

High-resolution micro-Doppler imaging during neurosurgical resection of an arteriovenous malformation: illustrative case

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OBJECTIVE Given the high-risk nature of arteriovenous malformation (AVM) resections, accurate pre- and intraoperative imaging of the vascular morphology is a crucial component that may contribute to successful surgical results. Surprisingly, current gold standard imaging techniques for surgical guidance of AVM resections are mostly preoperative, lacking the necessary flexibility to cater to intraoperative changes. Micro-Doppler imaging is a unique high-resolution technique relying on high frame rate ultrasound and subsequent Doppler processing of microvascular hemodynamics. In this paper the authors report the first application of intraoperative, coregistered magnetic resonance/computed tomography, micro-Doppler imaging during the neurosurgical resection of an AVM in the parietal lobe.

OBSERVATIONS The authors applied intraoperative two-dimensional and three-dimensional (3D) micro-Doppler imaging during resection and were able to identify key anatomical features including draining veins, supplying arteries and microvasculature in the nidus itself. Compared to the corresponding preoperative 3D-digital subtraction angiography (DSA) image, the micro-Doppler images could delineate vascular structures and visualize hemodynamics with higher, submillimeter scale detail, even at significant depths (>5 cm). Additionally, micro-Doppler imaging revealed unique microvascular morphology of surrounding healthy vasculature.

LESSONS The authors conclude that micro-Doppler imaging in its current form has clear potential as an intraoperative counterpart to preoperative contrast-dependent DSA, and the microvascular details it provides could build new ground to further study cerebrovascular pathophysiology.

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KEYWORDS micro-Doppler imaging; arteriovenous malformations; surgical decision-making; imaging technique

Arteriovenous malformations (AVMs) are vascular pathologies that can be difficult to resect, with potentially high procedural morbidity and mortality depending on factors such as their size and the number and location of the feeding arteries and draining veins.¹⁻⁴ From a pathophysiological perspective, the absence of intervening capillaries, but presence of a nidus with high-flow arteries and dilated veins, makes an AVM prone to hemorrhage. Imaging the AVM's vascular morphology is a crucial step in surgical planning, intraoperative decision-making, and therefore ultimately, treatment success.

Current clinical practice relies heavily on preoperatively acquired images including contrast-enhanced computed tomography angiography (CTA), contrast-enhanced magnetic resonance angiography (MRA), or digital subtraction angiography (DSA), the latter of which remains the gold standard for AVMs to this day.^{3,5,6} Preoperatively acquired images all present the same intraoperative difficulty: they cannot completely cater to the dynamic changes in the operative field as the surgery progresses. First and foremost, the craniotomy and durotomy itself, as well as the evacuation of hematoma and

ABBREVIATIONS 3D-DSA = three-dimensional rotational digital subtraction angiography; AVM = arteriovenous malformation; CDI = color Doppler image; CT = computed tomography; CTA = computed tomography angiography; DSA = digital subtraction angiography; ECG = electrocardiogram; fUS = functional ultrasound; MR = magnetic resonance; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; PDI = power Doppler image; ROI = region of interest.

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circumferential isolation of the malformation, can lead to a physical shift in brain tissue, introducing a mismatch between preoperative images and the intraoperative *in vivo* anatomy, even when using the latest neuronavigation software. What is more, the actual hemodynamics of the malformation can change as the surgery progresses and more and more blood flow to the malformation is sequentially interrupted. This is particularly problematic when the neurosurgeon sees no initial surface manifestation of the malformation as an anatomical reference for the remainder of the surgery.^{3,4} Intraoperative DSA^{7–10} allows the surgeon to circumvent brain shift-related issues, but it is a laborious technique, especially when used for repeated imaging during the surgical procedure: it is time-consuming, disrupts surgical flow, and repeatedly exposes the patient to contrast. What is more, if the contrast catheter is left *in situ* for longer periods of time to facilitate repeated imaging, heparin is often indicated, which is far from ideal in the context of cerebral AVM resection. Therefore, in our center, intraoperative DSA is often only used limitedly to confirm extent of AVM resection.

