CT perfusion for acute ischemic stroke: Vendor-specific summary maps, motion correction and application of time invariant CTA
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Chapter 5

Automatic Selection of CT Perfusion Datasets

Unsuitable for CTP Analysis due to Head Movement of Acute Ischemic Stroke Patients

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ABSTRACT

CT Brain Perfusion (CTP) datasets with severe head movement can deteriorate accurate perfusion analysis on acute ischemic stroke patients. We developed an automated selection of unsuitable CTP data with excessive movement. A 3D image-registration of the dynamic CTP data with non-contrast CT data provides transformation parameters. When these parameters exceeded threshold values, the data set was rejected for perfusion analysis. Threshold values were derived using controlled CTP phantom experiments. The automatic selection was compared to manual selection of unsuitable data by 2 experienced radiologists. ROC characteristics were calculated to determine the optimal threshold. In 114 CTP datasets, the optimal threshold was 1.0°, 2.8° and 6.9° for pitch, roll and yaw limit, and 2.8mm for z-axis translation. This resulted in a sensitivity and specificity of 91.4% and 82.3%. We conclude that registration of CTP datasets allows an automated and accurate selection of CTP datasets that should be removed from perfusion analysis.

Keywords—CT Brain Perfusion, Computer Aided System, Ischemic Stroke, ROC
INTRODUCTION

CT Brain Perfusion imaging (CTP) is evolving towards a promising diagnostic tool for initial evaluation of acute ischemic stroke patients [1-4]. In CTP images, areas with brain perfusion defects can be detected after the onset of clinical symptoms and can facilitate the differentiation between the irreversibly damaged infarct core and the potentially reversibly damaged infarct penumbra [5-9], which is important in choosing the most suitable therapy [10-12].

The patient’s head movement during scanning, however, limits the applicability of CTP. Since CTP analysis assumes that a specific location in the images is associated with a single anatomical position [13, 14], it is likely that head movement deteriorates CTP analysis results, as shown in an example in Figure 1. While it is indeed well recognized that head movement is a common problem during CTP acquisition of stroke patients [15-17], automated procedures for exclusion of unsuited CTP data are lacking, requiring substantial manual work by radiologists.

Figure 1. Example of summary map in CTP analysis, disturbed by head movement: the red arrows point out double falx cerebri due to moderate head movement (A); deformation of brain images due to severe head movement (B).

Thus, in clinical practice, a radiologist must first visually check the CTP datasets to conclude whether it is affected by head movement, and to decide whether the data set is suitable for accurate perfusion analysis. If the data set is approved, registration, commonly available in software analysis packages, is applied to correct for small motion. Alternatively, certain time frames of the CTP acquisition that could disturb the perfusion analysis can be
removed. The visual inspection is performed for all 25-30 time frames and is commonly conducted in 2D maximum intensity projections. Next to being time consuming, the selection of out-of-plane head movement acquisitions with this method is sometimes difficult. Furthermore, it relies on the subjective interpretation whether CTP data sets are considered suitable for analysis.

The goal of this study is to develop and validate an automatic selection for unsuitable CTP data subject to excessive head movement. To this end, we used an image registration based technique to quantify the head motion. We utilized our previous phantom study to estimate threshold values of the head motion parameters beyond which unacceptable deviations of perfusion analysis results occurred. These threshold parameters were combined with the quantified motion parameters to come to an automated selection of CTP data unsuitable for analysis.

**METHODS**

**CTP Data Acquisition**

We collected 114 CTP data set from 100 patients who were suspected of acute ischemic stroke and underwent non-contrast CT and CTP in our medical centre (AMC) during 2010-2012. 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. 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. Because the results of the evaluation of the images for the purpose of the current study were performed retrospectively, they could not influence clinical decisions.

For the 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. During acquisition, a standard foam headrest was used to provide patient with comfortable position and to minimize the head movement.
An ncCT scan is always present for patients suspected of stroke; therefore no additional scan was required [2, 18, 19]. The ncCT scan of the brain was acquired at admission using 120 kV and 300-375 mAs, with a reconstructed slice thickness of 5mm. The ncCT is scanned in a much shorter time period than the CTP acquisition. Therefore no, or only minimal, image degradation due to head movement is expected during the ncCT acquisition. In case severe head movement occurred during ncCT scanning and this was noticed by a technician, this ncCT was repeated.

