Assessment of Thrombus in Acute Middle Cerebral Artery Occlusion Using Thin-Slice Nonenhanced Computed Tomography Reconstructions

Christian H. Riedel, MD; Ulf Jensen, MD; Axel Rohr, MD; Marc Tietke, MD; Karsten Alfke, MD; Stephan Ulmer, MD; Olav Jansen, MD

Background and Purpose—We sought to evaluate how accurately length and volume of thrombotic clots occluding cerebral arteries of patients with acute ischemic stroke can be assessed from nonenhanced CT (NECT) scans reconstructed with different slice widths.

Methods—NECT image data of 58 patients with acute ischemic stroke with vascular occlusion proven by CT angiography were reconstructed with slice widths of 1.25 mm, 2.5 mm, 3.75 mm, and 5 mm. Thrombus lengths and volumes were quantified based on these NECT images by detecting and segmenting intra-arterial hyperdensities. The results were compared with reference values of thrombus length and volume obtained from CT angiography images using Bland-Altman analysis and predefined levels or tolerance to find NECT slice thicknesses that allow for sufficiently accurate thrombus quantification.

Results—Thrombus length can be measured with high accuracy using the hyperdense middle cerebral artery sign detected in NECT images with slice thicknesses of 1.25 mm and 2.5 mm. We found mean deviations from the reference values and limits of agreement of \(-0.1 \text{ mm} \pm 0.6 \text{ mm}\) with slice widths of 1.25 mm and \(0.1 \text{ mm} \pm 0.7 \text{ mm}\) for slice widths of 2.5 mm. Thrombus length measurements in NECT images with higher slice width and all evaluated thrombus volume measurements exhibited severe dependence on the level and did not match the accuracy criteria.

Conclusion—The length of the hyperdense middle cerebral artery sign as detected on thin-slice NECT reconstructions in patients with acute ischemic stroke can be used to quantify thrombotic burden accurately. Thus, it might qualify as a new diagnostic parameter in acute stroke management that indicates and quantifies the extent of vascular obliteration. 

Key Words: acute care ■ acute stroke ■ CT ■ embolic stroke ■ embolism ■ imaging ■ neuroradiology ■ stroke care ■ stroke management ■ thrombolysis

In acute anterior ischemic stroke, nonenhanced CT (NECT) may demonstrate a hyperdense middle cerebral artery sign (HMCAS) as a highly specific marker of thrombotic vascular occlusion. So far, the sign has not been used to assess clot burden because standard NECT slices are typically too thick to accurately delineate thrombus. Using thin-slice reconstructions of standard NECT data, thrombotic clots should contrast better with surrounding tissue due to diminished volume averaging effects. The high spatial resolution of such reconstructions can even outweigh their low signal-to-noise levels and therefore permit quantifying intravascular thrombus by accurate segmentation of the HMCAS.

The HMCAS was discovered \(>25\) years ago.\(^1\) Since then, authors have pointed out that the sign is highly specific for thrombus occluding cerebral arteries\(^2\) and that it predicts poor outcome of intravenous thrombolysis in acute strokes.\(^3–5\) Outcome furthermore depends on the location of the intravascular hyperdensity and on its size.\(^6\) The smaller, peripherally located variant of the HMCAS, the middle cerebral artery dot sign, is associated with a better outcome of intravenous thrombolysis compared with the HMCAS.\(^7,8\) However, a recent study reports that patients with HMCAS with acute stroke benefited more from intra-arterial than from intravenous thrombolysis.\(^9\) Thus, future decisions about the optimal therapy for acute strokes should take into consideration the total extent of vascular occlusion by thrombus. Recently, a technique for measuring the volume of intravascular thrombus using thin-section NECT scans was developed.\(^10\) Using additional high-resolution CT scans, the authors were able to detect thrombus in nearly all cases of acute stroke in which CT angiography had proven occlusions of the middle cerebral artery an internal carotid artery. Unfortunately, this quantitative method was not validated by any references such as CT angiography or MRI. Furthermore, the
A multidetector row CT scanner with 64 detector rows (Brilliance 64; Philips, Best, The Netherlands) was used for NECT and CTA. A multidetector row CT scanner with 64 detector rows (Brilliance 64; Philips, Best, The Netherlands) was used for NECT and CTA. The corresponding thick-slab MIP image of the NECT shows a HMCAS in exactly the same location where the contrast gap is found in the CTA image. The 4 MIP images show the results of the segmentation of clot in the left MCA by seeded region-growing using NECT images reconstructed with 5-mm, 3.75-mm, 2.5-mm, and 1.25-mm slice widths (sw). The thin dark gray lines superimposed on the segmentation results represent the calculated middle axes of the clots.

