Utility of intra-arterial cone beam CT angiography in detection of intracranial micro-arteriovenous malformations

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Aims and objectives

Although cerebral microarteriovenous malformations (mAVMs) are considered a rare subgroup of all cerebral AVMs accounting for approximately 8 % in the surgical series, they represent 21% of AVMs diagnosed following hemorrhagic presentation, especially in young adults. Yasargil defined mAVMs as a particular entity of pial AVMs characterized by a nidus of 1 cm or smaller and differentiated this subgroup from occult AVMs which are not visualized on angiography, by the surgeon or even in a gross pathology specimen, but assumed to be present as cryptic AVMs, only identified histopathologically if the associated hematoma was carefully removed. mAVMs can be suspected on angiography as an abnormal draining vein with non-distinguished feeding artery or nidus and suggestion of small coalescing arterioles. These findings makes the diagnosis more challenging and broaden the differential diagnosis to include the possibility of a dural or pial AVF.

Introduction of digital flat detector technology has improved the capabilities of modern angiographic platforms with the feasibility to provide 3D rotational digital subtraction angiography (3DR-DSA) and CBCTA with multiplanar reconstructions. CBCTA incorporates the high spatial vascular resolution of 3DR-DSA techniques with an increased contrast resolution to visualize the peripheral osseous and soft tissue structures approaching the quality of conventional CT scanners. Previous reports have described the use of CBCTA for the anatomic localization of intracranial and spinal dural AVFs. In this case series, we compared the diagnostic accuracy of DSA versus CBCTA in the evaluation of mAVMs with respect to their angiographic characterization and anatomic localization.
Methods and materials

Institutional review board approval was obtained for a retrospective study including five patients (3F:2M), age range (10-49 year) who underwent both DSA and IA-CBCTA procedures and revealed intracranial mAVMs between 2012 and 2015. Baseline patient demographics, presentation, AVM classifications according to Spetzler-Martin grading, arteries injected for tandem DSA and IA-CBCTA imaging, and management are cumulatively summarized in Figure 1.

Image Acquisition

The study was performed at two tertiary academic institutions with identical biplane angiography suites (Artis zee/zeego Flat Detector Biplane-Angiosuite, Siemens, Forchheim, Germany) and acquisition protocols. IA-CBCTA scanning was performed with a biplane flat detector rotational fluoroscopy and angiography unit (2k detector, amorphous silicon cesium iodide scintillator; 1920×2480 pixel resolution, 3.25 lp/mm; size 30×40 cm). The motorized frontal C-arm was used to acquire 496 projection frames over a 200° arc with 5-8 second rotation times at 80 kV and 260 mA. The radiation dose was set at 1.2 uGy per frame. Although acquisition parameters remained constant, IA-CBCTA techniques varied slightly with respect to IA contrast injection rates dependent on vessel injection sites, including the internal carotid artery (4 mL/s) and vertebral artery (3 mL/s) with total volumes (15-32 mL), Shorter acquisition times and non-diluted contrast assisted with opacification of subtle microvascular anatomy without venous contamination, other than abnormal early venous drainage.

IA-CBCTA acquisition data were transferred to an independent 3D postprocessing workstation (Leonardo, Siemens Medical Solutions). Multiplanar CT reconstructions (sagittal, coronal, and axial planes) and maximum intensity projections (overlapping 0.5 mm and 2-5 mm slice thickness) were generated and transferred to a picture archiving and communication system (PACS, Centricity Imaging; GE Healthcare, Milwaukee, Wisconsin, USA) for direct visualization on the workstation.

Image Analysis

Images were retrospectively and independently reviewed by two experienced neurointerventionalists on a de-identified PACS system (including postprocessed multiplanar IA-CBCTA reconstructions). Both observers scored the DSA (biplane and magnified oblique views) images without access to the IA-CBCTA dataset. Subsequent IA-CBCTA (multiplanar reconstruction) images acquired from the same IA injection site were scored by the observers. Qualitative image analyses were performed on high-definition LCD monitors routinely used for reporting and based on the level of image
quality, anatomic, and angiographic characterization on a scale of 0-2 (2: excellent/good; 1: relevant visibility with restrictions; 0: poor, non-diagnostic). The following parameters were scored: (a) arterial feeders (anatomic localization and course); (b) venous drainers (anatomic localization, course, single versus multiple draining veins); (c) nidus site (anatomic localization, angiographic delineation and differentiation from AV shunting). The total score for each modality was defined as the overall diagnostic value for interpretation. The difference between DSA and IA-CBCTA scores for each parameter and the overall diagnostic values were defined as relative IA-CBCTA efficacy values.

