Patients with substantial internal carotid artery (ICA) narrowing are at an increased risk of transient ischemic attack and ischemic stroke in the carotid territory of the brain. Treatments for ICA stenosis include carotid endarterectomy (CEA) or carotid artery stenting (CAS), depending on the category of stenosis. Several major randomized controlled trials involving CEA or CAS, in both symptomatic and asymptomatic patients with ICA stenosis, have attempted to address the effects of surgery in preventing major stroke. As a result, the various benefits of these methods have been established and reported. A typical method of ICA stenosis quantification using digital subtraction angiography (DSA) is described in the report on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) angiographic method. A novel ultrasonography measurement of internal carotid artery stenosis: comparison with the North American Symptomatic Carotid Endarterectomy Trial angiographic method

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Introduction

Patients with substantial internal carotid artery (ICA) narrowing are at an increased risk of transient ischemic attack and ischemic stroke in the carotid territory of the brain. Treatments for ICA stenosis include carotid endarterectomy (CEA) or carotid artery stenting (CAS), depending on the category of stenosis. Several major randomized controlled trials involving CEA or CAS, in both symptomatic and asymptomatic patients with ICA stenosis, have attempted to address the effects of surgery in preventing major stroke. As a result, the various benefits of these methods have been established and reported. A typical method of ICA stenosis quantification using digital subtraction angiography (DSA) is described in the report on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) angiographic method. A novel ultrasonography measurement of internal carotid artery stenosis: comparison with the North American Symptomatic Carotid Endarterectomy Trial angiographic method

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Internal carotid artery (ICA) stenosis is a cause of stroke. ICA stenosis is generally measured using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) angiography method, though ultrasonography (US) is often used in practice. This study aimed to identify the correlation between ultrasonographic and angiographic findings in the calculation of ICA stenosis degree using the NASCET method. US and angiography were performed in 42 patients. The ICA stenosis grades calculated using the angiographic NASCET method were compared to those from ultrasonographic findings of longitudinal views (Longitudinal axis NASCET method), transverse views (Transverse axis NASCET method), and the peak systolic velocity (PSV method). The values obtained on the Transverse axis NASCET method ($r = 0.80, p < 0.01$), the Longitudinal axis NASCET method ($r = 0.74, p < 0.01$), and the PSV method ($r = 0.75, p < 0.01$) significantly correlated with the percent stenosis measured by the angiographic NASCET method. The error of the Transverse axis NASCET method was significantly lower than that of the Longitudinal axis NASCET method ($p = 0.022$). The Transverse axis NASCET method is more closely correlated with the angiographic NASCET than the Longitudinal axis NASCET or PSV methods.

Keywords: internal carotid artery stenosis, NASCET, ultrasonography

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tomy Trial (NASCET). Although DSA based on the NASCET method is conventionally used to assess the grade of ICA stenosis, the method is not suitable for screening because of its invasiveness. In fact, cerebral angiography carries a 0.5–5% risk of causing permanent neurologic deficits.

On the other hand, magnetic resonance angiography (MRA) has been reported to have an excellent correlation (almost equal to DSA) with the measurement of ICA stenosis. However, MRA is contraindicated for patients with claustrophobia or implanted metal and is therefore not appropriate for everyone. As a result, non-invasive techniques with few contraindications, such as ultrasonography (US), are useful.

US has shown excellent reproducibility in the assessment of ICA stenosis, and is usually used as a first-line investigational technique in practice. US can also be used to estimate the plaque properties of the lesion site. In Japan, the grade of ICA stenosis is evaluated in respect to US using the following four techniques: area stenosis, European carotid surgery trial (ECST), NASCET, and peak systolic velocity (PSV) methods. Previously, several authors have reported a good correlation between the PSV and angiography methods.

The grade of ICA stenosis on the US image is generally calculated using the NASCET method on the basis of measurement of the degree of diameter of the stenosis in longitudinal views (Longitudinal axis images). However, the values measured by the US image and those measured by DSA are often different. One of the reasons is that it is difficult to accurately visualize the blood vessel lumen in the meandering artery using longitudinal views. The accuracy of the NASCET method using US images is sometimes poor, particularly in patients with ICA tortuosity or obscure distal ICA images.

For that reason, we postulated that transverse views (Transverse axis images) might allow for more accurate delineation of the degree of luminal reduction at the narrowest part of the stenosis, resulting in a more accurate prediction of the grade of ICA stenosis.

The purpose of this study is to compare the calculations of ICA stenosis based on US Longitudinal axis images, Transverse axis images, and the PSV method with those based on angiographic views (DSA or MRA) obtained using the NASCET method.