To make this new tool relevant for imaging in acute ischemic stroke, we have to comply with 2 requirements. First, thrombus should be depicted from standard NECT scan data to avoid additional scanning. On multidetector row CT scanners, this can be realized with thin-section reconstruction of NECT data scanned using standard protocols. Second, we have to determine how precisely thrombus extent can be delineated using these images with high spatial resolution but low signal-to-noise ratio. To determine the true extent of vascular obliteration, CT angiography images with intravascular contrast proximal and distal to the obstructed site can be used as a reference. The purpose of this study was to determine how accurately thrombus volume and length can be measured using thin CT slice reconstructions of standard NECT scans.

Methods

Patients

Between April 2008 and March 2009, we monitored a group of patients who presented with acute stroke in the middle cerebral artery (MCA) territory within 6 hours from symptom onset in a prospective case series. Patients were only included when pretreatment NECT was followed by CT angiography (CTA), which had to prove occlusion of the most proximal segment (M1) of the MCA. Furthermore, 2 neuroradiologists reading the NECT and CTA images independently had to agree on a close match between the location and spatial extent of focal hyperdensities representing thrombus in NECT images and intravascular contrast voids observed in the corresponding CTA images (Figure 1A–B). This means that in all included patients, sufficient retrograde blood flow across collateral vessels allowed for contrasting the obliterated vessel distally to the site of occlusion.

Demographic data of all included patients were recorded.

Data Acquisition

A multidetector row CT scanner with 64 detector rows (Brilliance 64; Philips, Best, The Netherlands) was used for NECT and CTA. The standard NECT protocol entailed a collimation of 16×0.625 mm, a tube voltage of 120 kV, a tube current of 320 mAs, and selection of a high-resolution focal spot. Incremental scanning and a smooth reconstruction kernel, optimized for brain imaging, yielded 2.5-mm thick NECT slices. Cranial CTA was initiated by visual contrast bolus tracking in the cervical arteries after infusion of an 80-mL bolus of 350 mg I/mL at a rate of 5 mL/s followed by 40 mL of saline flush. The vessels were scanned in helical mode with a volume pitch of 1.2 and a collimation of 64×0.625 mm, a tube voltage of 80 kV, and a tube current of 280 mAs.

Image Preprocessing

All NECT images were reconstructed offline with a slice width of 0.625 mm. All other reconstruction parameters of the standard cranial NECT protocol were kept constant. Subsequently, these thin slices were resampled using a B-Spline interpolator for gantry tilt correction. After resampling, additional reconstructions with slice widths of 1.25 mm, 2.5 mm, 3.75 mm, and 5 mm were calculated using averages of the original thin slices.

Thrombus Segmentation and Quantitative Analysis of Thrombotic Burden in NECT Images

Thrombus size was measured after semiautomated segmentation. Therefore, 1 neuroradiologist manually had to define regions of interest around the course of cerebral arteries of the anterior circulation in all preprocessed CT data sets. In these regions, every image voxel with a density between 55 and 80 Hounsfield units was regarded as a potential seed for a subsequent segmentation using a seeded region-growing algorithm. This segmentation process included all seed neighbor pixels with a density between 45 and 80 Hounsfield units. These conditions allowed for maximizing segmented thrombus volume without leakage affecting the surrounding tissue. Thrombus volume was computed using the segmented object by multiplying the number of object voxels by the voxel dimensions. To derive the thrombus length, the segmentation result first had to be reduced to a medial axis representation. Therefore, it was reduced to a skeleton by applying a topology-preserving morphological thinning operation. Finally, the maximum euclidean length of the resulting skeleton was calculated. The erosion distance of the skeletonization operation was added twice to this length to account for the shortening of the skeleton with respect to the thrombus by the morphological thinning procedure. Examples of the
results of the segmentation and skeletonization algorithm are shown in Figure 1C.

Data Validation
To define a reference value for thrombotic burden, the occluded arterial segment was measured using the CTA images along with the NECT images. For this purpose, the CTA and NECT images first had to be registered using a rigid 3-dimensional affine transform. Next, a medial axis of the occluded arterial segment was manually defined. Therefore, a polygon was drawn by connecting points in the vessel center proximally and distally to the occlusion site. Because the occluded segments could not be expected to follow a straight line between the patent proximal and distal vascular segments, their best medial axis representations had to be defined by using the hyperdense artery signs that were superimposed onto the CTA images by the preceding registration.

