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Total number of authors:
12

Published in:
Ultrasound in Medicine and Biology

Link to article, DOI:
10.1016/j.ultrasmedbio.2020.05.021

Publication date:
2020

Document Version
Peer reviewed version

Title

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Abstract

Noninvasive assessment is preferred for monitoring arteriovenous dialysis fistula (AVF). Vector concentration assesses flow complexity, which may correlate with stenosis severity. We evaluated if vector concentration could assess stenosis severity in dysfunctional AVF. Vector concentration was estimated in four stenotic phantoms at different pulse repetition frequencies. Spectral Doppler peak velocity and vector concentration were measured in 12 patients with dysfunctional AVF. Additionally, digital subtraction angiography (DSA) was obtained from five patients. In phantoms, vector concentration showed an inverse relationship with stenosis severity and was less affected by aliasing in severe stenoses. In nine stenoses of five patients undergoing DSA, vector concentration correlated strongly with stenosis severity (first stenosis: r=-0.73, p=0.04; other stenoses: r=-0.69, p=0.02) and midstenotic diameter (first stenosis: r=0.87, p=0.006; other stenoses: r=0.70, p=0.02) as opposed to peak velocities (p>0.05). Vector concentration is less affected by aliasing in severe stenoses and correlates with DSA in patients with dysfunctional AVF.

Keywords: Vector flow imaging, spectral Doppler ultrasound, digital subtraction angiography, arteriovenous dialysis fistula, flow complexity, stenosis assessment, patient study, phantom study

Introduction

Arteriovenous dialysis fistula (AVF) is the recommended method of vascular access for hemodialysis therapy due to superior long-term patency and reduced risk of infection compared with arteriovenous prosthetic grafts (Allon and Robbin 2002; Huber et al. 2003). However, AVF requires continuous surveillance with Doppler ultrasound or the Ultrasound Dilution Technique to identify stenosis and dysfunction (NKF-KDOQI 2006), and maintenance with percutaneous transluminal angioplasty (PTA) is essential in end-stage renal disease to uphold patency (Aktas et al. 2015; Beathard et al. 2003). AVF patency is commonly assessed with spectral Doppler ultrasound by determining volume flow and resistive index in the feeding artery, while measurements on the venous side remain complicated due to the convoluted course of the veins and the turbulent flow downstream of the anastomosis (Smith et al. 2012; Zamboli et al. 2014).

Vector flow imaging (VFI) is an angle independent ultrasound technique that produces two-dimensional velocity vectors (Jensen and Munk 1998). Several *in-vivo* studies have used VFI to estimate flow velocity and volume flow with high precision compared with magnetic resonance imaging, spectral Doppler ultrasound, and Ultrasound Dilution Technique (Bechsgaard et al. 2017; Brandt et al. 2016; Brandt et al. 2018; Hansen et al. 2014). Flow complexity calculated from VFI images has been associated with differences in the diameters of the carotid artery (Goddi et al. 2018), and a decrease in a VFI-derived parameter for flow complexity called vector concentration has been associated with arterial and aortic valve diseases (Hansen et al. 2017; Hansen et al. 2019a; Saris et al. 2019).

In this proof-of-concept study we investigated the use of vector concentration as a diagnostic tool to distinguish different stenosis severities from one another, as well as a tool for monitoring an effect of a treatment. Vector concentration was estimated in an experimental setup and *in-vivo,* where scans were performed on stenotic vessel segments. Vector concentration was estimated in four stenotic phantoms at various pulse repetition frequencies (PRF) to determine its robustness to aliasing. Furthermore, vector

concentration was compared with spectral Doppler peak velocities and digital subtraction angiography (DSA) measurements before and after balloon angioplasty in patients with dysfunctional AVF. The aim was to evaluate if vector concentration could assess stenosis severity and the effect of treatment in dysfunctional AVF by scanning directly on the lesions.