**Quantification of Head Movement**

The range and direction of head movement were quantified by the 3D registration of every time frame in the CTP data set with the ncCT image data of the same patient. Because the ncCT covers a larger volume than the CTP time frames, it is suitable as target for 3D registration.

The rigid registration resulted in 6 motion parameters: three angles of rotations: pitch (Rx), roll (Ry), and yaw (Rz); and three spatial translations in the x-, y- and z-direction (Tx, Ty, and Tz) (Figure 2). The registration was performed using Elastix [20, 21], with the normalized correlation coefficient as a similarity measure and the use of the gradient descent algorithm to solve the optimization.

The extent of movement was determined for each time frame, providing 25x6 temporal motion parameter values, using the first time frame as a reference.

**Figure 2.** Head movement parameters. Rx is the rotation around the x-axis (pitch), Ry is the rotation around the y-axis (roll), and Rz is the rotation around the z-axis (yaw).
Estimation of Threshold Values with Phantom Experiment

Small movement is not expected to deteriorate the CTP analysis result. To define the threshold values for which we expect serious effects, we investigated the effect of head movement on CTP analysis result (Fahmi et al; submitted for publication, 2013) using CTP phantom data [22].

To simulate head movement, the CTP phantom data were rotated and translated using Transformix, a companion tools of Elastix [20]. Controlled translations and rotations were performed along and around each coordinate axis. The simulated rotation angles were set from -10 to +10 degrees around the z-axis (yaw), and from -5 to +5 degree around the x-axis (pitch) and y-axis (roll), with steps of one degree. The translations were set from -10 to +10 mm for all three axes.

The original and transformed CTP datasets were processed using Philips Extended Brilliance Workspace version 3.5, Brain CT Perfusion Package (Philips Healthcare, Cleveland, OH) to obtain the perfusion maps. We calculated the volume similarity and the spatial agreement between summary maps generated from the original and rotated phantom data. The agreement was expressed with the Dice Similarity Coefficient (DSC) [23, 24], expressing agreement not only for size but also location of infarct core and penumbra in between summary maps. The DSC, which value is ranging from 0 to 1, is defined as twice the volume of the intersection divided by the sum of the two volumes.

Rotation angles and translations related to given DSC values were used as thresholds. We explored DSC values ranging from 0.4 to 0.8 to obtain candidate threshold parameter sets for our automated motion detection. In our experiments we excluded the in-plane translations in x- and y-direction because the experiments showed that the CTP analysis software can correct these translations, and these translations do not have an effect on the analysis results. A set of threshold values therefore consists of roll, pitch and yaw rotation angle, and translation in z-axis.

Automated Selection

The decision to reject or accept a CTP dataset was based on the comparison of quantified motion parameters resulting from the registration with the threshold values that is associated with given DSC values resulting from the CTP phantom data experiments. If one
or more of these 4 movement parameters exceeded the threshold values, it was rejected; otherwise the CTP dataset was accepted.

**Manual Selection**
Two radiologists (CM and LFB, both with more than 10 years experiences) qualitatively graded the severity of the patient’s head movement in CTP data as “Accepted”; CTP data with no or minor head movement that could be corrected by the CTP analysis software registration, or as “Rejected”; when the CTP datasets showed severe movement that was expected to affect the CTP analysis and as such should be excluded. This manual selection of CTP data was used as ground truth for the validation of the automatic selection.

**Statistical Analysis**
We use a binomial classification test in the comparison of the automatic selection result with the manual selection to evaluate the performance of this method. True positive rate, false positive rate, true negative rate, and false negative rate were determined. Diagnostic accuracy, sensitivity and specificity of the automatic method were calculated for each set of threshold values with 95% confident interval. Furthermore, receiver-operating characteristics (ROC) for the different threshold values were calculated. The area under the ROC curve was also determined.

**RESULTS**
In total, 114 CTP datasets from 100 patients were included in the analysis. During visual inspection, the radiologists rejected 35 CTP dataset because of severe movement and accepted the remaining 79 CTP datasets.

**Motion parameters**
The mean value of the rotation angles of all CTP datasets was $1.7^0 \pm 3.0^0$, $2.1^0 \pm 6.2^0$ and $3.3^0 \pm 7.7^0$ for roll, pitch, and yaw respectively. The mean value of the translation was $2.2 \pm 4.1$ mm, $1.2 \pm 2.0$ mm and $1.6 \pm 2.2$ mm for translation in x, y and z direction. The largest rotation recorded was in-plane (yaw) movement with maximum rotation angles up to $61.3^0$. Figure 3 shows an example presenting the dynamic behavior of motion parameters profiles for each time frame during CTP acquisition.
Figure 3. Examples of the six movement parameters (rotation on the left, translations on the right) for 25 time frames as a result of the head movement quantification. This figure indicates that there is a large yaw rotation and z-translation around the 17th time frame.

