Evaluation of the Usefulness of Multidetector Computed Angiography for the Diagnosis of Extracranial Internal Carotid Artery Stenosis by Comparing with Digital Subtraction Angiography

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Abstract
Among patients who were diagnosed with extracranial internal carotid artery stenosis and underwent carotid stenting procedures, patients that underwent both Digital Subtraction Angiography (DSA) and Multidetector Computed Tomography Angiograms (MCTA) were compared for usefulness in the assessment of extracranial internal carotid artery stenosis was evaluated. Between August 2005 and December 2013, 80 patients were diagnosed with extracranial internal carotid artery stenosis by both DSA and CTA (MCTA), and underwent carotid stenting procedures. A retrospective review was performed on these patients. The degree of artery stenosis was evaluated by the method of the North American Symptomatic Carotid Endarterectomy Trial collaborators (NASCET). The degree of stenosis was classified into 3 levels: 0 -31 % (mild), 31 - 71 % (moderate), and 71 - 100 % (severe). Both DSA and CTA classified the same 7, 52, and 21 patients as having ‘mild’, ‘moderate’, and ‘severe’ stenosis, respectively. The average percent diameter stenosis was not different between DSA and CTA (p≥0.05). An average stenosis of 56.37 ± 18.67 % was obtained by DSA, and an average of 55.14 ± 18.13 % was obtained by CTA (MCTA). In conclusion, for the diagnosis of extracranial internal carotid artery stenosis, DSA test is invasive and the risk of side effects is high whereas CTA (MCTA) is relatively non-invasive, the test time is short, and the risk of side effects is low.

Keywords: Extracranial Internal Carotid Artery, Digital Subtraction Angiography(DSA), Multidetector Computed Tomography Angiography(MCTA), North American Symptomatic Carotid Endarterectomy Trial collaborators (NASCET).

INTRODUCTION
Cerebrovascular disease is a major cause of death worldwide. According to the data reported by the bureau of , in Korea, cerebrovascular disease was the second leading cause of death in 2014 [1]. Additionally, it is a significant cause of disabilities in the geriatric population. Therefore, in the aging modern society, substantial medical expenses are spent for cerebrovascular diseases every year, which results in social burdens and 14 economical loss [2]. Reportedly, extracranial internal carotid artery lesions are the cause in 20~30% of ischemic stroke cases [3, 4]. Atherosclerotic carotid stenosis is the most common cause of cerebral infarction. In the past half century, efforts have been made to prevent cerebral infarction by widening blood vessels and improving blood flow. Since 1953, carotid endarterectomy has been performed widely as the first-line treatment procedure for carotid artery stenosis [5]. In 1980, carotid angioplasty using a balloon catheter was reported, and begun to be used limitedly for inoperable patients [6, 7]. Initial functional changes of atherosclerosis are reductions of the local availability of nitric oxide released from damaged vascular endothelial cells, increased expression of cell adhesion molecules, alteration of inflammatory markers, cytokine production, and peroxidation of lipoprotein [8, 9]. Although the structural alteration of vascular wall appears later than functional changes, changes such as the thickening of vascular wall and calcification are manifest a few years earlier than clinical symptoms do [10]. In this respect, it is very important to detect and treat cerebrovascular diseases as early as possible. Characteristically, the symptoms of cerebral infarction are neurological defects such as quadriplegia, dysaesthesia, visual disturbance, aphasia, ataxia, sphincter deficiency, pronounced disorder, behavioral disorders, and vascular dementia. Once the symptoms develop, complete cure is difficult, and severe impairments mostly remain. Thus, the importance of early diagnosis has been raised. Among various methods to diagnose and assess atherosclerotic carotid artery stenosis, cerebral angiography applying Digital Subtraction Angiography (DSA) is the most accurate diagnosis method. However, in consideration of the risk of development of side effects in the central nervous system due to the invasiveness of the test itself and the use of contrast agents, and because of long test duration, DSA cannot be used occasionally emergency patients [11]. Recently, with the development of
ultrasonography, Magnetic Resonance Image (MRI), and Computed Tomography (CT), non-invasive diagnostic techniques have gradually been applied in clinics. Particularly, Multidetector Computed Tomography (MDCT) provides high resolution vascular images a short time, it is of great help for the diagnosis for not only cardiovascular diseases but also intracranial and extracranial internal carotid artery stenosis [12-15]. In our study, the diagnostic value in the assessment of the degree of extracranial internal carotid artery stenosis was compared between MDCT and DSA.

