Ruptured cerebral aneurysm is a medical emergency, accounts for 80% of all spontaneous subarachnoid hemorrhages (SAHs), and can lead to a high rate of mortality and severe complications.1,20 Thus, prompt detection and treatment of cerebral aneurysm are extremely important for the patient’s prognosis.4 Currently, 3D digital subtraction angiography (DSA) is considered the gold standard for detecting cerebral aneurysms because of its high spatial resolution and large field of view.12,14,25 However, this technique is an invasive procedure associated with a small but definite risk of neurological morbidity and rebleeding.13,19,23 In addition, DSA needs to be performed by experts, especially in unstable patients. Therefore, it is very important to find an accurate noninvasive imaging method to diagnose cerebral aneurysms.

Multidetector CT angiography (CTA) is a noninvasive
Methods

Patient Population
Between February 2011 and August 2015, 721 patients with suspected cerebral aneurysm were enrolled in this study. Of these, 30 patients had previously undergone endovascular coiling or surgical clipping of cerebral aneurysms, and these 30 patients were excluded from this study. Another 29 patients did not undergo DSA due to rapid clinical deterioration and were also excluded. Thus, our study population consisted of 662 patients (338 men, 324 women; age range 18–91 years; mean age 56 years). Patients were assigned to VCTA by physician referral based on symptoms and signs suggestive of cerebral aneurysm.

Of the 662 patients, 402 patients had SAH; 71 had SAH and intraventricular hemorrhage; 38 had SAH and intraparenchymal hemorrhage; 36 had SAH, intraventricular hemorrhage, and intraparenchymal hemorrhage; 27 had intraparenchymal hemorrhage; and the remaining 88 patients had a variety of indications, including headache, ocular motor paralysis, tumor, and hydrocephalus. All VCTA and DSA examinations were performed within 3 days, without any intervening surgical or endovascular treatment. In no case was DSA performed only for the purpose of the present study. The study was approved by the institutional review board, and informed written consent was obtained from patients or from a close family member.

Protocol for 320-Detector Row VCTA Image Acquisition
All 662 patients underwent VCTA with a 320-detector row volume CT scanner (Aquilion ONE, Toshiba Medical Systems Corporation) using volumetric cine scanning without helical imaging. The patient was instructed to lie with eyes and mouth closed during the entire scan. The procedure was performed in the caudocranial direction from skull base to vertex. For VCTA, 50 ml of 370 mg I/ml iodinated contrast material (Ultravist; Bayer Schering Pharma) was injected at 5.0 ml/sec using an 18-gauge catheter inserted into the antecubital vein. This was followed by 20 ml of saline at the same rate. The CT scanning parameters were as follows: 320 × 0.5 mm detector width; 512 × 512 matrix; 180– to 240-mm field of view; 80-kV tube voltage; 300-mA tube current; and a total of 10 scans. Timing and scheduling of the dynamic scans were as follows. The first scan was made beginning 5 seconds after the start of the injection. This scan could be considered as a nonenhanced scan (the contrast has not yet arrived in the region of interest) and was used as a mask for postprocessing. The 9 continuous enhanced scans of VCTA were performed every 2 seconds beginning 12.8 seconds after the start of the injection. Thirty-six patients with agitation, confusion, or both were administered intravenous sedation, and no patient required general anesthesia before the VCTA examination.

The subtraction process was started by loading both the nonenhanced and enhanced data into the software of the console. Data from the 9 enhanced scans were subtracted and archived as 9 new DICOM files by applying the subtraction process. After loading of the subtracted files in the 4-dimensional application of the scanner, the images could be viewed in every desired direction like a DSA examination. The nonsubtracted and subtracted data were used for 3D visualization using maximum-intensity projection (MIP) and volume-rendering technique (VRT).