Defining Threshold Values
The deterioration of CTP analysis results is illustrated by plotting DSC as a function of motion parameters. We derived 5 sets of threshold values at DSC of 0.4, 0.5, 0.6, 0.7, and 0.8 (Figure 4). This figure shows that the direction of movement is also important for the accuracy of the perfusion analysis result. For example, this figure shows that for an in plane rotation of more than 6 degrees there is only a small deviation resulting in a DSC value, whereas a pitch rotation of 1 degree has a large effect as expressed with a DSC value of 0.5.
Figure 4. DSC graph resulting from phantom study indicating the accuracy of the CTP analysis when CTP data from a moved phantom is analyzed. The red line describes the accuracy of the infarct core volume estimations, the green line for the accuracy of the infarct penumbra (adapted from Fahmi et al; submitted for publication, 2013) The yellow dots represent interpolation for given DSC values. The x-values of these dots represent the threshold values for roll (A), pitch (B) and yaw(C) rotation angle, and the translation in the z-direction (D) used in the automated selection procedure.

A list of the rotation and translation thresholds for each DSC value is listed in Table 1. The translations in the x- and y- direction are here omitted because the CTP analysis software is insensitive to in-plane movement.
Table 1. Threshold values of the motion parameters associated with DSC values derived from the phantom experiments.

<table>
<thead>
<tr>
<th>DSC value</th>
<th>Rx [deg]</th>
<th>Ry [deg]</th>
<th>Rz [deg]</th>
<th>Tz [mm]</th>
</tr>
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<tr>
<td>0.4</td>
<td>1.97</td>
<td>5.01</td>
<td>7.15</td>
<td>8.14</td>
</tr>
<tr>
<td>0.5</td>
<td>1.04</td>
<td>2.80</td>
<td>6.99</td>
<td>6.14</td>
</tr>
<tr>
<td>0.6</td>
<td>0.83</td>
<td>1.85</td>
<td>6.83</td>
<td>3.34</td>
</tr>
<tr>
<td>0.7</td>
<td>0.62</td>
<td>1.39</td>
<td>6.68</td>
<td>1.93</td>
</tr>
<tr>
<td>0.8</td>
<td>0.42</td>
<td>0.92</td>
<td>6.52</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Accuracy

For each DSC value, the automated selection was performed and compared with the manual classifications, as shown in Table 2. In this comparison the manual selection was used as ground truth. The diagnostic accuracy was calculated for 5 sets of motion thresholds associated with the DSC values presented in this table (see Table 1 for the specific motion thresholds).

The ROC curve is shown in Figure 5 with an area under curve of 0.94. The optimal threshold was for DSC value of 0.5 (predictive power 0.79) with a diagnostic accuracy of 85.1% (95%CI: 78.6%-91.6%), sensitivity of 91.4% (95%CI: 86.3%-96.5%) and a specificity of 82.3% (95%CI: 75.3%-89.3%).

Table 2. Diagnostic accuracy of the automated selection of CTP datasets for different DSC value.

<table>
<thead>
<tr>
<th>DSC value</th>
<th>TP*</th>
<th>TN†</th>
<th>FP‡</th>
<th>FN§</th>
<th>PPV§</th>
<th>NPV§</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>PP**</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4</td>
<td>24</td>
<td>76</td>
<td>3</td>
<td>11</td>
<td>89%</td>
<td>87%</td>
<td>68.6%</td>
<td>96%</td>
<td>88%</td>
<td>0.77</td>
</tr>
<tr>
<td>0.5</td>
<td>32</td>
<td>65</td>
<td>14</td>
<td>3</td>
<td>70%</td>
<td>96%</td>
<td>91.4%</td>
<td>82%</td>
<td>85%</td>
<td>0.79</td>
</tr>
<tr>
<td>0.6</td>
<td>35</td>
<td>54</td>
<td>25</td>
<td>0</td>
<td>58%</td>
<td>100%</td>
<td>100%</td>
<td>68%</td>
<td>78%</td>
<td>0.74</td>
</tr>
<tr>
<td>0.7</td>
<td>35</td>
<td>44</td>
<td>35</td>
<td>0</td>
<td>50%</td>
<td>100%</td>
<td>100%</td>
<td>56%</td>
<td>69%</td>
<td>0.67</td>
</tr>
<tr>
<td>0.8</td>
<td>35</td>
<td>28</td>
<td>51</td>
<td>0</td>
<td>41%</td>
<td>100%</td>
<td>100%</td>
<td>35%</td>
<td>55%</td>
<td>0.58</td>
</tr>
</tbody>
</table>