RESEARCH SUBJECTS AND METHODS

A. Research subjects
Selected from patients who visited our hospital from August 1, 2005, to December 31, 2013, diagnosed as extracranial internal carotid artery stenosis by cerebral digital subtraction angiography, and who underwent carotid artery stenting procedures, the subjects were 80 patients who received Multidetector Computed Tomography Angiography (Fig. 1).

Figure 1. An angiographic image after carotid artery stent insertion procedures upon the diagnosis of intracranial internal carotid artery stenosis

B. Experiment equipment and research methods
For cerebral angiography, the Bi-plane DSA (Axiom Artis / dBA RF-1000-125, SIEMENS, Munich, Germany) was used. Experiment conditions were 1200 cm Distance source to detector, 0.153 mm Image pixel spacing, 0.3 mm Focal spot, 75 kVp, and 800 mA. For analysis, the software VB31E080813 (SIEMENS, Munich, Germany) was used.

The non-ionic contrast agent Ultravist (Bayer Korea, Seoul, Korea) was administered using an automatic injector. The injection rate for the external carotid artery was 5ml/sec, and a total 7ml contrast agent was injected. The injection rate for the internal carotid artery was 4ml/sec, with a total of 4ml contrast agent. The injection rate for the vertebral artery was 3ml/sec, with a total of 5ml contrast agent was injected. For computed tomography angiography, Definition (WCT-500-140, SIEMENS, Munich, Germany) 64 Detector was used. The detailed experiment conditions were 0.6mm Slice, 0.5mm Interval, 120 kVp, 1.2 mm Focal spot, H31s algorithm, and 0.6mm/0.5mm Recon. The non-ionic contrast agent Ultravist was injected using an automatic injector at an injection rate of 4.5ml/sec with a total of 90ml contrast agent. When the common carotid artery reached 100HU (Hounsfield Unit), the scan was initiated after 6 seconds of delayed time. After the scanning, images were reconstructed with the volume rendering technique (CT VRT) from the CT Row Data.

The input for the volume rendering algorithm was a 3D array of scalars. The array is called a volume, and each element of the array is called a voxel. Although some volume rendering algorithms assume that each voxel represents a small cube in space with a constant scalar value, we assumed a voxel to represent a point sample of a continuous scalar function. Volume rendering is an approximate simulation of the propagation of light through a participating medium represented by the volume (Fig. 2) [16].

\[ \vec{V} \cdot \nabla L(r, \omega) = -\Phi_t(r)L(r, \omega) + \epsilon(r, \omega) + \int_{S} \kappa(r, \omega' \rightarrow \omega) L(r, \omega') d\omega' \]

(1)

\( \Phi_t(r) \) is the extinction coefficient (with units of m\(^{-1}\)) which equals the probability per unit distance that a photon traveling along the ray will be either absorbed or scattered into a different direction by the volume. 

\( \epsilon(r, \omega) \) is the emission function (with units of W/m\(^4\)-sr) that accounts for photons emitted within the volume.

\( \kappa(r, \omega' \rightarrow \omega) \) is the scattering kernel (with units of sr\(^{-1}\)/m\(^3\)) which is the probability per unit solid angle per unit distance that a photon moving in direction \( \omega' \) will scatter into direction \( \omega \). We integrated this function against the incoming radiance from all directions (denoted by \( S^{2} \_m \)) to account for the photons scattered into the ray.
Equation 1 is a first order differential equation known as the differential form of the equation of transfer. It can be written in the equivalent integral form [16]:

\[ L(r, \omega) = e^{-\tau(r, r_B)} L_B(r_B, \omega) + \int_{r}^{r_B} L(r', \omega) Q(r', \omega) \, dr' \]  

(2)

\( \tau(r, s) \) is the integral of the extinction coefficient along the straight-line path between points \( r \) and \( s \) [16]:

\[ \tau(r, s) \equiv \int_{r}^{s} \phi_t(r', \omega) \, dr' \]  

(3)

The path between the two points is denoted by \( \tau(r, s) \). The \( e^{-\tau(r, s)} \) is the integrating factor used to convert Equation 1 into Equation 2.

\( L_B(r, \omega) \) is a function specifying boundary conditions over a closed surface surrounding the volume. The point _ED is the intersection between the closed surface and the ray from _in direction \( \omega \).

\( Q(r, \omega) \) is short-hand for the sum of the emission and scattering terms [16]:

\[ Q(r, \omega) \equiv \epsilon(r, \omega) + \int_{2}^{\omega} s \kappa(r, \omega') L(r, \omega') \, d\omega' \]  

(4)

This function can be thought of as a generalized source function that accounts for all of the gains in the energy balance equation.

