Two-dimensional flow imaging in the carotid bifurcation using a combined speckle tracking and phase-shift estimator: a study based on ultrasound simulations and in-vivo analysis

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Abstract

A 2D blood velocity estimator is presented combining speckle tracking (ST) and phase-shift estimation (PE) to measure lateral (vx) and axial (vz) velocities respectively. Estimator properties were assessed in a carotid bifurcation using ultrasound simulations based on computational fluid dynamics, allowing validation towards a ground truth. Simulation results were supported with in vivo data of a healthy carotid. ST and PE estimates were combined as: 1) **vx from 2D-ST** and vz from PE, 2) **vx from 2D-ST** and vz from PE with aliasing correction based on ST, 3) vz from PE and only lateral ST for vx. Regression analysis showed a 35-77 % decrease in standard deviation for vz for PE compared to ST. Aliasing correction based on ST improved results but also introduced spurious artifacts. A marginal decrease in performance was observed when only tracking laterally. Further work will focus on in vivo trials in patients with carotid plaques.

Key words: 2D flow imaging, speckle tracking, phase-shift estimation, CFD, ultrasound simulations, in-vivo

Introduction and Literature

Ultrasonic blood flow imaging is commonly applied in clinical practice, although still mainly limited to 1D Doppler-related techniques like Pulsed Wave Doppler (PWD) and Color Flow Imaging (CFI). Multidimensional flow imaging is however desirable since complex flow fields are present throughout the arterial system in bends, bifurcations and especially in diseased arteries showing obstructive plaques. Better assessment of the flow field and its associated hemodynamic parameters would potentially improve cardiovascular risk assessment and increase the understanding of the origin and development of cardiovascular disease. In particular, clinically relevant hemodynamic parameters like wall shear stress, well known as a stimulus of endothelial function and involved in atherosclerosis (Glagov et al, 1988), could be derived from multidimensional flow measurements.

Extensive research has been done on 2D flow imaging, mainly focusing on two research lines: speckle tracking (ST) (Trahey et al, 1987) and crossed-beam vector Doppler (VD) (Fox, 1978). The former relies on tracking the movement of speckle patterns, created by the interference of the ultrasonic waves backscattered by the red blood cells. The latter is the natural extension of 1D Doppler techniques, insonifying the blood vessel in two different directions, allowing construction of the velocity vector through triangulation. The performance of these estimators has been analyzed for analytically described flow patterns as well as in-vitro flow phantoms (e.g. Bohs et al (1998) for ST and Kripfgans et al (2006) for VD). Both methods have also been preliminary tested in healthy in-vivo conditions (e.g. Udesen et al (2008) for ST and Pastorelli et al (2008) for VD). However, to our knowledge these methods have yet to reach clinical practise, perhaps owing to a lack of robustness or practical applicability.

To investigate the accuracy and applicability of these techniques, accurate knowledge on the actually imaged flow field is indispensable. For this purpose, we developed an ultrasound (US) simulation environment based on computational fluid dynamics (CFD), which allows solving the Navier-Stokes equations and thus flow fields in complex geometries. The phantom for the ultrasound simulations (Field II) is built from random point scatterers representing the red blood cells, which are propagated for each emitted ultrasound beam according to the CFD velocity field. In Swillens et al (2009a,b), we described and validated this CFD-based ultrasound simulation environment in detail. We further used our multiphysics environment to compare the estimator properties of speckle tracking and vector Doppler (Swillens et al, in press). The ST-estimates were obtained by applying a sum-absolute-difference algorithm on the envelope data. Crossed-beam VD was implemented using one linear array transducer with a central transmit aperture and two sliding receive apertures to keep a fixed angle in depth. For each receive direction, the phase-shift was estimated with the autocorrelation method (Kasai et al, 1985), as commonly applied in CFI. We demonstrated ST to be the better lateral (perpendicular to US beam) velocity estimator and crossed-beam VD the better axial (parallel to US beam) estimator, based on a statistical analysis of Poiseuille flow in a tube and velocity estimations in a carotid bifurcation model (Swillens et al, in press).

In this paper, we present a natural extension of this work by combining speckle tracking and phase-shift estimation in one 2D flow estimator. A single scan procedure similar to conventional CFI-scanning is applied, and the received US-signals are processed with an ST-algorithm for the lateral flow component and with a phase-shift estimation (PE) method (autocorrelation technique) for the axial flow. In a first step, we analyze the combined estimator in a carotid bifurcation using our CFD-based ultrasound simulation environment, allowing direct comparison of the estimated flow with the reference CFD flow field. Finally, in-vivo data measured in the carotid bifurcation of a healthy volunteer will be analyzed using our different estimator setups to validate and support simulation results.

