Thin-Slice Reconstructions of Nonenhanced CT Images Allow for Detection of Thrombus in Acute CT Stroke

Christian H. Riedel, MD; Julia Zoubie, MD; Stephan Ulmer, MD; Janne Gierthmuehlen, MD; Olav Jansen, MD

Background and Purpose—The purpose of this study was to investigate whether thin-slice image reconstructions of cranial nonenhanced CT scans could be used to significantly increase sensitivity for detecting intraluminal thrombus in patients with acute ischemic stroke due to proximal occlusion of the middle cerebral artery.

Methods—In a prospective case series, the raw data of nonenhanced CT scans from 54 patients presenting with acute ischemic stroke and proven vascular obliteration of the middle cerebral artery were collected along with the same data from patients not having a stroke but the same sex and age. All raw data were reconstructed with a slice thickness of 5 mm and as thin slices with a thickness of 0.625 mm. Three observers independently evaluated the 5-mm nonenhanced CT reconstructions and 5-mm maximum intensity projections of the thin slices and rated the likelihood of a clot obliterating the middle cerebral artery trunk or first-order branches using a 5-point scale. The results were evaluated in comparison with base data using receiver operating curve analysis. Interobserver agreement was measured using Cohen $\kappa$ for every pair of observers.

Results—The area under the curve for the receiver operating curve analysis for the thick slices ranged from 0.63 to 0.67, whereas for the maximum intensity projection images of the thin slice reconstructions, receiver operating curve analysis revealed areas under the curve between 0.94 and 0.97. Interobserver agreement was higher for thin-slice ($\kappa$, 0.69–0.83) versus thick-slice nonenhanced CT reconstructions ($\kappa$, 0.38–0.45).

Conclusions—Thin-slice reconstructions of standard cranial nonenhanced CT raw data allow for more sensitive and reliable detection of clots occluding the proximal middle cerebral artery. (Stroke. 2012;43:00–00.)

Key Words: clot imaging CT embolic stroke neuroradiology stroke management

In acute ischemic strokes, nonenhanced CT (NECT) is used to exclude cerebral hemorrhage and early signs of extensive brain infarction before a patient is treated with intravenous thrombolysis.1–5 Because intravenous thrombolysis often fails to recanalize vessels occluded by large clots1 and mechanical thrombectomy devices are increasingly applied in these cases, imaging of the position and size of clots is helpful in choosing the best therapy.6,7 We therefore investigated if NECT raw data can be reconstructed in a way that allows for a more sensitive detection of thrombus in patients with acute cerebral artery occlusion.

Thrombotic occlusion of the middle cerebral artery (MCA) can be detected with high specificity by the well-known hyperdense middle cerebral artery sign (HMCAS).8–11 Unfortunately, several studies report only a low sensitivity for detecting an HMCAS in cases of proven MCA occlusion with detection rates ranging between 26% and 47%.10–12 This low sensitivity can either be explained by different consistencies of clots13 or by the spatial resolution of standard NECT images reconstructed with slice widths between 5 and 10 mm. These thick CT slices cannot reliably display thrombus in vessels with luminal diameters $<$ 3 mm such as the MCA.10,14 Using a special thin-slice CT protocol with high x-ray dosage has been proven recently to show that most patients with MCA stroke exhibit an HMCAS.15

To use high spatial resolution NECT imaging for patients with stroke without additional scanning, NECT raw data can be reconstructed with small slice width on all modern multidetector CT scanners. We hypothesized that these thin image slices would significantly increase thrombus contrast, that enhanced contrast would outweigh the inherently elevated image noise levels, and that clots could therefore be reliably detected. Thus, the purpose of this study was to investigate whether thin-slice image reconstructions of standard NECT data can be used to significantly increase sensitivity detecting intraluminal thrombus in patients with acute ischemic stroke.

