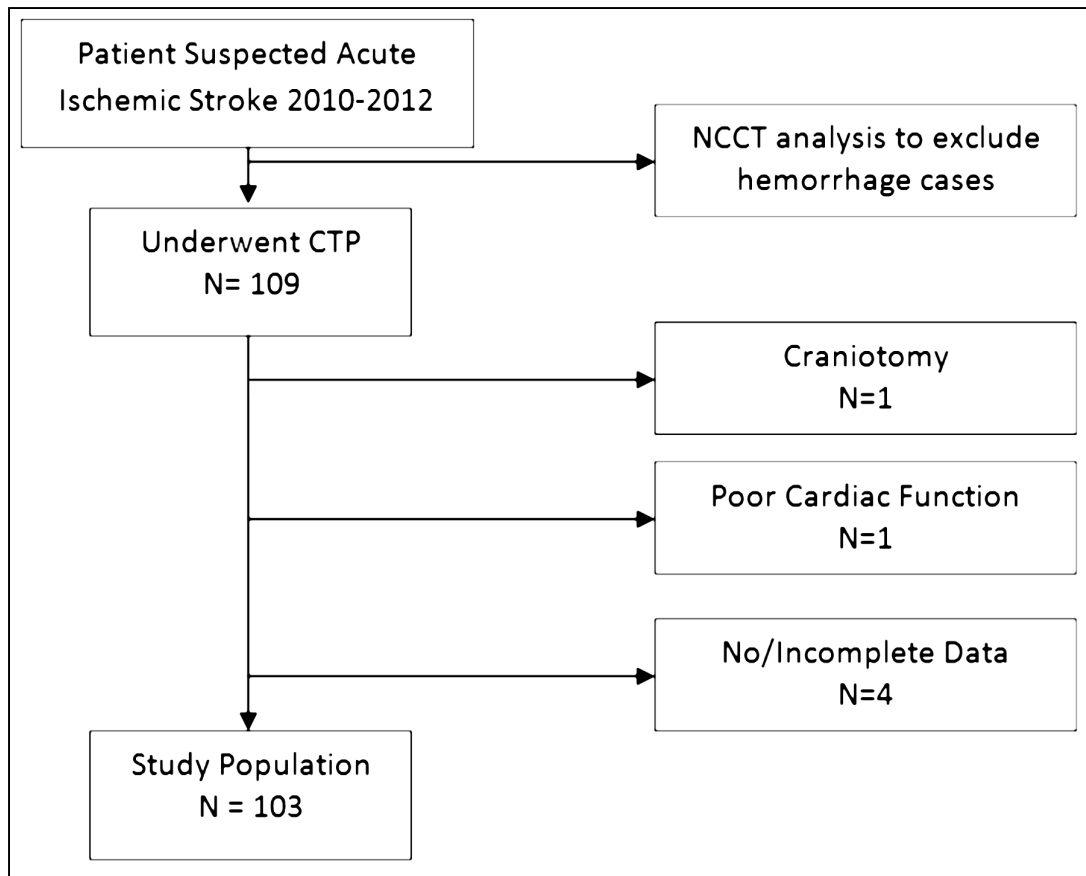
Up to now, head movement has not yet been studied quantitatively. The goal of this study is to analyze and quantify the extent, frequency and severity of head movement during CTP acquisition in a population of patients suspected of acute ischemic stroke. Furthermore, we studied the relation between the severity of head movement with the neurological condition of patients at admission, as expressed by the National Institute of Health Stroke Scale (NIHSS) score and with the baseline characteristics: age and gender.

## Materials and Methods

### Patient population

We retrospectively included all patients admitted to our medical center between January 2010 and February 2012, who were suspected of acute ischemic stroke and underwent CTP. Non-contrast CT (ncCT) was performed on all patients suspected of ischemic stroke. If intracranial hemorrhage was ruled out, CTP was performed. Exclusion criteria for this study

were: patients with previous craniotomy and patients with poor cardiac function. A flow diagram to sum up patient population is shown in figure 2. The NIHSS score of the patients was retrieved from our neurology stroke database. Permission of the medical ethics committee was given for this retrospective analysis of anonymous patient data. Informed consent was waived because no diagnostic tests other than routine clinical imaging were used in this study.