With all four assumptions, Equation 2 reduces to the volume rendering equation [16]:

\[ L(x) = \int_{x}^{x_B} e^{-\int_{x}^{x'} \phi_t(x'')}} d x' \epsilon(x) \, dx' \]  

(5)

In this equation the radiance in terms of a one-dimensional position variable \( x \) representing distance along a viewing ray. The upper limit of integration is \( x_B \), the point at which the ray exits the volume [16] (Fig. 3).

For the measurement of blood vessels, Marosis M-view (Infinitt healthcare, Seoul, Korea) was applied; the vascular test angle of extracranial internal carotid artery angiography and the vascular test angle of VRT imaging were superimposed (or overlapped), and stenosis sites as well as the degree of stenosis were assessed (Fig. 4). The rate (degree) of stenosis was calculated by measuring the area with the most severe stenosis and the normal blood vessel in the distal area of stenosis site according to the guidelines of the North American Symptomatic Carotid Endarterectomy Trial collaborators (NASCET) [17].

\[ \text{NASCET} = \left(1 - \left(\frac{A}{B}\right)\right) \times 100 \% \]  

(6)

Where, \( A \) is the area of blood vessel in the stenosis area, and \( B \) is the area of normal blood vessel in the distal area of the stenosis area.

The calculated stenosis rate was classified into 3 levels: 0 - 30.9% (mild), 31 - 70.9% (moderate), and 71 - 100% (severe). The differences in the vascular stenosis were compared between cerebrovascular angiography and computed tomography angiography.

**C. Data treatment and analysis**

Based on general characteristics of the subjects, technical statistics and a frequency analysis were performed. To analyze the stenotic areas and the stenosis extent, the frequency analysis was performed between the two angiography methods. To assess the difference in the degrees of stenosis between the two test methods, \( t \)-test was conducted. The data was analyzed using the SPSS 18.0 (SPSS, Chicago, USA), with a 95% confidence level (\( p < 0.05 \)).
RESULTS

A. The characteristics of research subjects
As stated above, 80 patients had undergone both DSA and MCTA, among whom 60 were males and 20 were females. The mean age was 71.90 ± 8.74 years for males, 71.00 ± 8.62 years for females.

B. The characteristics of the type of stenosis
Regarding the angle to measure stenosis, RAO was 42.5 %, LAO 32.5 %, LAT 17.5 %, and AP 7.5 %. RAO showed the highest frequency, and AP showed the lowest frequency. As for laterality, there were 34 stenoses on the left side and 46 on the right (Table 1).

Table 1. Characteristics of stenosis type

<table>
<thead>
<tr>
<th>Variables</th>
<th>Classification</th>
<th>Frequency(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement Angle</td>
<td>AP</td>
<td>6(7.5)</td>
</tr>
<tr>
<td></td>
<td>LAT</td>
<td>14(17.5)</td>
</tr>
<tr>
<td></td>
<td>LAO</td>
<td>26(32.5)</td>
</tr>
<tr>
<td></td>
<td>RAO</td>
<td>34(42.5)</td>
</tr>
<tr>
<td>Location of Stenosis</td>
<td>LT</td>
<td>34(42.5)</td>
</tr>
<tr>
<td></td>
<td>RT</td>
<td>46(57.5)</td>
</tr>
</tbody>
</table>

C. Comparison of the stenosis rates and degrees according to equipments
The degree of stenosis was assessed using images obtained by DSA and CTA. Then, the patients were classified according to the degree of stenosis into 3 levels by NASCET (%). Both images revealed the same patients as having ‘Mild’ stenosis in 7 patients, ‘Moderate’ in 52 patients, and ‘Severe’ in 21 patients. There were no differences in patient classification between the angiography methods. On t-test analyses of all 3 types of classification, no significant difference was found between the two tests (p > 0.05). In conclusion, the rates of stenosis for DSA and 55.14 ± 18.13 % for CTA, without a significant difference was found between the two tests (p > 0.05). (Table 2). In addition, due to its invasiveness, complications have been reported, such as bruise or rupture of blood vessels, local hematoma, allergy, high fever, sepsis, and cerebral ischemia [19].