Methods

Subjects
Between April 2009 and February 2011 we conducted a prospective case study of patients who presented with acute MCA stroke within 6 hours from symptom onset. The Institutional Review Board

Received January 17, 2012; final revision received May 8, 2012; accepted May 17, 2012.
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Stroke is available at http://stroke.ahajournals.org
DOI: 10.1161/STROKEAHA.112.649921
approved the study. Patients were only included when pretreatment NECT was followed by CT angiography (CTA), which had proven occlusion of the middle cerebral artery trunk or of a first order (M2) branch of the MCA by intraluminal thrombus. Furthermore, patients were excluded when they presented with early signs of infarction exceeding one third of the MCA territory or cerebral hemorrhage on admission NECT scans. Demographic data of all patients were recorded. Every patient with proximal MCA occlusion was matched with a control patient of the same sex and age but without MCA occlusion. We included patients without vascular obliteration to analyze changes in specificity for thrombus detection due to the reconstruction of thin NECT slices. These exhibit increased noise levels and we expected that areas of spuriously increased density due to image noise might misleadingly be interpreted as clots.

**Data Acquisition**

All patients were scanned using a multidetector CT scanner with 64 detector rows (Brilliance 64; Philips, Best, The Netherlands). The standard NECT protocol entailed a collimation of $16 \times 0.625$ mm, a tube voltage of 120 kV, a tube current of 280 mAs, and a high-resolution focal spot. Incremental scanning and a smooth reconstruction kernel, optimized for brain imaging, yielded 5-mm-thick NECT slices. After CTA using our standard clinical protocol, a neuroradiologist reviewed these studies for matching inclusion criteria. For every selected patient, the database of the CT scanner was searched for control patients of the same age and sex scanned with the same NECT protocol. To be included in the study, the control patients had to lack a clinical history and NECT signs of acute stroke; additionally, CTA raw data had to be available for reconstruction of 0.625-mm-thick slices. If more than one patient was found who matched with a patient with stroke, the corresponding control patient was chosen randomly from among the matches. If no close match was detected in the initial search, a follow-up survey was used to find an eligible patient. In all patients with stroke and control subjects, NECT raw data were reconstructed with slice thickness of $0.625$ mm, keeping all remaining reconstruction parameters constant. The original NECT reconstructions with a slice width of 5 mm were used for subsequent data analysis without any further processing. All CT images reconstructed with a slice thickness of $0.625$ mm were subsequently converted into 5-mm-thick slices using maximum intensity projections (MIPs) without a reconstruction increment. Finally, exchanging the clinical information in the image header with a unique ID anonymized the reconstructed CT images.

**Observational Study**

Two experienced neuroradiologists and a junior resident physician who were not informed about the composition of the patient population independently evaluated the anonymized and randomly arranged NECT data regarding the detectability of a hyperdense artery sign in the MCA trunk and M1 branches of the MCA. The observers did not receive any corresponding CTA images nor did they do any subsequent consensus reading. They reviewed all prepared CT images on a standard radiological viewing and reporting workstation (IMPAX; Agfa-Gaevert, Mortsel, Belgium) and rated the probability of finding thrombotic obliteration of a vessel in one of the anterior cerebral hemispheres based on a 5-point scoring system. A score of 4 was given if they were completely confident in detecting intraluminal thrombus, 3 if they were less confident they had detected occlusion, 2 if they were uncertain of thrombotic burden (with equal chances of both possibilities), 1 if they were less confident that they had detected occlusion, and finally a score of 0 was given if they did not detect intraluminal thrombus.

**Data Collection and Validation**

For every observer, a list of all image data with IDs and corresponding ranking scores was collected and matched with the original list of patient data containing the baseline data on thromboembolism in one of the cerebral arteries. Only when the clinical information regarding the neurological deficit matched signs of vascular obliteration on NECT and CTA images was a true obliteration regarded proven.

Finally, a neuroradiologist measured clot lengths using CTA images that were registered with the thin-slice NECT images. The resulting overlay of the HMCAS on the CTA images allowed for following the exact course of the occluded vascular segment. The CTA images were images for defining the proximal and in most cases also the distal ends of the clot. In cases in which the branches distally to the site of occlusion were not opacified by contrast dye due to insufficient collateral flow, the distal end of the clot corresponded to the distal end of the HMCAS. The measurements were performed manually using a standard ruler tool on the viewing workstation to determine the lengths of the occluded vascular segments.

