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Automatic intraoperative estimation of blood flow direction during neurosurgical interventions

Daniel Høyer Iversen · **Lasse Løvstakken** ·
Geirmund Unsgård · **Ingerid Reinertsen**

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Abstract *Purpose:* In neurosurgery, reliable information about blood vessel anatomy and flow direction are important to identify, characterize and avoid damage to the vasculature. Due to ultrasound Doppler angle-dependencies and the complexity of the vascular architecture, clinically valuable 3-D flow direction information is currently not available. In this paper, we aim to clinically validate and demonstrate the intraoperative use of a fully automatic method for estimation of 3-D blood flow direction from free-hand 2-D Doppler ultrasound.

Methods: A 3-D vessel model is reconstructed from 2-D Doppler ultrasound, and used to determine the vessel architecture. The blood flow direction is then estimated automatically using the model in combination with Doppler velocity data. To enable testing and validation during surgery, the method was implemented as part of the open source navigation system CustusX (www.custusx.org).

Results: Ten patients were included prospectively. Data from four patients were processed postoperatively, and data from six patients were processed intraoperatively. In total, the blood flow direction was estimated for 48 different blood vessels with a success rate of 98%.

Conclusions: In this work, we have shown that the proposed method is suitable for fully automatic estimation of the blood flow direction in intracranial vessels during neurosurgical interventions. The method has the potential to make the understanding of the complex vascular anatomy and flow pattern more intuitive for the surgeon. The method is compatible with intraoperative use, and results can be presented within the limited time frame where they still are of clinical interest.

Keywords Blood flow · Neurosurgery · Intraoperative · Ultrasound

Daniel Høyer Iversen · Lasse Løvstakken
Dept. Circulation and Medical Imaging, Norwegian University for Science and Technology (NTNU), Trondheim, Norway

Daniel Høyer Iversen
St. Olavs Hospital - Trondheim University Hospital, Trondheim, Norway

Geirmund. Unsgård
Dept. Neurosurgery, St. Olav University Hospital, Trondheim, Norway
Dept. of Neuromedicine and Movement Science, Norwegian University for Science and Technology (NTNU), Trondheim, Norway

Ingerid Reinertsen · Daniel Høyer Iversen
SINTEF Health, Dept. Medical Technology, Trondheim, Norway

1 Introduction

In neurosurgery, reliable information about blood flow is important in a number of procedures. During tumor resection it is important to avoid damage to major vessels. In vascular neurosurgery such as treatment of arteriovenous malformations (AVMs) and hemangioblastomas, accurate identification of feeding arteries and draining veins is crucial. An arteriovenous malformation (AVM) is an abnormal connection between the arteries and veins in the brain, bypassing the capillary vessel network. AVMs can be treated by embolization in combination with microsurgery or microsurgery alone, where the larger abnormal feeding vessels (also called feeders) are clipped to reduce the flow in the AVM. In [15] it was shown that navigated ultrasound is useful for identification and clipping of feeders to AVMs. With this method the direction of the blood flow is important to discern feeding arteries from draining veins and surrounding vessels.

The standard procedure for identification of feeders is visual inspection of 2-D slices (axial, coronal, sagittal) of the pre-operative MRA and sometimes rotational angiography. This is a highly challenging task as the vessels bend in and out of the image plane making it difficult to fully understand the 3-D geometry of the vessels. The visualization of the complete vessel geometry in a 3-D navigation scene greatly decreases the cognitive load required to understand the vessel geometry, and makes identification of the feeders intuitive and easy. The addition of Doppler ultrasound to the navigation scene increases the navigation accuracy through the correction for brain-shift, and in some cases also detects feeders not seen on MRA. If the surgeon misses a feeder, the nidus will remain filled with blood and there is a risk of bleeding if the surgeon starts the resection of the nidus. In these cases, it can be difficult and time consuming to track down the remaining feeder(s) that might not be visible in MRA. The clipping of a vein could cause sudden intraoperative hemorrhage and damage to the brain. It is therefore important to preserve the draining veins until all the feeders are secured.

Hemangioblastoma is a vascular tumor in the central nervous system that can be operated in a similar way as AVM by clipping the feeding vessels. As for AVMs, it is critical to accurately identify arteries and veins in order to correctly place the clips on the feeding arteries. After clipping of intracranial aneurysms, information about blood flow is advantageous when identifying and securing flow in the distal branches.