A B-Spline approximation of the polygon was used to smooth the resulting vascular axis. This medial axis was examined from 3 orthogonal maximum intensity projection images and eventually corrected to align accurately with the vascular axis. Finally, this skeleton representation of the artery was cut at the proximal and distal ends of the occlusion site defined by the void of intravascular contrast. The resulting segment length was used as a reference length of the thrombus. To define a reference volume for each thrombus, the HMCAS was quantified using NECT images reconstructed with a slice thickness of 0.625 mm. Thrombus volume was quantified in the same way as in NECT images with slice widths between 1.25 mm and 5 mm as described previously. Two neuroradiologists independently measured the reference lengths and volumes of all clots to evaluate interobserver variability.

Statistical Analysis
Data analysis started with processing the patients’ personal statistics. In the next step, we defined tolerance levels for the measurements of thrombus length and thrombus volume. Based on a typical NECT voxel width of approximately 0.5 mm in the axial plane, we considered a tolerance level of ±1 mm appropriate because this corresponds to an error of 1 voxel on each side of the clot. Assuming a typical diameter of the MCA of 2.5 mm and a tolerance of ±1 mm for thrombus length measurements, we defined a tolerance level for clot volume measurements of ±10 mm³. Subsequently, the Bland and Altman method was used to analyze the interobserver errors of the reference measurement results of thrombus volume and length. Therefore, the differences between the measurements by both observers were used to calculate the mean of the differences and upper and lower values of the 95% limits of agreement. The same technique was used to compare thrombus lengths and volumes in groups of equal CT slice width with the associated reference values. For every NECT slice width, the spread of these differences was evaluated with Bland-Altman plots for independence of the magnitude of thrombus volume and thrombus length. In cases of independence, the CO for the upper and lower limits of agreement was calculated using a pairwise t test. Finally, the mean of the differences and the upper and lower values of the 95% limits of agreement were compared with the tolerance levels defined above to find those NECT slice widths that allow for measuring thrombus length and volume with sufficient precision compared with the reference technique.

Results
Patients
A total of 58 people matched the inclusion criteria. Thirty-six patients were male with a median age of 62 and an age range from 43 to 79 years. In all included cases, CTA imaging proved MCA obliteration. All patients had either pure obliteration of the MCA main stem or from occlusion of the MCA main stem with thrombus reaching the supraclinoid segment of the ipsilateral internal carotid artery.

Image Processing
In all cases, preprocessing of the NECT image data by selecting a region of interest around the course of the anterior circulation vessels resulted in compact seeds within the intravascular hyperdensities. Seeded region growing resulted in well-defined thrombus representations in all patients with NECT slice widths of 1.25 mm and 2.5 mm. When a NECT slice thickness of 3.75 mm was chosen, no thrombus was detected in 4 of the 58 patients (6.9%). With a NECT slice thickness of 5 mm, clots were missed in 14 patients (24.1%).

Quantitative Thrombus Analysis
The interobserver variability for the reference data of thrombus length and volume was found to be within the limits of the predefined tolerance levels. The mean thrombus length deviation was 0.2 mm (limits of agreement: ±0.6 mm); the mean volume deviation was 2.3 mm³ (limits of agreement: ±4.3 mm³).

The magnitude-dependent differences between thrombus lengths measured in different NECT reconstructions on the 1 hand and thrombus length reference data on the other are demonstrated in Bland-Altman reconstructions in Figure 2. The equivalent comparisons for thrombus volume measurements are shown in Figure 3. For all measurements of thrombus volumes and lengths, the mean deviations and the limits of agreement as well as the CIs of the limits of agreement are listed in the Table.

According to Figure 2, thrombus length measurements are only independent of the level when they are based on NECT images reconstructed with a slice thickness of 1.25 mm or 2.5 mm. Only under these conditions, the limits of agreement and their upper and lower confidence levels as estimated by the t test are within the limits of the predefined tolerance level of ±1 mm (see the Table). Furthermore, the mean deviation between NECT measurements and reference lengths is very close to zero. As the NECT slice thickness increases beyond 2.5 mm, the mean deviation of thrombus length rises above the upper limit of the tolerance levels and the level of agreement exceeds the tolerance level by more than a factor of 4.

The measurements of thrombus volumes from NECT images with slice widths between 1.25 mm and 5 mm all deviate from the reference data with mean differences exceeding the defined tolerance levels. Thus, none of the evaluated NECT data sets can be used to evaluate thrombus volume with sufficient precision compared with the reference data.