**Statistical Tests and Evaluation of False-Negative Results**

The ranking scores for vascular obliteration for all 3 observers were analyzed against baseline data using receiver operating curves analysis using paired samples. The pairs were formed by standard 5-mm-reconstruction images with their corresponding thick slab MIP image projection data. First, the area under the curve for both tests was compared for every observer. Second, the SD for every single area under the curve and for the area under the curve between the paired samples was calculated. Because ordinal values were used to describe the probability of each observer finding a positive hyperdense artery sign, Kendall $\tau$ correlation was used to compare the 2 tests’ true-positives and false-positives. Furthermore, $z$-statistics and one-tailed probability values were calculated to test the hypothesis that the receiver operating curve results could differ by chance. To analyze interobserver agreement among the 3 readers, Cohen $\kappa$ was calculated for every pair of readers. All statistics were calculated using Aabel (Gigawiz Ltd Co, Tulsa, OK), Version 3.0.5. Finally, we described the specific imaging findings in cases with false-negative clot detection. We therefore considered a detection false-negative when a site of occlusion was rated between 0 and 2 by at least 2 readers.

**Results**

**Patients**

Of a total of 158 patients presenting with clinical signs of anterior circulation stroke (75 male, 83 female; median National Institutes of Health Stroke Scale, 8; range, 3–28; median age, 61 years; range: 38–86 years) within 6 hours after symptom onset, 54 patients (26 male, 28 female; median National Institutes of Health Stroke Scale, 13; range, 7–28; median age, 66 years; range, 41–86 years) were identified as matching the inclusion criteria. Most of the excluded patients had minor strokes ($n=63$) and did not receive a CTA scan; the remaining patients either had a cerebral hemorrhage ($n=18$) or presented with early extensive infarction ($n=23$). For every case a corresponding control patient of the same age and sex was identified. In all patients with stroke, a vascular occlusion site was identified and the lengths of the occluded segments were measured definitively (occluded segments: $n$ [internal carotid artery/M1] = 12, $n$ [M1] = 17, $n$ [M1/M2] = 18, $n$ [M2] = 7). The clot lengths ranged from 1.2 mm to 34.5 mm (median, 6.1 mm). With 54 NECT data sets from patients with stroke and the same number of images from control subjects, both reconstructed with slice widths of 5 mm and 0.625 mm, every observer had to rate a total of 216 NECT data sets. In Figure 1, standard 5-mm NECT reconstructions of 3 patients with stroke are compared with the corresponding images reconstructed with a slice width of 0.625 mm to exemplify how clots were visualized during rating.
Receiver Operating Curve Analysis and Failed Clot Detection

The calculated receiver operating curves are displayed in Figure 2 and all associated statistics are summarized in Table 1. In all observers, a high difference in areas under the curve for detection of the HMCAS was found for the 2 different CT slice widths. In NECT images with a standard slice width of 5 mm, the clots are missed in a large number of cases by all observers, whereas they are nearly always found in the 5-mm MIP images based on the thin-slice reconstructions. There was a one-sided $P<0.001$ of the difference occurring by chance. For thin-slice NECT reconstructions, the areas under the receiver operating curves for detecting a clot were all close to 0.95 and had a small SE. Only minor correlation ($\leq 0.21$) was found for paired comparison.

The results for Cohen $\kappa$ analysis for interreader agreement are shown in Table 2. For all pairs of readers, even for the inexperienced reader, agreement regarding clot detection is much higher in thin-slice reconstructions compared with thick.

Finally, we looked at those stroke cases that had false-negative (vessel obliterated, score $<3$) results in at least 2 observations using thin NECT slices ($n=3$). All 3 observers failed to detect a thrombus in 2 cases with clot lengths of 1.2 mm and 1.4 mm. Two observers did not detect a clot with a length of 2.4 mm that was partly hidden by a CT beam-hardening artifact superimposed by the adjacent clinoid process.

Discussion

The primary finding in this study is that thrombotic occlusion of the MCA can be detected with high sensitivity, specificity, and reliability in thin-slice reconstructions of standard NECT raw data using thick slab MIPs. Detectability is only slightly reduced in cases with very small clots or if the site of occlusion is superimposed with imaging artifacts. Furthermore, the high detection rate is not much influenced by the experience of the observer. In NECT images with a standard slice width of 5 mm, detection of clots is not much better than guessing.