Materials and Method

1. Data acquisition

Both for the simulations and the in-vivo data, we maximized the frame rate by using a scan acquisition scheme typically used in conventional color flow imaging (CFI), called beam interleaving (Chesarek, 1989). This technique is used when the chosen pulse repetition frequency (PRF) of the emitted ultrasound beams is lower than the theoretical maximum (PRF_{max}), as determined by the imaging depth. In case of shallow depths like in peripheral vascular imaging (e.g. carotid artery), the Doppler PRF is typically much lower than the maximum available PRF_{max}, so that sufficient sensitivity is obtained for the expected range of blood velocities.

Interleaving refers to the division of the image into lateral subregions or interleave groups (IG), where the neighbouring beams within the interleave group are acquired at a rate of PRF_{max} and the frame rate of the interleave group corresponds to the slow-time Doppler PRF. The number of beams in an interleave group, i.e. the interleave group size (IGS), is given by:

$$IGS = \left\lfloor \frac{PRF_{max}}{PRF} \right\rfloor \cdot PRB, \tag{1}$$

where PRB (Parallel Receive Beams) is the number of beams received in parallel for each beam emission, as commonly applied in high-end ultrasound systems.

2. 2D velocity estimation

Phase-shift estimation (PE)

The autocorrelation method for phase-shift estimation was applied, as proposed for ultrasound applications by Kasai et al (Kasai et al, 1985):

$$v_z = \frac{cPRF}{4\pi f_0} atan(\frac{Im(\hat{R}(1))}{Re(\hat{R}(1))}), \quad (2)$$

with v_z the estimated axial velocity, c the ultrasound wave speed in blood (1540 m/s), PRF the pulse repetition frequency of the emitted ultrasound beams, f_0 the center frequency of the ultrasound pulse and $\hat{R}(1)$ the estimated autocorrelation function at lag 1. The $\hat{R}(1)$ estimate was averaged over an ensemble of slow-time samples. The factor $\frac{cPRF}{4f_0}$ is the Nyquist velocity limit of the autocorrelation method. A velocity higher than the Nyquist velocity will alias, i.e. wrap around the velocity scale and show with incorrect magnitude and direction.

Speckle Tracking (ST)

Speckle tracking is applied by identifying a kernel region in a first image acquisition and searching for a best match inside a search region of a later acquisition, as illustrated in fig. 1-B. In this work, the match between the kernel inside the search region was determined using the sum-of-absolute differences (SAD) algorithm, given by:

$$\epsilon(\alpha, \beta, n) = \sum_{i=1}^{l} \sum_{j=1}^{k} |X_0(i, j) - X_n(i + \alpha, j + \beta)| \quad (3)$$

with ϵ the SAD coefficient, l and k the lateral and axial dimension of the kernel in beam and range samples, (α,β) defining a kernel displacement in the lateral and axial direction, and n referring to the lag between the acquisitions used for tracking. Using the kernel displacement corresponding to the minimal SAD-value (α_m,β_m), the velocity magnitude and angle can be estimated:

$$V_n = \frac{\sqrt{(\alpha_m \Delta x)^2 + (\beta_m \Delta z)^2}}{nT}, \Theta_n = atan\frac{\alpha_m \Delta x}{\beta_m \Delta z}, \tag{4}$$

with Δx and Δz the lateral and axial sampling distances and T the time between subsequent acquisitions. The procedure was performed for individual lags (n=1) in a packet of speckle images and the median of these estimates was calculated in order to minimize the effect of spurious tracking errors. **Since the velocity resolution in speckle tracking is at first determined by the image grid (see further), we interpolated the SAD matrix (parabolic fitting, (Cespedes et al, 1995)) to improve the accuracy. In order for this to work, we should have a starting image which is sufficiently sampled. Hence, we interpolated the image in both the axial (1x) and lateral (3x) directions.**

Speckle tracking imposes restrictions on the maximal and minimal velocity which can be measured. Concerning the lateral tracking, the maximal trackable velocity $V_{max,x}$ scales with PRF according to:

$$V_{max,x} = \left\lfloor \frac{S_x - K_x}{2} \right\rfloor \cdot \Delta x \cdot PRF \tag{5}$$

S_x is the lateral search region size, K_x the lateral kernel size and Δx the lateral sampling distance after envelope interpolation. In case of beam interleaved acquisition, the maximum size of S_x is given by the interleave group width as determined by the image depth (PRF_{max}), the slow-time PRF, and the receive beam overlap. **The interleave groupsize is the limiting factor for S_x since speckle decorrelation occurs across interleave groups, making it difficult to perform speckle tracking in a search region larger than the IGS.** The minimal trackable lateral velocity or resolution velocity $V_{res,x}$ scales with PRF as follows:

$$V_{res,x} = \frac{\Delta x \cdot PRF}{n} \tag{6}$$

with n the lag between the acquisitions used for tracking (n>1 is referred to as multilag tracking). Without substantial interpolation, $V_{res,x}$ is coarse compared to the expected range of velocities in clinical applications. **We illustrate this with a theoretical example.** When tracking one kernel (width of 4 beams) in an interleave region given according to a PRF of 4 kHz, PRF$_{max}$ of 16 kHz, Δx of 0.14 mm, and PRB of 2, the maximal lateral velocity V_{max} is 1.12 m/s and the minimal lateral velocity $V_{res,x}$ is 0.56 m/s. This can for instance be compared to the expected velocities in the common carotid, ranging from 0.1-1 m/s in healthy subjects. Concerning axial tracking, equation 6 is equally valid but using the axial resolution distance. However, the maximal axial velocity can be defined with more flexibility compared to the maximal lateral velocity restricted by equation 5, **since the interleaving concept is only a restricting factor when tracking in the lateral dimension** .

