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Superior performance of cone-beam CT angiography in characterization of intracranial atherosclerosis

Clinical article

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Object. Intracranial atherosclerotic disease (ICAD) carries a high risk of stroke. Evaluation of ICAD has focused on assessing the absolute degree of stenosis, although plaque morphology has recently demonstrated increasing relevance. The authors provide the first report of the use of ultra-high-resolution C-arm cone-beam CT angiography (CBCT-A) in the evaluation of vessel stenosis as well as plaque morphology.

Methods. Between August 2009 and July 2012, CBCT-A was used in all patients with ICAD who underwent catheter-based angiography at the authors' institution (n = 18). Lesions were evaluated for maximum degree of stenosis as well as plaque morphological characteristics (ulcerated, calcified, dissected, or spiculated) via digital subtraction angiography (DSA), 3D-rotational angiography (3DRA), and CBCT-A. The different imaging modalities were compared in their assessment of absolute stenosis as well as their ability to resolve different plaque morphologies.

Results. Lesions were found to have similar degrees of stenosis when utilizing CBCT-A compared with 3DRA, but both 3DRA and CBCT-A differed from DSA in their assessment of the absolute degree of stenosis. CBCT-A provided the most detailed resolution of plaque morphology, identifying a new plaque characteristic in 61% of patients (n = 11) when compared with DSA and 50% (n = 9) when compared with 3DRA. CBCT-A identified all lesion characteristics visualized on DSA and 3DRA.

Conclusions. CBCT-A provides detailed spatial resolution of plaque morphology and may add to DSA and 3DRA in the evaluation of ICAD. Further prospective study is warranted to determine any benefit CBCTA-A may provide in clinical decision making and risk stratification over existing conventional imaging modalities.
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Key Words • **cone-beam CT** • **atherosclerosis** • **stroke** • **vascular disorders**

Despite medical, surgical, and endovascular treatment options, intracranial atherosclerotic disease (ICAD) continues to be a morbid disease that carries a high 1-year risk of stroke estimated at between 12.2% and 25%.[8,9] This risk has been reported to be most elevated in patients who are found to have severe stenosis (70%–99%) of a major intracranial artery.[14,29] Most previous reports on ICAD have focused exclusively on the absolute degree of stenosis as the major factor leading to stroke.[4,8,25] However, the absolute degree of stenosis may not be the only risk-determining factor, and multiple reports on ICAD have noted that plaque morphology as well as plaque evolution may determine a patient's stroke risk.[3,12,27] It may therefore be of value for treating clinicians to classify ICAD with imaging modalities focused on assessing both the degree of stenosis and plaque characteristics.

Assessment of the intracranial vasculature and ICAD evaluation has historically been accomplished with catheter-based digital subtraction angiography (DSA).[25] Currently, DSA remains the gold standard in the evaluation of patients and is the modality used in most clinical trials and reports.[8,11,18,28] Advances in the last decade in neurointerventional imaging have led to the use of 3D-rotational angiography (3DRA) and, more recently, to the development of ultra–high resolution cone-beam CT angiography (CBCT-A) for evaluation of neurovascular disorders. CBCT-A was initially intended for identification of early hemorrhage and decreased perfusion and the assessment of hydrocephalus in the periprocedural time period.[16,19,21] More recently, CBCT-A has been used to evaluate intra-

Abbreviations used in this paper: CBCT = cone-beam CT; CBCT-A = CBCT angiography; CBCT-A-N = CBCT-A–normal; CBCT-A-S = CBCT-A–sharp kernel; CTA = CT angiography; DSA = digital subtraction angiography; HU = Hounsfield unit; ICA = internal carotid artery; ICAD = intracranial atherosclerotic disease; MIP-MPR = maximum intensity projection multiplanar reconstruction; MRA = MR angiography; TCD = transcranial Doppler ultrasonography; TIA = transient ischemic attack; 3DRA = 3D-rotational angiography.

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cranial stent placement during aneurysm treatment,[20,22] and delineate cerebral[15,16] and spinal arteriovenous malformations.[1] Furthermore, CBCT-A has since been shown to have excellent spatial resolution of the intracranial vasculature, including the ability to resolve submillimeter objects such as stent struts measuring 50–70 μm.[13] Despite these uses of CBCT-A in evaluation of intracranial vessels, its utility in determining stenosis and plaque morphology in ICAD has not been previously evaluated.

Given the high spatial resolution provided by CBCT-A, we have, since August 2009, obtained imaging studies in all patients undergoing catheter-based angiography for ICAD using this modality, in addition to contemporaneous standard DSA and 3DRA. We sought here to compare and quantify the resolution of CBCT-A compared with 3DRA as well as DSA in the evaluation of ICAD. We present the initial report of additional plaque characteristics identified by CBCT-A in patients with ICAD.