What could significantly aid the neurosurgical success of AVM resections would be a technique that allows for frequent or even continuous, real-time, hemodynamic feedback of the operative field. So far, literature shows multiple examples of grayscale, color Doppler imaging (CDI) or angle-independent blood flow sonographic imaging, which demonstrate the power of ultrasound as a mobile, affordable, and easy-to-use imaging technique capable of real-time morphological and hemodynamic feedback during AVM resections.^{4,11–15} However, conventional (Doppler) ultrasound is limited in its spatiotemporal resolution, mostly bottlenecked by current limitations on high data-rate processing in the intraoperative setting.

In this paper, we present the first case of high-resolution micro-Doppler imaging during a neurosurgical AVM resection. This unique micro-Doppler imaging technique relies on high frame rate (HFR) ultrasound and subsequent Doppler processing. Thus, it facilitates real-time detection of microvascular hemodynamics with submillimeter, subsecond precision.^{16–18} Previously, our team has demonstrated the potential of micro-Doppler imaging and its functional counterpart called “functional Ultrasound” (fUS) during awake tumor resections, where we showed highly detailed functional maps and vascular morphology of a range of low- and high-grade gliomas.¹⁸ Here, we demonstrate how intraoperative micro-Doppler imaging can identify with high resolution the key anatomical and hemodynamic features of a parietal AVM. Compared to preoperative three-dimensional-reconstructed rotational digital subtraction angiography (3D-DSA), micro-Doppler imaging could identify more vascular details, even at high depths (>5 cm), in real time during the surgical procedure. We also demonstrate the power of high-resolution micro-Doppler imaging in providing intraoperative contextual vascular information of, for example, healthy surrounding tissue, which could have direct surgical benefits, as well as long-term benefits for increasing our understanding of the cerebrovasculature. Finally, we discuss the necessary future steps to push micro-Doppler imaging to actual clinical maturity.

Illustrative Case

History and Preoperative Imaging

A male in his 30s presented with acute headache, left-sided hemianopsia, and left hemi-inattention, without evident motor symptoms. Consecutive CTA and magnetic resonance imaging (MRI)/MRA scans showed a parenchymal hemorrhage of 3.8 × 4.7 cm in

the right parieto-occipital region. 3D-DSA confirmed an underlying AVM with a compact nidus of 16 mm (S1V0E0/A2B0C0). Two superficial draining veins and two dominant arterial feeders originating from the medial cerebral artery could be identified (Fig. 1A–C).

Micro-Doppler Data Acquisition

Micro-Doppler acquisitions were performed using an experimental research system (Vantage 256, Verasonics) interfaced with the commercially available L8-18I-D linear array hockey stick transducer (7.8 MHz, 0.15 mm pitch, GE) or 9L-D Logiq 9 linear array transducer (5.3 MHz, 0.23 mm pitch, GE). For all scans we acquired continuous angled plane wave acquisition (10–12 angles equally spaced between –12 degrees and 12 degrees) with a pulse repetition frequency ranging from 667 to 800 Hz depending on the imaging depth and transducer. The average ensemble size (number of frames used to compute one power Doppler image [PDI]) was set at 200 angle-compounded frames from which the live PDIs were computed, providing a live Doppler frame rate ranging between 3 and 4 Hz. The PDIs as well as the raw, angle-compounded beamformed frames were stored to a fast PCIe SSD hard disk for offline processing purposes. Parallel to our micro-Doppler acquisitions, the patient's vital signs (electrocardiogram [ECG], arterial blood pressure) were recorded using a National Instruments' CompactDAQ module (NI 9250) at 500 Hz and stored for postprocessing purposes.

Imaging Procedure

The transducer was placed in a sterile cover containing ultrasound gel intraoperatively. Prior to durotomy as well as postresection, hand-held 3D volumes of the AVM or resection cavity were obtained by acquiring two-dimensional (2D) images during a 60-second sweeping motion along continuous trajectories. Additionally, stable acquisitions of 120 seconds were made by placing the probe over a region of interest (ROI) containing the AVM using a modified intraoperative surgical arm (Trimano, Getinge) with a transducer holder. Saline was added frequently to the operating field by the operating room nurse to ensure adequate acoustic coupling during imaging.