*Figure 2. Flow chart of the study population*

### **CT data acquisition**

All CT image acquisitions were performed on a sliding gantry 64 slice Siemens scanner (Somatom Sensation 64, Siemens Medical Systems, Erlangen Germany) in the emergency room. The ncCT scan of the brain was acquired at admission using 120 kV and 300-375 mAs, slice thickness was 5mm. In case head movement occurred during ncCT scanning, this CT was repeated. For each series of CTP acquisition, 40 ml iopromide (Ultravist 320; Bayer HealthCare Pharmaceuticals, Pine Brook, New Jersey) was infused at 4 ml/s using an 18

gauge canula in the right antecubital vein followed by 40 ml NaCl 0.9% bolus. Acquisition and reconstruction parameters were: 80 kV tube voltage, 150 mAs, collimation 24x1.2 mm, FOV 300 mm, reconstructed slice width of 4.8 mm. Each volume consisted of 6 slices with total coverage up to 3 cm in the -z direction. In two series, images were acquired for the duration of 50 sec at 2 sec intervals, first at the level of the third ventricle and second after approximately 3 minutes at the level of the roof of the lateral ventricles, each resulting in 25 time frame CTP volumes.

During acquisition, a standard foam headrest was used to provide patient with comfortable position and to minimize the head movement. For some patients, a follow-up CTP was taken within 2-3 days after the baseline CTP study if it is considered necessary.

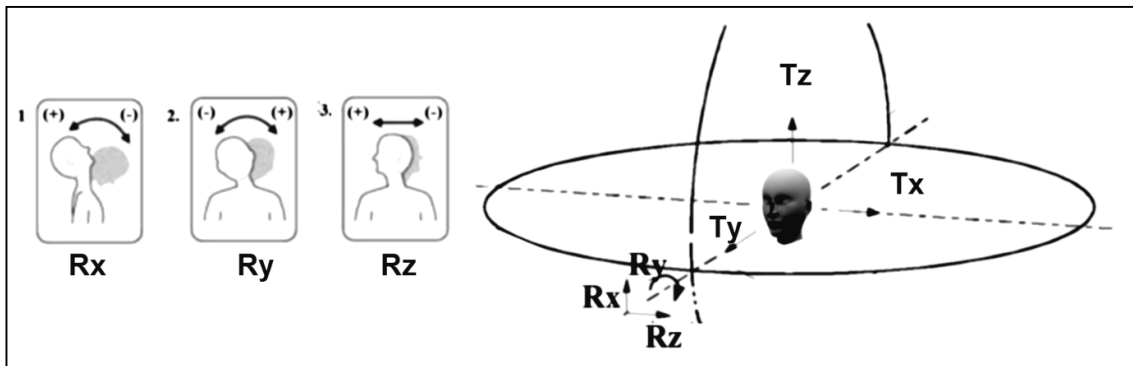
### **Qualitative Score**

A consensus reading was conducted by two experienced radiologists (LB and CM), both with more than 10 years experiences, to qualitatively grade the severity of the patient's head movement in all CTP datasets in one of 4 categories. Group 0 (no movement) was considered to be free from head movement; group 1 (minimal movement) contained CTP datasets with only slight movements that, as judged by the observers, could be corrected by the image registration available in CTP software packages. Group 2 (moderate movement) consisted of CTP datasets with head movement and were considered too large to be corrected by the registration available in the CTP analysis software. Group 3 (severe movement) consisted of CTP datasets with severe movement that was expected to affect the CTP analysis in a major part of the brain. The categorization was presented for every CTP dataset as well as for every patient in separate analysis. The patient was categorized according to its most severe CTP dataset.

### **Head Movement Quantification**

For all CTP datasets, the range and direction of head movement were quantified by 3D registration of every time frame within the CTP data set with the ncCT admission image data of the same patient. An ncCT scan is always performed for patients suspected of stroke<sup>19, 20</sup>. Therefore, no additional scan was required for the movement quantification. The ncCT is scanned in a much shorter time period than the CTP acquisition. Therefore no, or only minimal, head movement is expected during the ncCT acquisition. It covers a larger volume

than the CTP, thus it is suitable as a target for registration. The registration was performed using Elastix<sup>21</sup> with the normalized correlation coefficient as a similarity measure and gradient descent algorithm to solve the optimization problem. The rigid registration was described with 6 motion parameters: three angles of rotations: pitch (Rx), roll (Ry), and yaw (Rz); and three spatial translations in the x- (Tx), y- (Ty) and z-direction (Tz) (Figure 3). The extent of movement was determined for each time frame separately, providing 25x6 temporal motion parameter values for each CTP data set, comparing to first time frame as a reference. The range of each motion parameter was defined as the largest value subtracted by the smallest value for the whole CTP acquisition. The speed of head movement during acquisition was estimated as the difference in motion parameters in consecutive time steps divided by the time between the 2 acquisitions (2 seconds).