Protocol for DSA Acquisition
A standard biplane DSA unit with rotational capabilities (Artis Zee Biplane; Siemens Medical Systems) was used. Nonionic contrast material (Omnipaque 300 mg I/ml; Amersham Life Science) was injected with a power injector (Medrad). The runs consisted of a 38-cm field of view (anteroposterior), a 30-cm field of view (lateral and oblique), and a 1024 × 1024 matrix. The spatial resolution was 0.32 × 0.32 mm. Selective angiograms consisted of 1 anteroposterior, 1 lateral, and 1 or 2 oblique views. The 3D DSA acquisition was performed in bilateral ICAs, even if no aneurysm was visible on conventional angiography.

Review Process
All VCTA and 3D DSA images were independently evaluated by 5 neuroradiologists. Two readers (W.C. and C.W.) evaluated the nonsubtracted VCTA images and 2 readers (W.X. and Z.H.) evaluated the subtracted VCTA images. The 4 VCTA readers were blinded to the assessments of the other investigator, who only knew that these were patients with suspected cerebral aneurysm. Subtracted and nonsubtracted volume data were transported to a workstation (VOXAR; Toshiba Medical Visualization Systems) with VRT and MIP. Arterial phase images were selected by providing the best depiction of the aneurysm. The 4 readers assessed the presence of an aneurysm, its location, and its morphology. The image quality of subtracted VCTA was rated according to the following criteria: 1) excellent quality: images without apparent artifacts had sufficient quality for interpretation; 2) moderate quality: images had mild artifacts that did not interfere with interpretation; and 3) poor quality: images had severe artifacts that interfered with interpretation.

Upon completion of the procedure, the 3D DSA runs were immediately sent to an adjacent 3D workstation (InSpace; Siemens Medical Systems). After ascertaining the presence of cerebral aneurysm, the neuroradiologist reader (Q.W.) measured each aneurysm’s maximum diameter on 3D DSA images. The largest diameter of each aneurysm was measured in millimeters to 1 decimal place. Aneurysms < 3 mm in largest diameter were considered small cerebral aneurysms and included in this study. The 3D DSA reader assessed the presence, shape (saccular,
mastoid, or irregular), and location of the cerebral aneurysms.

**Statistical Analysis**

In this study, 3D DSA was considered the diagnostic standard of the cerebral aneurysms. Two-by-two tables were designed from true-positive, true-negative, false-positive, and false-negative results for 320-detector row nonsubtracted and subtracted VCTA compared with 3D DSA. Sensitivity, specificity, accuracy, and positive and negative predictive values were compared on a per-aneurysm basis. Two-sided 95% (exact) confidence intervals based on binomial probabilities were calculated for the 4 independent VCTA readers. Comparisons between groups were made by Fisher’s exact test. Differences with a p value < 0.05 were considered significant. All statistical analyses used Stata 9.2 for Windows (Stata Corp.).

**Results**

There were no technical failures during 320-detector row CT scanning. All subtracted VCTA images were diagnostic, with 642 cases judged excellent quality, 20 cases moderate quality, and no cases poor quality. The moderate quality was caused by incomplete bone subtraction due to head motion during the VCTA scanning.

**Small Cerebral Aneurysm Characteristics**

According to the 3D DSA results, 98 small cerebral aneurysms were confirmed in 90 of 662 patients (39 men, 51 women). No aneurysm was identified using 3D DSA in 246 patients: 198 negative findings, 32 arteriovenous malformations, and 16 moyamoya diseases. Ninety patients had at least 1 small cerebral aneurysm: 82 patients had 1 small aneurysm, and 8 patients had 2 small aneurysms.

Eighty-three small aneurysms were saccular, 12 were mastoid, and 3 were irregular in morphology. The most common location for all of the small aneurysms was the anterior communicating artery (29%, 28 of 98), and the second most common location was the internal carotid artery (ICA) (21%, 21 of 98).