MR/CT Co-Registration

Our transducers were made trackable by Brainlab neuronavigation software by attaching the conventional optical tracking geometry to the transducer casing using custom-made 3D-printed attachments. Building on Brainlab's 'Cranial Navigation' and 'Intra-Operative Ultrasound' calibration modules, we could in real-time coregister our intraoperative PDIs to patient-registered MR/CT data and display these images on the conventional, clinical Brainlab interface. Using the 'IGTLink' research interface, we could access and store the real-time tracking data for offline postprocessing purposes. Preoperative 3D-DSA reconstructions were not available to the neurosurgeon intraoperatively through registration in the neuronavigation software but were registered to the intraoperatively used navigational volumes (MR/CT) postoperatively using the General Registration (BRAINS)¹⁹ module in 3D Slicer.²⁰ Any remaining brain shift-related mismatches were also corrected offline using a rigid linear transform in 3D Slicer²⁰ to visually match the MR/CT/DSA to the PDI.

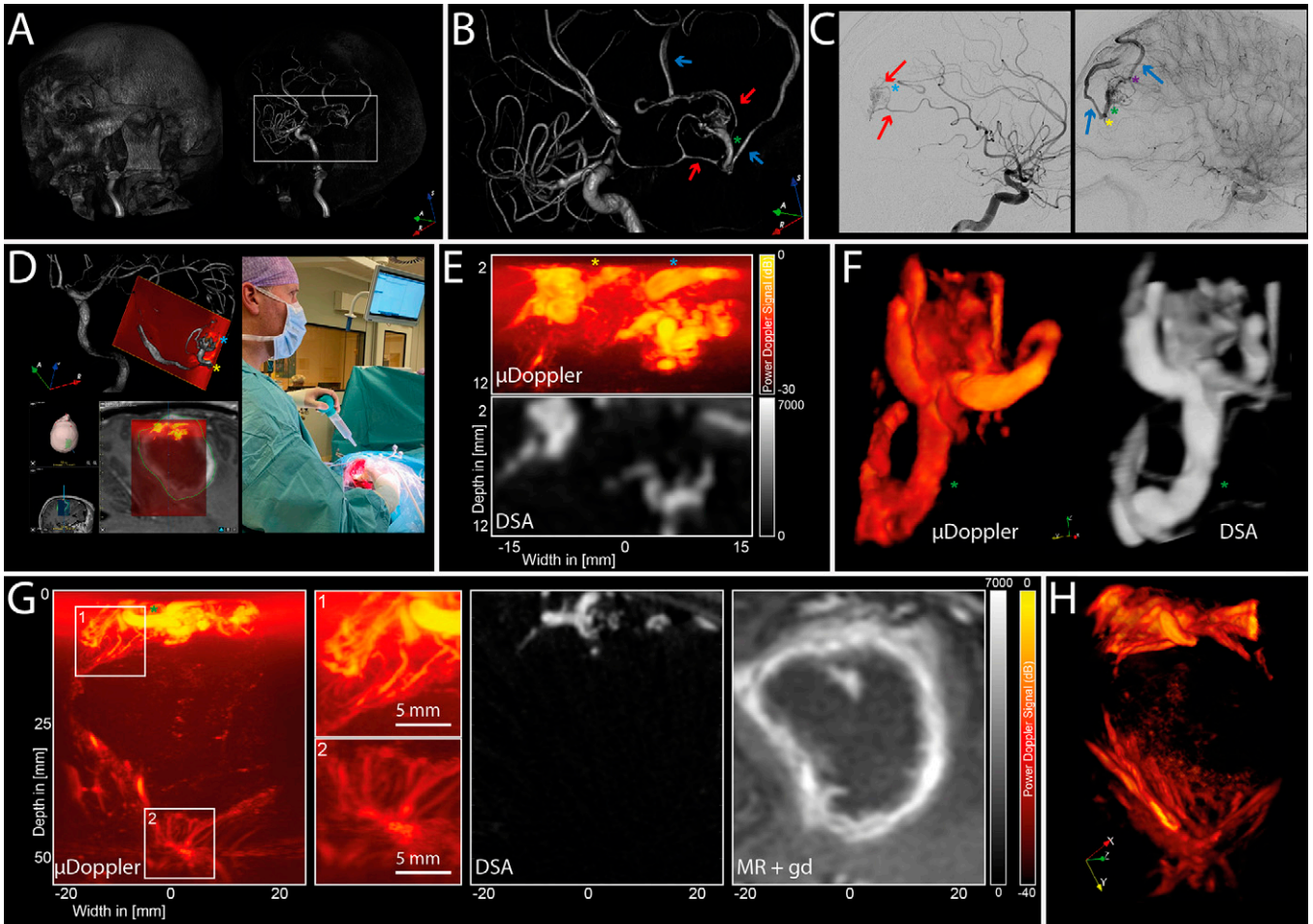


FIG. 1. Intraoperative micro-Doppler versus preoperative DSA images of an AVM. **A:** 3D reconstruction of preoperative 3D-DSA images with (*left*) and without (*right*) the skull in view, demonstrating the parietal localization of the AVM. The *white box* marks the area depicted in panel B. **B:** Magnified preoperative 3D-DSA showing the AVM's angioarchitecture. A total of two feeding arteries (*red arrows*), originating from the middle cerebral artery, and 2 superficial draining veins (*blue arrows*) could be identified. *Green asterisk* indicates the large beginning of a draining venule, which serves as a clear anatomical identifier. **C:** Preoperative 2D-DSA images of the arterial (*left*) and venous (*right*) phase, showing the same anatomical landmarks as described in panel B. The nidus spans approximately 16 mm, and its borders are marked by *purple* and *yellow asterisks* (*right*). The *blue asterisk* (*left*) indicates an ROI in panel E. **D:** Intraoperative micro-Doppler acquisitions. Offline reconstruction of the position of an intraoperatively acquired stable 2D micro-Doppler image relative to the preoperative 3D-DSA (*upper left*). *Asterisks* indicate ROIs in panel E. Screenshot of the intraoperative view