MR angiography is the leading image modality for imaging of blood vessels in the brain preoperatively [1]. Preoperetive MR angiography can be imported in navigation systems for intraoperative identification of vessels. Intraoperative 3-D ultrasound imaging is a cost and time efficient modality that has proven useful for providing information about the vessel structures during surgery. Ultrasound can provide updated images, that also is more sensitive to show smaller blood vessels, particularly near the brain surface [12, 10].

In [18] a clinical study was presented where the feeding vessels of the AVMs in 31 patients were clipped before resection of the *nidus*. They concluded that microsurgical extirpation assisted by navigated 3-D ultrasound angiography is an effective and safe method for removing AVMs, but also commented that the flow direction is important information to differentiate the feeding arteries from the draining veins. The lack of information about the direction of the blood flow is mentioned as a limitation in currently available technology. Current methods for real-time ultrasound flow evaluation in neurosurgery include spectral Doppler, power Doppler (PD), and color-Doppler imaging (CDI). These methods have previously been used to investigate the hemodynamics in intracranial blood vessels [17, 16, 3, 4, 15, 19, 20, 14]. In [6] ultrasensitive power Doppler imaging is used for intraoperative functional ultrasound imaging.

Conventional Doppler-based ultrasound modalities are limited by an angle-dependency in that they only provide a measurement of the flow velocity parallel to the ultrasound beam axis. Further, the measurable velocity scale is limited, and the imaging system must typically be set to image either low or high velocities present during the cardiac cycle. Detailed 3-D information of flow direction is therefor currently not available to the surgeons, but could provide important clinical information when making key decisions during an operation.

This article is a continuation of earlier published work presented in [7]. In [7], a method to correctly estimate the flow direction and angle-corrected velocities was presented. The presented method uses a model-based approach where 3-D vessel models generated from navigated 3-D freehand scanning is used as *a priori* information of vessel geometry and orientation at each scan plane. The method presented in [7] required some manual steps, and was only tested retrospectively with data from three patients and a sub-optimal Matlab implementation of the code. In this paper, we present a fully automatic method, including a more robust vessel centerline algorithm, implemented in an open source navigation system, and tested intraoperatively during surgery of six patients. The fully automatic method is also validated on retrospective data from four patients. In the previous work [7], we evaluated the robustness of angle-correction of velocity data on *in vitro* data. However, In neurosurgical applications, the blood flow direction is of higher clinical interest than the angle-corrected velocity. Consequently, the main focus of this paper is the evaluation of the accuracy and robustness of fully automatic intraoperative estimation of the blood flow direction.

This paper has been organized as follows. In Section II, the background and methodology are presented. In Section III, *in vivo* results from the intraoperative validation are presented. Results, potential future work and conclusions are discussed in Section IV and V.

2 Methods

2.1 Intraoperative setup

The intraoperative setup used in the operating room is shown in Fig. 1 with our open-source navigation platform CustusX (`www.custusx.org`, SINTEF Medical technology, Trondheim, Norway) [2]. To acquire ultrasound images, we used a GE Vingmed E9 ultrasound scanner with a GE 11L linear array transducer (GE Vingmed Ultrasound, Horten, Norway) connected to the navigation system.

The navigation system is also connected to an optical position tracker (NDI Polaris Spectra; Northern Digital, Waterloo, Canada) for acquisition of the the position and orientation of the ultrasound probe and surgical tools including the navigation pointer, ultrasonic aspirator and the biopsy forceps. All navigated tools are visualized relative to both preoperative and intraoperative images on the navigation screen. A screenshot from the navigation system is shown in Figure 8.

2-D ultrasound images were obtained by free-hand scanning over the region of interest, where the position and orientation of each 2-D frame were stored during acquisition. The ultrasound scanner transmits 2-D ultrasound frames to the navigation system via a digital research interface. Each frame contains separated tissue data, Doppler velocity data and power Doppler data. The power Doppler data are used to generate a 3-D volume of the blood vessels by mapping the 2-D ultrasound frames into a single volume by a Voxel Nearest Neighbor (VNN) algorithm as described in [9]. The velocity data are required for estimating the blood flow direction in the blood vessels.

