Flow Complexity Estimation in Dysfunctional Arteriovenous Dialysis Fistulas using Vector Flow Imaging

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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](https://doi.org/10.1016/j.ultrasmedbio.2020.05.021)

Publication date:
2020

Document Version
Peer reviewed version

[Link back to DTU Orbit](#)

Citation (APA):
Nguyen, T. Q., Traberg, M. S., Olesen, J. B., Heerwagen, S. T., Brandt, A. H., Bechsgaard, T., Pedersen, B. L., Moshavegh, R., Lönn, L., Jensen, J. A., Nielsen, M. B., & Hansen, K. L. (2020). Flow Complexity Estimation in Dysfunctional Arteriovenous Dialysis Fistulas using Vector Flow Imaging. *Ultrasound in Medicine and Biology*, 46(9), 2493-2504. <https://doi.org/10.1016/j.ultrasmedbio.2020.05.021>

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1 **Title**

2 Flow Complexity Estimation in Dysfunctional Arteriovenous Dialysis Fistulas using Vector Flow Imaging.

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21

22 **Abstract**

23 Noninvasive assessment is preferred for monitoring arteriovenous dialysis fistula (AVF). Vector
24 concentration assesses flow complexity, which may correlate with stenosis severity. We evaluated if vector
25 concentration could assess stenosis severity in dysfunctional AVF. Vector concentration was estimated in
26 four stenotic phantoms at different pulse repetition frequencies. Spectral Doppler peak velocity and vector
27 concentration were measured in 12 patients with dysfunctional AVF. Additionally, digital subtraction
28 angiography (DSA) was obtained from five patients. In phantoms, vector concentration showed an inverse
29 relationship with stenosis severity and was less affected by aliasing in severe stenoses. In nine stenoses of
30 five patients undergoing DSA, vector concentration correlated strongly with stenosis severity (first stenosis:
31 $r=-0.73$, $p=0.04$; other stenoses: $r=-0.69$, $p=0.02$) and midstenotic diameter (first stenosis: $r=0.87$, $p=0.006$;
32 other stenoses: $r=0.70$, $p=0.02$) as opposed to peak velocities ($p>0.05$). Vector concentration is less affected
33 by aliasing in severe stenoses and correlates with DSA in patients with dysfunctional AVF.

34

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

37

38 Introduction

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

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

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

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

66

67 **Materials and Methods**

68 *Phantom setup*

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

82

83

84 *Study population*

85 The project was approved by the Danish Data Protection Agency (Journal number 30-1202, ID number
86 02867). The local Ethics Committee waived approval, since ultrasound scanning of vessels is considered a
87 routine procedure (protocol number: 17030576). Inclusion criteria were patients with a dysfunctional AVF
88 referred for DSA-guided PTA at the Department of Diagnostic Radiology or ultrasound-guided PTA at the
89 Department of Vascular Surgery, Rigshospitalet, Denmark. Informed and written consents were obtained
90 from all participants.

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

99

100 *In-vivo setup*

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

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

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

118

119 *Vector flow imaging*

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

126 The vector concentration method utilizes the vector angle distribution to derive a parameter for flow
127 complexity (Pedersen et al. 2014). Estimation of vector concentration is performed by marking a ROI and
128 defining a time segment for analysis (Fig. 2). Vector concentration is measured on a scale ranging from 0 to
129 1, where 1 indicates a completely laminar flow, while an increase in flow complexity decreases the value

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

133

134 *Spectral Doppler ultrasound*

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

142

143 *Angiography*

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

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

151

152 *Statistical analysis*

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

158

159 **Results**

160 *Phantom model experiment*

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

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

168

169 *In-vivo measurements*

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

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

175 Vector concentration was not associated with stenosis severity when including all stenoses ($r = -0.29$, p
176 $= 0.24$), but showed a strong inverse correlation, when the first stenosis of each AVF was analyzed
177 separately from the second and third stenoses (first stenosis: $r = -0.73$, $p = 0.04$; other stenoses: $r = -0.69$, p
178 $= 0.02$). Vector concentration also showed a moderate linear association with midstenotic vessel diameter
179 ($r = 0.50$, $p = 0.03$), which was stronger when the first stenosis was analyzed separately from the second
180 and third stenoses (first stenosis: $r = 0.87$, $p = 0.006$; other stenoses: $r = 0.70$, $p = 0.02$). Spectral Doppler
181 peak velocity for all ultrasound scans ($n = 20$) showed a moderate and inverse linear association with vector
182 concentration ($r = -0.43$, $p = 0.006$), but was not associated with any DSA measurements (Table 3). Vector
183 concentration and spectral Doppler velocities have been plotted against DSA in Fig. 7.