of the Brainlab neuronavigation software (*lower left*), where our experimental micro-Doppler images were coregistered to preoperative CT/MR images in real time. Here, the postcraniotomy brain shift is already visible. A hand-held linear acquisition by the surgeon (*right*). **E:** Cut-out of a 2D micro-Doppler image acquired using the intraoperative arm, as shown in panel D. Multiple components of the AVM's angio-architecture are in view at once, including a draining vein (*yellow asterisk*, also depicted in C and D) and a feeding artery (*blue asterisk*, also depicted in C and D). As compared to the preoperative 2D-DSA image, the micro-Doppler image can provide a much more detailed overview of the vascular morphology intraoperatively. **F:** A side-by-side 3D reconstruction of the main draining venule (*green asterisk*) and its surrounding angioarchitecture using micro-Doppler imaging (*redscale*) and DSA (*grayscale*). As demonstrated, the reconstructed hand-held linear micro-Doppler scan can depict as much angio-architectural detail intraoperatively as the DSA that was made preoperatively. **G:** A second intraoperatively acquired, stable 2D micro-Doppler image depicting the main draining venule (*green asterisk*). This image further demonstrates the power of micro-Doppler imaging. In magnification *boxes 1* and *2*, we highlight high-resolution vascular details of neighboring healthy cortical vessels (*box 1*) as well deep (5 cm) vascular structures surrounding the hematoma cavity (*box 2*). In the corresponding DSA image, both of these superficial and deep vascular details are completely absent. In the corresponding gadolinium-enhanced MR image, we see a clear depiction of the cavity borders of the hematoma, without any of the microvascular details seen with micro-Doppler. **H:** The 3D reconstruction of the vascular morphology in the area covering the 2D image depicted in panel G. In the top layers of the reconstruction, the AVM vessels are reappearing. Now in-depth details are depicted even more clearly: the vascular structures (deep medullary veins) surrounding the hematoma's cavity. These vessels were not in sight intraoperatively or in any of the preoperative modalities, depicting the unique contextual vascular information which could be gained by using micro-Doppler as a routine intraoperative imaging modality.