Methods

Case Selection

During the study time period of August 2009 to July 2012, all patients undergoing catheter-based angiography for the evaluation of ICAD were assessed in prospective fashion. Patients' medical charts, radiographic studies, and endovascular procedures were reviewed for pertinent history. Variables recorded included patient age, sex, clinical presentation, smoking status, alcohol use, prior anticoagulation medication use, prior stroke or transient ischemic attack (TIA), and the presence of hypertension, coronary artery disease, diabetes mellitus, or hyperlipidemia. This study was approved by the institutional review board of Tufts Medical Center.

Procedure and Image Processing

All patients underwent catheter-based cerebral angiography including biplane 2D-DSA, 3DRA, and CBCT-A performed with the Siemens Axiom-Artis VB22N 060907 system. 3DRA was performed using 3 ml/second of contrast medium for 5 seconds with a 1.5-second preinjection delay; CBCT-A was performed using a 20-second acquisition while injecting contrast medium at 1 ml/second with a 2.0-second preinjection delay (Isovue-250, Bracco Imaging SpA). All raw 3D acquisition data were reconstructed using the Leonardo/Syngo workstation software (Siemens AG). 3DRA data were visualized using maximum intensity projection multiplanar reconstruction (MIP-MPR) using a Hounsfield unit (HU) "normal" kernel. CBCT-A volumes were reconstructed in the same manner using both HU "normal" and HU "sharp" kernels. These were labeled CBCT-A-N and CBCT-A-S, respectively. 2D-DSA data were analyzed using the OsiriX medical imaging software (OsiriX MD).

Lesion Classification

Two reviewers were provided the different imaging 3D volumes, without knowledge of the imaging modality being used, as well as 2D DSA and instructed on which vessel to assess for each patient in a scrambled nonconsecutive fashion. The degree of stenosis was calculated using a standardized and validated method for ICAD[25] on DSA, 3DRA, CBCT-A-N, and CBCT-A-S. This method for assessing ICAD stenosis has previously been used in the SAMMPRIS[8] and WASID[9] trials. Atherosclerotic plaque morphology was graded in a binary fashion by the 2 independent blinded reviewers, in regard to the presence or absence of the following 4 criteria: ulceration, calcium deposits within the plaque, dissection of the plaque, and spicule formation. Reviewers were blinded to each other's findings and to patient history or any radiographic reports that noted the classification of plaque morphology. An ulcerated plaque was defined as a plaque lacking a smooth contour. Calcium deposits were defined as hyperdense lesions within the plaque consistent with calcium. A plaque was considered to have dissection if a dissection flap or membrane into the core of the plaque was noted or if contrast was seen filling into a false lumen. Finally, a spicule was defined as a sharp and acute protrusion of the core of the plaque into the lumen of the vessel at any point along the plaque wall.

Statistical Analysis

Statistical analysis was completed using the JMP 10.0 statistical software package (SAS Institute). Standard mean, median, and standard deviations were calculated in regard to demographic information. Matched pair analysis as well as Pearson correlation coefficients were used to compare stenosis measurements between the different imaging modalities. Inter-reader reliability was calculated using Cohen's kappa values to verify grader agreement for plaque morphology classifications. Differences in the morphology-detecting capabilities of the various modalities are summarized as the absolute number of patients with a lesion visualized as well as the percentage of patients showing a novel finding when transitioning from any one imaging modality to another.

Results

Patient Demographics

Eighteen consecutive patients underwent DSA, 3DRA, and CBCT-A in relation to ICAD during the time period of the study (Table 1). Most patients were male (n = 14, 78%). The average age was 63.5 years (range 50–81 years). The majority of patients presented with transient ischemic attack (TIA) or stroke. Thirteen (72%) of the 18 patients in this series had lesions in the anterior circulation that were believed to be responsible for their symptoms. Five patients (28%) had lesions in the posterior fossa and presented with vertigo, gait instability, and/or double or blurry vision. Most patients had significant comorbidities, which included hypertension in 14 cases (78%), coronary artery disease in 4 (22%), diabetes mellitus in 16 (89%), and hyperlipidemia in 12 (67%). Twelve patients (67%) were former or current smokers. Only 5 patients (28%) reported alcohol use.

Assessment of Lesion Stenosis

Lesions were found to have similar degrees of stenosis when imaged with a 3D modality (Fig. 1; Table 2).