Discussion
According to our results, reconstructions of standard cranial NECT data with a slice width of ≤2.5 mm using simple image postprocessing tools allow for the accurate measurement of the length of a thrombus in a cerebral artery of the circle of Willis. However, the same tools fail to identify the volume of thrombus with sufficient precision with all other NECT slice widths we evaluated. The latter finding is most likely due to the different influences of partial volume effects on the spatial extent of the HMCAS as slice thickness increases. However, partial volume averaging only has a minor impact on the middle axis representation of the thrombus used for length measurements. It only degrades the
middle axis significantly as the CT slice width increases beyond 2.5 mm.

Thus, thrombotic burden can be described accurately by thrombus length if standard cranial NECT scanning protocols with multidetector row CT scanners are used. It requires only a few seconds of extra reconstruction time and no additional scanning, which ultimately saves radiation dose and time needed for subsequent treatment. Furthermore, because a slice width of 2.5 mm still permits sufficiently accurate delineation of thrombus extent, this slice width could initially be used as a reconstruction parameter for the standard NECT protocol.

A recently published technique for measuring thrombus volume for the first time from thin-slice NECT image quantitatively defined thrombotic burden in acute strokes. These results are highly encouraging for establishing a valuable new prognostic parameter in acute strokes. This might even eventually guide therapeutic decisions. Our study results show that the same technique is applicable to standard thin-slice NECT data obviating additional scanning. We furthermore confirm the gray scale thresholds described for thrombus segmentation by seeded region-growing. These correspond well with density values of thrombus reported in earlier studies. In contrast to the preceding work on volumetric assessment of thrombus, our results show that thrombotic burden might be more accurately defined by thrombus length than by volume. Thrombus extent along the vascular axis very recently has been used as a prognostic parameter for patient outcome using scoring systems for occlusion on CTA images. These systems associate scores with different vessel segments. These scoring systems have been shown to correlate well with treatment success and patient outcome.

Figure 2. Bland-Altman plots showing the differences between the reference thrombus lengths (TL_{reference}) measured using CTA images and thrombus lengths (TL_{HMCAS}) measured using the HMCAS in NECT images with reconstruction slice widths (sw) of 1.25 mm (A), 2.5 mm (B), 3.75 mm (C), and 5 mm (D). Differences are plotted against the mean of both length measurements. The mean of the difference is indicated by the dotted line; the solid lines define the upper and lower 95% limits of agreement.
Our technique has the potential to advance these systems to describe thrombotic burden in a more reproducible way. Thus, we have defined a new parameter for the management of acute ischemic stroke that directly describes the cause of patients’ states and symptoms. The technique can be applied immediately at most stroke units using modern multidetector row CT scanners with high-resolution detectors. The required thin-slice NECT images can simply be reconstructed using standard scanning protocols. Therefore, the data required for thrombus length analysis will not

Table. Results of Bland-Altman Analysis Describing How Accurately Thrombus Length and Volume Can Be Measured From NECT Reconstructions With Slice Widths of 1.25 mm, 2.5 mm, 3.75 mm, and 5 mm Compared With Reference Data of Thrombus Length and Volume

<table>
<thead>
<tr>
<th>NECT Slice Width</th>
<th>1.25 mm</th>
<th>2.5 mm</th>
<th>3.75 mm</th>
<th>5 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombus length, mm</td>
<td>Mean difference</td>
<td>−0.1</td>
<td>0.1</td>
<td>4.2</td>
</tr>
<tr>
<td>Limits of agreement: upper/lower limit</td>
<td>0.6/−0.7</td>
<td>0.8/−0.5</td>
<td>10.6/−2.2</td>
<td>12.3/0.1</td>
</tr>
<tr>
<td>Ct: upper/lower limit</td>
<td>0.7/−0.8</td>
<td>0.9/−0.6</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Thrombus volume, mm³</td>
<td>Mean difference</td>
<td>10.3</td>
<td>31.6</td>
<td>47.0</td>
</tr>
<tr>
<td>Limits of agreement upper/lower limit</td>
<td>16.4/4.2</td>
<td>37.7/25.4</td>
<td>53.1/40.8</td>
<td>61.9/49.6</td>
</tr>
<tr>
<td>Ct: upper/lower limit</td>
<td>17.3/3.3</td>
<td>…</td>
<td>…</td>
<td>…</td>
</tr>
</tbody>
</table>
necessitate additional radiation and the time needed for 1 additional reconstruction is negligible. Because current studies aim to define simple clinical and NECT imaging parameters to guide patients in acute stroke, quantification of thrombotic burden might become included as a standard parameter into the guidelines for management of acute ischemic stroke. Thrombus length might particularly be useful as a parameter to decide in which patients intravenous thrombolysis will most likely fail to recanalize the occluded vessels. If this parameter is generally accepted, it might even be used to evaluate the success of therapy by detecting and measuring residual thrombus.