Table 2. Comparisons of the rate and degree of stenosis assessed on DSA and CTA

<table>
<thead>
<tr>
<th>Classification</th>
<th>Mean ± SD</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DSA</td>
<td>CTA</td>
<td>DSA - CTA</td>
</tr>
<tr>
<td>Mild</td>
<td>18.80 ± 7.67</td>
<td>21.22 ± 5.83</td>
<td>-2.43 ± 5.81</td>
</tr>
<tr>
<td>Moderate</td>
<td>52.97 ± 11.74</td>
<td>51.06 ± 11.49</td>
<td>1.91 ± 9.6</td>
</tr>
<tr>
<td>Severe</td>
<td>77.31 ± 4.84</td>
<td>76.58 ± 4.88</td>
<td>0.73 ± 4.99</td>
</tr>
<tr>
<td>Total</td>
<td>56.37 ± 18.67</td>
<td>55.14 ± 18.13</td>
<td>1.22 ± 6.46</td>
</tr>
</tbody>
</table>

DISCUSSION
An acute cerebral infarction caused by proximal internal carotid artery blockage or severe stenosis is associated with a high mortality rate and results in severe sequelae. Since internal carotid artery stenosis induced by the continuous progression of atherosclerosis is directly associated with the development of cerebral stroke, early diagnosis is important and should be given attention. Since Moniz successfully conducted cerebral angiography for the first time in 1927 [18], it has become the most important test for the diagnosis of cerebral aneurysm, cerebral arterial stenosis, and other cerebrovascular diseases. However, it is difficult to assess an accurate anatomical structure through cerebral angiography if blood vessels are turned around or overlapped. In addition, due to its invasiveness, complications have been reported, such as bruise or rupture of blood vessels, local hematoma, allergy, high fever, sepsis, and cerebral ischemia [19]. The incidence of complications in the central nervous system reaches approximately 0.1 -2.6 % in healthy individuals undergoing cerebral angiography [20]. Because of such problems, the non-invasive test methods of magnetic resonance angiography (MRA) and cerebral CT angiography have more recently been used for the diagnosis of cerebral artery stenosis and cerebrovascular diseases. Although the usefulness of MRA for intracranial vascular diseases has been accepted [21], its shortcomings are that if the neurological condition of patient is poor at the time of test or for patients with claustrophobia, the test is difficult, since the imaging time is long. Images may be distorted due to movements, and the test cannot be performed in patients wearing an artificial pacemaker or certain prostheses [22]. In comparison, cerebral CT angiography has become popular, which could potentially replace the conventional angiography [23, 24], and reports on the usefulness of cerebral CT angiography as a primary diagnosis tool are on the rise [25–27]. After 1980s, in cerebral angiography applying MDCT, spiral CT areas engaged in clinics were expanded to cerebral blood vessels [28]. According to previous reports, in comparison with magnetic resonance angiography (MRA), correlation of CTA with DSA is high, spatial resolution power of CTA is also high, influence on CTA from the flow of blood flow is small, and CTA provides more information of extra- as well as intra- blood vessels (29, 30).) In the past, similarly, studies on carotid artery stenosis applying CTA and its usefulness have been conducted. In countries except Korea, Josephson et al. [14], Bartlett et al. [15, 31] and other investigators have studied to carotid artery stenosis using CTA. Particularly, the study reported by Dillon et al. showed that CTA could deliver abundant information related to carotid artery stenosis [32]. According to the research results reported by Silvennoinen et al., correlation was high between DSA and CTA, and thus CTA was suggested to be an alternative to DSA in the assessment of carotid artery stenosis [33]. In Korea, researches have been conducted on carotid artery stenosis and on cerebral aneurysm using DSA and CTA [34]. The findings from previous studies support the usefulness of CTA, and consolidate the purports of the current study. Our current study is limited in that there is an inevitable peculiarity of the NASCET evaluation that measurement
areas and standard points are selected by investigators subjectively. However, this limitation was somewhat overcome through the method that one identical investigator selected and measured stenosis areas on DSA and CTA images, and a different investigator confirmed the measurement. Our study shows that CTA for the diagnosis of extracranial internal carotid artery stenosis is non-invasive in comparison with invasive DSA, provides high resolution blood vessel images within a short test period, and produces similar accuracies in the evaluation of external carotid arteries. Therefore, CTA can provide an important direction for the diagnosis of extracranial internal carotid artery stenosis, to establish treatment strategy, and to determine prognosis.

CONCLUSION
In the assessment of extracranial internal carotid artery stenoses, the stenosis rates were not significantly different between DSA and CTA. Therefore, in measuring the degree of stenosis for the diagnosis and treatments such as stent insertion procedures, due to the advantages that it is relatively user-friendly, time-effective, and suitable in emergency conditions, CTA will be applied increasingly, and considered to play an useful and important role continuously.

REFERENCES