Materials and Methods

Phantom setup

Four straight vessel phantoms carrying stenosis of 0%, 40%, 70%, and 90% were fabricated in-house. The manufacturing process has been described elsewhere (Lai et al. 2013; Olesen et al. 2018). A flow system (CompuFlow 1000, Shelley Medical Imaging Technologies, Toronto, Canada) induced a pulsating flow pattern for the blood-mimicking fluid (BMF-US, Shelley Medical Imaging Technologies, Toronto, Canada). A 5.5 MHz wide linear transducer (10L2w, BK Medical, Herlev, Denmark) was positioned with the color box for VFI covering the stenosis. VFI data were obtained at 30 frames per second and stored as sequences of 10 seconds on the ultrasound scanner (bk5000, BK Medical, Herlev, Denmark). Presence of aliasing was visually evaluated on the scanner display, and the lowest PRF setting with no noticeable aliasing was defined as the baseline PRF setting for each phantom. Gain was increased to fill the vessel lumen while avoiding blooming artifacts. Wall filtering was automatically set by the scanner. To test repeatability, 10 repeated sequences were obtained at baseline PRF for each of the phantoms. Subsequently, one acquisition was obtained on every PRF setting between 0.2 kHz to 11.9 kHz, resulting in an additional 14 sequences of each phantom.

Study population

The project was approved by the Danish Data Protection Agency (Journal number 30-1202, ID number 02867). The local Ethics Committee waived approval, since ultrasound scanning of vessels is considered a routine procedure (protocol number: 17030576). Inclusion criteria were patients with a dysfunctional AVF referred for DSA-guided PTA at the Department of Diagnostic Radiology or ultrasound-guided PTA at the Department of Vascular Surgery, Rigshospitalet, Denmark. Informed and written consents were obtained from all participants.

Sixteen patients participated in the study: seven were treated at the Department of Diagnostic Radiology and examined with ultrasound and DSA, while nine patients were treated at the Department of Vascular Surgery using only ultrasound guidance. Four patients were excluded from the study: two occluded AVF had no measurable flow on ultrasound before PTA and rescue was not attempted, one AVF had no measurable flow by ultrasound after PTA, and one patient requested the PTA-procedure to be discontinued. Furthermore, one stenosis defined on DSA was not identified on ultrasound, and two stenoses could not be ultrasound scanned after PTA due to post-procedural bandages obstructing the scan areas. Flowcharts illustrating the patient and stenosis distribution are shown in Fig. 1A and 1B.

In-vivo setup

Ultrasound scans were performed using a commercial ultrasound scanner (bk5000, BK Medical, Herlev, Denmark) before and after PTA. The color box position and size for VFI were adjusted to cover the region of interest (ROI), ideally fitting a mid-stenotic, pre-stenotic and the adjacent post-stenotic segment. If the stenosis did not fit inside the color box due to its length or out-of-plane geometry, multiple acquisitions were made along the stenosis. PRF was set to the lowest setting with no noticeable aliasing on the scanner display, but if aliasing occurred at the highest setting, i.e. PRF 11.9 kHz, VFI data were obtained at this

setting. Gain was increased to fill the vessel lumen while avoiding blooming artifacts and wall filtering was automatically set by the scanner. A surgical skin-marker was used to indicate the transducer position before PTA, easing reproduction of the transducer position after PTA. One VFI sequence was obtained at each stenosis before and after PTA, respectively. All sequences were obtained at a frame rate of 30 frames per second and contained 10 seconds of VFI data.

All patients were ultrasound scanned within two hours prior to PTA and one hour after PTA except for two post PTA scans, where the patients requested the examinations to be postponed to the following day. A mean vector concentration was calculated from three estimations of each stenosis. Corresponding estimations of peak velocities were obtained with spectral Doppler. Three acquisitions of spectral Doppler peak velocities were obtained at each stenosis, and a mean spectral Doppler peak velocity was calculated for comparison.

Vector flow imaging

All scans were obtained on a commercially available ultrasound scanner (bk5000, BK Medical, Herlev, Denmark) using a 5.5 MHz wide linear transducer (10L2w, BK Medical, Herlev, Denmark). Flow vectors were visualized within the color box with the direction and magnitude shown by a color wheel. Vector arrows were superimposed onto the velocity field in real time to ease flow interpretation during ultrasound scanning. The obtained VFI data were processed and analyzed offline using an in-house built graphical user interface in MATLAB (MathWorks, Natick, MA, USA) (Moshavegh et al. 2016).