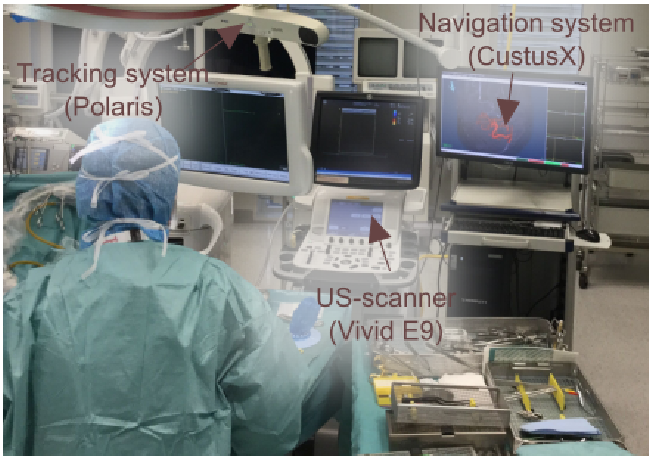


Fig. 1: The experimental setup used in the operating room, showing the tracking system, the ultrasound scanner and the navigation system (CustusX). Tracking frames were attached to the patient bench and the ultrasound probes.

2.2 Estimation of blood flow direction

The 3-D volume with blood vessels was smoothed with an Itk Gaussian image filter [21] with a smoothing parameter of 0.25. Further, we extracted the vessel centerlines from the smoothed 3-D volume. The vessel centerlines were used as *a priori* information of the vessel orientation. In [7] a thinning method [5] was used to obtain the centerline. This gives separate points along the center of the blood vessels. A continuous centerline is required to get *a priori* information about the blood vessel orientation. In [7] a manual step was required to obtain such centerlines. An automatic method for estimation of blood vessel centerlines is required to be able to estimate the flow direction automatically during surgery.

A new method for automatic estimation of the blood vessel centerline was presented in [13], and provides a continuous and more robust estimation of the centerlines. The centerline method runs on the GPU and do segmentation by region growing in parallel. This method is implemented as part of the navigation system, CustusX, and the source code for the algorithm is available at `https://github.com/smistad/Tube-Segmentation-Framework` . We have used the parameter setting called *Neuro-Vessels-USA*, that is the recommended parameter setting for neuro ultrasound angio data.

From the centerlines and the registered orientation of each 2-D ultrasound image, the angle, θ, between the true velocity and the measured velocity for measurement j was calculated as:

$$\cos\theta_j = \frac{\mathbf{f}_j \cdot \mathbf{p}_j}{||\mathbf{f}_j||_2 ||\mathbf{p}_j||_2}, \tag{1}$$

where $\mathbf{f}_j$ is a vector describing the flow direction and $\mathbf{p}_j$ describes the direction of the velocity measurement, as illustrated in Fig. 2. Here $\cdot$ denotes the scalar product of the two vectors and $||\cdot||_2$ denotes the Euclidean norm of the vector. So the flow direction is averaged over a vessel segment.

To estimate the flow direction, $\hat{d}$, in a vessel segment, we assume that more than half of the velocity measurements (pixels) are less the maximum of the measurable velocity limit (not aliased) for most of the frames. The flow direction is then estimated as

$$\hat{d} = \frac{1}{\sum_{i=1}^{N} W_i} \sum_{j=1}^{N} W_j \frac{v_{\text{Measured},j} \cos(\theta_j)}{|v_{\text{Measured},j} \cos(\theta_j)|}, \qquad (2)$$

where $|\cdot|$ is the absolute value, j denotes measurement number j, $v_{\text{Measured},j}$ is estimated flow velocity from the ultrasound data, the sum is over all, N, measurements in a vessel segment and W_j is a weight function. More details can be found in [7] and the same parameter settings are used here.

The method is implemented as a standalone program and as a plugin in the CustusX navigation platform. The source code is available at `https://github.com/Danielhiversen/AngleCorr` and executables can be downloaded from `www.custusx.org`. A block diagram showing the main data processing steps from the ultrasound probe to the final 3-D model with flow information is shown in Fig. 3.