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TABLE 1: Demographic characteristics, clinical presentation, and comorbidities*

Case No.	Age (yrs), Sex	Clinical Presentation	Lesion Location	HTN	CAD	DM	HL	Prior CVA or TIA	Smoking	Alcohol	Anticoag Med Prior to CBCT-A
1	69, F	TIA (garbled speech, rt arm weakness)	lt MCA	yes	no	yes	yes	yes	no	no	clopidogrel, warfarin
2	58, M	rt pst HA, tinnitus, nausea, presyncope	rt VA	yes	yes	yes	yes	no	former	yes	aspirin, clopidogrel
3	81, M	unsteady gait, visual disturbances	lt VA	yes	yes	yes	yes	no	no	no	aspirin, clopidogrel
4	78, M	TIA (shaking of lt side when standing)	rt ICA	yes	no	yes	yes	yes	former	no	aspirin, warfarin
5	71, M	rt eye blindness	rt ICA	yes	yes	yes	yes	no	former	no	aspirin
6	50, M	TIA (rt facial droop, ptosis, tongue deviation)	lt MCA	yes	no	yes	yes	yes	yes	yes	aspirin, dipyridamole
7	57, M	rt hemiparesis	lt ICA	no	no	no	yes	yes	yes	no	none
8	73, M	vertigo, blurred vision, gait instability	BA	yes	no	yes	no	no	no	yes	aspirin, clopidogrel
9	51, M	TIA (lt face & arm weakness)	rt MCA	no	no	no	yes	yes	yes	yes	aspirin, warfarin
10	56, M	CVA (lt arm/hand weakness)	rt ICA	no	no	yes	yes	yes	yes	yes	none
11	50, F	CVA (aphasia, rt hemiparesis)	lt MCA	no	no	yes	no	yes	no	no	none
12	58, M	CVA (rt facial droop, numbness)	lt MCA	yes	no	yes	no	yes	yes	no	none
13	58, M	TIA (lt face, arm weakness, numbness)	rt MCA	yes	no	yes	no	yes	no	no	none
14	75, F	lt eye blurriness & positional rt-side weakness	lt CCA	yes	no	yes	yes	no	former	no	aspirin
15	63, F	TIA (intermittent aphasia)	lt ICA	yes	no	yes	yes	yes	yes	no	none
16	52, M	TIA (double vision, gait instability, lt arm/leg numbness)	BA	yes	no	yes	no	yes	no	no	none
17	73, M	TIA (confusion, aphasia)	lt ICA	yes	yes	yes	yes	no	former	no	aspirin, clopidogrel
18	67, M	positional vertigo, dysarthria	rt VA	yes	no	yes	no	no	former	no	aspirin, clopidogrel

* Anticoag = anticoagulant; BA = basilar artery; CAD = coronary artery disease; CBCT-A = cone-beam CT angiography; CCA = common carotid artery; CVA = cerebrovascular accident; DM = diabetes mellitus; HA = headache; HL = hyperlipidemia; HTN = hypertension; MCA = middle cerebral artery; med = medication; pst = posterior; VA = vertebral artery.

CBCT-A-N and CBCT-A-S did not differ in the maximum degree of stenosis from 3DRA utilizing matched pair analysis (CBCT-A-N vs 3DRA, mean maximum percent stenosis 57.78% vs 60.22% [SE of the difference between matched pairs 2.28%], p = 0.30; CBCT-A-S vs 3DRA. 59.94% vs 60.78% [SE 2.53%], p = 0.75). In addition, assessment of stenosis by the different 3D modalities demonstrated good correlation (CBCT-A-N vs 3DRA, R = 0.746; CBCT-A-N vs CBCT-A-S, R = 0.833; Fig. 1). In contrast, measurement of stenosis by 2D DSA correlated poorly with the 3D modalities (3DRA vs DSA, R = 0.291; CBCT-A-N vs DSA, R = 0.460; Fig. 1; Table 2) despite mean values across groups being statistically indistinguishable (3DRA vs DSA, 60.22% vs 60.78% [SE 3.18%], p = 0.86, CBCT-A-N vs DSA, 57.78% vs 60.78% [SE 3.06%], p = 0.34, CBCT-A-S vs DSA, 59.94% vs 60.78% [SE 2.53%], p = 0.75). Further analysis revealed that 2D DSA did not consistently either under- or overestimate the degree of stenosis when compared with the other 3D modalities.