**Figure 3.** Different types of head rotation

From PET studies it is known that head movement occurs more frequently as scanning time progresses<sup>15</sup>. To study whether such an effect is also present in the CTP acquisitions, the average motion parameters for all patient data sets as a function of time were determined.

Since it is expected that CTP analyses are accurate for all CTP datasets in category 0 and 1 (no or minimal head movement), the quantitative analysis was only performed for data sets in category 2 and 3 (moderate or severe head movement).



## Statistical Analysis

Means and SD of the range of the motion parameters and velocity were calculated for the two categories. The relationship between head movement and the NIHSS score was studied using a multinomial logistic regression. The significance test with the final model chi-square and the Wald test was our statistical evidence of the overall relationship between NIHSS score and movement categorization, as well as to evaluate whether or not the NIHSS score is statistically significant in differentiating between patient groups of movement. Student's unpaired t-test was used to compare patients' baseline characteristic (age and gender) between groups of head movement.

## Results

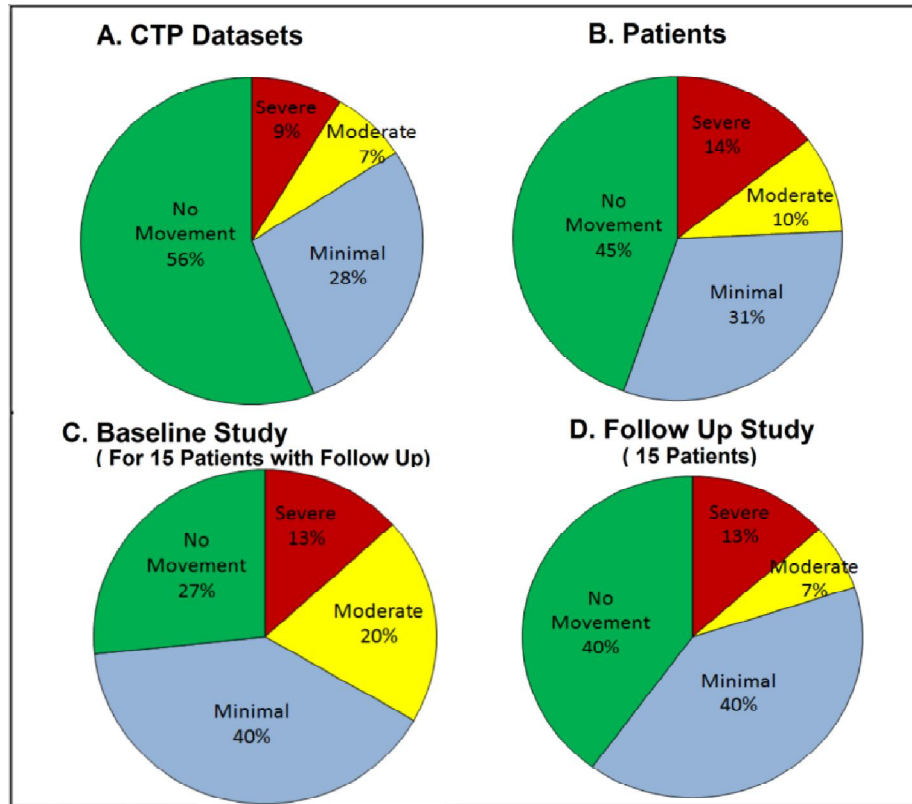
A total of 220 CTP datasets of 103 patients were included. For most patients (89/103), the CTP study consisted of two CTP series at two brain levels. For 14 patients, CTP data were only available for one series at a single level. We also included 15 follow-up CTP study available (13 patients with two series, 2 patients with only one). Sixty-five patients (62.5%) were male. The average age was 62 years, ranging from 19 to 90 years. Detail of patient's characteristic is listed in Table 1.