A major potential pitfall when applying the thrombus segmentation technique might result from conditions different from thrombotic vascular occlusion leading to hyperdensities of intracranial vessels. Calcified arterial walls and a high hematocrit could cause vascular hyperdensities resembling thrombus. This underlines the limitations of our study. In the relatively small patient population we studied, thrombotic vascular occlusion was well defined by arterial hyperdensities in all cases. In none of the patients was segmentation of intraluminal thrombus due to arterial calcification or an increase in x-ray attenuation in the bloodstream a problem. Because both of these conditions have to be expected in a larger patient population, it is highly important to apply the technique in a larger prospective study. Furthermore, it would be very helpful if a reference standard for thrombus length measurements could be established that would be completely independent from the NECT and CTA imaging. This reference might use MR sequences optimized for displaying thrombotic clots.

**Conclusion**

In summary, standard NECT protocols for imaging of acute stroke can easily be extended by thin-slice reconstructions that allow for assessing clot burden accurately by thrombus length. The occluded length can be used to predict patient outcome and the success rate of intravenous lysis. If subsequent studies define a limit of thrombus length above which intravenous thrombolysis most likely fails because the lyrics simply never successfully penetrate the whole thrombus extent, then this limit will define a threshold above which intra-arterial thrombolysis would have to be strongly considered. Thus, further studies will have to show the feasibility of the technique we described in a larger patient population. This population should be analyzed further with respect to their treatment plans and clinical outcomes to decide whether intra-arterial hyperdensities can be used to define the best treatment option in acute ischemic stroke.

**Disclosures**

None.

**References**

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Assessment of Thrombus in Acute Middle Cerebral Artery Occlusion Using Thin-Slice Nonenhanced Computed Tomography Reconstructions

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背景和目的: 预探索应用平扫 CT(NECT) 不同层厚的重建技术, 测量脑动脉闭塞的急性缺血性卒中患者其血栓长度和体积的准确性。

方法: 共纳入 58 例经 CT 血管造影 (CTA) 检查证实存在血管闭塞的急性缺血性卒中患者。患者的 NECT 影像分别以 1.25 mm、2.5 mm、3.75 mm 和 5 mm 的层厚进行重建。通过检测和分割患者 NECT 影像中的动脉内高密度征, 对血栓的长度和体积进行量化。其结果分别与通过 CT 血管造影得到的血栓长度及体积的参照值进行比较。应用 Bland-Altman 分析和预定义的标准或可接受范围, 得出可以对血栓进行准确量化的 NECT 重建影像的层厚。

结果: 以 1.25 mm 和 2.5 mm 层厚重建的 NECT 影像, 通过检测其大脑中动脉高密度征能够准确测量血栓的长度。1.25 mm 和 2.5 mm 层厚的测量结果与参照值和一致性界限的平均差分别为 –0.1 mm ± 0.6 mm 及 0.1 mm ± 0.7 mm。以更大层厚重建的 NECT 影像所测量的血栓长度和所有关于血栓体积的测量结果均显示了对重建层厚的高度依赖性，并且其结果不能与参照值相匹配。

结论: 在急性缺血性卒中患者中, 应用 NECT 薄层重建技术所检测到的大脑中动脉内高密度征长度可以准确量化血栓负荷。因此, 大脑中动脉高密度征长度可能会成为一个新的急性卒中治疗管理的诊断参数, 用此参数来表明和定量血管闭塞的程度。

关键词: 急性期治疗, 急性卒中, 计算机断层扫描, 血栓形成性卒中, 血栓, 影像, 神经放射学, 卒中治疗, 卒中治疗管理, 血栓溶解

大脑中动脉高密度征 (HMCAS) 作为血栓闭塞血管的一个高度特异性标志, 常可见于急性前循环缺血性卒中患者的平扫 CT(NECT) 影像之中。由于标准 NECT 的层间距太大, 不能准确描述血栓情况, 因此, 目前尚未应用 HMCAS 对血栓栓子进行评价。应用平扫 CT 薄层重建影像技术, 可以减少体积平均效应, 因而血栓栓子能与周围组织形成更好的对比。薄层重建得到的高空间分辨率图像, 其质量甚至优于低信噪比水平的图像。因此, 通过精确地测量每截段内的 HMCAS, 能够对血管内血栓进行量化。