Micro-Doppler Data Processing

PDIs were computed using an adaptive SVD clutter filter over each ensemble and mapped onto a 100- μm grid using zero padding in the frequency domain. For the stable measurements, the PDIs were further subjected to rigid motion compensation by registering every PDI to the median PDI using the inbuilt Matlab function 'imregtform.m'. The ensemble size was adaptively set to match one average cardiac cycle based on the acquired ECG signal, before averaging the power Doppler signal. Color Doppler images were computed by taking the mean of the difference of the instantaneous phase signal for all frames in one ensemble, as described by Kasai et al.²¹

All initial micro-Doppler data processing was performed using custom scripts in Matlab 2020b (MathWorks, Inc.). Offline 3D reconstructions of the linear micro-Doppler scans were made by computing a power Doppler signal for each voxel, based on the 3D position and orientation of the closest ultrasound frames, as measured intraoperatively through the *IGTLink*. Using Paraview (Kitware, Inc.), the 3D volumes of both the micro-Doppler and 3D-DSA images were further thresholded and smoothed for visualization purposes.

Surgical Procedure

The surgery was scheduled a few weeks after the bleeding, in our hybrid operating room. With the patient under general anesthesia, a standard parietal craniotomy was performed using MR/CT-guided neuronavigation to have the AVM, feeding arteries, and draining veins centered in the craniotomy. Circumferential dissection was performed saving the major draining veins. At the end of the resection the draining veins "turned blue," and the hematoma was evacuated.

Intraoperative DSA confirmed the nidus and venous drainage were no longer visible postresection. A total of 6 hand-held linear micro-Doppler scans and 2 stable scans with the help of the intraoperative arm were performed predurotomy. A total of 3 hand-held linear scans of the resection cavity were made postresection (Fig. 1D). Total intraoperative recording time was 11 minutes.

Postoperative Course

Postoperatively, the patient presented conform preoperative assessment, with no additional neurosurgical deficits. The patient returned to the rehabilitation center for further recovery.

Micro-Doppler Results

Intraoperative micro-Doppler versus Preoperative 3D-DSA

Intraoperative 2D micro-Doppler imaging was successful in identifying the key anatomical features of the AVM including draining veins, supplying arteries and microvasculature in the nidus itself (Fig. 1E). As compared to the corresponding millimeter scale preoperative DSA image, the micro-Doppler images could delineate and discern vasculature structures in submillimeter scale detail. Comparison between offline 3D reconstruction of hand-held linear micro-Doppler scans and the preoperative 3D-DSA scan further confirmed the striking vessel correspondence between the two techniques, indicating that hand-held intraoperative micro-Doppler in its current form could potentially compete with contrast-dependent preoperative DSA (Fig. 1F) (Video 1).

VIDEO 1. Clip showing micro-Doppler imaging versus DSA of an AVM. Click here to view.

Micro-Doppler's Resolution and Depth Penetration

The striking difference in resolution between intraoperative micro-Doppler and preoperative DSA is further demonstrated in Fig. 1G, a 2D micro-Doppler image of the most dominant draining venule. As compared to DSA and contrast-enhanced MR, micro-Doppler can delineate vasculature of both the AVM as well as the neighboring healthy cortical vessels in more detail. This resolution is also present at high depths of penetration, as demonstrated in this same image by the unique microvascular pattern surrounding the cavity of the hematoma at a depth of 5 cm. In the postresection scans, more unique healthy vascular patterns were captured, as depicted in Fig. 2A and B, in which we see vasculature spanning multiple gyri, the falx, and even into the contralateral hemisphere. These depth-resolved microvascular details may not be directly pathophysiological in this case but could provide contextual information during the surgical procedure as well as increase potential understanding of cerebrovascular pathophysiology, as will be explained in the *Discussion*.

Color Doppler Images

As depicted in Fig. 3, color Doppler processing of the intraoperative micro-Doppler images could visualize directionality of blood flow with a similar level of detail as the micro-Doppler images in Figs. 1 and 2.

Discussion

Observations

This paper describes the first application of high-resolution, depth-resolved micro-Doppler imaging during the neurosurgical resection of an AVM. We show how this new, contrast-free, affordable, and easy-to-use sonography-based imaging technique provides images that are highly detailed, perhaps even more detailed than its preoperative clinical counterpart of 3D DSA. These vascular details are not limited to superficial or pathophysiological structures only but include structures at great depths (>5 cm) and surrounding healthy vessels, which could serve as additional contextual information during surgical resection.

