

Dynamic assessment of venous anatomy and function in neurosurgery with real-time intraoperative multimodal ultrasound: technical note

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The relevance of the cerebral venous system is often underestimated during neurosurgical procedures. Damage to this draining system can have catastrophic implications for the patient. Surgical decision-making and planning must consider each component of the venous compartment, from the medullary draining vein to the dural sinuses and extracranial veins. Intraoperative ultrasound (ioUS) permits the real-time study of venous compartments using different modalities, thus allowing complete characterization of their anatomical and functional features. The B-mode (brightness mode) offers a high-resolution anatomical representation of veins and their relationships with lesions. Doppler modalities (color, power, spectral) allow the study of blood flow and identification of vessels to distinguish their functional characteristics. Contrast-enhanced US allows one to perform real-time angiosonography showing both the functional and the anatomical aspects of vessels.

In this technical report, the authors demonstrate the different applications of multimodal ioUS in neurosurgery for identifying the anatomical and functional characteristics of the venous compartment. They discuss the general principles and technical nuances of ioUS and analyze their potential implications for the study of various venous districts during neurosurgical procedures.

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KEYWORDS intraoperative imaging; contrast-enhanced ultrasound; intraoperative ultrasound; cerebral veins; extracranial veins; dural sinuses

KNOWLEDGE of the venous functional anatomy is essential for the safe and effective execution of neurosurgical operations. The most critical issues to understand are the contribution of each venous structure to the drainage of each brain compartment and the dynamic nature of this behavior in pathological conditions.^{9,23} In cases such as tumors and vascular malformations, the physiological architecture of the venous compartment can be subverted with the creation of reversible shunts, anastomoses, and collaterals and, in some cases, even completely replacing the normal angioarchitecture.⁴ The highly dy-

amic nature of the cerebral veins' response to head positioning and mechanical stimuli and their reorganization under different conditions (tumor presence, bone and tumor decompression, shunts, patient positioning) highlight the need for a real-time intraoperative imaging modality able to identify dynamic venous modifications.

Intraoperative ultrasound (ioUS) can provide useful real-time information in planning the management of vessels, notably venous structures. It is a rapid tomographic modality not requiring any changes in patient positioning or the intraoperative setting, while at the same time of-

ABBREVIATIONS AVM = arteriovenous malformation; CEUS = contrast-enhanced ultrasound; DAVF = dural arteriovenous fistula; GBM = glioblastoma; IJV = internal jugular vein; ioUS = intraoperative ultrasound.

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TABLE 1. Technical principles of ioUS

Applications/Characteristics	
Probe selection	
Linear (high frequency)	Study of superficial structures (higher definition/lower penetration)
Convex/linear (low frequency)	Study of deep structures (lower definition/deeper penetration)
US mode	
B-mode (grayscale)	Initial evaluation, orientation, structure (including vessel), & lesion detection
Doppler (echo color & power)	Vessel identification, flow direction, & characterization (arterial/venous)
CEUS	Enhanced vessel identification (both arterial & venous), lesion & structure characterization (arterial, venous, & late phase)

fering significant spatial and temporal resolution.¹⁸ Moreover, it provides multiple imaging modalities. The B-mode (brightness mode) has a spatial resolution comparable to that of preoperative volumetric MRI, thus allowing the study of anatomical details in real-time, given its incomparable temporal resolution.¹⁸ Power Doppler permits vessel localization relying on blood flow. Color Doppler can be used to assess flow direction in a region sensitive to flow velocity, although it is limited by the insonation angle. Spectral Doppler permits the quantification of flow velocity and its representation in waveform. Contrast-enhanced ultrasound (CEUS) represents the most specific and sensitive US technique to describe blood flow in arterial, capillary, and venous districts through the use of an intravascular contrast agent to enhance backscattering from the vessels and to suppress the signal from the remaining part of tissues, thus permitting angiosonography. Its use in neurosurgery has been recently included in the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines.^{13,16–18,20}

In this paper, we provide technical background on which modalities to apply when evaluating the venous circulation in neurosurgical procedures, and we review different clinical scenarios, demonstrating how the combination of different US modalities has the potential to detect all those dynamic changes that take place within the venous system during cranial surgery, and discuss the importance of the assessment of the extracranial venous system and its impact on cerebral venous drainage.