首次报道 HMCAS 至今已超过 25 年 [1]。自那时起, 即有学者指出该征象是血栓闭塞大脑动脉的特异性标志 [2], 并且是急性卒中患者静脉内溶栓治疗预后不良的预测因子 [3-4]。此外, 卒中患者的预后与其血管内高密度征的位置和大小相关 [5]。与密度均匀一致的 HMCAS 相比, 周边存在密度混杂区的 HMCAS, 即大脑中动脉样征越小, 则血管内溶栓治疗的预后越好 [7-8]。然而, 近来一项研究结果显示具有 HMCAS 的急性卒中患者应用动脉内溶栓治疗比静脉内溶栓治疗将获益更大 [9]。因此, 将来为急性卒中患者选择治疗决策时, 应考虑到血栓对血管闭塞的整体程度。近年来, 应用薄层 NECT 扫描测量血管内血栓体积的技术已得到发展 [10]。对 CT 血管造影检查已证实存在大脑中动脉闭塞的患者, 应用额外的高分辨率 CT 扫描成像, 几乎可以检测到所有患者的血栓。遗憾的是, 尚无研究应用 CT 血管造影或 MRI 检查来证实该定量测量方法的有效性。此外, 该方法需要额外的扫描, 因此势必会导致放射线暴露量及时间增加。

对急性卒中患者应用这一新的影像检查技术,
必须要符合两个条件。首先，为了避免患者接受不必要的扫描，应仅对 NECT 扫描已发现血栓的患者才实行该项检查。对于多排 CT 扫描的检查者来讲，应严格按照标准操作规程来进行平扫 CT 薄层重建成像。其次，我们必须明确应用原始图像如何清晰地描述血栓的范围，以及应该使用高空间分辨率成像，而不是低信噪比技术来获取原始图像。为了确定血管闭塞的真实范围，应用 CT 血管造影结果作为参照标准对闭塞位置近端及远端进行分析。本研究旨在探讨如何应用平扫 CT 薄层重建成像技术，对血栓体积和长度进行准确测量。

数据采集
所有患者的 NECT 及 CTA 检查均采用荷兰飞利浦公司生产的 64 排 CT (Brilliance 64 ; Philips, Best, The Netherlands) 来完成。标准的 NECT 操作规程要求采用准直 16×0.625 mm、管电压 120 kV、管电流 320 mAs 及选择高分辨率焦点进行扫描。最佳的脑成像附加扫描和顺利重建内核技术，其采用的是 2.5 mm 较厚的NECT层厚。颅脑 CTA 采用造影剂跟踪技术成像，需在颈动脉内以 5 mL/s 的速率团注 350 mg I/mL 的造影剂 (总量 80 mL), 随后注射 40 mL 生理盐水。血管扫描选用螺距 1.2、准直 64×0.625 mm、管电压 80 kV、管电流 280 mAs 的螺旋模式。

图像预处理
对所有 NECT 影像进行脱机重建，采用重建层厚为 0.625 mm。所有其他的操作参数与标准的头颅 NECT 操作规程保持一致。随后，应用 B 条件插补器[1]对机架倾斜校正后，对薄层重新取样。之后，应用原始薄层的平均数据，重建层厚分别选取 1.25 mm、2.5 mm、3.75 mm 及 5 mm 对图像进行重建。

NECT图像中血栓的影像分割和血栓负荷的定量分析
在对图像半自动分割之后，进行血栓尺寸的测量。因此，在所有 CT 数据的预处理时，一位放射学医师需要围绕前循环的脑动脉人为定义感兴趣区域。
在这些区域内，每一个密度在 55-80 Hu 之间的体素都会被认为是一个潜在的种子，随后应用种子区域生长算法对图像进行分割。分割过程包括了所有种子周围密度在 45-80 Hu 之间的像素。利用分割对象计算血栓体积，目标体素的数量乘以体素的尺寸。为了得到血栓的长度，分割结果首先必须简化至由中心轴表示。因此，应用保留拓扑结构的形态学细化操作，简化到得出血栓的结构骨架。最后计算剩余骨架的最大欧几里得（欧氏）长度。例如图 1C 所示的影像分割和骨架化计算法。

数据验证
为了定义血栓负荷的参照值，闭塞部位的动脉节段需要经过 NECT 及 CTA 两项检查的测量。首先，NECT 及 CTA 影像必须应用严格的三维仿射变换技术，来确定两影像间的对应关系。其次，手动确定闭塞动脉节段的中心轴。通过连接闭塞部位近端至远端血管各节段的中心点，得到了一个多边形。因为处于开放血管近端和远端之间的闭塞节段不可能是沿着一条直线的，因此，必须根据预先叠加到 CTA 影像上的高密度征象以及 CTA 与 NECT 图像间的对应关系，来确定最佳中心轴的位置。