In order to reduce the variance of the tracking estimates, it is desirable to do spatial averaging. This however implies that the tracking estimates should lie in close vicinity of each other, in order to retain sufficient spatial resolution. When using a low PRF, this means several tracking estimates are needed for each interleave region. The number of tracking estimates that fit inside an interleave group is given by:

$$N_K = \left\lfloor \frac{IGS - 2 \cdot \left\lfloor \frac{V_{max,x}}{V_{res,x}} \right\rfloor - K_x + 2}{K_x - overlap} + 1 \right\rfloor \tag{7}$$

with N_K the number of kernels in the interleave group and *overlap* the number of overlapping beams for each kernel (with $1 \leq overlap \leq K_x - 1$).

Combining ST and PE

The same scanning procedure was applied for ST and PE, and two different imaging setups were investigated, using a PRF of 2 kHz and 4 kHz respectively. Further, a PRF$_{max}$ of 16 kHz and a transducer centre frequency of 5 MHz was applied, two receive lines were acquired in parallel, and a packet size of 10 was acquired for clutter filtering and averaging the estimated flow velocities. Using this setup, the autocorrelation method resulted in a maximal measurable velocity of 15 cm/s and 31 cm/s for respectively 2 and 4 kHz. For speckle tracking, an interleave groupsize of 16 and 8 beams was obtained for respectively 2 and 4 kHz. The lateral beam density was close to the Rayleigh criterion for both setups, and resulted in 9 and 18 interleave groups for 2 and 4 kHz respectively, and an overall frame rate of 22 frames per second (fps). A kernel size of 0.88 x 0.52 mm (lateral x axial) was chosen. **For both setups, we chose a maximal trackable velocity of 85 cm/s and 65 cm/s in respectively the lateral and axial direction, a trade-off between the acquisition/averaging setup and the possible maximum velocity. This choice resulted in a search region of 1.36 x 1.53 mm for 2 kHz and 0.94 x 1.14 mm for 4 kHz (both smaller than IGS, cfr. fig. 1-C).** According to equation 7, two kernels were fitted in the 2 kHz interleave region and one kernel in the 4 kHz interleave region. After envelope interpolation, the velocity resolution for ST was 7 cm/s and 14 cm/s laterally for respectively 2 and 4 kHz. In the axial direction, the resolution velocity was 3 cm/s (2 kHz) and 6 cm/s (4 kHz).

Three different possibilities of combining the lateral velocity v_x from ST ($v_{x,ST}$) and axial velocity v_z from PE ($v_{z,PE}$) were investigated:

(1) $v_{x,ST}$ **from 2D speckle tracking** and $v_{z,PE}$ are combined by replacing the axial estimate of ST by the phase-shift estimate, further labeled as *ST-PE*,

(2) $v_{x,ST}$ **from 2D speckle tracking** and $v_{z,PE}$ are combined but $v_{z,PE}$ is corrected for aliasing artifacts based on $v_{z,ST}$:

$$\angle\hat{R}(1)_{corrected} = \angle\hat{R}(1) + sign(v_{z,ST}) \cdot \lfloor |v_{z,ST}| / v_{Nyquist} \rfloor \cdot 2\pi \quad (8)$$

with $\angle\hat{R}(1)$ the angle of the estimated autocorrelation function at lag 1 and $v_{Nyquist}$ the Nyquist velocity limit. This method is further labeled as *ST-PE: unwrapped*,

(3) a simplified speckle tracking where the axial kernel displacement corresponds to $v_{z,PE}$ while the search region is confined to lateral tracking **(1D-ST)** only. This method is

further labeled *ST-simplified* and is also illustrated in fig. 1-C for the 4 kHz setup.

The variance of the velocity estimates was reduced through spatial averaging: (1) PE-estimates were averaged in a region of 3 beams and 2 pulselengths, (2) estimates from ST and the combined ST-PE methods were median filtered in a 5x3 kernel region.

Performance analysis

A linear regression analysis was performed, taking into account all spatial and temporal velocity measurements below the Nyquist limit and above the clutter filter cut-off velocity, further called the normal range of velocities. The accuracy of the estimated velocity vector field was further quantified with a temporal analysis of the mean absolute deviation $|V_{US} - V_{CFD}|$ of each velocity component for each frame. To directly compare the performance of both imaging setups, the 2 kHz estimates (2 kernels per IG) were interpolated to the 4 kHz kernel positions (1 kernel per IG). Estimator performance was also investigated using two different signal-to-noise ratios (SNR) during postprocessing. A default SNR of 20 dB was applied for all simulations. The effect of high noise levels was investigated by applying an SNR of 5 dB. If no noise level is especially mentioned in the text or figures, the 20 dB SNR was applied.