Multimodal ioUS and Applications for Real-Time Venous Imaging and Management: Technical Principles

The operator should have received specific training in the use of ioUS; therefore, the general steps in the use of US are not discussed herein. Table 1 summarizes the various US modalities used in general practice and their neurosurgical applications specifically in terms of vein visualization and management. The latter requires not only a basic theoretical knowledge of US other than the B-mode, which is provided by educational courses, but also, as already established for other organs, supervised training regarding normal and pathological US findings of brain diseases.¹²

The US probe and parameters should be chosen according to the lesion type, dimensions, and field depth

and, in general, the information that has been collected about the area of interest. Multiple probes can be used and changed during the same intervention. Smaller probes can be used to fit smaller craniotomies or resection cavities, but they have lower resolution. Usually the entire evaluation can be performed with multifrequency linear probes with frequencies ranging from 5 to 18 MHz.¹⁸

The main parameters to be set are depth and frequency. In adjusting the depth, it is possible to have a shallower or deeper image. With greater depths the image will be smaller, whereas with reduced depths the image becomes larger, although the spatial resolution will be decreased. Frequency changes allow one to modulate the spatial resolution: the higher the frequency, the higher the spatial resolution and the lower the penetration of the US beam.¹⁸

Patient positioning is crucial: the head should be elevated as compared to the thorax, the abdomen should be free, and the neck should be as supple as possible in order not to obstruct the jugular veins and the vertebral plexuses, thus facilitating venous outflow.^{10,26} From an imaging standpoint, the surgical field should be as parallel as possible to the floor to facilitate acoustic coupling between the probe and the organ.¹⁸

The first part of the evaluation is performed using the B-mode. It is conducted in two orthogonal planes, tilting and shifting the probe to visualize the entire lesion and its anatomical relationships with major landmarks (dural structures, sinuses, ventricles, choroid plexuses, and arachnoidal folds). Frequency is set to permit the maximum resolution possible that is compatible with the depth needed.¹⁸ Care should be taken not to apply too much pressure on the structures as veins are easily compressible and the simple application of the probe can modify their caliber.

The power Doppler mode is typically used to visualize vessels as it has high sensitivity and is less dependent from the insonation angle,¹⁸ whereas color Doppler and spectral Doppler should be used to study flow velocity, direction, and waveform.¹⁸ Doppler parameters should be set according to the depth and size of the vessels, speed of the flow, and angle of insonation.

The use of CEUS has been described in other papers from our group.^{13–20} In general, the US contrast agent is prepared and injected through a peripheral vein. Different vascular phases are analyzed: basal, arterial, peak, parenchymal, and venous. Functional characteristics are derived from the intensity of vessel scattering, the direc-