应用多边形的 B 样条逼真算法，对得到的血管中心轴结果进行平滑处理。这个中心轴经过 3 个正交最大强度投影图像的校正，最终调整至准确的血管轴位置。

最后，将闭塞部位从近端至远端在血管骨架中剪切下来，闭塞部位即血管内造影剂缺失的部位。剪切节段的长度即作为血栓的参考长度。应用 0.625mm 层厚重建的 NECT 影像对 HMCAS 进行量化，其结果作为血栓体积的参照标准。再分别应用如前描述的 1.25mm 和 2.5mm 层厚重建的 NECT 影像，对血栓体积进行量化。两位神经放射学医师分别测量所有患者的血栓长度和体积，并评价其一致性。

统计分析
首先，对受试者的个人数据进行整理分析。其次，对血栓长度和体积测量结果的可接受水平进行定义。基于典型 NECT 的横切面上像素宽度大约为 0.5mm，并且血栓的每侧边界都相应会有 1 个像素的误差，因此，我们认为其可接受的水平为 ± 1 mm。假定 MCA 的直径为 2.5 mm，同时血栓长度测量的可接受范围为 ± 1 mm，那么我们则可定义血栓体积测量的可接受水平为 ± 10 mm³。随后，对于两位神经放射学医师关于血栓体积和长度的判读结果，应用 Bland-Altman 分析比较两组数据之间的一致性。因此，根据两者测量数据间的差值，计算出差值的均数及 95% 一致性界限的上下限。应用同样的方法比较血栓长度和体积测量结果与参照值之间的一致性。应用 Bland-Altman 描绘图评价不同层厚重建的 NECT 影像关于血栓长度及体积的测量结果与参照值之间的差别范围。对与参照值一致性较好、可独立应用的数据，应用配对 t 检验分析其一致性界限上下限的可信区间。最后，差值的均数和 95% 一致性界限的上下限分别与上述所定义的可接受水平进行比较，最终确定可以精确地测量出血栓长度和体积的 NECT 的适宜层厚。

结果
受试患者
共有 58 例患者符合入选标准，其中 36 例为男性，中位年龄为 62 岁（范围 43-79 岁）。所有入选患者均经 CTA 影像证实存在 MCA 闭塞，其中部分患者为单纯 MCA 主干闭塞，其余患者为 MCA 主干至同侧颈内动脉床突上段闭塞。

图像处理
所有患者 NECT 影像数据的预处理均需围绕前循环血管选择一个感兴趣区，以便感兴趣区内的血管内高密度成为致密的种子点。应用种子区域生长法，采用 1.25mm 和 2.5mm 的重建层厚，但在所有患者均可以显示出界限清楚的血栓。当重建层厚选择 3.75mm 和 5mm 时，则分别有 4 例（4/58, 6.9%）和 14 例（14/58, 24.1%）患者未显示出血栓影像。

血栓栓子的定量分析
两位神经放射学医师对于血栓长度和体积判读结果之间的差异处于预先定义的可接受水平之内。血栓长度的平均差为 0.2mm（一致性界限：± 0.6mm）；血栓体积的平均差为 2.3mm³（一致性界限：± 4.3mm³）。

Bland-Altman 描绘图显示了不同 NECT 重建图像中实际测量的血栓长度与参照长度之间的差值（图 2）。图 3 则为血栓体积测量值与参照值间的比较。所有关于血栓长度及体积测量的平均差、一致性界限及其可信区间的详细数据已在本文表中列出。
如图2所示，以1.25 mm和2.5 mm层厚的重建影像测量的血栓长度，其结果与参照值有很好的符合度，该方法可以独立应用。应用t检验对可独立应用的数据进行分析，一致性界限和其上下限的可信区间均处于预先定义的可接受的±1 mm水平内。此外，这两组结果与参照值之间的平均差非常接近于0。当NECT的重建层厚超过2.5 mm时，血栓长度的平均差也随之升高，超过了可接受水平的上限，并且一致性超出可接受水平4个单位以上。

图2 Bland-Altman图显示了应用CTA影像得出的血栓长度参照值(TL_reference)与应用NECT重建影像中HMCAS测量的血栓长度值(TL_mm)之间的差别。NECT的重建层厚(sw)分别为1.25 mm(A)、2.5 mm(B)、3.75 mm(C)和5 mm(D)。根据两个长度测量结果的均值描绘其差别。虚线代表了差值的均数，实线代表95%一致性界限的上下限。