**Statistical Analysis**

Interobserver agreement between the two readers for qualitative image criteria was assessed using Kendall's # coefficient. Kendall's # coefficient varies between 0 and 1, with 0 representing no agreement and 1 representing complete agreement. # Values of >0.8, >0.5 to 0.8, >0.2 to 0.5, and #0.2 were considered to indicate excellent, good, fair, and poor agreement, respectively. Wilcoxon's test was used to compare scores of image quality parameters, as appropriate. A p value of <0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS statistical software (V.16.0, SPSS Inc, Chicago, Illinois, USA).
**Fig. 1:** Baseline presentations, AVM grading, injection sites, and management

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Results

Blinded observer analysis was performed on DSA and multiplanar IA-CBCTA images from 5 patients with suspected intracranial mAVMs (table 2). Both observers graded IA-CBCTA for all the components of the mAVMs as grade 2 (excellent visualization) while there were differences in DSA grading with fair agreement ($\kappa=0.43$).

Both observers assigned significantly higher scores to IA-CBCTA for overall diagnostic value (both observers: $p<0.004$, observer 1: $p<0.004$, observer 2: $p<0.038$). Although no significant differences were seen between DSA and IA-CBCTA scores (low relative IA-CBCTA efficacy value) when evaluating venous drainage (both observers: $p=0.3$), both observers assigned significantly higher scores to IA-CBCTA (high relative IA-CBCTA efficacy value) when evaluating arterial feeders (observer 1: $p<0.038$, observer 2: $p=0.034$) and nidus (both observers: $p<0.038$). This resulted in high relative IA-CBCTA efficacy value (overall diagnostic value of IA-CBCTA minus DSA) with no significant difference between the two observers.

There were no complications related to the IA-CBCTA procedure. Three patients underwent surgery for hematoma evacuation and two patients underwent micro-surgical resection of the micro-AVM.

Two illustrative cases demonstrated in figures 2 and 3.
### Table 1: Qualitative DSA (DA) and IA-CBCTA (CBA) image scoring by observers

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Fig. 2: 31 years old female with history of surgical evacuation to right cerebellar intraparenchymal hematoma (A); Right vertebral artery angiogram (Towne's antroposterior projection) shows early opacification of a right cerebellar hemispheric vein (black arrow heads) related to the distal posteroinferior branch of the right anterior inferior cerebellar artery (AICA) (white arrow head). (B): Right vertebral artery angiogram (oblique projection) shows Focal subtle increased vascularity (black arrow) suggesting arteriovenous shunting between the right cerebellar hemispheric vein and AICA. (C, D & E): Axial right vertebral IA-CBCTA images, (C) shows small right cerebellar mAVM nidus (white arrow), (D) shows the arterial feeder from the AICA (white arrow head) and (E) shows the course of the venous drainage into the right cerebellar hemispheric vein (curved arrow) which ascends along the cerebellar surface with subsequent venous outflow posteriorly along the tentorium via the superior vermian vein. There is no evidence of intracranial flow induced or venous aneurysms.

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Fig. 3: 49 year old male presented with recent right PCA and small right thalamoperforator infarcts as well as prominent venous vascularity along the tentorium on MRA head imaging suggesting early opacification of the straight sinus (A & B); Right vertebral artery angiogram (lateral projections), (A) shows hypertrophied superior cerebellar artery (white arrow heads) supplying a subtle increased region of vascularity along the inferomedial margin of the tentorium (black arrow) and (B) shows early venous drainage into the vein of Galen (black arrow heads) and straight sinus. (C & D); Sagittal reconstructed right vertebral IA-CBCTA images, (C) shows mAVM nidus within the anterior cerebellar vermis (black arrow) and (D) shows venous drainage into the vein of Galen (black arrow head) which demonstrates subtle segmental narrowing and straight sinus. (E & F); Axial right vertebral IA-CBCTA images, (E) shows the nidus measurements and (F) shows the
arterial supply from the right superior cerebellar artery (white arrow heads). There is no evidence of intracranial flow induced or venous aneurysms.

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The diagnosis of mAVMs can be challenging, requiring a high degree of suspicion especially in patients < 40 years in age with large cortical based hematomas. mAVMs can be assessed with a variety of imaging modalities including CT/CTA, MR/MRA, and DSA each has its advantages and drawbacks. Alén et al\textsuperscript{11} reported the role of high-resolution fast spin echo T2-weighted sequences in detection of a small nidus as subtle flow voids that correspond to nidal vasculature with the supplementary value of contrast-enhanced MRI/MRA over time of flight MRA techniques for nidus delineation, especially when the mAVM is in close apposition to the hematoma, due to better background suppression without contamination from hyperintense methemoglobin. However these findings combined MRI and contrast enhanced MRA failed to identify mAVMs in 6 out of 21 patients who required DSA to confirm the diagnosis.