According to these results, an observer would be able to detect thrombus in the proximal cerebral arteries of the anterior circulation with a chance of considerably $<50\%$ if 5-mm NECT reconstructions are used. Results from the literature are in agreement with this. The thick-slab MIPs derived from thin-slice NECT images, however, allow for detection of thrombus in nearly all cases of vascular obliteration at the level of the circle of Willis. The fact that the observers could miss very small thrombi might have only minor clinical impact in practical handling of stroke cases.
This can be expected because patients in whom a so-called media dot sign, a smaller variant of the HMCAS, was found show a significantly better outcome compared with patients presenting with an HMCAS.17 The findings in this study are consistent with the literature regarding the high specificity of the HMCAS used to describe thrombotic burden.10 It was also previously reported that sliding MIP images of thin-slice NECT reconstructions improve detection of thrombotic vascular occlusion. With this technique, a sensitivity of 67% for thrombus detection was found using a reconstruction slice width of 2.5 mm.18 The most significant result of this study, showing that slices reconstructed with 0.625 mm thickness allow for detection of nearly all sites of thrombotic vascular occlusions, is new. Due to high levels of image noise resulting from thin-slice reconstruction of standard NECT data, it could be anticipated that thrombotic clots do not show sufficient contrast with surrounding tissue to be detected at a higher rate. Nevertheless, it has been pointed out before that small objects can often be more easily detected on CT images if these images are reconstructed with smaller slice width without increasing the applied x-ray dose.6 A smaller slice width generally results in less partial volume averaging, leading to higher object contrast.17,19,20 This gain in contrast is higher than the associated contrast decline by higher levels of image noise if the object size is close to the spatial resolution limit. This condition is fulfilled for the vessels of the circle of Willis because they run predominantly within the NECT scan plane and their diameter is typically close to the slice width.

The most important clinical lesson to be drawn from this work is the fact that a HMCAS can be detected in nearly all patients if the NECT data are properly reconstructed and displayed. This has an important impact on the relevance of the HMCAS in imaging of patients with acute stroke. Although until recently this was mainly associated with poor patient prognosis and low sensitivity, it now has to be re-evaluated regarding its prognostic value in acute stroke.12,21 Because the HMCAS can be detected easily in thin-slice NECT reconstructions, it should be possible to describe the obliterated vascular segments and the spatial extent of the thrombus. These descriptors can be used as parameters for therapeutic decisions and to predict the clinical outcome.7

Limitations of our study are mainly due to the relatively small variation in reconstruction parameters. Although we focused on the smallest available slice width for MIPs of thin-slice reconstruction, the standard slice width generally used is 5 mm in cranial NECT imaging. By extending the proposed techniques to reconstruction slice widths between 0.625 and 2 mm, it might even be possible to improve detection rates further.

### Table 1. Receiver Operating Characteristic Curves (ROCs) Analysis for Paired Comparisons

<table>
<thead>
<tr>
<th></th>
<th>Observer 1</th>
<th>Observer 2</th>
<th>Observer 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>NECT slice width, mm</td>
<td>5</td>
<td>0.625</td>
<td>5</td>
</tr>
<tr>
<td>AUC</td>
<td>0.67</td>
<td>0.96</td>
<td>0.66</td>
</tr>
<tr>
<td>SE</td>
<td>0.06</td>
<td>0.02</td>
<td>0.06</td>
</tr>
<tr>
<td>Correlation</td>
<td>0.21</td>
<td>0.18</td>
<td>0.13</td>
</tr>
<tr>
<td>Z</td>
<td>5.14</td>
<td>5.39</td>
<td>4.88</td>
</tr>
<tr>
<td>P value (one-tailed)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The area under the ROC curves (AUC) and SDs of AUC curves are calculated and compared. The correlation of paired comparisons is derived from Kendall’s τ correlation of the 2 tests’ true-positives and false-positives. Z statistics relate the differences in AUC to their SE. The one-tailed P values define the probability that differences between ROC curves could occur by chance.

NECT indicates nonenhanced CT.