### Subjects and Methods

1. **Patients**

We prospectively analyzed the DSA/MRA and US data of 42 patients at Kansai Electric Power Hospital (39 males and 3 females; mean age: 72 years; range 46–87 years) examined between May 1, 2013 and April 30, 2014. Fifty-one carotid arteries were found to be stenosed. Nine arteries with massive plaque calcification found by B-mode imaging were excluded due to technical issues.

2. **Ultrasonography**

The US procedure was performed by experienced clinicians using an Apio 500 (Toshiba Medical Systems, Tochigi, Japan) or Prosound F75 (Hitachi, Tokyo, Japan) diagnostic ultrasound system with high-frequency linear probes in accordance with the Japanese guidelines.

Three independent, experienced observers measured the degree of stenosis of the carotid artery using each of the methods. Each observer was blind to the measurements made by the other observer and to the clinical details. The Doppler gain was adjusted such that the blood flow signal was clearly confirmed and no noise appeared. When color Doppler images showed stenotic lesions on US images, the sample volume was moved slowly, proximally to distally, in the ICA stenosis to obtain the optimal portion. The time phase for measuring color Doppler is diastolic basically.

The degree of ICA stenosis was calculated using the area stenosis, ECST, and PSV methods in addition to the NASCET method in order to compare the US imaging with the angiographic imaging (DSA/MRA). Briefly, in the NASCET method with angiographic imaging, the minimal residual ICA diameter ($D_s$) and the normal ICA diameter ($D_n$) distal to the stenosis were measured (Fig.1A), and the degree of stenosis was calculated as $(1 - [D_s/\bar{D}_n]) \times 100$. On US longitudinal axis images, $D_s$ was also defined as the minimal residual ICA, and $D_n$ was defined as the normal ICA diameter distal to the stenosis, as shown in Fig.1B. The degree of stenosis was described in the Longitudinal axis NASCET using the same equation. Furthermore, on US transverse axis images, $D_s$ and $D_n$ were defined as the minor axes of the transverse views (Fig.1C). This value was described as the Transverse axis NASCET.

To measure blood flow velocity on the longitudinal scans, a 3–7 mm sample was displayed linearly in the ICA. When the color Doppler images showed the narrowest stenotic
lesions on the US Longitudinal axis images, the sample volume was moved to obtain the highest flow velocity.

3. DSA and MRA

DSA was performed using Artis zee BA Twin (SIEMENS, Munich, Germany), and MRA was performed using MAGNETOM Skyra (SIEMENS) angiography systems.

4. Data analysis

To compare the angiographic NASCET, Longitudinal axis NASCET, Transverse axis NASCET, area stenosis, ECST, and PSV methods, linear or best-fitting nonlinear regression analyses were performed according to the formula $y = a + bx$, where $y$ is the dependent and $x$ is the independent variable (i.e., one of the four methods), $a$ is the intercept, and $b$ is the slope. Errors were calculated on the basis of the differences between the angiographic and ultrasonographic NASCET results. Sensitivity, specificity, predictive values, and likelihood ratios were calculated to characterize the ability of the US methods to detect moderate or severe stenosis as defined by the angiographic NASCET method. In the NASCET method, stenosis was classified as mild (0–49% stenosis), moderate (50–69% stenosis), severe (70–99% stenosis), or complete occlusion. For the PSV method, stenosis was classified as mild ($< 150$ cm/s), moderate ($150–200$ cm/s), or severe ($> 200$ cm/s).

Descriptive variables were summarized by means of medians and standard deviations, and tested using Student’s $t$-tests as appropriate. Statistical significance was defined as $p < 0.05$.

**Results**

The correlation between stenosis demonstrated by the Transverse axis NASCET method and the area stenosis method was $0.81$ ($p < 0.01$), and the correlation between the Transverse axis NASCET method and the ECST method was $0.78$ ($p < 0.01$) (Fig.2). The values obtained on the Transverse axis NASCET method ($r = 0.80, p < 0.01$), the Longitudinal axis NASCET method ($r = 0.74, p < 0.01$), and the PSV method ($r = 0.75, p < 0.01$) significantly correlated with the percent stenosis measured by the angiographic NASCET method (Fig.3). The correlation coefficient using the former method was greater than those obtained using the latter methods, but there were no statistically significant differences in the correlation coefficients between the three groups ($p = 0.55$ for the Transverse axis NASCET method versus the Longitudinal axis NASCET method, and $p = 0.61$ for the Transverse axis NASCET method versus the PSV method). The difference mean ($\pm$SD) between the Transverse axis NASCET and the angiographic NASCET was $9.57 \pm 0.9\%$, while the difference between the Longitudinal axis NASCET and the angiographic NASCET was $11.11 \pm 1.3\%$. Thus, the error range of the Transverse axis NASCET method was found to be significantly lower than that of the Longitudi-
Fig. 2 Scatterplots
A: Showing the correlation between the degree of stenosis by Transverse axis NASCET and Area stenosis methods \( (r = 0.81, p < 0.01) \).
B: Showing the correlation between the degree of stenosis by Transverse axis NASCET and ECST methods \( (r = 0.78, p < 0.01) \).