In contrast to conventional millimeter scale (Doppler) ultrasound,^{4,12-15} our micro-Doppler technique presents with an unprecedented resolution in the submillimeter range, allowing for actual morphological delineation and inspection of microvasculature intraoperatively. Conventional ultrasound and micro-Doppler still share a common enemy: the skull bone. Conventional transcranial Doppler²²⁻²⁴ or transcranial color-coded duplex sonography²⁵ are used sparsely for preoperative diagnostics or postoperative follow-up of AVMs and other brain pathologies, given their low resolution and ability to capture only those major cerebral arteries accessible through limited ultrasonic windows.²⁶ The transcranial counterpart of micro-Doppler might be more promising, although requiring contrast enhancement. Recent advances in ultrafast ultrasound combined with intravenously injected microbubble contrast have demonstrated the possibility to perform transcranial imaging of in-depth human vasculature, including a deep-seated aneurysm, at microscopic scales.²⁷ These promising developments form the first steps toward possible preoperative ultrasound-guided surgical planning, in addition to micro-Doppler as an intraoperative surgical tool.

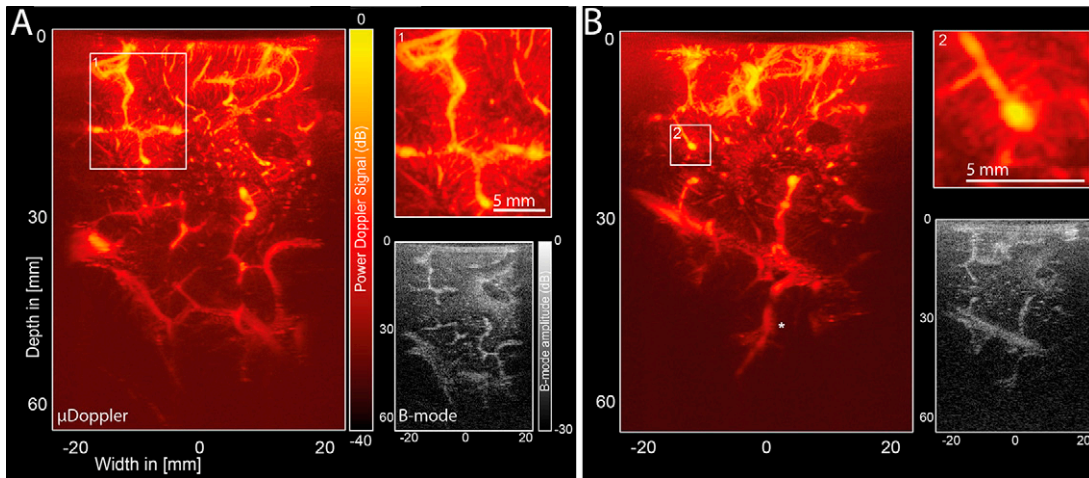


FIG. 2. High-resolution micro-Doppler details of healthy vasculature. **A:** Intraoperative micro-Doppler imaging of AVMs would also allow for high-resolution imaging of surrounding vasculature, here up to depths >5 cm. In this image we see multiple vascular structures following a gyral pattern, as also becomes clear from the corresponding B-mode. In the magnified panel, we can appreciate the vascular detail that is now available to the neurosurgeon intraoperatively. **B:** A second intraoperative micro-Doppler image of surrounding vasculature, here including the falx cerebri starting at a depth of 3 cm. Vessels originating from the midline and penetrating the parenchyma both ipsi- and contralateral (*white asterisk*) to the hemisphere containing the AVM are clearly visualized in the micro-Doppler image and confirmed in the B-mode. In the magnified view, we can appreciate the vascular details of a healthy, feather-like cortical vessel. Both images were acquired postresection of the AVM.