The vector concentration method utilizes the vector angle distribution to derive a parameter for flow complexity (Pedersen et al. 2014). Estimation of vector concentration is performed by marking a ROI and defining a time segment for analysis (Fig. 2). Vector concentration is measured on a scale ranging from 0 to 1, where 1 indicates a completely laminar flow, while an increase in flow complexity decreases the value

toward 0. Vector concentration estimation of *in-vivo* data was performed by splitting the sequence into three partitions of 100 frames. This allowed the ROI to be repositioned to accommodate any operator or patient motion occurring during scans.

Spectral Doppler ultrasound

Peak velocities were obtained with spectral Doppler ultrasound on the same scanner setup as VFI. The range gate was positioned in the center of the stenosis with the range gate adjusted to cover the central one third of the lumen. Angle correction was manually adjusted to achieve an insonation angle of maximum 60 degrees relative to the direction of blood flow (Fig. 3). PRF was automatically adjusted by the ultrasound scanner, when the baseline was adjusted to fit the spectrograms. Velocities were measured on screenshots of the spectrograms in an offline graphics editor, GNU Image Manipulation Program (The GIMP Development Team, Berkeley, USA).

Angiography

In an angio-suite (Toshiba Infinix VF-i/SP, Toshiba Medical Systems Corporation, Otawara, Japan), a direct puncture of a superficial adjacent vein in local anesthesia was followed by a placement of a 4 or 5 French short sheath. Guided by fluoroscopy and DSA, iodine contrast (Visipaque 270 mg/mL, GE Healthcare AS, Oslo, Norway) was injected to visualize the vessels. Midstenotic and adjacent nonstenotic diameters of the vessels were measured on the anteroposterior projection of the AVF on a PACS workstation (AGFA Impax, AGFA Technical Imaging Systems, Ridgefield Park, New Jersey) (Fig. 4). Stenosis severity was calculated as (Ota et al. 2005):

$$Severity = 1 - \frac{Midstenotic\ diameter}{Nonstenotic\ diameter}$$

Statistical analysis

Data were pooled before statistical analysis. Statistical significance was defined as $p < 0.05$. Pearson correlation coefficient, *r*, was used to test the linear relationship between ultrasound and DSA measurements. Differences before and after treatment were calculated using paired t-tests. All analyses were performed in the statistical programming software, R (R Foundation for Statistical Computing, Vienna, Austria).

Results

Phantom model experiment

At baseline PRF, mean vector concentration declined when stenosis severity inclined above 40%, indicating an inverse relationship (Fig. 5, Table 1).

PRF was gradually reduced from 11.9 kHz in each phantom to evaluate the effect of aliasing on vector concentration. This led to an initial visually stronger flow signal that was accompanied by an increase in vector concentration, which declined when aliasing occurred (Fig. 6). The decline in vector concentration due to aliased flow was more pronounced in the 0% and 40% stenosis phantoms than the 70% and 90% stenosis phantoms.

In-vivo measurements

Flow was consistently aliased in all first stenoses with VFI both before and after PTA, while three second stenoses and three third stenoses were aliased. Paired t-tests found a significant increase in mean

midstenotic vessel diameter after PTA (p = 0.0002) and a decrease in mean stenosis severity (p = 0.0007). This change was accompanied by a significant increase in vector concentration (p = 0.01), while no change was found for mean spectral Doppler peak velocities (p = 0.84) (Table 2).

Vector concentration was not associated with stenosis severity when including all stenoses (r = -0.29, p = 0.24), but showed a strong inverse correlation, when the first stenosis of each AVF was analyzed separately from the second and third stenoses (first stenosis: r = -0.73, p = 0.04; other stenoses: r = -0.69, p = 0.02). Vector concentration also showed a moderate linear association with midstenotic vessel diameter (r = 0.50, p = 0.03), which was stronger when the first stenosis was analyzed separately from the second and third stenoses (first stenosis: r = 0.87, p = 0.006; other stenoses: r = 0.70, p = 0.02). Spectral Doppler peak velocity for all ultrasound scans (n = 20) showed a moderate and inverse linear association with vector concentration (r = -0.43, p = 0.006), but was not associated with any DSA measurements (Table 3). Vector concentration and spectral Doppler velocities have been plotted against DSA in Fig. 7.