184 No linear association was found between change in vector concentration and stenosis severity ($r = -$
185 0.57 , $p = 0.11$), nor between change in vector concentration and midstenotic vessel diameter ($r = 0.51$, $p =$
186 0.16). Due to the small sample size, changes were only analyzed as a pool of all stenoses. One outlier
187 amongst the first stenoses was noted to have a large increase in vector concentration (from 0.38 to 0.95)
188 compared with other first stenoses. Stenosis severity in this lesion was reduced from 49% to 0%.
189 Furthermore, the post PTA ultrasound scan for the outlier was performed on the day after PTA, which may
190 have affected the results. Exclusion of this measurement from the correlation analysis resulted in a
191 significant association between change in vector concentration and midstenotic vessel diameter ($r = 0.79$, p
192 $= 0.02$), and a tendency for an inverse association between change in vector concentration and stenosis
193 severity ($r = -0.68$, $p = 0.07$). Change in spectral Doppler peak velocities did not correlate with a change in
194 stenosis severity ($r = -0.11$, $p = 0.78$) or midstenotic vessel diameter ($r = -0.26$, $p = 0.50$). The analyses were

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

197

198 **Discussion**

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

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

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

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

231 Besides measuring peak flow velocities, stenoses may also be identified with other Doppler ultrasound
232 techniques. Spectral broadening can be observed with conventional Doppler ultrasound in turbulent flow
233 and is often present beyond the stenosis (Beach et al. 2010; Corriveau and Johnston 2004; Doelman et al.
234 2005). However, spectral broadening is routinely not evaluated when assessing stenoses (NKF-KDOQI
235 2006). VFI obtains additional flow information compared with conventional Doppler ultrasound due to the
236 angle independency. This allows the user to assess flow complexity in the live situation and quantitative
237 estimation could eventually become a supplemental tool to improve flow assessment in the clinic.

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

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

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

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

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

270 The velocity range at a given PRF measured with VFI is limited similar to conventional pulsed Doppler
271 systems. Therefore, simultaneous measurement of fast and slow flow is not possible. Several different
272 methods have been proposed to counteract this limitation (Ekroll et al. 2016; Posada et al. 2016; Saris et al.
273 2016; Villagómez Hoyos et al. 2016). One of the proposed methods is an adaptive PRF approach that uses
274 unfocused pulse emissions for VFI to simultaneously measure fast and slow flow (Villagómez Hoyos et al.
275 2016). Some of the shortcomings encountered in stenoses with a large velocity gradient could be alleviated
276 if an adaptive PRF approach was implemented into the presented VFI setup. This could result in a reduction
277 in the amount of noise vectors observed in areas of slow flow and potentially correct the reduction in
278 vector concentration, when the PRF is set inappropriately high.

279 AVF patency is commonly assessed with spectral Doppler ultrasound or the Ultrasound Dilution
280 Technique (Hansen et al. 2014; Wijnen 2006). While spectral Doppler ultrasound is considered to be an
281 accurate method for detecting arterial stenoses (Zamboli et al. 2014) and categorizing stenosis severity in
282 carotid and renal arteries (Granata et al. 2009; Grant et al. 2003), it did not correlate with any DSA
283 measurements in our study, where midstenotic velocities were measured on the venous side of AVF.
284 Velocity estimation with spectral Doppler ultrasound relies on an assumption of the direction of peak flow.
285 However, the flow angle may have considerable variation near stenoses, and misalignment of the Doppler
286 beam may result in inaccurate velocity estimation (Hatle et al. 1980). Additionally, vessels in AVF are often
287 near parallel to the skin surface, resulting in velocity estimation being performed at near perpendicular
288 flow angles. Adjustment of the Doppler beam to an insonation angle of 60 degrees or less is an often
289 accepted procedure for velocity estimation, but can still result in inaccurate and imprecise measurements
290 (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

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

327

328 **Conclusion**

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

335

336

337 **Conflicts of interest**

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

341

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455 **Figure captions**

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

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

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

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

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

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

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

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

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482 **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)
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487 *Table 1: Baseline PRF settings and mean vector concentration for 10 repeated measurements. Baseline PRF*
488 *was defined as the lowest PRF setting that displayed flow without aliasing. VC = Vector concentration. SD =*
489 *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

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

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	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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