### Table 2. Agreement Between Readers Expressed by Cohen Kappa

<table>
<thead>
<tr>
<th></th>
<th>Inexp/Exp1</th>
<th>Inexp/Exp2</th>
<th>Exp1/Exp2</th>
</tr>
</thead>
<tbody>
<tr>
<td>κ (0.5-mm reconstruction)</td>
<td>0.38</td>
<td>0.45</td>
<td>0.39</td>
</tr>
<tr>
<td>κ (0.625-mm reconstruction)</td>
<td>0.71</td>
<td>0.69</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Observer 1 is the inexperienced reader (Inexp); Observers 2 and 3 are the experienced readers (Exp1 and Exp2). For all κ test results, we found P<0.001.
Another point of critique is that the readers in our study might have been biased in detecting clots by the appearance of early signs of infarction. Because these signs are much easier to detect in high-contrast thick-slice reconstructions compared with noisy thin-slice NECT images, this bias would have resulted in higher clot detection rates in thick slices. Because our study results demonstrate the opposite, we considered this bias effect negligible.

Conclusions
Using thick-slab MIPs of NECT images that are reconstructed with a slice thickness of less than a millimeter allows for detecting intraluminal thrombus in the trunk or M2 branches of the MCA in cases of acute stroke with a very high sensitivity, specificity, and reliability. This additional information about proximal MCA obliteration can easily and quickly be obtained on all modern multidetector CT scanners without additional scanning time or radiation burden. Thrombus localization and extent are important parameters for outcome prediction and decision-making when it comes to choosing the right therapy in acute stroke. Therefore, it may prove helpful to quantify and correlate this additional information in subsequent acute stroke imaging trials with chosen therapy and clinical outcome.

Sources of Funding
This study was supported by a grant from the Medical Faculty of the Christian-Albrechts-University.

Disclosures
None.

References
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Stroke. published online June 21, 2012;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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非造影 CT 画像の Thin-Slice 再構成により急性期脳卒中における血栓の検出が可能

Thin-Slice Reconstructions of Nonenhanced CT Images Allow for Detection of Thrombus in Acute Stroke

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背景および目的：本研究の目的は、頭蓋非造影 CT スキャンの thin-slice 画像再構成を使用して、中大脳動脈の近位閉塞による急性期血栓性脳卒中患者における頸内血管の検出精度を有効に上昇させることができるか否かを調べることである。

方法：急性期血栓性脳卒中を呈し中大脳動脈の血管閉塞が証明された 54 例の患者の非造影 CT スキャンの生データを、性別と年齢が同じで脳卒中を有さない患者の同じデータとともに前向きに収集した。すべてのデータを、スライス厚 5 mm (thick-slice) と厚さ 0.625 mm の thin-slice として再構成した。5 mm の非造影 CT 再構成および thin-slice の 5 mm の最大値投影の評価を 3 名の観察者がそれぞれ単独で行い、中大脳動脈幹または一次分枝を閉塞する凝血塊の可能性を 5 段階評価を用いて評価した。結果を、受信者動作曲線 (ROC) 解析を用いてベースデータと比較して評価した。観察者のすべてのパーセについて Cohen k を用いて観察者間信頼性を測定した。

結果：Thin-slice の ROC 解析の曲線面積は 0.63 ～ 0.67 の範囲であったのに対して、thin-slice 再構成の最大値投影画像では、ROC 解析で明らかになった曲線面積は 0.94 ～ 0.97 であった。観察者間一致性は、thin-slice (κ, 0.69 ～ 0.83) の方が thin-slice 非造影 CT 再構成 (κ, 0.38 ～ 0.45) より高かった。

結論：標準的頭蓋非造影 CT 生データの thin-slice 再構成により、近位中大脳動脈を閉塞する凝血塊のより高感度で信頼性の高い検出が可能となる。

Stroke 2012; 43: 2319-2323

図 1 左側の NECT 画像は 3 例の異なる脳卒中患者（A ～ C）のオリジナルの 5 mm 厚の NECT 画像であり、右側の画像はそれに対応する 0.625 mm で再構成した NECT 画像による thick-slab MIP 画像である。最初の患者（A）の左側の頸動脈先端部にはわずかな動脈の高吸収が検出できるが、対応する thin-slice 画像ではさらに MCA 主幹へと広がる凝血塊が明らかに認められる。右 MCA 主幹および分歧（B）および左 MCA の M2 分岐（C）の凝血塊は thin-slice 再構成でのみ検出できる。NECT：非造影 CT。MIP：最大値投影、MCA：中大脳動脈。