尚未得出可评价血栓体积的足够精确的测量结果。

讨论

本研究结果显示对标准头颅NECT数据应用普通影像后处理工具以≤2.5 mm的层厚进行重建，此方法可以准确测量Willis环水平脑动脉中的血栓长度。然而，本研究中采用的几种重建层厚按照同样的方法，却并不能准确测量出血栓的体积。分析其原因可能是由于随着重建层厚的增加，HMCAS空间范围的部分容积效应也存在不同的影响。然而，部分容积的平均值对用于血栓长度测量的中心轴仅有一定的影响。仅当CT的层厚超过2.5 mm时，才
表 1 应用 1.25 mm、2.5 mm、3.75 mm 和 5 mm 层厚重建的 NECT 影像测量的血栓长度和体积值与参照值之间的 Bland-Altman 分析结果

<table>
<thead>
<tr>
<th>NECT 层厚</th>
<th>1.25 mm</th>
<th>2.5 mm</th>
<th>3.75 mm</th>
<th>5 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>血栓长度, mm</td>
<td>差值的均数</td>
<td>-0.1</td>
<td>0.1</td>
<td>4.2</td>
</tr>
<tr>
<td>一致性界限：上限 / 下限</td>
<td>0.6/-0.7</td>
<td>0.8/-0.5</td>
<td>10.6/-2.2</td>
<td>12.3/0.1</td>
</tr>
<tr>
<td>可信区间：上限 / 下限</td>
<td>0.7/-0.8</td>
<td>0.9/-0.6</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>血栓体积, mm³</td>
<td>差值的均数</td>
<td>10.3</td>
<td>31.6</td>
<td>47.0</td>
</tr>
<tr>
<td>一致性界限：上限 / 下限</td>
<td>16.4/4.2</td>
<td>37.7/25.4</td>
<td>53.1/40.8</td>
<td>61.9/49.6</td>
</tr>
<tr>
<td>可信区间：上限 / 下限</td>
<td>17.3/3.3</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>
的血栓负担。这些结果大大鼓舞了研究人员为急性卒中患者建立一个有价值的新的诊断参数。我们研究结果显示同样的技术也适用于标准薄层 NECT 数据，并且不需要额外的扫描。此外，本研究还确定了应用种子生长方法描述血栓节段的灰度等级图。这些结果与早期研究报道的血栓密度值之间有良好的一致性。与之前关于血栓体积评价的研究相比，本研究结果显示血栓长度与体积的测量结果更加准确。最近，有研究显示应用 CTA 影像的闭塞评分系统可对血管内的血栓程度进行评分，并且其评分已经被用作为判断患者结局的预后参数。这些系统将不同的血管节段与评分相联系，同时评分系统与治疗效果和患者预后结局之间已经显示了良好的相关性。我们的研究技术可能会以更加可重现的方式，促进这些关于血栓负荷系统的评价。

因此，我们已确定了一个新的处理急性缺血性卒中结果参数可以直接描述患者的状态和疾病的发展。这一技术在大多数具有高分辨探测器的多排 CT 检查设备的卒中单元中都可以直接应用。应用标准扫描规程可以直接对薄层 NECT 影像进行重建。因此，血栓长度分析所需要的数据不必额外的辐射量，并且图像重建所需要的时间很短，可忽略不计。鉴于本研究的目的在于确定简便的临床和影像参数，用于指导急性卒中患者的治疗，因此，进行低剂量的血栓负荷作为一个标准参数，可能被纳入急性缺血性卒中治疗指南。血栓长度可能是决定治疗决策的一个有用参数，尤其对于判断哪些患者的静脉内溶栓治疗不能使血管再通会有帮助。如果此参数能够被广泛接受，可能进一步指导溶栓治疗决策的选择。我们的研究能够确定一个血栓长度的界限，如血栓长度在此界限之上，则溶栓剂不能穿透整个血栓范围，导致静脉内溶栓治疗极易失败。那么这一界限将作为对判断急性缺血性卒中患者选择最佳的治疗策略。

### 参考文献


### 结论

总的 NECT 薄层重建技术可以准确地评价血栓长度，并且急性卒中患者的 NECT 影像的操作规程易于推广。闭塞的长度可预测患者的预后和静脉内溶栓治疗的成功率。期待随后的研究能够确定一个血栓长度的界限，如血栓长度在此界限之上，则溶栓剂不能穿透整个血栓范围，导致静脉内溶栓治疗极易失败。那么这一界限将作为评价进行静脉溶栓治疗的阈值。因此，下步的研究将着重显示在大样本人群中此技术的可行性。还应将研究人群的治疗计划和临床结局纳入分析，以判断是否动脉内密度征可帮助急性缺血性卒中患者选择最佳的治疗策略。