**Accuracy of 320-Detector Row Nonsubtracted VCTA in Detecting Small Cerebral Aneurysms on a Per-Aneurysm Basis**

Nonsubtracted VCTA identified 90 small cerebral aneurysms (including both true-positive and false-positive) in 83 of 662 patients (37 men, 46 women) by the 2 independent readers. Ten small cerebral aneurysms found on 3D DSA were initially missed by the 2 nonsubtracted VCTA readers. The 10 small aneurysms were considered false-negative interpretations for nonsubtracted VCTA. When false-negative images were reviewed, 5 aneurysms were displayed on the nonsubtracted VCTA images (Fig. 1), and the other 5 aneurysms were still not detected (Fig. 2). Two small aneurysms shown on nonsubtracted VCTA were not detected by 3D DSA. These 2 small aneurysms were considered false-positive interpretations for nonsubtracted VCTA.

Data on false-negative and false-positive small aneurysms of nonsubtracted VCTA are listed in Table 1 for readers 1 and 2. The results of the 2 nonsubtracted VCTA readers were consistent, and the results of only 1 reader were provided. The sensitivity, specificity, and accuracy of nonsubtracted VCTA in detecting small cerebral aneurysms were 89.8% (95% CI 82.0%–95.0%), 99.2% (95% CI 97.1%–99.9%), and 96.5% (95% CI 94.0%–98.2%), respectively, on a per-aneurysm basis. The positive predictive value and negative predictive value of nonsubtracted
VCTA in depicting small cerebral aneurysms were 97.8% (95% CI 92.2%–99.7%) and 96.1% (95% CI 92.9%–98.1%), respectively, on a per-aneurysm basis. There was a statistically significant difference in accuracy between nonsubtracted VCTA and 3D DSA (Fisher’s exact test, p = 0.039).

### Accuracy of 320-Detector Row Subtracted VCTA in Detecting Small Cerebral Aneurysms on a Per-Aneurysm Basis

Subtracted VCTA identified 97 small cerebral aneurysms (including both true-positive and false-positive) in 88 of 662 patients (39 men, 49 women) by 2 independent readers. Three small cerebral aneurysms that were visible on 3D DSA were initially not detected by the 2 subtracted VCTA readers. The 3 small aneurysms were considered false-negative interpretations for subtracted VCTA (Fig. 3). When false-negative subtracted images were viewed retrospectively, 1 aneurysm was detected, and the other 2 aneurysms were still undetected.

Two small aneurysms diagnosed by subtracted VCTA were invisible on 3D DSA. These 2 small aneurysms were considered false-positive interpretations for subtracted VCTA (Fig. 4). The false-negative and false-positive small aneurysms of subtracted VCTA are also listed in Table 1 for readers 3 and 4. Due to consistency of observations between subtracted VCTA readers 3 and 4, the results of only reader 3 were offered.

The sensitivity, specificity, and accuracy of subtracted VCTA in depicting small cerebral aneurysms were 96.9% (95% CI 91.3%–99.4%), 92.2% (95% CI 97.1%–99.9%), and 98.6% (95% CI 96.7%–99.5%), respectively, on a per-aneurysm basis. The positive predictive value and negative predictive value of subtracted VCTA in depicting small cerebral aneurysms were 97.9% (95% CI 92.7%–99.7%) and 98.8% (95% CI 96.5%–99.7%), respectively, on a per-aneurysm basis. There was no statistically significant difference in accuracy between subtracted VCTA and 3D DSA (Fisher’s exact test, p = 1.000). However, significant differences occurred between nonsubtracted and subtracted VCTA (Fisher’s exact test, p = 0.016).

### Patient Demographic Data and Small Cerebral Aneurysm Treatment

Overall, 77 of 90 patients with small cerebral aneurysms presented with SAH, and 85 of 98 small cerebral aneurysms were detected in the presence of SAH. Of the 77 patients presenting with SAH, 59 cases were thought to be due to a small cerebral aneurysm rupture and the other 18 were thought to be due to the rupture of another aneurysm ≥ 3 mm in maximal diameter. Fifty-six small cerebral aneurysms were treated by embolization, 6 small cerebral aneurysms were treated with surgery, and the other 36 small cerebral aneurysms were followed but not treated (Fig. 2).