No linear association was found between change in vector concentration and stenosis severity (r = -0.57, p = 0.11), nor between change in vector concentration and midstenotic vessel diameter (r = 0.51, p = 0.16). Due to the small sample size, changes were only analyzed as a pool of all stenoses. One outlier amongst the first stenoses was noted to have a large increase in vector concentration (from 0.38 to 0.95) compared with other first stenoses. Stenosis severity in this lesion was reduced from 49% to 0%. Furthermore, the post PTA ultrasound scan for the outlier was performed on the day after PTA, which may have affected the results. Exclusion of this measurement from the correlation analysis resulted in a significant association between change in vector concentration and midstenotic vessel diameter (r = 0.79, p = 0.02), and a tendency for an inverse association between change in vector concentration and stenosis severity (r = -0.68, p = 0.07). Change in spectral Doppler peak velocities did not correlate with a change in stenosis severity (r = -0.11, p = 0.78) or midstenotic vessel diameter (r = -0.26, p = 0.50). The analyses were

performed on only 9 out of the 10 stenoses due to the absence of one post PTA ultrasound scan. The plots for changes in DSA and ultrasound measurements can be found in Fig. 8.

Discussion

Vector concentration was not directly associated with the stenosis severity in dysfunctional AVF and only moderately associated with midstenotic diameter. However, when stenoses were analyzed separately in subgroups, the associations became strong. Changes in vector concentration were also associated with changes in midstenotic vessel diameter following PTA with a tendency for an association with stenosis severity. However, these results were based on a limited sample size and a larger study is needed to verify these findings. The current findings support previous studies of vector concentration, where the parameter was used to assess aortic valve stenosis and stenosis of the superior femoral artery (Hansen et al. 2019a; Hansen et al. 2016). Additionally, VFI found increased flow complexity in infants with congenital heart disease, adults with aortic valve stenosis, and adults with carotid stenosis compared with healthy subjects (Hansen et al. 2017; Hansen et al. 2019b; Saris et al. 2019). One study found the presence of complex flow to be associated with the difference in diameter between the common carotid artery and internal carotid sinus (Goddi et al. 2018), further advocating for an association between vector concentration and vessel narrowing.

The absence of an association between vector concentration and stenosis severity when all stenoses were pooled may be explained by how the first stenoses influence flow going toward the second and third stenoses. Fig. 7 illustrates that first stenoses tended to have a lower vector concentration compared with second and third stenoses of similar severity. This indicates that upstream vessel geometry affects flow to downstream stenoses. Similarly, no association was found between changes in measurements before and after PTA until an outlier was excluded from the analyses. The outlier may be explained by the extended delay between PTA and post ultrasound scan as well as the limitation of 2D acquisition performed with

both VFI and DSA, as out-of-plane movement may conceal essential information about flow and stenosis geometry.

Our spectral Doppler peak velocities correlated moderately with vector concentration, but not with any DSA measurements. Our findings differ from the excellent results reported by Doelman et al., who found midstenotic spectral Doppler peak velocities above 375 cm/s to be a strong predictor of a stenosis severity above 50% regardless of location (Doelman et al. 2005). Meanwhile, our data indicate that the first stenosis in a row tended to have higher peak velocity compared with downstream stenoses of similar stenosis severity. Wo et al. found midstenotic spectral Doppler peak velocities above 500 cm/s to be a reliable predictor of a stenosis severity above 50%, but needed to exclude all stenoses at the anastomosis site due to the presence of consistently high peak velocities (Wo et al. 2017). A single peak velocity criterion may not be viable for the whole segment of stenoses. Instead, separate criteria for the different stenosis subgroups are warranted.

Besides measuring peak flow velocities, stenoses may also be identified with other Doppler ultrasound techniques. Spectral broadening can be observed with conventional Doppler ultrasound in turbulent flow and is often present beyond the stenosis (Beach et al. 2010; Corriveau and Johnston 2004; Doelman et al. 2005). However, spectral broadening is routinely not evaluated when assessing stenoses (NKF-KDOQI 2006). VFI obtains additional flow information compared with conventional Doppler ultrasound due to the angle independency. This allows the user to assess flow complexity in the live situation and quantitative estimation could eventually become a supplemental tool to improve flow assessment in the clinic.