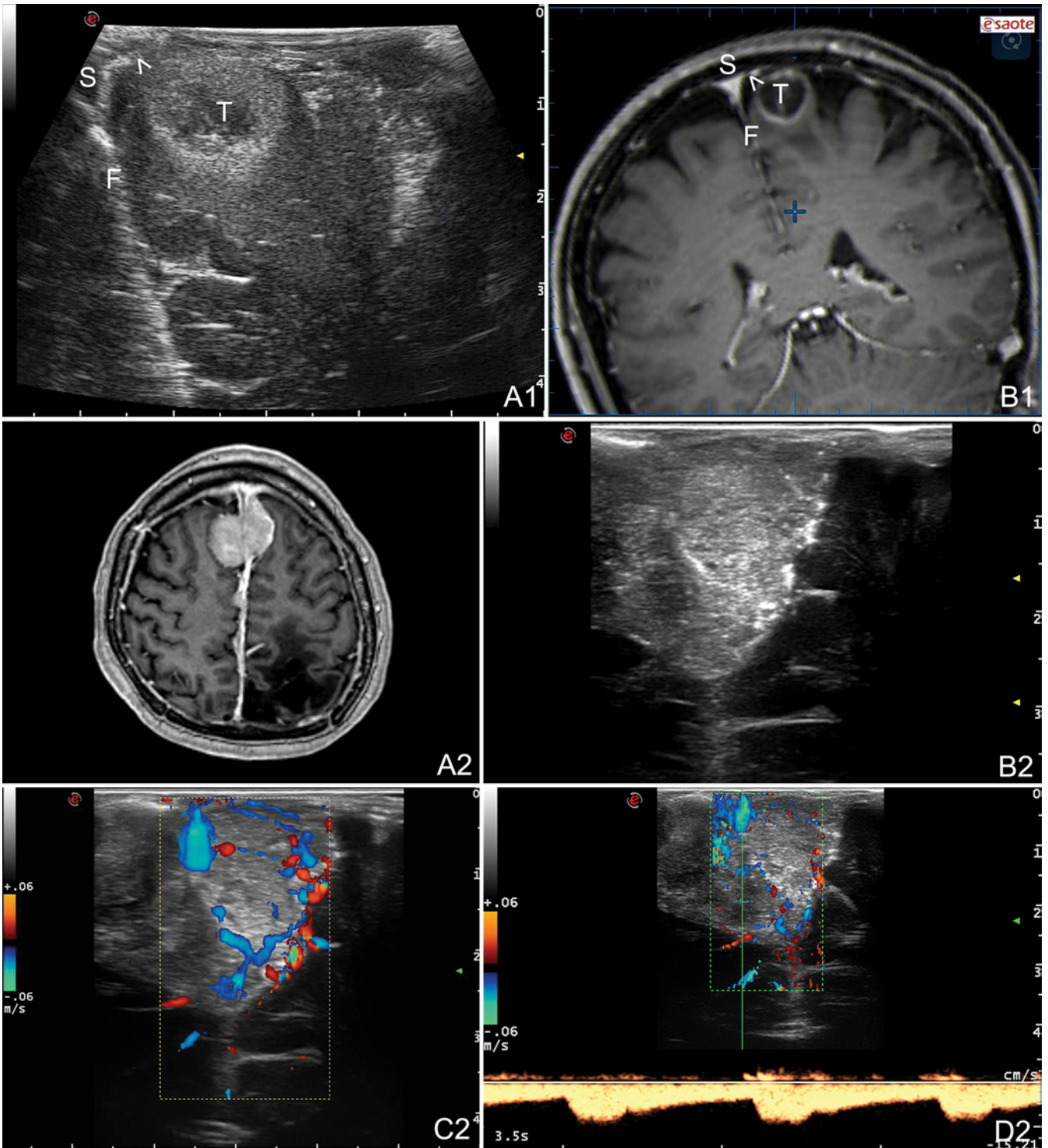


FIG. 1. Transdural multimodal US allows one to characterize the venous functional anatomy. Right frontal parasagittal meningioma (**A1 and B1**): ioUS permits one to tailor the dural opening, sparing the superior sagittal sinus and bridging veins. *Arrowheads* indicate the sinus lateral limit. Bilateral frontal sagittal meningioma (**A2–D2**): on preoperative MRI (**A2**), the superior sagittal sinus appears closed. With B-mode imaging (**B2**), one is unable to evaluate the patency of the sinus. Color Doppler imaging (**C2**) demonstrates relevant flow in the sinus, bridging veins, and collateral venous drainage. Spectral Doppler imaging (**D2**) allows one to study flow in the superior sagittal sinus. F = falx; S = sinus; T = tumor.

TABLE 2. Clinical applications of ioUS

Application	ioUS Technique	Surgical Implication
Management of dural sinuses & superficial veins	B-mode, power Doppler, color Doppler, spectral Doppler, CEUS	Venous structures localization & morphological assessment to aid in dural opening & arachnoidal dissection
Management of basal dural sinuses & basal bridging veins	Power Doppler, color Doppler, spectral Doppler, CEUS	Venous structures localization & morphological assessment influences the surgical corridor & dural opening
Management of deep venous circulation	Power Doppler, color Doppler, spectral Doppler, CEUS	Visualization of disrupted anatomy of venous system & its changes during surgery prior &/or after dissection & targeting of the lesion
Assessment of intraop dynamic change in venous circulation	Power Doppler, CEUS	Comprehension of specific functional anatomy of the vascular tree in different lesions & its changes during surgery
Assessment of changes in brain perfusion associated w/ venous drainage	CEUS	Evaluation of parenchymal blood flow in different vascular phases, including the venous phase, to evaluate brain perfusion
Assessment of extracranial venous drainage & implications for neurosurgical procedures	Color Doppler, spectral Doppler	Extracranial venous circulation (jugular & vertebral veins) during surgery planning & patient positioning

tion and velocity of bubbles and vessels, enhancement of the lesion, time to peak enhancement, and duration of the parenchymal phase. Anatomical features are derived by observing the flow of bubbles and the vessel-enhancement position with regard to the lesion.^{17,18} The examination can be repeated several times to understand the functional vascular anatomy.

In the sections that follow, we describe the use of multimodal ioUS in various cases and scenarios, highlighting the technical nuances of its application in neurosurgery.

Multimodal ioUS Applications for Venous Imaging and Management: Clinical Scenarios

Management of the Dural Sinuses and Superficial Veins

Dural venous sinuses have great variability among patients with potential extension several centimeters from the midline (e.g., venous lacunae),³ whereas bridging veins can join the dura at great distances from the sinus edges before entering into it. The exact location of venous structures is extremely difficult to assess before opening the dura, thus leading to the risk of inadvertent damage.²³

A B-mode US scan before dural opening allows the surgeon to identify the anatomical location and morphology of vessels, sinuses, and dural folds. Both CEUS and Doppler allow one to characterize the functional aspects of various vessels, differentiating high versus low flow, direction of the flow, flow speed, and vessel dimensions. Furthermore, the possibility of visualizing the lesion (intra- or extraaxial) together with the vessels allows one to tailor the dural opening to the intraoperative anatomy (Fig. 1 and Table 2). This is particularly helpful in cases such as parasagittal meningiomas.^{5,9,23} Multimodal ioUS permits one to assess the position of the lesion and the venous bridging vessels, revealing the most suitable surgical corridor and thus allowing one to tailor the durotomy accordingly.