**Table 1.** Patient Baseline Characteristics

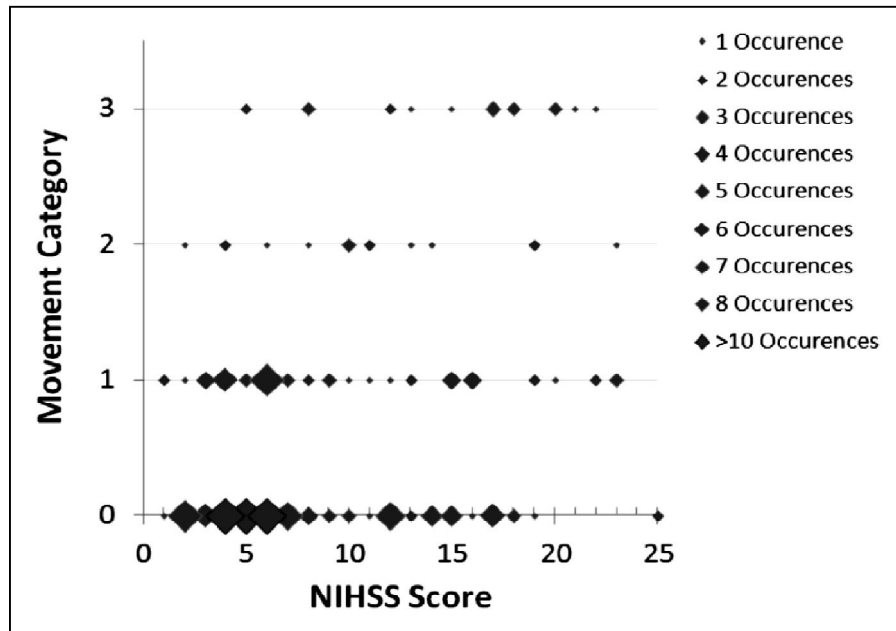
	All	Movement 0-1	Movement 2-3
ΣPatients	103	78 (76%)	25 (24%)
Female (%)	38 (37%)	28 (36%)	10 (40%)
Age (years)	62±16	61±15	64±15
NIHSS	10.7±7.42	10.2±7.63	13.1±5.91

Thirty-five out of 220 CTP datasets (16%) were categorized as moderate or severe head movement (groups 2 and 3) (Figure 4). Twenty-five patients of 103 (24%) had at least one CTP dataset with moderate or severe movement with 15 of 103 patients (14%) having severe movement during CTP acquisition.

Head movement occurred in both baseline and follow-up CTP study: from the 15 patients, 33% of baseline study and 20% of follow up study was classified as having moderate or severe movement (Figure 4).



**Figure 4** Pie charts proportions of movement severity classifications for all datasets (a) and all patients (b). The lower pie charts show the movement classification of patients with follow-up CTP for admission CTP, baseline (c) and the follow-up study (d).