3. CFD-based ultrasound simulations

Ultrasound simulations

The backscattered ultrasound signals were simulated with the Field II software (Jensen and Svendsen, 1992; Jensen, 1996), which is based on the spatial impulse response estimation as described by Tupholme (Tupholme, 1969) and Stephanishen (Stepanishen, 1971). In this approach, blood is modeled as a collection of random point scatterers with normally distributed amplitude. The density of the scatterers is related to the imaging system bandwidth, with approximately 10 scatterers per resolution cell assuring Gaussian distributed RF-signals. To mimic realistic scatterer displacement in complex blood flow conditions, numerically computed flow fields are necessary to propagate the scatterers correctly. In Swillens et al (2009a), we presented a method which couples the output of computational fluid dynamics (CFD) with the Field II software. For each emitted beam, the scatterer position is updated based on the CFD-velocity fields. In this approach, spatial interpolation is necessary to interpolate the CFD velocity vectors from the irregular CFD grid to the random scatterers. Further, temporal interpolation is performed to match the CFD and ultrasound timescales (5 ms versus $62.7\mu s$ for a PRF of 16 kHz). We refer to Swillens et al (2009a) for further details on the CFD-US coupling procedure.

2x4 cm scans were simulated with a 192 element linear array transducer of 5 MHz centre frequency. Each transducer element was divided into 4 mathematical elements which ensured that every scatterer was imaged in the far-field of each individual element. A fixed transmit focus of 2 cm in depth was chosen, with an F-number of 2.5 on transmit. Dynamic focusing and an expanding aperture were used to retain an F-number of 1.4 on receive. Rectangular and cosine tapered apodization were used on transmit and receive respectively. A sinusoidal excitation pulse of 2.5 pulse periods was applied. No frequency dependent attenuation was included in the simulations. For further details on the imaging setup, we refer to the ST-setup mentioned in Swillens et al (in press). Although the tissue surrounding the blood vessel was not simulated, the effect of clutter filtering on the blood signal was included by assuming all clutter is attenuated by the filter. A second order polynomial regression filter was applied prior to PE (cut-off is 1.94 and 3.88 cm/s for respectively 2 and 4 kHz) and a fourth order FIR filter was used prior to ST (cut-off is 2.53 and 5.05 cm/s for respectively 2 and 4 kHz). The time-invariant FIR filter was used for ST to identically filter subsequently acquired speckle images.

CFD

A carotid artery bifurcation was reconstructed from MRI-scans of a healthy volunteer (Mimics, Leuven, Belgium), in which we artificially added an eccentric plaque in the internal branch (cfr. fig. 1-A). The commercial CFD-software Fluent 6.2 was used to numerically solve the Navier-Stokes equations with a finite volume method. The applied boundary conditions were a velocity profile at the common carotid, measured with PW-Doppler in a healthy volunteer, and a 45-55% externa-interna flow division. Incompressible Newtonian blood behaviour was assumed with a viscosity of 3.5 mPas and a density of 1050 kg/m^3. For further details on the CFD-setup and according phantom construction, we refer to Swillens et al (2009a).

4. In-vivo data

Raw IQ-data were recorded during examination of the carotid artery of a healthy volunteer using a 7L probe for vascular imaging and a GE Vingmed Vivid 7 ultrasound system (GE Vingmed Ultrasound, Horten, Norway). Color flow images were recorded with an imaging setup equal to the simulations (both 2 and 4 kHz). Hence, the in-vivo ST and PE estimates were obtained with the same processing as the simulations. The 2D flow estimates were superimposed on color flow images, and the flow angle was investigated in segments of the carotid artery where flow is expected to be aligned with the geometry. For this purpose, the mean and standard deviation (std) of the flow angle was analyzed in the common carotid in-vivo (the first four lateral lines) and in the external carotid for the simulations (the last four lateral lines). The external carotid was chosen for the simulations since swirling flow was present in the common carotid for several frames.

Results

1. CFD-based ultrasound simulations

The performance of ST and the three ST-PE combination techniques was compared to the reference CFD flow field with vector plots of the complete cardiac cycle. Note that the comparison is based on dynamic CFD vector fields, taking into account the location and timing of the fired ultrasound beams in order to provide correct reference values (Swillens et al, 2009a). Two important phases of the cardiac cycle are shown in fig. 2: systolic acceleration (frame 2) and the onset of diastole (frame 5), as indicated by the red part on the flow curve. Frame 2 shows zoomed-in plots of the external carotid artery, the location where the highest velocities of the complete cardiac cycle prevail. A higher PRF demonstrated reduced aliasing and improved ST performance. Both ST and the unwrapped version of ST-PE show a good qualitative agreement with the reference CFD flow field. Integrating the PE-estimate without unwrapping (*ST-PE* and *ST-simplified*) shows obvious aliasing artifacts for both PRF's. Frame 5 shows vector plots zoomed in on the common carotid during the onset of diastole, showing a large vortex in the internal bulb and a smaller one on the opposite side. Both the 2 and 4 kHz imaging setups are able to capture the large zone of swirling flow. Low velocities dominate during this stage and hence the influence of the clutter filter becomes important. The 4 kHz setup estimates suffer most from clutter filtering, and all methods imaged with 4 kHz have difficulties capturing the smaller vortex near the external carotid, which is not the case for 2 kHz. **To provide a full overview on the results from the complete cardiac cycle, we refer to the additional multimedia material.**