Characteristics of Lesion Morphology

Agreement between reviewers on the assessment of plaque morphology (smooth, ulcerated, dissected, calcium deposits, spiculated, or a combination of multiple morphologies) was independent of the imaging modality. Interreader reliability was calculated for the 2 reviewers using Cohen's kappa values and was 0.84 for DSA, 0.96 for 3DRA, 0.83 for CBCT-A-N, and 0.87 for CBCT-A-S. Plaque morphology features were more frequently identified when moving from a 2D modality (DSA) to any 3D modality (3DRA, CBCT-A-N, CBCT-A-S). Furthermore, CBCT-A provided the most detailed identification of plaque morphology compared with any other modality, including 3DRA (Figs. 2–4; Tables 3 and 4). Specifically, whereas 2D-DSA suggested only 3 ulcerated lesions and 15 smooth stenotic lesions, CBCT-A-S revealed 12 ulcerations, 6 dissections, 1 spicule impinging into the lumen, and 5 calcific components (Table 3). CBCT-A identified a new plaque characteristic in 61% of patients (n = 11) when

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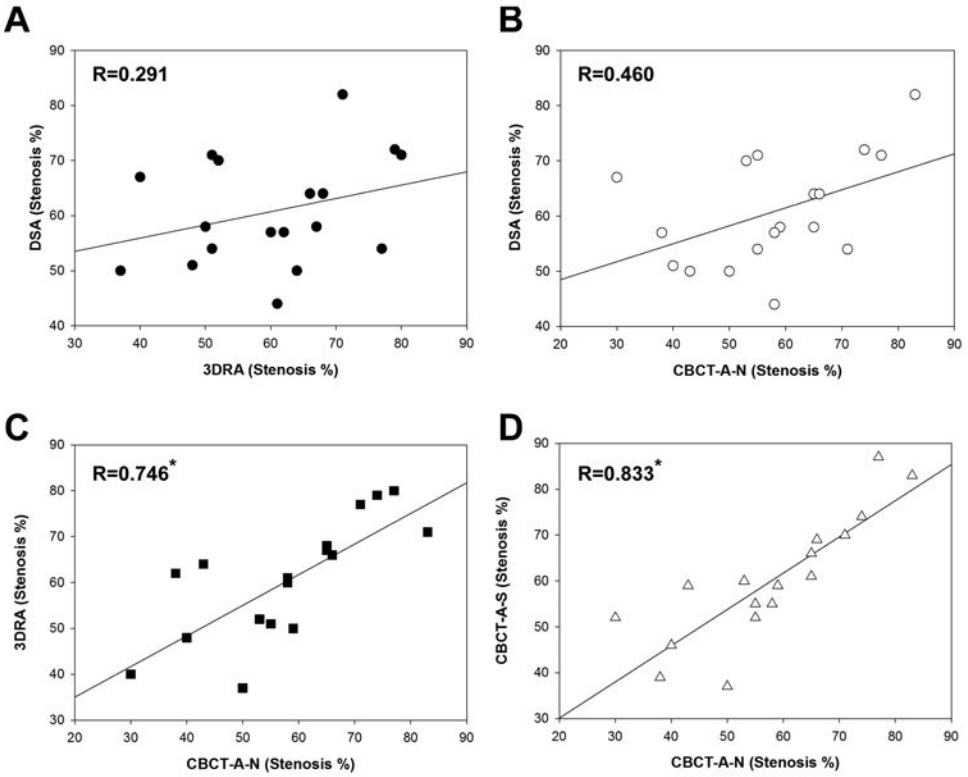


Fig. 1. Multiple scatter plots with linear regression comparing percent stenosis measurement in the 18 patients by different modalities. **A:** Percent stenosis measured on DSA compared with 3DRA. There is weak correlation (R = 0.291). **B:** Percent stenosis measured on DSA compared with CBCT-A-N. There is weak correlation (R = 0.460). **C:** Percent stenosis measured on 3DRA compared with CBCT-A-N. There is a significant correlation (R = 0.746). **D:** Percent stenosis measured on CBCT-A-S compared with CBCT-A-N. There is a significant correlation (R = 0.833). *p < 0.05.

compared with DSA and identified a new lesion in 50% of patients (n = 9) when compared with 3DRA (Tables 3 and 4). No morphological characteristic discovered on DSA was missed by either 3DRA or either CBCT-A modalities. Likewise, no lesion discovered on 3DRA was missed by either CBCT-A modalities.

CBCT-A Effect on Clinical Management

After cerebral angiography 8 patients were maintained on maximal medical therapy and 10 patients underwent endovascular therapy with either balloon- or stent-mediated angioplasty (Table 5). CBCT-A influenced the treatment decision in 6 of the 10 patients treated with endovascular therapy. Four of 10 patients would have been treated with endovascular therapy even if they had not undergone CBCT-A imaging. The most common reason for a change in management strategy based on CBCT-A included the finding of a vulnerable plaque with ulcerations, dissections, and/or spicules thought to be responsible for an embolic phenomenon or threatening complete vessel occlusion.