For the AVMs the feeding vessels were clipped during the surgery, so the true flow direction was verified by the surgeon at this point. We have also manually studied the data afterwards to identify the true blood flow direction. CustusX has the ability to replay the operation afterwards, as shown in Fig. 8 where the neurovascular tree and the recorded ultrasound Doppler data with the corresponding probe orientation is visualized. This functionality was used to find the true flow direction postoperatively by carefully interpreting the 2-D ultrasound Doppler data, the corresponding position and orientation of the ultrasound probe and the orientation of the 3-D blood vessels.

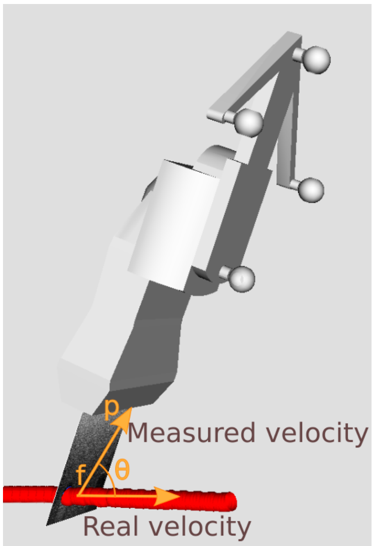


Fig. 2: An illustration of the 3-D angle-correction procedure, where the estimated angle between the 3-D model and the ultrasound image plane is used to estimate the mean blood velocity of a vessel segment.

Due to brain-shift the preoperative MR images will be inaccurate after opening of the skull. The shift of the MR images are corrected by registering the centerlines from the blood

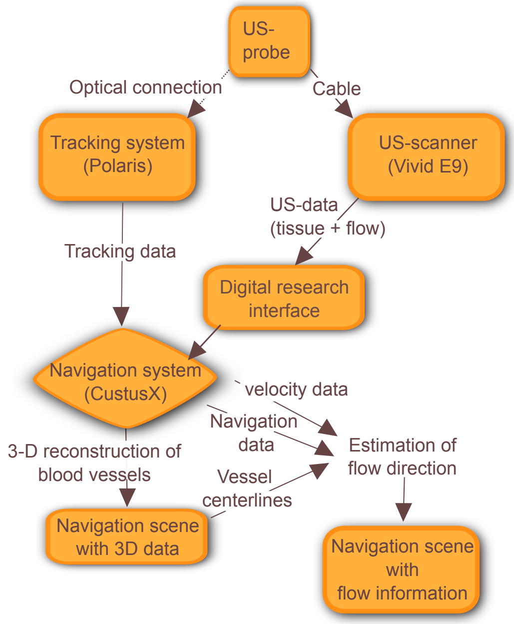


Fig. 3: Block diagram showing the main processing of data from the ultrasound probe to the finale 3-D model with flow information.

vessels imaged with ultrasound and MR. The method is integrated as part of the navigation system CustusX, and described in detail in [11].

2.3 In vitro data for optimization of the work flow

In vitro data from tube models and *in vivo* data from two patients with an aneurysm and one patient with an AVM were used to further develop and validate the algorithm presented in [7]. To test the robustness of the fully automatic implementation new *in vitro* data were acquired. A straight tube flow phantom (ATS Laboratories, Bridgeport, CT, USA) was used to acquire data with a variation of beam-to-flow angle and different direction of probe movements. These data were used to optimize and automate the work flow, and to test and validate the implementation of code in c++.

2.4 Patient data for automatic estimation of flow direction

After the implementation and optimization of the work flow, the method were tested fully automatically on data from ten patients. The method were tested with the same parameter settings and implementation in CustusX is applied for all ten patients. Four of the patient data were acquired earlier and tested post operatively, and for six of the patient data the method was tested live during surgery.

Data from four patients with a brain tumor with nearby blood vessels are presented in Tab. 1, and used for postoperative validation. Finally, the method was tested intraoperatively during surgery of six patients with AVM, hemangioblastoma and brain tumor. The patient data used for intraoperative testing are also presented in Tab. 1 as patient 5-10. The ultrasound data were acquired after the bone flap had been temporarily removed from the skull. The collection of data for the study was approved by the local ethics committee and informed consent to participate in clinical research was given by all patients included in the study.