Furthermore, in most cases in which meningioma invades or is close to the sinus, a collateral drainage system can develop, enveloping the lesion or impeding the surgical corridor.^{4,9,23} Preoperative workup should include

an angiographic study to assess the patency of the superior sagittal sinus;^{9,22–25} however, because the study is performed while the patient is supine with a closed skull, it does not always reflect intraoperative findings.^{1,2,27} In some cases, such as in the parasagittal meningioma featured in Fig. 1, it must be noted that, despite the appearance of an occluded sinus on preoperative imaging, venous flow was restored intraoperatively after bone flap removal, as demonstrated by Doppler and CEUS examinations (Fig. 1 and Table 2). In these cases, the sinus should be preserved after tumor debulking because it can regain its functionality.

Management of Basal Dural Sinuses and Basal Bridging Veins

In subtemporal, pretemporal, or transsylvian approaches, retraction of the temporal lobe or access to the optico-carotid region is commonly restricted by bridging veins toward the basal sinuses.⁷ In this setting, vein sparing is mandatory. An ioUS scan before dural opening, as well as during resection, permits one to visualize the bridging veins without the need for direct exposure. In particular Doppler modalities, especially those performed in combination with CEUS, one can visualize all vessels including those at different depths within the field of view, both arterial and venous, independently of the angle of insonation (Fig. 2 and Table 2). This feature can influence surgical decision-making as regards the better corridor to reach the target and to open the dura accordingly.

Management of Deep Venous Circulation

When dealing with lesions close to the deep venous system, it is important to visualize the entire vascular tree and how it is distorted by tumor. Even if not properly encased by the lesion, the deep venous system represents a critical aspect of tumor debulking and dissection. The B-mode coupled with vascular imaging via Doppler or CEUS allows one to visualize the lesion to study its vascularity as well as the disrupted anatomy of the venous system and can be repeated several times, permitting one to follow its changes during various phases of the surgery. In particular, CEUS is useful as it allows one to perform