*Figure 5. Movement categorization plotted against the NIHSS scores.*

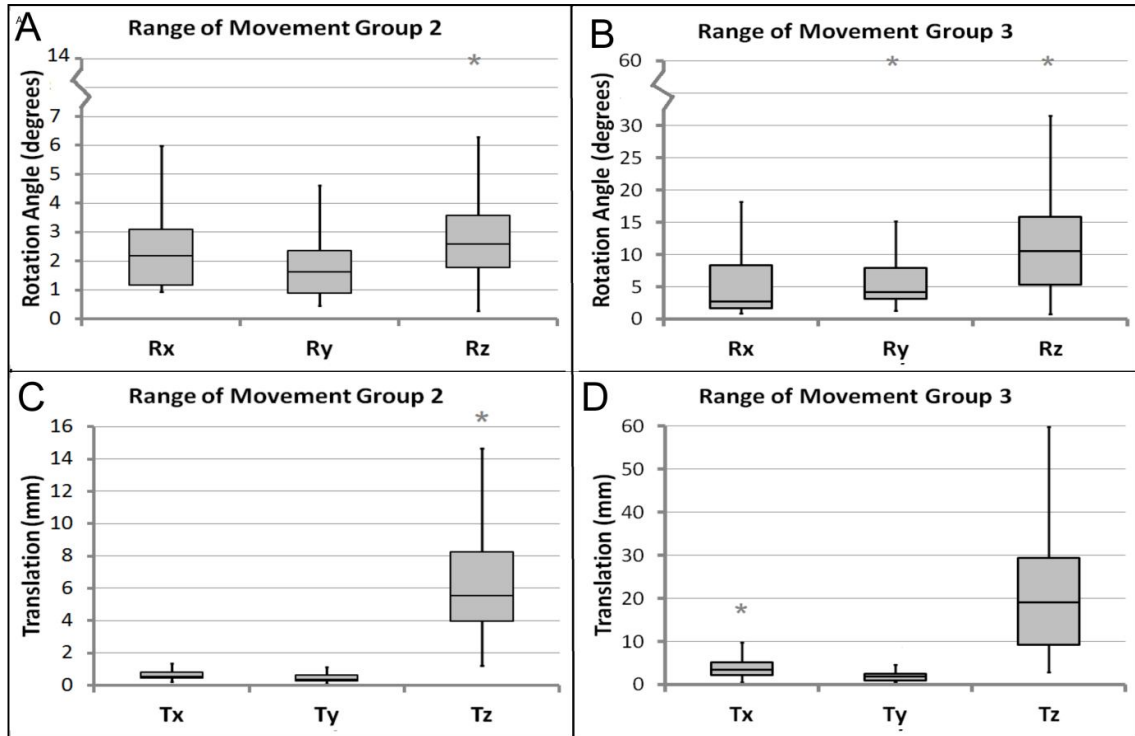
In Figure 5, the movement classification is plotted against the NIHSS scores. This figure shows that the head movement was almost equal for all NIHSS scores. In the multinomial logistic regression analysis, the probability of the model chi-square (2.5) was 0.47 ( $P > 0.05$ ), indicating that there was overall no relationship between NIHSS score and movement categorization. In the comparison to group 3 (severe movement), the probability of the Wald statistic for group 0, 1, and 2 was (0.96) 0.43, (0.93) 0.15, and (0.93) 0.24 respectively (all  $P$ -values  $> 0.05$ ), resulting in a statistically not significant difference of NIHSS score between each groups compared to group 3.

There was no statistically significant difference in age and gender in between the groups. The average age was  $61 \pm 15$  year for patients in groups 0 and 1 and  $63 \pm 15$  year for groups 2 and 3 ( $P = 0.5$ ). Within groups with moderate and severe head movement, the ratio between male and female was equally distributed, 60% and 40% respectively, and for the group with none and minimal movement the ratio was 64% and 36% respectively ( $P = 0.4$ ).

### **Quantitative result**

The range of motion parameters for all CTP series classified as moderate and severe movement is summarized in Table 2 and Figure 6. As expected, the quantitative assessment reveals larger rotational and translational movement for data sets categorized in group 3

than in group 2. The mean value of the rotation angles in group 2 was  $2.3^{\circ}$ ,  $2.0^{\circ}$  and  $3.6^{\circ}$  for roll, pitch and yaw respectively. For group 3, mean value of the rotation angles were  $5.7^{\circ}$ ,  $8.3^{\circ}$  and  $14^{\circ}$  for roll, pitch and yaw respectively. The mean speed of rotation ranged from  $0.04^{\circ}/s$  to  $0.8^{\circ}/s$  in group 2 and from  $2.17^{\circ}/s$  to  $5.46^{\circ}/s$  in group 3 (Table 3). In both groups, the largest rotation was in-plane (yaw).



**Figure 6** Range of head movement (a) and speed of head movement (b), group 2 (left) and group 3 (right). Note the different y-axis ranges for group 2 and 3. (\*) express the highest outlier value.