What makes ultrasound in general a favorable technique compared to conventional neuro-angiograms—be it 3D DSA, CTA, or MRA—is the actual ability to capture real-time hemodynamics, without being dependent on the presence of contrast in either arterial and/or venous compartments. micro-Doppler is also not phase-dependent such as 3D-DSA, which relies heavily on timing of contrast wash-out to differentiate between arterial feeders, nidus and

draining veins. Instead, directionality of these vessels could be visualized using well-established CDIs at micro-Doppler resolution, as exemplified in Fig. 3. Alternatively, our concomitant recordings of ECG signal could in future work become valuable for investigating temporal characteristics of the micro-Doppler signal in relation to the cardiac phase, which might give additional insight into feeding and drainage patterns.

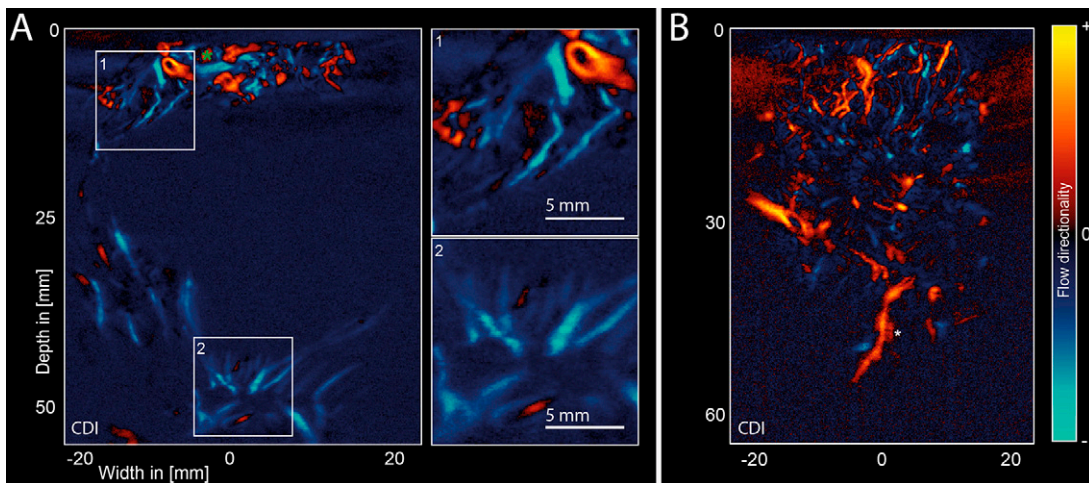


FIG. 3. CDI of the AVM and its surrounding angio-architecture. The color axis depicts flow directionality, with positive values indicating flow toward the transducer and negative values indicating flow away from the transducer. **A:** CDI corresponding to Fig. 1G, showing flow directionality in the main venule of the AVM (*green asterisk*), healthy cortical vessels adjacent to the AVM (magnification in *box 1*) and deeper-seated vasculature surrounding the hematoma cavity (magnification in *box 2*). Given the 2D nature of these images, 3D vascular structures will not necessarily align with the field of view. Thus, a 2D sample of, for example, the main venule (*green asterisk*) can appear to contain bidirectional flow because of the contribution of out-of-plane Doppler signal. **B:** CDI corresponding to Fig. 2B, showing flow directionality in cortical and deeper-seated vessels, assumed to be healthy vasculature.

Lessons

Micro-Doppler in the form currently presented has not yet reached its full intraoperative potential. First and foremost, our current use on linear probes dictates the 2D nature of our real-time micro-Doppler images. As of yet, we reconstruct the offline 3D volumes by stacking these 2D images using positional data as saved through the neuronavigation software. A first step would be to facilitate real-time, intraoperative volumetric reconstructions of these 2D acquisitions. Ultimately, our team is developing 3D micro-Doppler using matrix probes, which could facilitate actual real-time, intraoperative 3D acquisitions. Overlaying 3D maps with real-time information on directionality using color Doppler, as well as quantitative measures of blood flow, would complete the package and render 2D out-of-plane limitations such as described in Fig. 3A obsolete. With such 3D vascular maps, vascular-based calibration instead of the usual bone-based calibration for neuronavigation, could also potentially solve postcraniotomy brain shift problems.

Although our micro-Doppler images can achieve exceptional resolution without needing contrast agent, future work involving ultrasound localization microscopy^{28,29} with the aid of intraoperative microbubble contrast agent would be valuable to produce unique superresolution vascular maps of in vivo AVMs. Microscopic scale images of an AVM might not be necessary for surgical decision-making but could add significant new insight into our understanding of AVM morphology and hemodynamics.