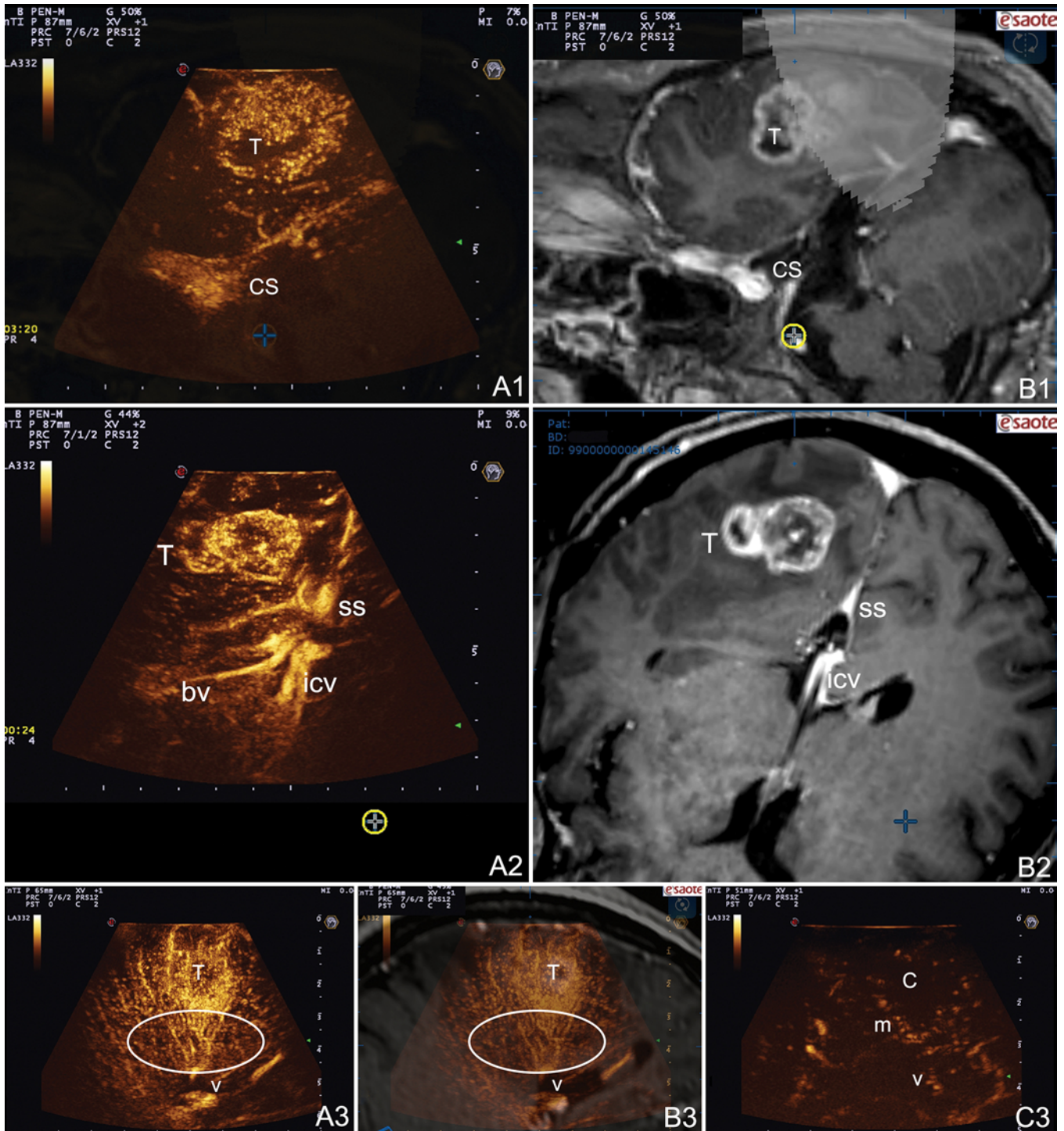


FIG. 2. Intraoperative multimodal US permits one to visualize and characterize the entire vascular venous tree and its changes during surgery. A case of right temporal GBM allows for the study of both arterial and venous relationships; the cavernous sinus is visualized together with the basal venous tributaries on navigated CEUS (A1) and the corresponding coplanar preoperative MRI (B1). A case of right parietooccipital GBM: a CEUS scan (A2) and the corresponding coplanar preoperative gadolinium-enhanced MR image (B2). A case of left parietooccipital GBM (A3–C3): CEUS highlights tumor together with venous, capillary, and arterial vessels and permits the study of deep veins up to a depth of 9 cm from the surface, allowing their identification in the deeper part of the lesion or in cases of deep-seated lesions. Pre-resection CEUS examinations highlight venous drainage through small vessels directed toward the ventricle (*ellipses*, A3 and B3). After complete resection, venous drainage disappeared (C3). bv = basal vein; C = cavity; CS = cavernous sinus; icv = internal cerebral veins; m = margins; ss = straight sinus; T = tumor; v = ventricle.