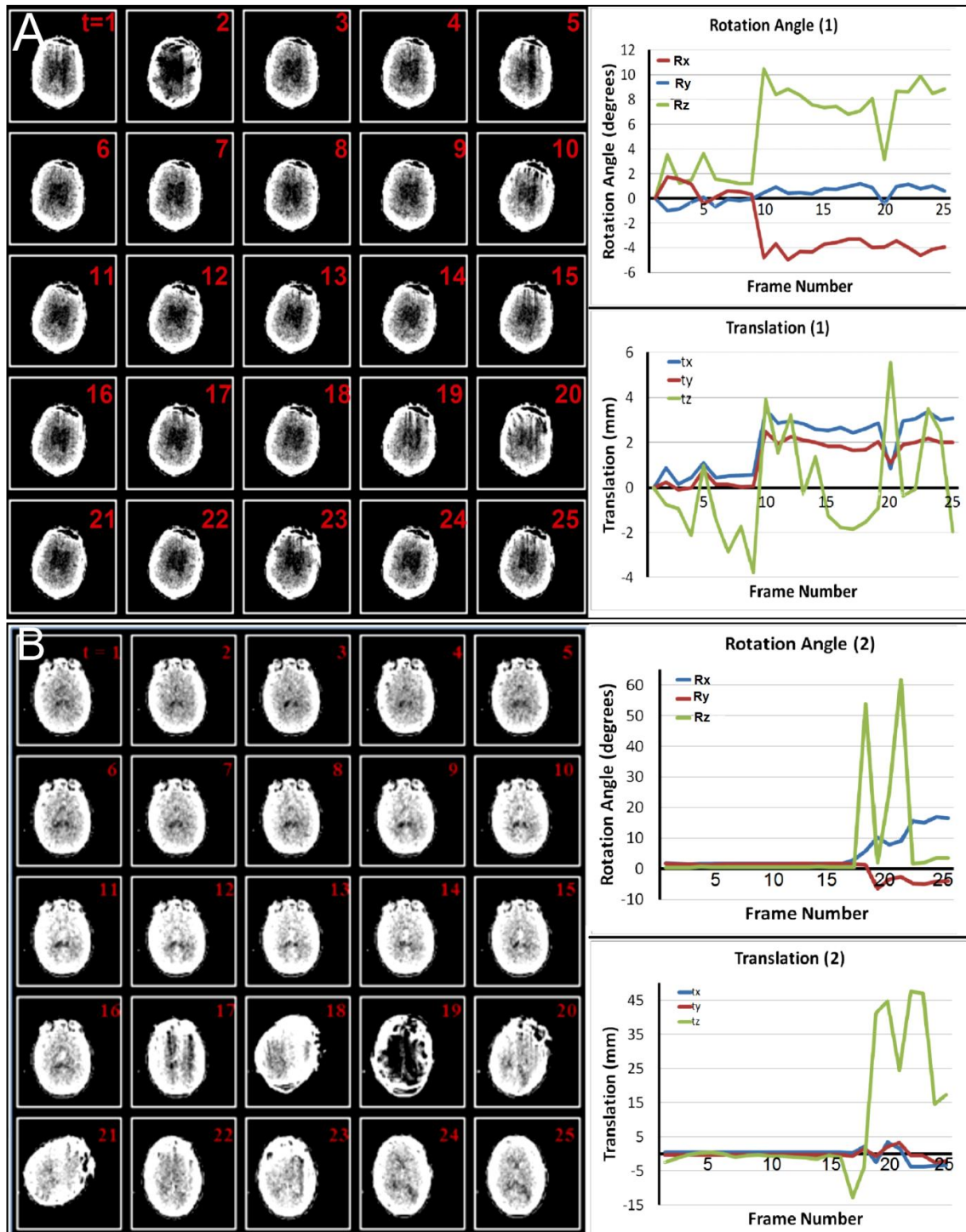
**Table 2.** Range of head movement parameters.  $R_x$ ,  $R_y$ , and  $R_z$  are the rotation angles around the x-, y-, and z-axis.  $T_x$ ,  $T_y$ , and  $T_z$  are the translation in x-, y-, and z- direction.

	Group 2 (28 CTP series)						Group 3 (27 CTP series)					
	Rotation (degree)			Translation (mm)			Rotation (degree)			Translation (mm)		
	$R_x$	$R_y$	$R_z$	$T_x$	$T_y$	$T_z$	$R_x$	$R_y$	$R_z$	$T_x$	$T_y$	$T_z$
Max	5.56	5.55	14.4	2.07	3.35	19.8	18.8	62.9	61.3	15.6	5.56	69.3
Mean	2.30	1.97	3.55	0.96	0.90	9.08	5.62	8.25	14.0	4.11	2.05	22.6
$\pm$ SD	$\pm 1.35$	$\pm 1.51$	$\pm 3.54$	$\pm 0.48$	$\pm 0.87$	$\pm 5.85$	$\pm 5.70$	$\pm 13.7$	$\pm 14.5$	$\pm 3.33$	$\pm 1.38$	$\pm 18.0$