Fig. 3 Scatterplots
A: Showing the correlation between the degree of stenosis by angiographic and Longitudinal axis NASCET methods \( (r = 0.74, p < 0.01) \).
B: Showing the correlation between the degree of stenosis by angiographic and Transverse axis NASCET methods \( (r = 0.80, p < 0.01) \).
C: Showing the correlation between the degree of stenosis by peak systolic velocity and angiographic NASCET methods \( (C) \) \( (r = 0.75, p < 0.01) \).
The diagnostic performance of the three methods in identifying moderate or severe stenosis using DSA/MRA is summarized in Table 1. There were no significant differences between the 3 methods in terms of sensitivity, specificity, positive predictive value, or and negative predictive value. However, the positive likelihood ratio was 3.3 for the Longitudinal axis NASCET, 4.1 for the Transverse axis NASCET, and 2.8 for the PSV method. The negative likelihood ratio was 0.28 for the Longitudinal axis NASCET, 0.26 for the Transverse axis NASCET, and 0.32 for the PSV method (Table 1).

**Discussion**

In the present study, the US parameters for the Longitudinal axis NASCET, Transverse axis NASCET, and the PSV methods were found to correlate well with the degree of ICA stenosis determined by the angiographic NASCET method. In particular, the correlation and error range were better for the Transverse axis NASCET method than for the Longitudinal axis NASCET or PSV methods. Furthermore, the positive and negative likelihood ratios for identifying moderate or severe stenosis using DSA/MRA were better in the Transverse axis NASCET method compared to the other two US methods. It seems likely that the Transverse axis NASCET method using US images provides a better assessment of ICA stenosis than the Longitudinal axis NASCET and PSV methods in practice.

The Transverse axis NASCET method presented in this study used the diameter of the narrowest vessel lumen diameter in the transverse axis image of the ICA and the diameter of the peripheral side as measurement values. On the other hand, the NASCET method used conventionally in US uses the longitudinal image of ICA. In this case, it is possible that the narrowest part could not be accurately measured, e.g., in cases where the shape of the lumen of the lesion is irregular, close to the vessel wall, or in meandering cases. These failures do not occur in the Transverse NASCET method because the method evaluates the transverse image. We hypothesize that the Transverse axis NASCET method performed better because of these factors.

However, there are limitations to the Transverse axis NASCET method. Calcified lesions are a serious limitation. As a result, the PSV method is still recommended. Neither the area stenosis nor the ECST or NASCET methods can be used if the vascular lumen cannot be imaged by calcification. On the other hand, the PSV method also has limitations. For example, PSV cannot be used in cases with high-grade stenosis on the contralateral side or in cases of cardiac disease. Furthermore, the experience of the observer may cause errors in measurement speed due to the characteristics of the ultrasonic device. The observer must recognize the limitations of each method in order to properly evaluate the lesion.

Depending on disease severity, patients with ICA stenosis may undergo CEA or CAS in order to reduce the risk of suffering fatal ischemic stroke. Patients with moderate (50–69% stenosis) or severe symptomatic stenosis...
(> 70%) should receive surgical treatments in addition to the best medical care. The efficacy of surgical treatments in addition to the best medical care for patients with asymptomatic stenosis (> 60% stenosis) has been reported by several authors. Therefore, cases of moderate or severe stenosis must be identified.

In the present study, we found that using Transverse axis US images is useful for the accurate measurement of moderate or severe stenosis. By combining the Transverse axis NASCET with other US methods, we believe that ultrasonic devices can become more accurate diagnostic tools. To make the US parameters more clinically indispensable, observers should consider using the Transverse axis NASCET method as one of the US methods.

Conclusions

All US parameters in the present study were found to correlate well with the degree of ICA stenosis determined by the angiographic NASCET method, including DSA and MRA. In particular, the Transverse axis NASCET method closely correlated with the angiographic NASCET method. We believe that the use of a combination of US parameters in the study plays an important role in the accurate assessment of the degree of ICA stenosis.

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Disclosure Statement

The authors have no conflicts of interest directly relevant to the content of this article.

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