Pat.	Disease	Anatomical location
1	Tumor	Right insula
2	Tumor	Left frontal lobe
3	Tumor	Right frontal lobe
4	Tumor	Left temporal lobe
5	AVM	Left frontal lobe
6	Hemangioblastoma	Cerebellum
7	Hemangioblastoma	Cerebellum
8	AVM	Left temporal lobe
9	Tumor	Right parietal lobe
10	AVM	Left frontal lobe

Table 1: Patient data. Patient 1-4 is processed postoperative and patient 5-10 is processed intraoperative during surgery.

3 Results

After optimization of the work flow the angle correction method was included in the official version of CustusX. Some of the parameters can be changed from the gui, but the default values were sat from these initial trials. All the parameters were fixed during estimation of the flow direction for the ten patients and specified in more details in the previous work [7].

Data from four patients with a brain tumor with nearby blood vessels were used to postoperatively test the robustness of the method. The processing was done retrospectively, but completely automatically with fixed parameter settings. The results are presented in Tab. 2. Further, data from six patients with an AVM, hemangioblastoma or brain tumor were acquired and processed intraoperatively during the surgery. The results are also presented in Tab. 2 and the flow direction was estimated for 48 blood vessels in total. The correct flow direction was found for 47 of the blood vessels. This gives a success rate of 98%. 3-D scenes with the estimated blood flow direction are shown in Fig. 4, 5, 6, 7, 8, 9 and 10. The MR images were shift-corrected and used for visualization in combination with the estimated blood flow direction.

A video recorded during the surgery and commented by the surgeon shows the visualization of the flow direction can be seen here: `https://youtu.be/ZmS0esLulqU`.

Acquiring the ultrasound data takes about 15-40 seconds. Reconstruction of 3-D volume of the blood vessels takes about 7-15 seconds and smoothing and extraction of centerlines takes about 4-8 seconds. Finally the angle-correction and estimation of blood flow direction takes about 3-5 seconds. So the estimated blood flow direction can be available for the surgeon in less than 30 seconds after acquisition of the ultrasound data. The method does not require any extra ultrasound aquistion.

Pat.	No. vessels	No. vessels with correct flow direction
1	4	4
2	5	5
3	6	6
4	3	3
5	4	3
6	5	5
7	4	4
8	7	7
9	5	5
10	5	5
Total:	48	47

Table 2: Patient data results. Patient 1-4 is processed postoperative and patient 5-10 is processed intraoperative.

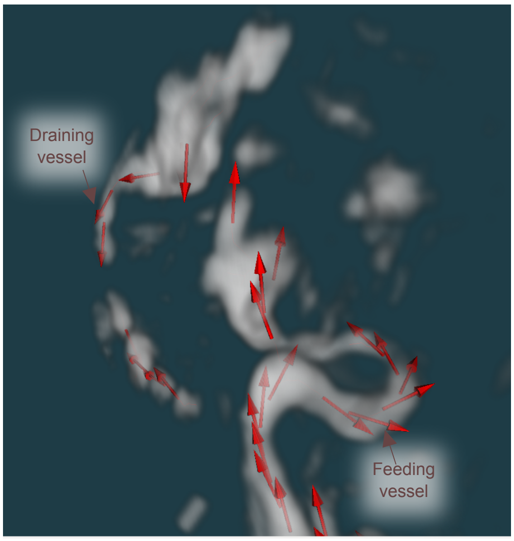


Fig. 4: Results of estimation of blood flow direction from Doppler data from the arteriovenous malformation (AVM) of patient number 5. The arrows indicate the estimated flow direction after angle-correction.

4 Discussion

In the earlier work [7], we have shown how calibrated 3-D flow images (velocity and direction) can be reconstructed from 2-D ultrasound image slices to provide clinically relevant information not previously available during neurosurgery. The approach is based on 3-D reconstruction and vessel segmentation, where the 3-D geometry and alignment of vessels can be used as *a priori* knowledge for estimation of blood flow direction.