The estimator performance is further compared to the CFD-reference for all velocity estimates in space and time, as shown in the scatterplots of fig. 3 and 4 (for SNR of 20 dB) for respectively the axial (v_z) and lateral velocity (v_x) component. Black circles indicate the normal range of velocities, blue squares the aliased range and red stars the clutter filtered range. Figure 3 quantifies the improved ST performance for v_z when using 4 kHz. In the normal range of velocities, a lowered spread can be observed for PE estimates for all setups. A bias can also be observed for PE variants; overestimation in the vicinity of the clutter filter transition region, while underestimation close to the Nyquist limit. Aliasing errors are apparent for PE but is partly corrected for by the proposed unwrapping procedure, especially for 4 kHz. Figure 4 demonstrates a larger spread in lateral estimates of the simplified ST-method when the axial estimates alias. A linear regression analysis was performed for the normal range of velocities, and table 1 and 2 provide the mean ($\bar{m}$) and standard deviation (std) on the differences between the ultrasound estimates and the reference flow, the slope (β) and the R^2 goodness-of-fit parameter of respectively v_z and v_x. For all imaging setups, the estimation of v_z improves for *ST-PE* compared to ST, in terms of decreased standard deviation (std) and an increased goodness-of-fit (R^2). A decrease in std of 37% (2kHz) and 35% (4kHz) was observed for high SNR (20dB), and of 77% (2kHz) and 50% (4kHz) for low SNR (5dB). Table 1 also quantifies a slightly deteriorated performance for v_x of the simplified ST method.

Figure 5 shows the temporal analysis of the mean absolute deviation of the estimated v_z with respect to the CFD-reference. The performance of all investigated estimators was analyzed for both imaging setups in the common and external carotid artery. As could be observed in the flow curve of the common carotid artery (cfr. fig. 2), low flow prevails throughout most of the cardiac cycle. Hence, fig. 5 is zoomed in on the deviations present during these frames in diastole. ST shows for both PRF's the largest deviation in the external carotid during the low flow frames (cfr. frame 12 - 22). For the common carotid artery, ST shows deviations similar to the PE approach for high SNR (20 dB), and higher deviations in case of low SNR (5 dB). During the aliased frames (especially frame 2 and 3), large deviations are present in the external carotid (0.15 m/s<deviation<0.35 m/s for 2 kHz and 0.1 m/s<deviation<0.5 m/s for 4 kHz). During systole (see frame 2 in fig. 2), the unwrapping method is the overall best performer and ST the worst performer for

2 kHz. For 4 kHz, both ST and the unwrapping method perform well during this frame, with a deviation close to each other.

2. In-vivo data

Figure 6 shows the *ST-PE* method superimposed on color flow images recorded in a healthy volunteer, for a frame in systole (frame 4) and diastole (frame 6) and for both imaging setups. The left panels of figure 7 show a temporal analysis of the in-vivo mean flow angle in the common carotid artery and its associated standard deviation for the investigated 2D flow estimators. The cardiac cycle comprised 11 frames but the 1st frame was not taken into account due to signal loss in the common carotid artery. ST tracks best the reference angle that was determined from geometrical considerations (dashed black line), but shows the highest standard deviation during most of the cycle. The right panels show the same angle analysis but based on the simulations. One should note that the simulation results were derived from the external carotid in order to analyze flow conditions which were aligned with the axis of the vessel. During the second half of the cycle (frame 10 - 22), ST is closest to the reference flow angle derived from CFD (solid black line), as was the case in-vivo. The estimators perform quite similar during most of the cardiac cycle regarding standard deviation. **A full overview on the results from the complete cardiac cycle can be found in the on-line multimedia material.**

Discussion and Summary

In previous work, we compared the performance of speckle tracking and crossed-beam vector Doppler in a patient-specific carotid bifurcation model by integrating CFD and Field II ultrasound simulations (Swillens et al, in press). In our examples, we demonstrated ST to be the superior lateral velocity estimator and VD the better axial velocity estimator. For a detailed discussion on the advantages and limitations of the simulation environment, we refer to (Swillens et al, 2009a). With the aim to develop a clinically applicable and robust 2D flow estimator, we investigated the natural extension of our previous work, combining speckle tracking and phase-shift estimation to measure v_x and v_z respectively. To the best of our knowledge, such a combined approach has not previously been investigated in detail.