*TP/TN = True Positive/Negative, †FP/FN = False Positive/Negative, ‡PPV/NPV = Positive/Negative Predictive Value, **PP = Predictive Power
DISCUSSION

We presented a method for automatic selection of unsuitable CTP data sets based on the quantification of motion between the time frames. These motion parameters were compared to threshold values based on simulations of CT perfusion analysis with a CTP phantom. Performance of this automatic selection method, as evaluated by comparison with manual qualitative classification of head movement severity by radiologists, was high. To our knowledge, this is the first study that quantitatively analyzes head movement during CTP acquisition using available image data only.

Based on simulations with the digital hybrid phantom, it was shown that head movement can only be corrected by the standard CTP analysis software when the range of movement is limited. We have shown in our previous study that head movement strongly alters estimated size and position of infarct core and penumbra in the CTP analysis. The range of movement parameters for which an accurate CTP analysis result can be expected with DSC value 0.5 were 1.0° for pitch, 2.8° for roll and 6.9° for yaw; and also 2.8mm
translation in z-axis. These values were defined as threshold values to accept or reject CTP data, and might be different for other software packages. Individual phantom studies should therefore also be conducted for other software packages in order to allow adequate automatic selection of motion-affected CTP analyses.

The ROC analysis provided an optimal threshold for DSC value of 0.5. The sensitivity of the proposed method with this threshold values is high, while the specificity is somewhat lower. This characteristic is more preferable for such a computer aided system where the radiologists are expected to check the suspected CTP data. It was shown that for this DSC value, the automatic detection of suspicious data sets resulted in a rejection of more data than the selection of the radiologists. For a higher DSC value of 0.6 the sensitivity of the automated selection could be set to 100% at the cost of a specificity decrease to 68%. The threshold values used in this study could be optimized for other CTP methods and scanners. However, this was beyond the scope of this study.

This study has some limitations. First, the required computational time needed for the automatic selection is currently too large for introduction in clinical practice. Time constraint is an important issue especially for hyper acute stroke patient situation [25-27]. The main time consuming process of this study was the simulation of CTP phantom data in order to derive the threshold values for the motion parameters. Once the threshold values defined, it requires only single rigid registrations of a CTP dataset with ncCT image. This process could be computationally fast with adequate computer resources. Another limitation of this study is that the used motion threshold values were derived from CTP phantom instead of using large clinical patient data. A difficulty of such the latter analysis is the absence of a ground truth for the CTP analysis result, which is important in deriving the threshold values. The use of CTP phantom data for this purpose is the more suitable. Head movement parameters measured in this study consider only motion between time frames and ignore the motion occurred during the acquisition of a single time frame. Therefore, only deterioration due to this kind of movement that can be minimized with automatic selection of CTP dataset, and artifacts due to motion during acquisition of single frame was beyond the scope of this study.

The presented method has the potential to be integrated in clinical practice such that any movement during CTP acquisition will be automatically detected allowing radiologists to remove suspicious image data from the CTP analysis.
CONCLUSIONS

We presented a method that automatically selects CTP datasets that are subject to excessive head movement. The accuracy of the method was 85.1% with a high sensitivity (91.4%) and good specificity (82.3%). It supports the accuracy of CTP analysis and assures that clinical decision is not based upon faulty image data due to excessive head movement.

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CONFLICT OF INTEREST

- Mr. Fahmi reports other grant from DIKTI Scholarship, Ministry of National Education, Government of Republic of Indonesia, outside the submitted work.
- Dr. Marquering has nothing to disclose.
- Dr. Streekstra has nothing to disclose.
- Dr. Beenen has nothing to disclose.
- Ms. Janssen has nothing to disclose.
- Prof. Dr. Majoie has nothing to disclose.
- Prof. Dr. van Bavel has nothing to disclose.

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

REFERENCES