TABLE 2: Pearson correlation coefficients for comparison of different modalities in assessing percent stenosis*

	DSA	3DRA	CBCT-A-N	CBCT-A-S
DSA	1			
3DRA	0.291	1		
CBCT-A-N	0.460	0.746†	1	
CBCT-A-S	0.605†	0.78†	0.833†	1

* CBCT-A-N = cone-beam CT angiography–normal kernel; CBCT-A-S = CBCT-A–sharp kernel; DSA = digital subtraction angiography; 3DRA = 3D-rotational angiography.
† $p < 0.05$.

Discussion

Two-dimensional DSA remains the standard for the diagnosis, evaluation, and risk stratification of ICAD. Patients are typically grouped according to the maximum degree of stenosis of the vessel in question. Based on this criterion, medical, surgical, or endovascular treatments are recommended. The major recent trials studying intracranial stenosis, including SAMMPRIS[8] and WASID,[7] have continued this trend and relied on measuring the maximum degree of stenosis assessed by DSA to stratify stroke risk. Recent literature and the current study, however, suggest that DSA may incorrectly estimate true stenosis when its findings are compared with those of other imaging modalities as well as measurements in histological specimens.[5,17,26] Although these studies were conducted in the extracranial carotid artery, this body of evidence raises a question about the validity of what is considered our gold standard. DSA may not provide an optimal assessment of plaque stenosis and morphology

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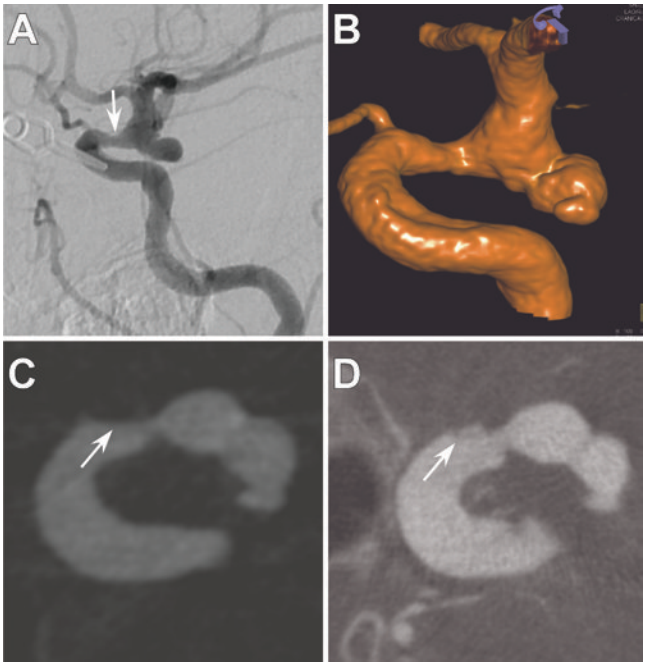


Fig. 2. Case 15. This 63-year-old woman with previous bilateral posterior communicating artery aneurysms had developed intermittent aphasia episodes. She was found to have a left supraclinoid ICA stenosis proximal to the aneurysm. **A:** Lateral left ICA DS angiogram demonstrating a 60% stenosis *(arrow)* in the supraclinoid ICA proximal to the aneurysm. The edges of the plaque seem smooth and non–flow limiting. **B:** 3D reconstruction of a left ICA 3D-rotational angiogram demonstrating the same stenosis once again as a smooth plaque. **C:** 3D rotational angiogram visualized using MIP-MPR once again demonstrating a smooth plaque *(arrow)*. **D:** CBCT-angiogram visualized using MIP-MPR demonstrating the same stenosis. An ulcerated plaque is demonstrated with contrast filling within the plaque *(arrow)*.



Fig. 3. Case 17. This 73-year-old man presented with multiple intermittent episodes of confusion and aphasia. He was found to have a left ICA stenosis. **A:** 3D reconstruction of a left ICA 3D-rotational angiogram demonstrating a 65% stenosis of the left ICA. The plaque distal to the stenosis appears smooth. **B:** 3D reconstruction of left ICA CBCT angiogram demonstrating the same stenosis. It is, however, noted that this plaque seems ulcerated and has a different appearance from that shown by 3DRA. **C:** 3D rotational angiogram visualized using MIP-MPR demonstrating a spicule *(arrow)*. No ulceration is evident distal to this spicule. **D:** CBCT angiogram visualized using MIP-MPR demonstrating the same spicule but also a more distal ulcerated plaque *(arrow)*, which was not evident on the 3D rotational angiogram.

in ICAD. A broader study of this topic and, if possible, histological correlation will be necessary to fully answer these questions.