VFI is based on conventional pulsed ultrasound emissions and is limited by aliasing similar to conventional pulsed wave Doppler ultrasound. Aliasing occurs at high blood flow velocities, when the Doppler shift exceeds the frequency that can be sampled according to the Nyquist Limit and results in erroneous estimation of velocity and direction (Nelson and Pretorius 1988; Terslev et al. 2017). Aliasing can be avoided by increasing the PRF to a higher frequency, which in turn lowers the sensitivity to slower flows.

Since vector concentration measures the vector angle distribution within a region of interest, the measure is not only affected by flow complexity, but also by aliasing where vectors are reversed. In this study aliasing was observed directly on the monitor but not analyzed due to lack of quantification tools. Combination of quantified aliasing and vector concentration may lead to a parameter better than vector concentration alone. As indicated in this and previous studies (Hansen et al. 2019a; Hansen et al. 2017), useful vector concentration estimation could potentially be performed in severe stenoses, but will likely be influenced by both flow complexity and aliasing.

Fig. 6 illustrates how the effect of aliasing was different depending on stenosis severity, with the decline being less pronounced in the 70% and 90% stenosis phantoms. When PRF was set too high, random "noise vectors" were present in areas with undetected slow flow, which resulted in a wide vector angle distribution, thus a decreased vector concentration. Reducing the PRF from the high setting allowed slower flow to be detected and resulted in an increased signal-to-noise ratio and vector concentration. When aliasing occurred at PRF 5.1 kHz in the 70% stenosis phantom, vector concentration decreased by 1.0% compared with baseline, and reducing PRF to 4.1 kHz resulted in a 4.9% decrease from the baseline value. Similarly, vector concentration decreased by only 1.1% compared with baseline, when PRF was reduced from 11.9 kHz to 5.1 kHz in the 90% stenosis phantom. The small changes could indicate that vector concentration remains robust in severe stenoses despite aliasing as already suggested by previous studies (Hansen et al. 2019a; Hansen et al. 2017). VFI data should be obtained at the lowest PRF setting without aliasing whenever possible since vector concentration seems to be affected by aliased vectors. This is also true for spectral Doppler estimation where adjustment of not only PRF, but also spectral baseline, Doppler gain, and angle correction are crucial for correct velocity estimation (Terslev et al. 2017).

Although aliasing may appear to cause problems in stenoses of lower severity, our tentative experiments have shown that VFI is capable of measuring flow velocities up to approximately 250 cm/s without aliasing at PRF 11.9 kHz. This range is sufficient for measuring some of the fastest blood flows in

normal physiology (Garcia et al. 2018). Accordingly, blood flow in healthy vessels and low severity stenoses is not expected to be aliased with VFI when used in a clinical setting, and the lower robustness observed in the low severity phantoms may not be relevant, when estimating flow in patients.

The velocity range at a given PRF measured with VFI is limited similar to conventional pulsed Doppler systems. Therefore, simultaneous measurement of fast and slow flow is not possible. Several different methods have been proposed to counteract this limitation (Ekroll et al. 2016; Posada et al. 2016; Saris et al. 2016; Villagómez Hoyos et al. 2016). One of the proposed methods is an adaptive PRF approach that uses unfocused pulse emissions for VFI to simultaneously measure fast and slow flow (Villagómez Hoyos et al. 2016). Some of the shortcomings encountered in stenoses with a large velocity gradient could be alleviated if an adaptive PRF approach was implemented into the presented VFI setup. This could result in a reduction in the amount of noise vectors observed in areas of slow flow and potentially correct the reduction in vector concentration, when the PRF is set inappropriately high.

AVF patency is commonly assessed with spectral Doppler ultrasound or the Ultrasound Dilution Technique (Hansen et al. 2014; Wijnen 2006). While spectral Doppler ultrasound is considered to be an accurate method for detecting arterial stenoses (Zamboli et al. 2014) and categorizing stenosis severity in carotid and renal arteries (Granata et al. 2009; Grant et al. 2003), it did not correlate with any DSA measurements in our study, where midstenotic velocities were measured on the venous side of AVF. Velocity estimation with spectral Doppler ultrasound relies on an assumption of the direction of peak flow. However, the flow angle may have considerable variation near stenoses, and misalignment of the Doppler beam may result in inaccurate velocity estimation (Hatle et al. 1980). Additionally, vessels in AVF are often near parallel to the skin surface, resulting in velocity estimation being performed at near perpendicular flow angles. Adjustment of the Doppler beam to an insonation angle of 60 degrees or less is an often accepted procedure for velocity estimation, but can still result in inaccurate and imprecise measurements (Hoskins 1996; Park et al. 2012). Meanwhile, VFI is an angle independent ultrasound technique that