While the concept of combining ST and PE is straightforward, its practical implementation is not. Challenges arise from the fact that a common acquisition scheme does not reconcile the acquisition and processing requirements of the individual techniques. To achieve satisfactory results with the PE approach, the slow-time PRF needs to be adapted to the velocity range of interest. Further, for the combined approach to work properly, the maximum axial velocity should lie below the Nyquist limit, to avoid obscuring the combined estimate. This means that the PRF will vary for different clinical applications, and can in many cases be quite high (e.g. 4-10 kHz). Considering the interleaved acquisition mode used, this poses some challenges. The interleaved acquisition is necessary to obtain a high frame rate speckle acquisition (in the kHz range), making tracking of complex blood movement feasible. The number of receive lines in each interleave group is, as described by equation 2, dependent on the depth of the scan (PRF_{max}) and the slow-time PRF, such that high PRF's or deep scanning leads to few interleaved beams. In this case the possible kernel width may become very small. However, the choice of the kernel size depends on the imaging system resolution, with the lower limit of K_x related to the in-focus -3dB beam width ($K_x = \lambda F_{2-way}$, λ the wavelength and F_{2-way} the two-way F-number), as put forward by Wagner (Wagner et al, 1983). Further, the tracking performance becomes also highly dependent on the spatial interpolation for high PRF's, due to the coarse velocity resolution initially given for ST. In particular, the lateral beam sampling is typically low to adhere to frame rate requirements. In this work, both linear interpolation of envelope-detected data as well as parabolic fitting around the SAD minimum was therefore needed to obtain a velocity resolution close to the clutter filter cut-off velocity.

Combining the requirements of both approaches and considering the carotid imaging setup described in this work, the optimal choice of slow-time PRF is difficult to find and consequently becomes a compromise in unifying the requirements of both approaches. In particular, adhering to a requirement of avoiding aliasing in a combined estimator might decrease performance when tracking high blood flow, compared to using ST alone at a lower PRF. An exception is the case where the speckle decorrelation is so rapid that extreme frame rates (high PRF's) are essentially needed to track any movement. In general, multi-lag tracking might increase performance for a broader range of velocities when using a high PRF. Decimation in time is then applied for ST and tracking is performed for every *nth* (n>1) speckle image within a packet of data. Such an approach is considered further work. On the other hand, unwrapping based on axial speckle tracking estimates may also help, as can be seen in the vector plots in fig. 2 and the scatter plots in fig. 3 and 4. However, due to the variance on the axial ST estimates, the direct approach used in this work may also lead to spurious errors when unwrapping. This explains why the standard deviation increases for the unwrapped combined estimator as seen in Table 1 and 2. Problems also emerge when axial velocities wrap around all the way into the clutter filter stop band for low PRF's, as can be observed for the 2 kHz setup in fig. 2, where the signal in the external carotid aliases substantially during systole. In any case, as aliasing artifacts may be difficult to avoid, they should be visible in the final display to notify the operator. This can for instance be achieved by visualizing arrows on top of a conventional color flow image as given for the in vivo examples in fig. 6.

An alternative approach that avoids interleaving issues would be to track only within the group of parallel receive beams, as previously reported in Bohs et al (2001). However, only a small number of PRB (2-4) can be utilized without reducing the transmit aperture and therefore the sensitivity. Further, artifacts due to the misalignment of transmit and receive beams should be corrected to ensure good performance (Hergum et al, 2009), increasing complexity and cost. Another alternative would be to use unfocused (plane) transmit beams and a high number of parallel receive beams as reported in Udesen et al (2007).

However, it remains to be shown whether this approach provides sufficient sensitivity in clinical practice.

A different acquisition aspect concerns the pulse length requirements for ST and PE. ST is a wide-band technique, as the related cross-correlation technique, benefiting from short ultrasound pulses and high spatial resolution. On the other hand, PE is a narrow-band technique benefiting from longer pulses (e.g. 4 to 8 periods). In our setup, a relatively short ultrasound pulse of 2.5 periods was used as a compromise. As can be observed in the in vivo example in fig. 6, the combined estimator works quite well for the given setup. In clinical practice, however, longer pulses will be necessary in many cases. A detailed investigation of ST or the combined estimator approach with regards to sensitivity and pulse length is considered future work. However, it is worth noting that with regards to sensitivity, the proposed acquisition setup using focused beams has an advantage. Using small apertures or unfocused transmit beams in conjunction with a high number of PRB, the transmitted pressure in depth quickly decreases and longer pulses are necessary.