In this work he have shown that the method is suitable for fully automatically estimation of the flow direction for intracranial blood vessels, within the limited time slot where the results still are of clinical interest. We have shown that the method may help the surgeon to identify the feeding vessels of an AVM or hemangiablastoma to ensure the correct vessels

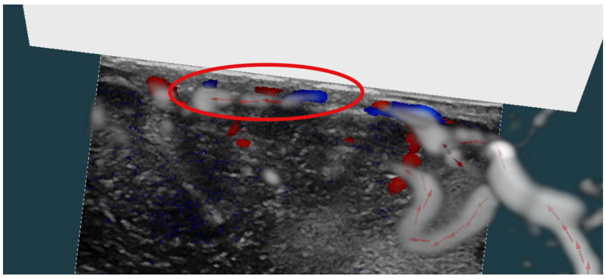


Fig. 5: Results of estimation of blood flow direction from Doppler data from the arteriovenous malformation (AVM) of patient number 5. The arrows indicate the estimated flow direction after angle-correction. The red circle marks the blood vessels where the wrong flow direction is found.

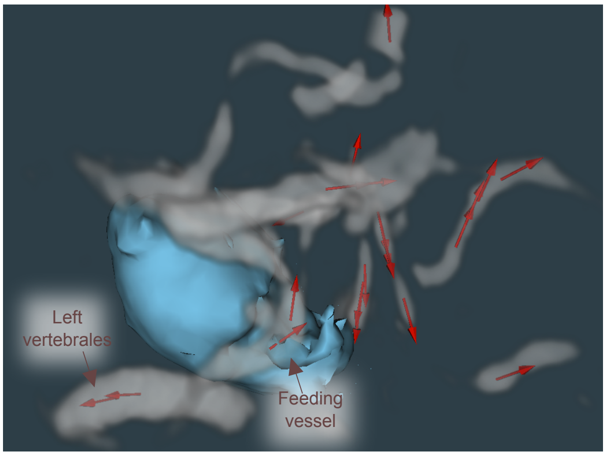


Fig. 6: Results of estimation of blood flow direction from Doppler data from the hemangioblastoma of patient number 6. The arrows indicate the estimated flow direction after angle-correction. The segmented cyst in front of the tumor is marked in turquoise.

are clipped before resection. Other applications may be to get an improved understanding of the surrounding vessel architecture during tumor resection.

For nine of the ten patient cases all clinical interesting blood vessels were detected with ultrasound and then also shown in the 3-D model of the vessel structure. Then the flow direction was estimated for all blood vessels of clinical interest. Even a few small, but clinically important, blood vessels were shown on the ultrasound images and not in the preoperative MRA images. For patient #7 the feeding vessels were located deep in the brain. These blood vessels were not possible to see on the ultrasound images because of the depth and possible shadowing from other structures such as tumor, cyst and other blood vessels. This is a limitation of ultrasound imaging in general, and not the method presented here. The draining vessels were closer to the ultrasound probe, hence easier to detect with ultrasound and the blood flow direction were also correctly estimated. This is shown in Fig. 7.

For patient #10 there were four feeding blood vessels to the AVM, as seen if Fig. 10. Only two of the feeding vessels were described by the radiologist from the preoperative MR

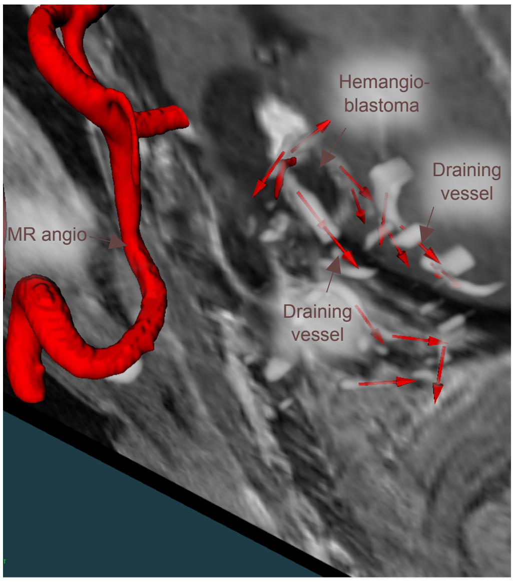


Fig. 7: Results of estimation of blood flow direction from Doppler data from the hemangioblastoma of patient number 7. The arrows indicate the estimated flow direction after angle-correction. Segmented blood vessels from MR-angio is shown in red and in the background is the MR T1 image shown.

images. From the first ultrasound acquisition we identified three feeding vessels. The last feeding vessel was not identified from the first ultrasound acquisition due to a complex vessel structure. After clipping the main feeders as seen in Fig. 9b, another ultrasound acquisition were acquired. Here the last feeding vessel was identity and the correct flow direction was estimated. After clipping the last feeder, another ultrasound acquisition showed that there was no more blood flow in the *nidus* that could be detected by ultrasound. The surgeon could then easily resect the *nidus* of the AVM.