### Discussion

With the rapid development of multidetector CT technology, the sensitivity and accuracy of conventional multidetector CTA has progressively improved in detecting cerebral aneurysms.2,18,24 Wintermark et al.24 reported that the sensitivity and accuracy for diagnosing cerebral aneurysms were 94.8% and 94.9%, respectively, on 4-detector CTA. Chen et al.2 studied 152 patients with suspected cerebral aneurysm who underwent 16-detector CTA and reported that the sensitivity and accuracy of detecting aneurysms were 97.8% and 98.7%, respectively. Pozzi-Mucelli et al.18 reported that the overall sensitivity and accuracy for detecting cerebral aneurysms were 92.8% and 99.4%, respectively, on 64-detector CTA.

Although previous studies had shown that conventional multidetector CTA had relatively high sensitivity and accuracy in the diagnosis of cerebral aneurysms, numerous reports also proved that conventional multidetector CTA had a relatively low sensitivity and accuracy in detecting small cerebral aneurysms.3,12,26 Teksam et al.21 reported that the sensitivity and accuracy of detecting cerebral aneurysms (≤ 5 mm) were 85% and 79%, respectively, on 4-detector CTA. Yoon et al.26 studied 85 patients with suspected cerebral aneurysm who underwent 16-detector CTA, and reported that the sensitivity and accuracy for...
the diagnosis of cerebral aneurysms (< 3 mm) were 74.1% and 81% for reader 1, and 77.8% and 83.3% for reader 2, respectively. Li et al. reported that the sensitivity of diagnosing cerebral aneurysms (< 3 mm) was 93.7% for reader 1 and 96.8% for reader 2 on 64-detector CTA.

Conventional multidetector CTA had a disadvantage in detecting cerebral aneurysms of small size and near the skull base due to the influence of overprojecting bone structures. Moreover, patient motion artifacts during CT scanning would also reduce conventional multidetector CTA image quality and sensitivity in diagnosing small aneurysms. With the recently introduced 320-detector row volume CT scanner, which significantly increased detector width (160 mm) and allowed whole-brain coverage in a single rotation of 0.75 seconds, these problems seemed less severe. Luo et al. studied 56 patients using 320-detector row VCTA and reported that the overall sensitivity, specificity, positive predictive values, and negative predictive values of subtracted VCTA were all 100%. Nevertheless, only 56 patients were enrolled in their study, and the sample size was relatively small.

In the current study, 662 patients were enrolled, and 320-detector row volume CT scanner was also used. The sensitivity, specificity, and accuracy of 320-detector row subtracted VCTA for detecting small cerebral aneurysms (< 3 mm) were 96.9%, 99.2%, and 98.6%, respectively, on a per-aneurysm basis. No statistically significant difference in accuracy was seen between 3D DSA and 320-detector row subtracted VCTA (p > 0.05). The greatest improvement with 320-detector row subtracted VCTA seemed to be in diagnosing small aneurysms in our study compared with the previous studies using conventional multidetector CTA.

In our study, we also compared the diagnostic performance of 320-detector row nonsubtracted VCTA with subtracted VCTA and 3D DSA for the evaluation of small cerebral aneurysms. We found that the 7 small aneurysms (70%) missed by nonsubtracted VCTA were located in the ICA (Table 1). Nonsubtracted VCTA had equal diagnostic accuracy to subtracted VCTA and 3D DSA for detecting small aneurysms located in the anterior cerebral artery, the anterior communicating artery, the middle cerebral artery (MCA), and the posterior communicating artery. Detection of small ICA aneurysms adjacent to the skull base was still a challenge for nonsubtracted VCTA due to the presence of overlying bone structures (Figs. 1 and 2). Therefore, the sensitivity of nonsubtracted VCTA for detecting small aneurysms was only 89.8% on a per-aneurysm basis in this study. Nonsubtracted VCTA was significantly less sensitive than subtracted VCTA and 3D DSA in detecting small aneurysms (p < 0.05). However, we found that subtracted VCTA also had some limitations, such as the atherosclerotic plaque and the relationship of aneurysms to bone structure that could not be shown (Fig. 5), which were very important for the aneurysm treatment.