Different lateral sampling requirements of ST and PE is also an issue. In conventional CFI, the image is often undersampled in order to yield a higher frame rate. Due to smoothing and the low dynamic range used in the color images, visible artifacts because of undersampling are limited. On the other hand, in order to produce high quality speckle and ensure a good tracking performance, undersampling should be avoided. In this work, marginal sampling of the RF signal variation was ensured by using (approximately) the Rayleigh criterion as the beam distance. This still infers undersampling by a factor of two for the envelope detected data, and performance might be suboptimal. Coherent interpolation of the RF-data within the interleave region or a group of parallel beams could be a solution to achieve sufficient sampling and frame rate. This imposes however the requirement that phase-cancellation between beams does not occur for the velocity range of interest. The practical limits of such complex interpolation with regards to arterial flow remain to be investigated. It is also worth noting that this approach would substantially increase computational demands.

Overall, the PE estimator showed decreased variance of the axial estimates, compared to using pure ST for the examples explored. This can be observed in the scatter plots of fig. 3 and the regression results in Table 1 and 2. One should note that a bias was noticeable for PE in our examples for both low and high velocities. Overestimation on the lower range can be attributed to the clutter filter, as polynomial regression filters are known to produce a bias close to the clutter filter transition region (H.Torp, 1997; Bjaerum et al, 2002). The underestimation for increased velocities can partly be attributed to averaging. When previously comparing ST and crossed-beam vector Doppler, we showed that ST was less robust towards added noise. Also, we showed ST performance decreased in out-of-focus areas and for increased out-of-plane blood movement (Swillens et al, in press). As can be observed by comparing Table 1 and 2, the combined estimator approach has advantages for ensuring robust axial estimates in unfavorable signal-to-noise conditions.

The simplified tracking approach, fully combining ST and PE, is particularly interesting, as potential variance attributed to the 2D search regions can be avoided. In principle, this approach may therefore produce more stable lateral tracking estimates. However, we did not observe this in our examples due to the biased autocorrelation estimates. Interestingly, results showed that the simplified tracking approach marginally decreased lateral tracking performance in the normal range of velocities for both SNR conditions investigated, as given in Table 1 and 2. The simplified approach also has obvious computational advantages compared to full 2D tracking, and a high potential for real-time operation on modern scanner systems. In any case, utilizing special purpose multimedia instruction sets (MME/SIMD) on modern CPUs or going towards a graphical processor unit (GPU) implementation will make real-time performance of blood flow speckle tracking feasible for a high number of tracking kernels.

As the performance of the estimators is highly dependent on the flow field, we analyzed the deviation of the estimated v_z with respect to the CFD-reference for each frame (cfr. fig.5). In the external carotid artery, ST showed the highest deviation from the reference during the low flow phases (both 2 and 4 kHz), and the combination approach proved advantageous. In the common carotid artery, the opposite occured and ST estimates resulted in the lowest deviation from the reference during these frames. It should be noted that in the common carotid artery, relatively low axial velocities were present since the flow direction was almost perpendicular to the beam. Hence, the axial velocities were often close to the clutter filter cutoff, where the PE approach suffers from a bias due to the clutter filter. Improved results for PE may be obtained for velocities close to the clutter filter transition region by using a different clutter filter than the polynomial regression type used in this work.

To illustrate the feasibility of the estimators in vivo, we recorded data from a healthy volunteer using the exact same 2 and 4 kHz imaging setup as for the computer simulations. As can be observed in fig. 6, the ST-PE method provides reasonable velocity vector fields compared to what one would expect in a healthy carotid bifurcation. To quantify the in vivo results and compare it to the simulation results, we calculated the estimated angle of the velocity vectors in areas where the flow is expected to be well aligned with the axis of the vessel. For the in vivo data, the common carotid artery was chosen, while for simulations only the external carotid artery was used due to the swirling flow otherwise present. As can be seen in fig. 7, the mean angle estimated by ST was closest to the reference for the in vivo data, but with an overall higher standard deviation. This may be attributed to the low axial velocity component due to the near perpendicular angle in the in vivo data, and hence to clutter filtering artifacts as previously discussed. On the other hand, in the simulated data, a larger angle and larger axial velocities were present. Similar results for ST and the combined approaches can here be observed. This can partly be attributed to the higher SNR of 20 dB used for the example, and improved results when incorporating PE are expected for lower SNRs as observed globally. Overall, it can be concluded that the in vivo application of speckle tracking and a combined estimator was feasible for the given carotid artery of a healthy volunteer. Further work is needed to map the potential for patients with varying SNR conditions and for complex flow patterns due to pathology.

Conclusion

When designing a 2D blood velocity vector estimator based on speckle tracking, the added axial velocity information available using the autocorrelation approach may be used to increase overall robustness. However, a unified acquisition which ensures good tracking performance and at the same time avoids aliasing is not always possible. Unwrapping using the axial speckle tracking estimate can be used with success to some extent, but may also introduce spurious unwrapping errors. A fully combined approach where only 1D lateral tracking is performed showed a marginal decrease in performance compared to 2D tracking, but has large computational advantages. Further work will focus on in vivo trials in patients with carotid plaques.