eliminates inaccuracies caused by erroneous angle adjustment. The technique determines the flow vectors within the color box and even allows measurements to be performed on flow moving perpendicular to the beam axis. Furthermore, peak velocities that are not located centrally in the lumen (Ford et al. 2008; Kamenskiy et al. 2011) may go unnoticed with conventional spectral Doppler ultrasound, but will be detected with VFI as long as they are in-plane with the ultrasound beam. Alternatively, a 4D/3D ultrasound method has been proposed and found good agreement with DSA in carotid stenosis (Macharzina et al. 2019).

The Ultrasound Dilution Technique is considered the reference standard for flow estimation in AVF, but is limited to being performed during dialysis sessions, thereby prolonging an already cumbersome procedure (Hansen et al. 2014). An additional limitation is that the dilution agent and blood may not mix sufficiently in AVF with slow flow, thus resulting in erroneous volume flow estimation (Hansen et al. 2014; Pavek et al. 1970). Volume flow derived with VFI was reported to have an increased precision and a strong correlation with the Ultrasound Dilution Technique in AVF (Brandt et al. 2016; Hansen et al. 2014), and may be a feasible alternative due to its ease of use.

This study had several limitations. While our results indicate that vector concentration may be used to assess AVF stenoses using separate criteria for first and other stenoses, the study population was limited with only a subgroup undergoing DSA. Furthermore, pre and post PTA results were pooled before correlation analysis due to the small sample size, resulting in the measurements not being independent. A larger study sample is necessary to verify the findings. DSA was obtained in only one plane and all stenoses were assumed to be circular. Likewise, ultrasound measurements were only acquired in 2D and out-of-plane vectors were not obtained. The solution may be a 3D VFI technique, which has been achieved and validated *in-vivo* with an experimental scanner setup (Holbek et al. 2017). Spectral Doppler peak velocities and VFI were obtained on the venous side of AVF, where flow is known to be turbulent (Zamboli et al. 2014). The combination of turbulence with the tortuous and bulbous geometry of the fistulas complicated

accurate velocity estimation. We used an in-house built graphic user interface in MATLAB to calculate vector concentration. Even though the method to calculate vector concentration has been described previously (Hansen et al. 2019; Pedersen et al. 2014), the user interface for vector concentration estimation is currently not commercially available. This is a limitation for other research groups who intend to conduct similar studies. Nevertheless, we encourage other researchers to investigate turbulence as a measure for evaluating vessel pathology with ultrasound. Noise could not be omitted from the vector concentration analysis and may have resulted in a decreased estimate when the PRF was set too high. The noise is currently filtered live on the scanner display, and we expect that the noise can be omitted from the analysis in a future build of the user interface. VFI and spectral Doppler peak velocities were obtained by a single operator and interobserver variability was not evaluated. Lastly, the methods were not performed simultaneously, and two post PTA ultrasound scans were performed the following day instead of immediately after PTA, which may have affected the results.

Conclusion

The vector concentration method had high precision and correlated strongly with DSA measurements, when scanning directly on 10 stenoses in 5 patients with dysfunctional AVF, whereas spectral Doppler peak velocities did not correlate with DSA. However, vector concentration estimation was affected by noise and aliasing artifacts, and a larger study sample is necessary to clarify whether it is a reliable parameter for stenosis severity. This proof-of-concept study demonstrated an approach to perform noninvasive stenosis assessment in dysfunctional AVF.

Conflicts of interest

Jacob Bjerring Olesen and Ramin Moshavegh are employed at BK Medical. Jørgen Arendt Jensen developed and patented the vector flow imaging technique, and receives royalties from the sale of BK Medical ultrasound scanners with the technique implemented.