For one blood vessel for patient #5, the angle between the ultrasound probe trajectory the vessel (beam-to-flow angle) was close to 90 degrees, as seen in Fig. 5. Hence, the vessel appears in very few 2-D ultrasound frames. This situation is probably the most challenging case for our method, and is the reason for the one blood vessel where the method estimates the wrong flow direction. Better filtering of blood vessels with beam to flow angle close to 90 degrees could have excluded this blood vessel from estimation of the blood flow direction. In a clinical setting is it important to only show trustworthy information, therefore flow directions with a high uncertainty should not be shown in the final 3-D models.

Imaging at near perpendicular beam-to-flow angles will result in drop-outs or thinning of the 3-D images. This can make it difficult to interpret how a blood vessel is connected to the *nidus* of an AVM, and then difficult to distinguish between a feeding and draining vessel even with an estimated blood flow direction. Here, a shift-corrected MR image is useful for interpret how the vessels are connected to the *nidus* of the AVM. In Fig. 10 the combination of the estimated flow direction and the shift-corrected MR image is presented in a 3-D scene. This makes it possible to identify the feeding blood vessels and understand how they connect to *nidus*. However, compounding of Doppler 2-D images with different transmit angles might reduce the number of drop-outs and improve the 3-D ultrasound image.

Another challenging case for our method is when two small blood vessels with opposite flow direction are located close to each other. If the distance between the vessels is small compared to the resolution of the Doppler ultrasound images, the two blood vessels may be interpreted as one vessel. This would result in a wrong flow direction for one of the two vessels. We had no such cases in this study, so the resolution of the ultrasound system might be high enough to separate most clinically important blood vessels in a neurosurgical setting.

Further work is required to evaluate the true clinical benefits of the method, so a clinical study with more patients would be necessary.

We also believe that an improved visualization of the flow direction may help the surgeon to interpret the direction information and make the right choice. Further work will look into how flow direction can be visualized in combination with other information such as MRA and B-mode ultrasound data using techniques such as volume rendering and augmented reality [8].

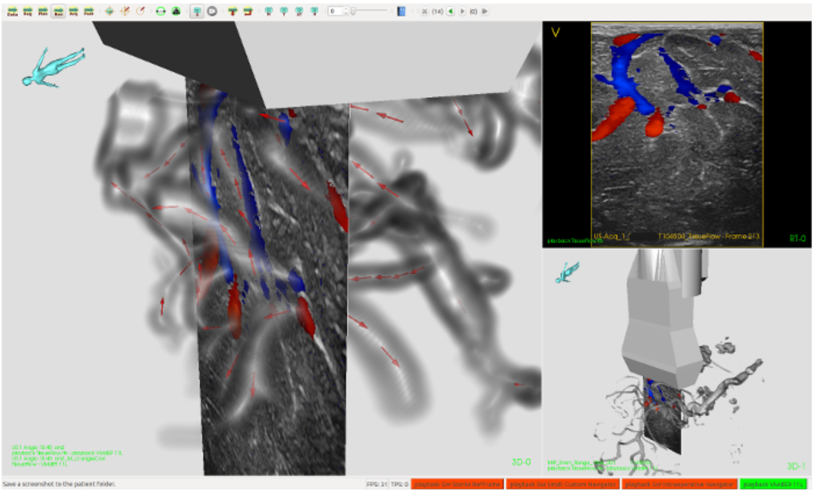
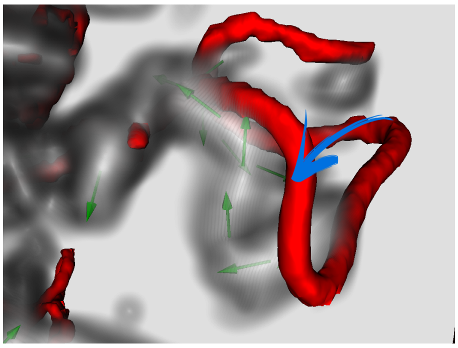