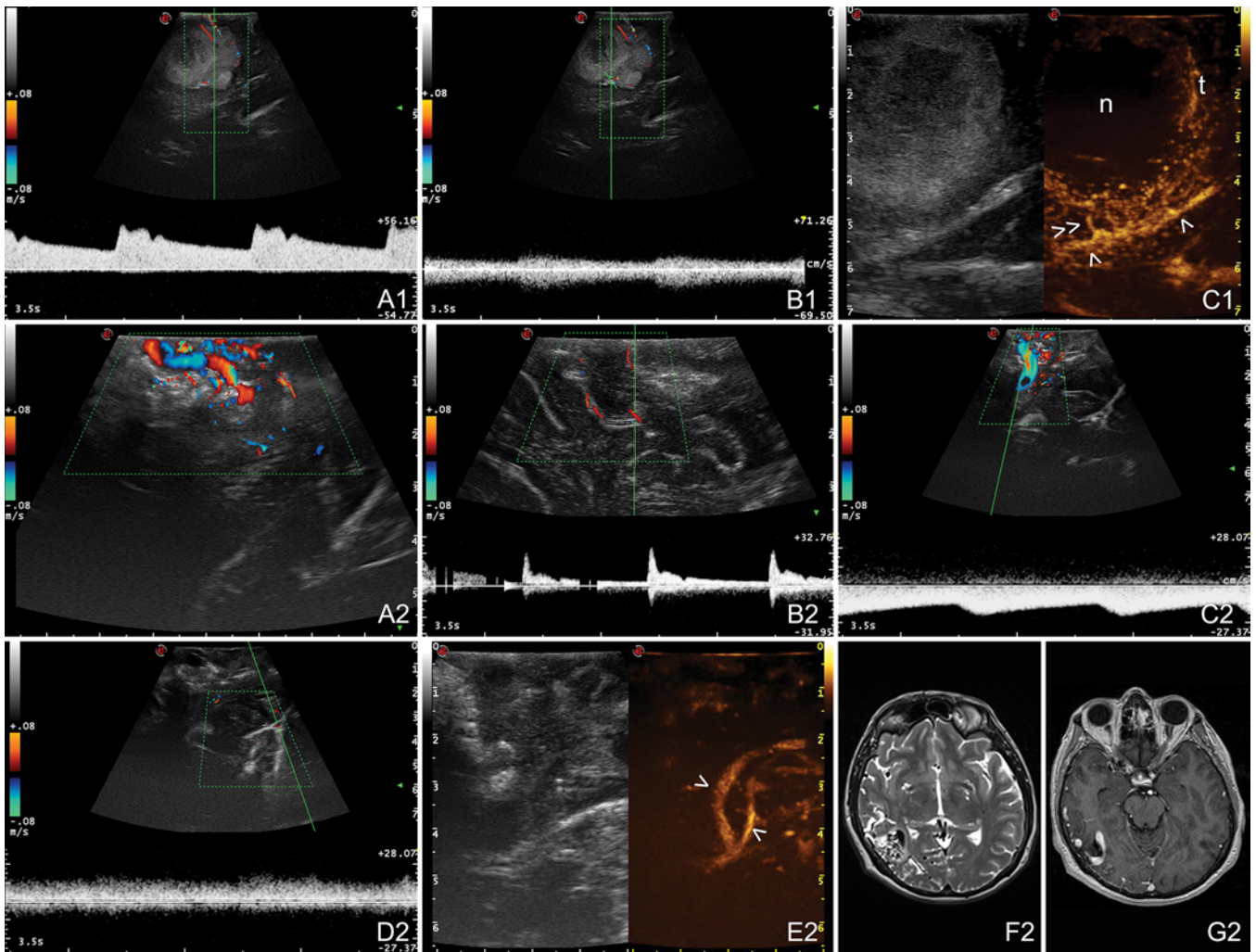


FIG. 3. Intraoperative multimodal US to characterize vascular functional anatomy of the lesion and surrounding vessels both on the surface and in depth. Right temporoparietal GBM (A1–C1): spectral Doppler demonstrates that the superficial vessel is an artery (A1) and the deeper vessel is a vein (B1); note the typical flow patterns. CEUS (C1) permits characterization of both tumor and surrounding vessels: in particular, the deep vein is part of the venous drainage of the lesion. Arrowheads indicate the vein visualized in B1; double arrowhead, the radial venous drainage toward the vein. Right parietooccipital AVM (A2–G2): color Doppler permits identification and study of each component of the AVM: arterial feeder (B2), venous enlargement (C2), and straight sinus (D2). Note the different flow patterns with different shapes and flow velocity for each vascular structure. CEUS (E2) highlights deep venous drainage toward the straight sinus (arrowheads). Preoperative T2-weighted (F2) and gadolinium-enhanced (G2) MRI studies. n = necrosis; t = viable tumor.

real-time angiosonography to visualize both the arteries and the veins simultaneously, even deep, small low-flow vessels (Fig. 2 and Table 2). The images are generated by the machine's reliance only on harmonic signals produced by intravascular microbubbles. This is particularly useful when dealing with deep-seated structures because the signal generated by the parenchyma is subtracted from the images, as in digital subtraction angiography, and only the vascular tree is displayed with great specificity and detail.

Assessment of Intraoperative Dynamic Changes in Venous Circulation

The different real-time dynamic modalities of iUS can not only integrate the information provided by preopera-

tive imaging but can also detect and highlight changes that occur during surgery, from bone flap removal with the expansion of compressed veins to flow normalization in arterIALIZED veins and the disappearance of arteriovenous shunts.

Intra- and extraaxial lesions display different patterns of venous drainage that can be studied before and after tumor removal, aiding in distinguishing between tumor-related veins and physiological veins (Figs. 1–3 and Table 2). Intraaxial tumors, such as glioblastoma (GBM), represent a sort of shunt with centripetal drainage toward the ependymal veins of the ventricles through hypertrophic medullary veins. After tumor removal, these hypertrophic medullary veins were no longer visible (Fig. 2).¹⁹