In the current study, CBCT-A did not differ significantly in assessing the absolute percent stenosis of lesions when compared with other 3D modalities such as 3DRA. However, both of these 3D modalities differed in the measurement of percent stenosis when compared with traditional 2D-DSA (Fig. 1 and Table 2). This difference is likely due to the fact that the vessel stenosis due to plaque occurs in a 3D manner and DSA is a 2D imaging modality, which effectively flattens these spatial features. Measuring a 3D phenomenon such as a stenosis on a 2D imaging modality likely has inherent error. As mentioned previously, the findings of the current study compel some hesitation in the wide reliance on DSA as the gold standard for maximum percent stenosis in ICAD and as the basis for stratification in 2 major clinical trials assessing this disease. We suggest that further analysis may be warranted to determine whether the use of DSA as the sole measurement of percent stenosis should be reassessed, or at least supplemented with additional imaging modalities such as CBCT-A.

Moreover, there is growing debate about whether lesion morphology should be added to the current criterion of percent stenosis in determining which patients to offer endovascular treatment. In recent studies, plaque vulnerability, or the propensity of a lesion to embolize distally, leading to stroke, may provide a better estimate of risk than maximal stenosis.[2,3,6] Factors that have been found to determine vulnerability include intraplaque hemorrhage, plaque erosion, calcification, inflammation, lipid-rich necrotic cores, thin fibrous caps, and ulcerations.[2,3,6] In addition to the aforementioned data indicating that DSA is a poor gauge of absolute percent stenosis, we have provided initial data to demonstrate that this imaging modality misses a great proportion of the plaque morphologies studied when compared with 3DRA and, specifically, CBCT-A. There may be a significant impact on the treatment of these patients if DSA alone is used to assess ICAD. In our current study 6 of 10 patients undergoing endovascular therapy were selected due to the addition of CBCT-A findings (Table 5). Without this imaging modality, these patients would have been advised to continue on maximal medical therapy based on current recommendations. Furthermore, these results are in agree-

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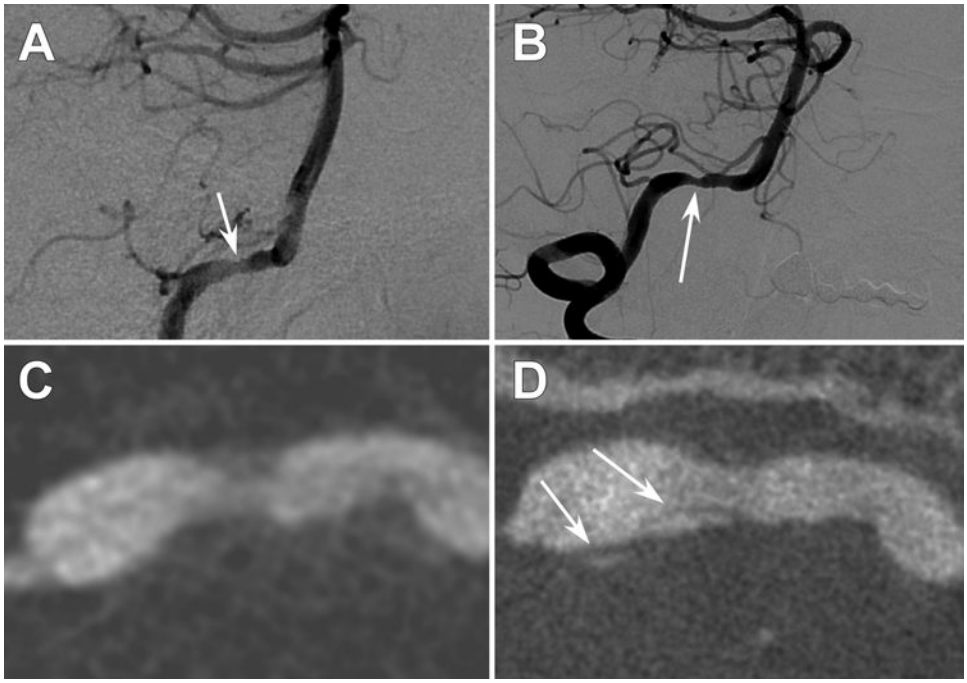