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Figure captions

Fig. 1: A) Overview of the patients in the study, "n" represents the number of patients. B) Overview of the stenoses in the study, "N" represents the number of stenoses. "Pre PTA" and "Post PTA" refer to examinations performed before and after PTA. The first stenosis in an AVF was referred as "First stenosis", while any second and third stenoses were pooled as "Other stenoses". SDUS = Spectral Doppler ultrasound.

Fig. 2: Vector concentration estimation in a 40% (A) and 70% (B) stenosis phantom. The two examples were examined with a linear transducer at PRF 2.6 kHz and 6.9 kHz, respectively. The red box delineates the ROI for vector concentration estimation.

Fig. 3: A) Velocity estimation with Spectral Doppler ultrasound of the first stenosis (*) in an AVF with three stenoses. B) VFI of the same stenosis. Small areas of aliasing can be seen in the midstenotic flow. Stenosis severity was determined to be 47% on DSA.

Fig. 4: Routine anteroposterior DSA in one plane before (A) and after (B) balloon angioplasty of the same AVF as illustrated in Fig. 3. Stenosis severity of the three lesions (marked 1-3) was reduced from 47%, 63%, and 66% to 35%, 43%, and 29% after balloon angioplasty, respectively.

Fig. 5: Mean midstenotic vector concentration measured in four stenotic phantom models of 0%, 40%, 70%, and 90% constriction.

Fig. 6: Dot plots illustrating the effect of adjusting PRF on vector concentration in four stenotic phantoms. The lowest PRF for each stenosis phantom that presented no aliasing was defined as the baseline PRF.

Fig. 7: Vector concentration and spectral Doppler peak velocities plotted against stenosis severity and midstenotic vessel diameter measured on DSA. Pre- and post-PTA results were pooled. The solid line illustrates the best linear fit for the first stenoses, while the dotted line is the best linear fit for the second and third stenoses. The open and filled symbols indicate if flow was nonaliased or aliased, respectively.

Fig. 8: In-vivo results of the change in vector concentration and spectral Doppler peak velocity plotted against change in stenosis severity and midstenotic vessel diameter following PTA.

Tables

Stenosis severity	PRF (kHz)	Mean VC (SD)
0 %	2.6	0.95 (0.01)
40 %	2.6	0.95 (0.02)
70 %	6.9	0.81 (0.02)

90 %	11.9	0.64 (0.02)	483

Table 1: Baseline PRF settings and mean vector concentration for 10 repeated measurements. Baseline PRF was defined as the lowest PRF setting that displayed flow without aliasing. VC = Vector concentration. SD = Standard deviation.

	Before PTA (SD)	After PTA (SD)	Mean difference [CI95]	*p*-value
Mean vector concentration	0.70 (0.24)	0.80 (0.17)	+ 0.13 [0.03; 0.22]	0.01
Mean peak SDUS (cm/s)	305.0 (130.1)	333.1 (112.6)	+ 5.75 [-54.2; 65.7]	0.84
Mean stenosis severity (%)	62 (16)	24 (14)	- 0.37 [-0.54; -0.21]	0.0007
Mean vessel diameter (cm)	0.23 (0.13)	0.49 (0.08)	+ 0.25 [0.14; 0.34]	0.0002

Table 2: Mean values and mean differences calculated with paired t-tests before and after PTA. Mean differences of vector concentration and spectral Doppler ultrasound (SDUS) peak velocities were calculated for all patients (n = 12). Mean difference of stenosis severity and midstenotic vessel diameter were calculated for 5 patients. SD = Standard deviation. CI95 = 95% confidence interval.

	Vector concentration	Spectral Doppler velocity
Stenosis severity, all stenoses	r = -0.29, p = 0.24	r = -0.11, p = 0.66
Stenosis severity, first stenosis	r = -0.73, p = 0.04	r = -0.16, p = 0.70
Stenosis severity, other stenoses	r = -0.69, p = 0.02	r = 0.10, p = 0.77
Vessel diameter, all stenoses	r = 0.50, p = 0.03	r = -0.25, p = 0.30
Vessel diameter, first stenosis	r = 0.87, p = 0.006	r = -0.53, p = 0.17
Vessel diameter, other stenoses	r = 0.70, p = 0.02	r = -0.26, p = 0.44

499 *Table 3: Pearson correlation coefficients, r, for in-vivo ultrasound and DSA measurements.*

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