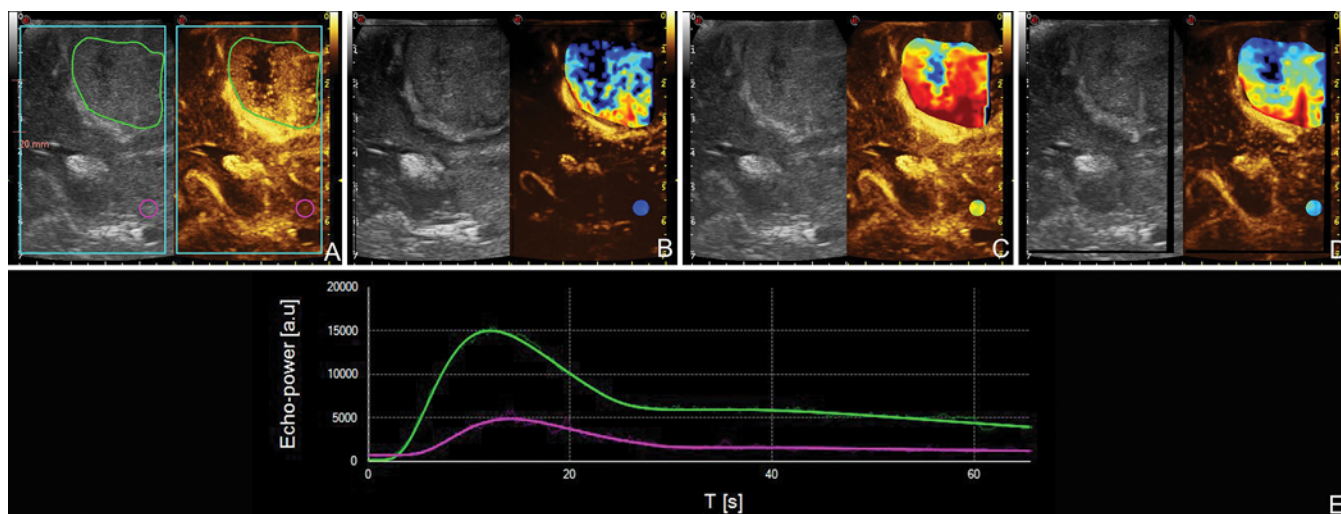


FIG. 4. CEUS perfusion analysis in a case of left frontal GBM. CEUS tumor intensity (*green*) is normalized to a region of interest (ROI; *purple*) placed on healthy parenchyma (A): arterial phase (B), peak phase (C), and venous phase (D). The clip featured in the time-intensity curve (E) was obtained during a 40-second registration, performed while keeping the probe still and processed using proprietary software for quantitative imaging (VueBox). Postprocedural analysis is conducted by analyzing different ROIs manually drawn along tumor borders, major vessels, and lobar parenchyma (tumor, *green*; healthy parenchyma, *purple*).

In extraaxial tumors, such as meningiomas, drainage is mediated by several subarachnoid veins that can also be confused with healthy brain vessels (Fig. 1).¹⁵ After tumor debulking, these veins were usually no longer significant.

In surgery for arteriovenous malformation (AVM) and dural arteriovenous fistula (DAVF), a critical aspect is recognizing the flow architecture in order to approach the lesion.^{14,16} CEUS allows one to visualize the direction of the flow and different components of the malformation without having to directly expose the structures prior to dural opening (Fig. 3 and Table 2). In cases of DAVF, CEUS permits one to study the arterial feeder and the arterialized veins in great detail. This feature can be decisive in cases of spinal DAVF in which a congested venous plexus can hide the fistula.¹⁶ Furthermore, the possibility of obtaining an ioUS scan after bone removal allows the surgeon to open the dura according to the malformation anatomy. Because US imaging presents a sectorial tomographic scan, it allows one to observe the whole surgical field, from the surface to the depth, without the need to directly expose all structures involved. It is also important to obtain multiple scans at different time points during the surgical procedure in order to assess the changes occurring over time.

Characterization of Brain Perfusion Changes Associated With Venous Drainage

Cerebral veins and sinuses are mainly viewed as hydraulic collectors, driving blood out of the head back to the heart. However, their role has larger implications, regulating parenchymal drainage and cerebrospinal fluid homeostasis and in general influencing intracranial pressure and brain perfusion.^{5,6,10,26,28} Rapid alterations of the venous system such as those occurring during surgery are implicated in localized parenchymal drainage altera-

tion with subsequent venous engorgement, local hypertension, parenchymal perfusion impairment, and eventually infarction.²³ CEUS allows one to analyze tissue perfusion.^{17,18} Microbubble quantification is performed using off-line dedicated software, providing information about parenchymal and lesion perfusion with multiparametric representations of time-intensity curves, as described in Fig. 4, and measuring the echo intensity enhancement in a given period of time in the selected region of interest. This allows one to quantitatively evaluate the flow in different vascular phases, including the venous phase, and thus indirectly assessing brain perfusion.