Fig. 4. Case 18. This 67-year-old man presented with positional vertigo and dysarthria. He was noted to have a right vertebral artery stenosis. **A:** Lateral DS angiogram demonstrating a 40% stenosis *(arrow)* in the right vertebral artery. The edges of the lesion seem smooth and non–flow limiting. **B:** Another lateral DS angiogram demonstrating the same 40% stenosis *(arrow)* in the right vertebral artery. Once again the edges of the lesion seem smooth and non–flow limiting. **C:** 3D-rotational angiogram visualized using MIP-MPR demonstrating a smooth 65% stenotic lesion. **D:** CBCT angiogram visualized using MIP-MPR demonstrating a severely ulcerated and dissected plaque *(arrows)*. The stenotic lesion is calculated at 65%, in keeping with 3DRA but differing from DSA.

ment with previous work showing that standard DSA has disappointing specificity and sensitivity for detecting ulceration and plaque morphology in known symptomatic patients.[23,26] It is with this impetus that we aimed to study imaging modalities that both assess the maximum degree of stenosis and resolve fine details of plaque morphology.

Multiple imaging modalities, including DSA, CT angiography (CTA), MRI or MR angiography (MRA), ultrasonography, and transcranial Doppler ultrasonography (TCD), have been studied to assess their accuracy in identifying plaque features that portend plaque rupture and stroke.[15,24] Recently, ultra–high resolution CBCT-A has found increasing utility in the neurovascular suite with praise for its ability to resolve morphological characteristics of the intracranial circulation,[10,13,22] though its role in ICAD imaging has not been studied. In the current first series on the utilization of CBCT-A in the evaluation of ICAD, CBCT-A revealed extremely detailed resolution of plaque morphology. This study demonstrates that CBCT-A provided greater resolution when compared with other catheter-based modalities such as DSA or 3DRA. A new plaque morphology was identified in 61% of patients when CBCT-A was used following standard DSA (Tables 3 and 4). Even more surprising, in 50% of patients, CBCT-A identified a new plaque characteristic that had not been identified with another detailed 3D modality—3DRA (Tables 3 and 4).

TABLE 3: Grading of lesions among multiple imaging modalities in all patients (n = 18)

Modality	Smooth	Ulcerated	Calcification	Dissection	Spicule
DSA	15	3	0	0	0
3DRA	8	10	0	2	1
CBCT-A-N	7	11	3	6	3
CBCT-A-S	6	12	5	6	5

Although further studies on the clinical benefit, if any, of this modality will need to be conducted, we have recently reported on a patient on dual antiplatelet therapy who presented with a TIA with a benign-appearing, non–flow-limiting, less than 50% stenotic lesion in the intracranial ICA using both traditional DSA as well as the more advanced 3DRA.[12] The addition of CBCT-A identified a dissected and ruptured lesion with overlying thrombus accounting for the patient's embolic symptoms. In our current series 11 of 18 patients had morphological characteristics that were missed on DSA and only identified with CBCT-A, further adding to the argument that DSA may not be as good a predictor of plaque morphology. CBCT-A may therefore provide important information about morphological characteristics without deficiency in assessing a lesion's maximum stenosis. This may have a major effect on clinical management beyond what is possible with standard 2D-DSA.

Study and Technology Limitations

Although we have mentioned some of the benefits

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TABLE 4: Plaque morphology and new lesions discovered when transitioning between different imaging modalities

New Lesions Discovered When Utilizing	Type of New Lesion Discovered*				Total No. of Pts Affected (%), n = 18
	Ulceration	Calcium	Dissection	Spicule	
3DRA compared to DSA	7 (38.89)	0 (0.00)	2 (11.11)	1 (5.56)	9 (50.00)
CBCT-A-S compared to DSA	9 (50.00)	3 (16.67)	6 (33.33)	5 (27.78)	11 (61.11)
CBCT-A-S compared to CBCT-A-N	0 (0.00)	0 (0.00)	0 (0.00)	2 (11.11)	2 (11.11)
CBCT-A-S compared to 3DRA	2 (11.11)	3 (16.67)	4 (22.22)	4 (22.22)	9 (50.00)

* Values represent numbers of patients (%) in whom new lesions were discovered with the specified transition in imaging modality.