Over the past 10 years, some techniques have been advanced, including hydrophilic guide wires, smaller catheters, and DSA units. However, the technical advances could not solve the patient-related risk factors associated with neurological complications in catheter cerebral angiography, and the risk of neurological complications is augmented by age. Fluoroscopic times longer than 10 minutes and cardiovascular disease were independent predictors of risk. Even in patients without vascular disease, neurological complications still appear. Lim et al. found that ruptured aneurysms located in anterior circulation with a high aspect ratio might have the risk of rebleeding during DSA, especially during 3D DSA. Therefore, the indications for catheter cerebral angiography should be limited.

Hayashida et al. reported that sufficient presurgical treatment information could be obtained using 320-detector VCTA alone in most patients with unruptured cerebral aneurysms. Willinsky et al. also supported the shift to a
noninvasive imaging method of the cerebral vessels. These findings confirmed the argument that patients with a higher risk should undergo a noninvasive imaging method of the craniocervical vessels, and catheter cerebral angiography should be avoided.

In our hospital, 320-detector row VCTA had been used as a first-line imaging modality in patients with SAH possibly caused by ruptured cerebral aneurysms. Compared with DSA, 320-detector row VCTA was more effective in an emergency setting. VCTA could be performed immediately after a diagnosis of SAH by a nonenhanced CT scan of the brain. In our study, only 36 uncooperative patients (5.4%) needed a short-acting sedative to complete a 320-detector row CT scan. In all cases, a complete diagnostic workup could be performed without general anesthesia, which was often required during the catheter angiography.

After 320-detector row VCTA data were obtained, VCTA images could be evaluated in almost unlimited projections in 3D formats. The 320-detector row VCTA images performed well in the characterization of elements of the circle of Willis, which was a major concern in the evaluation of risks associated with both neurosurgical and endovascular treatments. Subtracted VCTA images were clearer and more accurate in displaying aneurysm bodies and aneurysm necks, as well as the relationships of the artery with aneurysms and neighboring vessels (Figs. 1, 2, and 5).

**Study Limitations**

There are 3 limitations of our study. First, our study population included 547 patients (83%) with spontaneous SAH, raising the possibility of ruptured cerebral aneurysm. When there is high suspicion of the presence of an aneurysm, a high estimate of accuracy could result due to observer expectation bias. Therefore, the relative predominance of SAH in our population may have affected the diagnostic sensitivity of 320-detector row VCTA. Second, 3D DSA was considered the diagnostic standard for the cerebral aneurysms in our study. However, Hochmuth et al. found in their study that 1 cerebral aneurysm depicted on conventional DSA was not seen on 3D DSA because of its site, and the sensitivity of 3D DSA was actually not 100%. However, in previous studies, 3D DSA was also considered the reference standard for detecting cerebral aneurysms. Third, only a single neuroradiologist reader evaluated the 3D DSA analysis; thus, interobserver variability could not be calculated.

**Conclusions**

Subtracted 320-detector row VCTA shows promising and equivalent diagnostic accuracy to 3D DSA for detection of small cerebral aneurysms (< 3 mm). The accuracy of nonsubtracted 320-detector row VCTA is obviously low for small ICA aneurysms adjacent to the skull base. Noninvasive subtracted 320-detector row VCTA is sensitive enough to replace 3D DSA in the diagnosis of patients with small cerebral aneurysms (< 3 mm).

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**References**


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