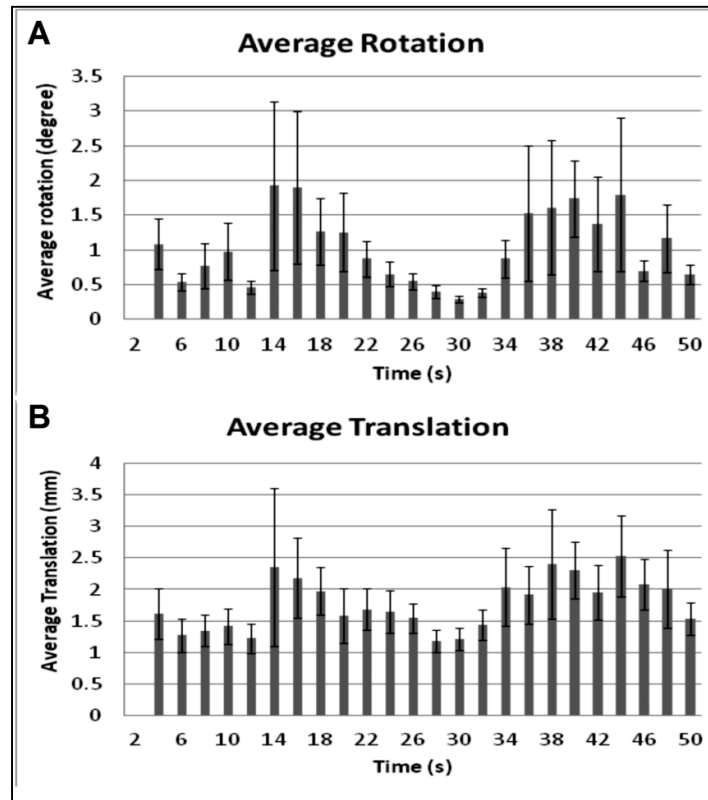
**Table 3.** Speed of head movement parameters.  $R_x$ ,  $R_y$ , and  $R_z$  are the rotation angles around the x-, y-, and z-axis.  $T_x$ ,  $T_y$ , and  $T_z$  are the translation in x-, y-, and z- direction.

	Group 2 (28 CTP series)						Group 3 (27 CTP series)					
	Rotation (degree/s)			Translation (mm/s)			Rotation (degree/s)			Translation (mm/s)		
	$R_x$	$R_y$	$R_z$	$T_x$	$T_y$	$T_z$	$R_x$	$R_y$	$R_z$	$T_x$	$T_y$	$T_z$
Max	1.49	1.79	3.13	0.50	0.82	5.79	9.26	31.5	29.9	5.88	1.89	34.6
Mean	0.43	0.42	0.83	0.21	0.18	1.74	2.17	3.49	5.46	1.55	0.78	8.01
$\pm$ SD	$\pm$ 0.48	$\pm$ 0.52	$\pm$ 0.89	$\pm$ 0.18	$\pm$ 0.25	$\pm$ 1.76	$\pm$ 2.62	$\pm$ 6.92	$\pm$ 6.67	$\pm$ 1.38	$\pm$ 0.58	$\pm$ 8.28

Figure 7 shows two examples presenting the dynamic behavior of motion parameters for each time- frame. Figure 7a is an example of data set classified as group 2 (moderate) and figure 7b classified as group 3 (severe). In Figure 8, the average movement as a function of time is shown for all data sets of the group 2 and 3 categories. This figure shows a slight increase around 1/4 and 3/4 of the scanning time period. Nevertheless, head movement seems to occur during the whole period of acquisition.



**Figure 7.** Example of CTP image data of group 2 (a) and group 3 (b). Graphs on the right shows related motion parameters. Rotation angle and translation parameters are presented for  $-x$  axis (blue line),  $-y$  axis (red line) and  $-z$  axis (green line) for each time step.



**Figure 8.** The average value (mean with standard error) of rotation angles (a) and translations (b) presented for all CTP datasets as a function of acquisition time.

## Discussion

In this study we have shown that in patients with acute ischemic stroke, moderate and severe head movement during CTP acquisition is rather common. In our population of 103 patients who presented with a suspicion of ischemic stroke, 24% had at least one CTP dataset showing moderate to severe head movement. Since CTP analysis assumes that a specific location in each time frame is associated with a single anatomical position, movement of the head alters time-attenuation curves and as such CTP analysis results.