Some would perhaps argue that even the submillimeter scale imaging as demonstrated here is an overkill for the surgical procedure of most AVMs. With this first in-human application we already demonstrate another benefit of high-resolution, real-time imaging of cerebrovascular hemodynamics and morphology: increasing our understanding of cerebrovascular pathology. In the patient presented here, we discovered an intricate in-depth vascular network surrounding the hematoma cavity, which was not visible in the operative field, nor in any of the preoperative images. Additionally, we could capture surrounding assumingly healthy cortical vasculature with submillimeter precision. None of these in vivo high-resolution images of human neurovasculature have been available for study yet. We might not directly be able to predict the significance of these vascular details, but as we continue to image during more AVMs of different shapes and sizes, in different anatomical locations, we will add a wealth of information on both healthy and pathophysiological vascular morphology. Feeding this into for example deep learning algorithms might allow us to discover new patterns in human vascular pathophysiology, which hopefully could circle back to improving surgical procedures. As we increase the number of AVMs we measure, we aim to in parallel move from qualitative morphological measures to more real-time quantitative morphological and blood flow measures to facilitate these artificial intelligence-based analyses. Especially during the different stages of the surgical procedure, as more and more of the AVM's angioarchitecture is devascularized, it would be very valuable to compare quantitative measures to better predict locations of the AVM harboring high risk of bleeding.

A final potential application of micro-Doppler would be in the context of functional brain mapping. The microvascular hemodynamics measured with micro-Doppler are indicative of changes in cerebral blood flow and cerebral blood volume.^{17,18,30} Through the principle of neurovascular coupling, these hemodynamics can serve as an indirect measure of neuronal activity and therefore brain functionality.^{17,18,31} In its functional counterpart, so-called fUS uses micro-Doppler-based imaging to produce high-resolution, depth-resolved intraoperative functional maps of the

brain. So far, applications of fUS have been described in rodents,^{32–36} pigeons,³⁷ primates,^{38,39} neonates,^{40,41} and adult humans.^{18,42} The latter involves functional brain mapping during awake tumor resections, where patients were able to perform simple functional tasks such as lip pouting or word repetition.^{18,42} AVMs are not resected routinely in awake patients,^{43,44} and passive tasks which can be performed under general anesthesia (e.g., passive limb movement, or sensory stimulation) are limited.⁴⁵ However, fUS might still be valuable in those cases where functionality is at risk and awake AVM-resection is possible and preferred.

A dynamic, high-risk surgical procedure such as the resection of an AVM could benefit from an equally dynamic technique which can in real-time guide surgical decision-making safely and effectively. In this paper we demonstrate the unique potential of high-resolution, depth-resolved intraoperative micro-Doppler imaging of an AVM and its surrounding healthy vasculature. As the technique progresses, micro-Doppler does not only have the potential to become a powerful new tool in the surgeon's intraoperative toolkit, but the microvascular details it provides could build new ground to further study cerebrovascular pathophysiology.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Soloukey, Kruizinga, Schouten. Acquisition of data: Soloukey, Verhoef, Schouten. Analysis and interpretation of data: Soloukey, Verhoef, van Doormaal, Generowicz, Kruizinga, Schouten. Drafting the article: Soloukey, Kruizinga, Schouten. Critically revising the article: Soloukey, van Doormaal, Dirven, De Zeeuw, Koekkoek, Kruizinga, Vincent, Schouten. Reviewed submitted version of manuscript: Soloukey, Verhoef, van Doormaal, Generowicz, Dirven, De Zeeuw, Koekkoek,

Kruizinga, Vincent, Schouten. Approved the final version of the manuscript on behalf of all authors: Soloukey. Statistical analysis: Soloukey, Generowicz. Administrative/ technical/material support: Soloukey, Verhoef, Dirven, De Zeeuw, Koekkoek, Kruizinga. Study supervision: Soloukey, Kruizinga, Vincent, Schouten.

Supplemental Information

Video

Video 1. <https://vimeo.com/739644097>.

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