Evaluation of the Extracranial Venous Drainage and Implications for Neurosurgical Procedures

Cerebral venous outflow has been extensively studied in recent years, and it has been correlated mainly to other CNS pathologies such as idiopathic intracranial hypertension, cerebrospinal venous insufficiency, and multiple sclerosis.^{8,11}

Cephalic venous drainage is guaranteed by two major systems—internal jugular veins (IJVs) and vertebral venous plexuses—representing an anastomotic drainage system between the extracranial and intracranial compartments.²⁶ The supine position favors cerebral venous flow through the IJV, while in the orthostatic position blood outflow is mainly redirected to the vertebral and azygos veins.^{6,26} Furthermore, in about 85% of subjects, IJV valves are present as phylogenetic remnants at the junction of the brachiocephalic trunk, potentially causing retrograde flow during the Valsalva maneuver.²¹

These positional modifications highlight the need to take into account the position of the head relative to the neck and the rest of the body in the operating room. It is necessary to understand the real venous functional anatomy, which cannot be demonstrated by preoperative stand-

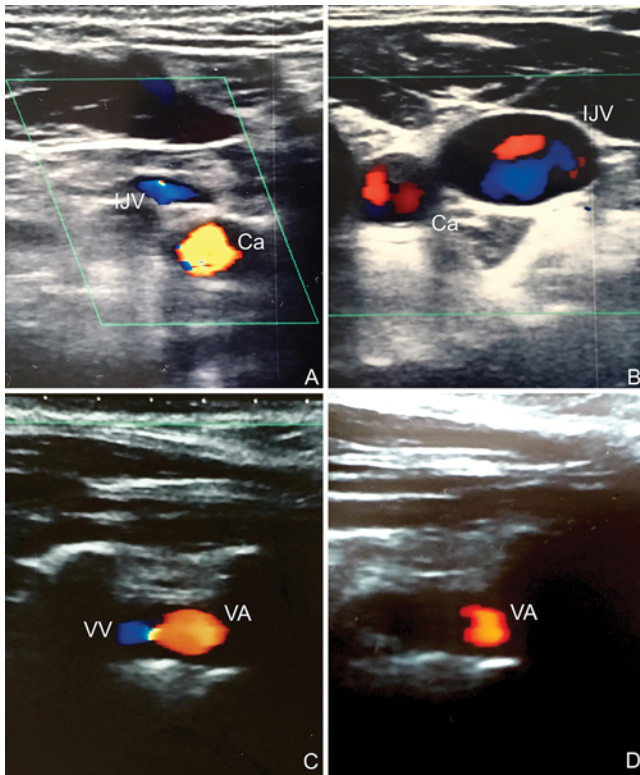


FIG. 5. Cerebral venous outflow. Area and flux direction in the IJV in a patient sitting (A) or supine (B). Transverse cervical color Doppler at the thyroid level showing the IJV and carotid artery (Ca); note the change in the IJV area when the patient is supine or sitting. Flux direction in the vertebral venous plexus (VV) in a patient sitting (C) or supine (D). Longitudinal cervical color Doppler at the level of the carotid bifurcation showing the VV and vertebral artery (VA); note the change in flux in the VV when the patient is sitting or supine. In the latter position, flow in the VV disappears.

ard imaging as it is usually performed in a supine patient with the head in a neutral position.

Venous outflow should be assessed during the preoperative workup to visualize postural changes as described in Fig. 5. The combination of morphological and hemodynamic parameters of color Doppler represents an ideal direct, real-time method for the study of hemodynamics of cerebral venous outflow.

The principal significance for neurosurgery is the objective need to consider extracranial venous outflow during surgical planning. Poor positioning of the patient with the head too rotated or flexed, lower than the chest, or with compression of the abdomen could lead to insufficient venous drainage with a consequent increase in intracranial pressure, brain swelling, and venous bleeding and less compliance if vein sacrifice is needed.

Conclusions

ioUS permits real-time, dynamic intraoperative characterization of the venous compartment not limited to the anatomical representation via the B-mode, but through multiple modalities allowing for the evaluation of blood flow, tissue and tumor perfusion, changes in venous dis-

tricts, and extracranial outflow. The main limitations of ioUS are its operator dependency and steep learning curve. As with surgery, ioUS is a technique that requires training and practice in order to fully understand its potential and to develop the ability to tailor and maximize its response to a patient's clinical and surgical needs. However, multimodal ioUS is a great tool, used alone or in a synergistic manner with other imaging modalities, in the surgical armamentarium.

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Disclosures

Dr. Mauri has been a consultant for Elesta SrL.

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