In general, rotation was more severe within the axial plane (yaw/Rz), and translation occurred predominantly in the longitudinal z-direction (Tz, scan direction). The quantitative movement assessment showed larger values for all motion parameters for CTP datasets that were qualitatively categorized as severe (group 3), than for the CTP datasets that were categorized as moderate (group 2).

We presented a method to quantify head movement during CTP acquisition based on a 3D registration technique utilizing the ncCT data. To our knowledge, this is the first

study that quantifies head movement during CTP acquisition using available image data only. This method allows an objective detection of movement that may exceed specific thresholds and that should therefore be excluded from the CTP analysis.

Using the quantification of head movement during CTP acquisition, we were also able to estimate the speed of head movement by calculating the difference of motion parameters between time steps. Previous studies on general axial CT scanning emphasized that the velocity of motion rather than the range of the movement is crucial<sup>22</sup>, even though the study investigated single-frame image quality and related parameters such as blurring, rather than dynamic sequences. Estimating the speed of movement during acquisition will give additional information in predicting flaws in CTP datasets.

Since CTP analysis is based upon the interpretation of time-intensity curves, it can be expected that head movement occurring early during the acquisition influences the analysis differently from movement late during the acquisition. We did not observe a strong dependence of head movement on the time point in the enhancement curve: movement was observed in all time frames. This observation is in contrast to PET studies, in which more movement was observed at the end of the acquisition<sup>23</sup>. However, we need to emphasize that the duration of a CTP acquisition is much shorter than PET acquisition.

From a limited number of follow-up CTP study (15 datasets), there was no difference regarding occurrences of head movement in follow-up compared to base line acquisitions, indicating that this problem may arise also in a more stable condition of patients.

We found no statistically significant correlation between the NIHSS score and the movement categories. With increasing NIHSS, we observed a small increase in probability of movement during scanning. However, the odd-ratios were close to 1 indicating that that the difference is small and clinically insignificant. As such this study suggests that the NIHSS score cannot be used as a predictor for head movement during CTP acquisition. It was also shown that there was no significant difference in distribution of age and gender between groups with and without head movement.

In our experience, the current registration techniques available in CTP analysis software are in many cases not sufficient to correct patient's head movement. The proposed quantification method allows identification of datasets with excessive movement which unsuitable for accurate CTP analysis and therefore should be excluded. This technique provides also a base for a more advanced registration to correct this head movement. We



suggest the correction of movement of should be performed by the 3D registration of CTP dataset with ncCT data to improve the reliability of core and penumbra estimations in CTP analysis.

Our study has some limitations. First, we could not quantitatively assess the accuracy of the registration technique. The Elastix software had been used in variety application using different modality like MR, CT and Ultrasound. Several publications provided accuracy measurement of Elastix and it is increasingly used as benchmark<sup>21, 24, 25</sup>. In our study, visual assessment of the registration showed a good correspondence of the ncCT scans with the registered CTP source images. Second, for every patient 1 to 4 datasets were included in our population. As a result, not all datasets were independent. This was neglected in our statistical analysis. Each CTP dataset was acquired separately and therefore we treated these multiple dataset as independent data. As an addition, we included also the patient-based analysis in this study. Third, we did not evaluate the precise effects of head movement on the result of CTP analysis, although impact of head movement on perfusion maps can obviously be observed as in Figure 1. An intrinsic difficulty of such an analysis is the absence of a ground-truth reference standard. The effects of head movement on CTP analysis results should be studied further in future studies.

## **Conclusion**

We have shown that head movement during CTP acquisition is common in our population of patients with acute ischemic stroke. Motion occurs during the whole acquisition period and is independent of the neurological condition. Almost a quarter of all patients showed moderate or severe head movement during CTP acquisition and therefore the CTP dataset was considered unsuitable for accurate CTP analysis. We presented a technique to quantify head movement with a good correlation with the qualitative classification.

## **Acknowledgements**

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## Conflict of Interest Statement

All authors declare that there is no potential conflict of interest including any financial, personal or other relationships with other people or organizations within three (3) years of beginning the work submitted that could inappropriately influence (bias) the work.

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