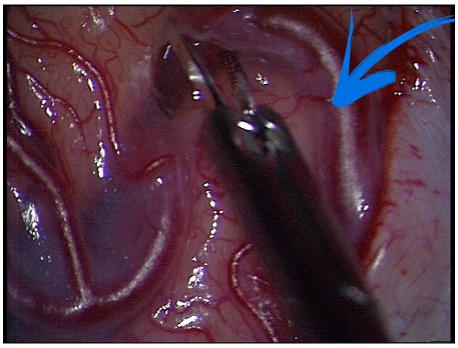
Fig. 8: Results of estimation of blood flow direction from Doppler data from the arteriovenous malformation (AVM) of patient number 8. The arrows indicate the estimated flow direction after angle-correction. The figure is a screenshot from the navigation system, CustusX.

5 Conclusion

By using a model-based approach to angle-correct Doppler measurements, 3-D information about blood flow direction was provided based on free-hand 3-D ultrasound imaging and position sensor information. In 98 % of the blood vessels the correct flow direction were found. We have shown that the method is suitable for intraoperative use where the results must be available within a limited time slot where the information is of clinical interest. The method is made freely available as part of the open source navigation system CustusX.



(a) Segmented blood vessels from MR-angio is shown in red, ultrasound angio in grey and the arrows indicate the estimated flow direction.



(b) Picture from the microscope when the surgeon is clipping one feeder. The clip is visible in front of the surgical tool.

Fig. 9: Results of estimation of blood flow direction from Doppler data from the arteriovenous malformation (AVM) of patient number 10. The image (a) shows one of the feeders marked with a blue arrow, and in image (b) the clip is placed on the feeder also marked with a blue arrow.

6 Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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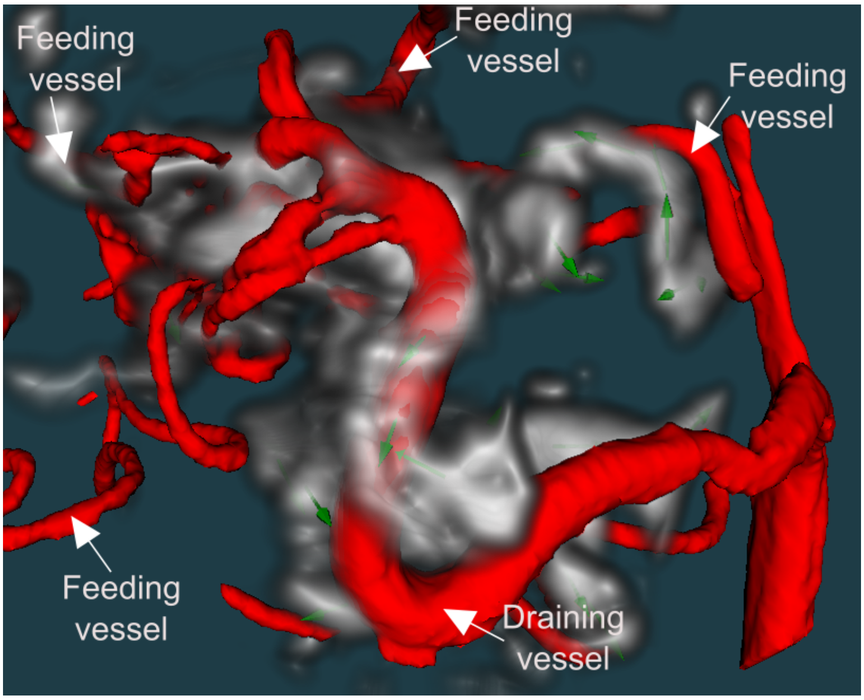

Fig. 10: Results of estimation of blood flow direction from Doppler data from the arteriovenous malformation (AVM) of patient number 10. The arrows indicate the estimated flow direction after angle-correction. The shift-corrected MR image with rigid transformation in red and the ultrasound angio image in gray. It is some deformation that is not accounted for by the rigid registration method.

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