Early conventional angiography in the setting of a large hematoma may obscure identification of mAVMs which can be secondary to various causes such as hemorrhage related vasospasm, sluggish flow through the lesion, compression of nidal of feeder/draining vessels by the hematoma, or intralesional thrombosis.\textsuperscript{12,13} Many authors reported initially negative DSA results in cases with acute intracerebral hemorrhage, proven later by histopathological studies or repeat angiography to be a mAVM.\textsuperscript{14,11,15} In 1992, Willinsky et al\textsuperscript{16} reported 2 of 5 patients with mAVMs that required superselective angiography to identify and define the topography of the lesion. Furthermore, Andreou et al\textsuperscript{2} in 2008 reported questionable standard DSA findings in 6 of 25 patients, and the diagnosis of a mAVM was confirmed after superselective angiography. In our series, two patients with initially negative or equivocal angiograms underwent repeat angiography including IA-CBCTA, without the need for superselective angiography, to confidently diagnose a mAVM as noted by both observers in our retrospective study. For these reasons, many authors\textsuperscript{2,11,15,16} agree that negative or questionable conventional DSA findings in young adults with atypical hemorrhage patterns should prompt superselective angiography or repetition of the study after resorption of the intracranial hemorrhage. We postulate that IA-CBCTA techniques may similarly enable precise localization and angioarchitectural characterization of these nearly occult lesions by increase the diagnostic power over traditional 2D DSA techniques. Additionally, IA-CBCTA techniques may limit the need for superselective catheterization and angiography, reducing the cost and risks of intracranial intervention.

Unlike large AVMs, the feeding artery of a mAVM is usually a single small branch of a pial artery\textsuperscript{11} with no trans-dural supply\textsuperscript{14} and a reported high incidence of associated saccular
In our series, a proximal flow related arterial aneurysm was observed in a single case. The draining vein of a mAVM is described as a "normal-sized vein" since it appears within the size range of visualized veins on angiography. In fact, these mAVM draining veins are often dilated, as they correspond to a small cortical vein usually not seen on angiography. The most common conventional 2D angiographic finding in the setting of a suspected mAVM is the presence of a "hidden vessel" in the arterial phase, corresponding to the early draining vein rather than a small nidus. However, early venous opacification is not specific for mAVM and can be found in the first 2 weeks after cerebral infarction or hemorrhage due to a local ischemic insult, increased blood brain permeability, or as angiographic manifestation of a dural/pial AVF. In our series, there was no significant difference between the DSA and IA-CBCTA regarding the identification of the early venous drainage with excellent inter-observer agreement between the two readers.

In the prior literature, biplane DSA and multidetector CT hybrid suites were shown to improve the diagnosis and management of various neurovascular diseases. Over the last decade, CBCT/IA-CBCTA techniques have emerged as a diagnostic tool replacing the need for hybrid suites for various peripheral and neurointerventional applications allowing sufficient cross-sectional localization of the vasculature relative to the peripheral soft tissues, organs, and osseous anatomy. Earlier studies used CBCT/IA-CBCTA to visualize embolic material during head and neck tumor embolizations, intrahepatic chemoembolization, and to evaluate post-procedure carotid and cerebrovascular stent apposition. It has been reported as a valuable tool for the rapid diagnosis and emergent management of intraprocedural complications such as intracranial hemorrhage. Additionally, IA-CBCTA has been shown to improve the anatomic delineation of both intracranial and spinal dural arteriovenous fistulas (AVFs) for preoperative or endovascular treatment planning.

Flat panel detectors improve the signal intensity-to-noise ratio and suppress geometrical distortion, enabling 3DR-DSA and IA-CBCTA to produce high contrast and spatial resolution imaging with radiation exposure and contrast dose reduction. Furthermore isotropic CBCT volumetric datasets allows for multiplanar and 3D reconstructions analogous to multidetector CT scanners. Advantages over traditional intravenous computed tomographic angiography (CTA) include singular spatial resolution (#1 mm maximally), selective IA contrast injections for territorial vascular analysis, rapid acquisitions (5-8 s) limiting venous contamination, possibility of subtraction and hemodynamic analysis (3DR-DSA), and the simultaneous ability to optimize visualization of the osseous structures and related soft tissues (IA-CBCTA).
In our series, both observers assigned higher scores for IA-CBCTA regarding the nidus and arterial feeder identification, they were able to delineate them with greater anatomic localization and more confident characterization. In addition to IA-CBCTA attaining a statistically significant higher total diagnostic score, it achieved excellent inter-observer agreement while conventional DSA was limited to fair agreement. Although conventional DSA still harbors superior spatial and temporal resolution, it has some limitations by its 2D acquisition and inherent vessel overlap.\textsuperscript{9} Even biplanar DSA can require multiple projections and/or superselective catheterizations to delineate the subtle anatomy of mAVMs. Moreover, the precise anatomic localization of mAVMs, especially for surgical treatment planning, can be challenging to ascertain with conventional 2D DSA techniques. Even intra-operatively the location of the nidus is nearly impossible unless the venous drainage is superficial and easy to follow the arterialized vein to the nidus in a retrograde fashion.\textsuperscript{11} In the future, IA-CBCTA may address the need for intraoperative 3D localization with stereotactic guidance for occult mAVMs as well as reducing operative times.

Our results are subject to the inherent limitations of a retrospective study. Although we attempted to partly mitigate bias with blinded analysis. Despite the rare nature of the mAVMs, sample sizes remain small which require future studies with a larger cohort.

We directly studied IA-CBCTA and DSA modalities in parallel to assess the relative efficacy of IA-CBCTA in the anatomic identification and localization of mAVMs. IA-CBCTA improves the anatomic delineation of mAVMs, particularly for the arterial feeder and nidus site enabling a more confident diagnosis and treatment plan.
Personal information

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