of CBCT-A, this modality does have some limitations. First, the evaluation of ICAD can be accomplished with noninvasive methods, such as MRA, CTA, and TCD, or with invasive catheter-based modalities. Although this study demonstrates that CBCT-A provides more detailed resolution of plaque morphology, this modality should be used to supplement and not replace noninvasive methods. Moreover, since DSA currently remains the standard for the evaluation of ICAD, we suggest that CBCT-A may be accomplished during the same procedure in which both DSA and 3DRA are being acquired with minimal additional risk. A major limitation of CBCT-A is that patients must hold relatively still for a relatively long 20-second acquisition period. This can be difficult for patients who are unable to cooperate or unable to hold their respiration for this period of time. With respect to safety, a single 20-second CBCT-A acquisition involves the delivery of 22 ml of contrast agent and is associated with approximately a 0.2-Gy radiation dose, compared with 3DRA, which involves 18 ml of contrast agent and 0.065 Gy; a standard DSA run utilizes 6–10 ml of contrast agent and is associated with a radiation dose of about 0.15 Gy. Although CBCT-A entails an additional radiation dose, it is important to recognize that utilizing multiple magnified-DSA runs to acquire appropriate visualization of an ICAD lesion may deliver a higher dose than a single CBCT-A run. Thus, the overall radiation dose delivered to a patient may in fact be higher with the traditional use of multiple DSA runs when compared with the use of 1 DSA run and an additional CBCT-A acquisition. Finally, another limitation of CBCT-A, like other CT modalities, is that it is limited by artifacts caused by metal (clips, stents, or coils), which may create a star-burst effect that can limit its use in ICAD where other intracranial pathologies have been treated (for example, after stent-assisted aneurysm coil embolization, aneurysm clip ligation, ar-

TABLE 5: Clinical presentation and management*

Case No.	Clinical Presentation	Lesion Location	Treatment	Did CBCT-A Finding Alter Management?	Relevant Finding on CBCT-A
1	TIA (garbled speech, rt arm weakness)	lt MCA	medical	no	NA
2	rt pst HA, tinnitus, nausea, pre-syncope	rt VA	stent angioplasty	no	none additional
3	unsteady gait, visual disturbances	lt VA	stent angioplasty	no	none additional
4	TIA (shaking of lt side when standing)	rt ICA	stent angioplasty	yes	ulcerated & dissected plaque
5	rt eye blindness	rt ICA	stent angioplasty	yes	ulcerated & dissected plaque
6	TIA (rt facial droop, ptosis, tongue deviation)	lt MCA	balloon angioplasty	yes	ulcerated & dissected plaque
7	rt hemiparesis	lt ICA	medical	no	NA
8	vertigo, blurred vision, gait instability	BA	balloon angioplasty	yes	ulcerated & dissected plaque
9	TIA (lt face & arm weakness)	rt MCA	balloon angioplasty	no	none additional
10	CVA (lt arm/hand weakness)	rt ICA	stent angioplasty	yes	spicule & ulcerated & dissected plaque
11	CVA (aphasia, rt hemiparesis)	lt MCA	medical	no	NA
12	CVA (rt facial droop, numbness)	lt MCA	medical	no	NA
13	TIA (lt face, arm weakness, numbness)	rt MCA	medical	no	NA
14	lt eye blurriness & positional rt-sided weakness	lt CCA	medical	no	NA
15	TIA (intermittent aphasia)	lt ICA	medical	no	NA
16	TIA (double vision, gait instability, lt arm/leg numbness)	BA	medical	no	NA
17	TIA (confusion, aphasia)	lt ICA	stent angioplasty	no	none additional
18	positional vertigo, dysarthria	rt VA	stent angioplasty	yes	ulcerated & dissected plaque

* NA = not applicable.

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teriovenous malformation treatments). Overall, the limitations of CBCT-A are relatively small when compared with the potential benefits of the superior spatial resolution that this technology provides.

In addition to the above limitations, our study is limited by a small sample size. We plan to continue to accrue to the current prospective database and analyze the added benefit of this imaging modality. Larger multicenter studies with much greater sample size as well as the addition of studies with more reviewers will be necessary before any definitive conclusions can be reached. Secondly, the current study does not report fully on clinical outcomes of these patients or the way that the additional information provided by CBCT-A informed clinical decision making. We propose that given the exquisite details that CBCT-A provides, it will aid in stratifying lesion severity both in terms of absolute stenosis as well as in high-risk plaque features. This, however, remains unproven until comparisons of clinical outcomes are used in simultaneous control groups evaluated only with DSA as compared with groups utilizing this new modality in treatment algorithms. Finally, this study only compares plaque morphology among catheter-based technologies. It will be important to assess whether the plaque morphologies evaluated on this imaging modality are similar or add any additional benefit in comparison with noninvasive but lower-resolution methods such as MRA and CTA.

Conclusions

We report the first case series of CBCT-A for the assessment of ICAD lesions. CBCT-A appears to provide greater spatial resolution and discrimination in assessing both absolute vessel stenosis as well as plaque morphology in intracranial atherosclerotic disease than other catheter-based modalities such as digital subtraction angiography or 3D-rotational angiography. CBCT-A should be studied further in the context of ICAD to determine its potential benefit for clinical decision making.

Disclosure

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