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Table 1

Linear regression analysis for the complete cardiac cycle of v_x and v_z as estimated by speckle tracking (ST), phase-shift estimation (PE), corrected phase-shift estimation (ST-PE: unwrapped) and the simplified tracking method (ST-simplified), compared to the CFD reference. Analysis was based on those values within the normal range of velocities, i.e. not influenced by clutter filtering and within the Nyquist range. Data are reported for both imaging setups (PRF=2 and 4kHz).

		ST		**ST-PE**		**ST-PE:unwrap**		**ST-simplified**	
		2 kHz	4 kHz	2 kHz	4 kHz	2 kHz	4 kHz	2 kHz	4 kHz
$\overline{m}$ (cm/s)	vx	2.05	2.69	2.09	2.75	2.09	2.72	1.90	2.28
	vz	-0.36	0.36	-0.01	0.21	0.04	0.63	-0.02	0.10
σ (cm/s)	vx	5.19	6.32	5.19	6.27	5.22	6.38	5.25	6.70
	vz	2.83	4.67	2.07	3.48	2.07	5.46	2.17	3.55
β $(slope)$	vx	0.86	0.84	0.86	0.84	0.86	0.84	0.86	0.83
	vz	0.92	0.81	0.95	0.88	0.94	0.87	0.96	0.88
$R^2(gof)$	vx	0.83	0.82	0.83	0.82	0.82	0.82	0.82	0.80
	vz	0.86	0.86	0.92	0.92	0.92	0.91	0.92	0.92

Table 2

Linear regression analysis for the complete cardiac cycle of v_x and v_z as estimated by speckle tracking (ST), phase-shift estimation (PE), corrected phase-shift estimation (ST-PE: unwrapped) and the simplified tracking method (ST-simplified), compared to the CFD reference. Analysis was based on those values within the normal range of velocities, i.e. not influenced by clutter filtering and within the Nyquist range. Data are reported for PRF=2kHz and low SNR (5dB).

		ST		**ST-PE**		**ST-PE:unwrap**		**ST-simplified**	
		2 kHz	4 kHz	2 kHz	4 kHz	2 kHz	4 kHz	2 kHz	4 kHz
$\overline{m}$ (cm/s)	vx	5.30	9.26	5.41	9.24	5.34	9.14	5.02	8.59
	vz	-0.65	-1.36	0.21	0.71	0.31	0.88	0.01	0.19
σ (cm/s)	vx	7.50	11.28	7.43	11.32	7.52	11.38	7.64	11.38
	vz	4.77	7.42	2.70	5.49	3.33	5.77	2.97	5.00
β $(slope)$	vx	0.70	0.58	0.70	0.57	0.69	0.49	0.69	0.51
	vz	0.85	0.84	0.84	0.75	0.83	0.75	0.87	0.79
$R^2(gof)$	vx	0.70	0.51	0.70	0.49	0.69	0.49	0.67	0.51
	vz	0.63	0.65	0.90	0.89	0.90	0.89	0.88	0.88

Figure captions

Figure 1 **Panel A**: Beam interleaved scansequencing of the patient specific CFD-based carotid phantom, illustrated for PRF=4kHz. **Panel B**: Speckle tracking principle: the region of interest is divided into kernels and the optimal match of a kernel in a surrounding search region is estimated over an ensemble of 10 speckle images using an SAD-algorithm. **Panel C**. The applied tracking setups for PRF=2 and 4kHz. Using a maximal trackable lateral velocity of 85 cm/s, 2 kernels fitted in the 2kHz region and 1 kernel in the 4 kHz region. The 2kHz region consisted of 16 receive lines and the power data were further interpolated to fit in 3 lines in between the original beams (indicated with x). The 4kHz region consisted of 8 lines and the same interpolation was applied. The 4kHz setup also shows the principle of 'simplified tracking': the autocorrelation estimate $v_{z,PE}$ is used to translate the kernel a distance Δz and only lateral motion (v_x) is estimated by ST.

Figure 2 Comparison of the four 2D flow estimators and the reference CFD flow field for frame 2 (systole) and frame 5 (diastole). A setup with PRF of 2 and 4kHz is shown. Movies for the different estimators are available for the complete cardiac cycle when clicking on the images. The lower panels show the color flow images corresponding to the phase shift estimates (SNR of 20 dB).

Figure 3 Scatterplots and associated linear regression analysis of the normal velocity range for the axial velocity component (PRF of 2 and 4 kHz), shown for the three different axial estimators: *ST*, *ST-PE* and *ST-PE: unwrapped* (SNR of 20 dB).

Figure 4 Scatterplots and associated linear regression analysis of the normal velocity range for the lateral velocity component (PRF of 2 and 4 kHz), shown for the two different lateral estimators: *ST* and *ST-simplified* (SNR of 20 dB).

Figure 5 Temporal analysis of the mean absolute deviation of the axial velocity component with respect to the CFD reference flow field. The common and external carotid are investigated seperately, for ST and the three ST-PE combination techniques, and for both PRF's (2 and 4 kHz). A SNR of 20 dB was applied during post-processing of the simulations (four upper panels), and high noise levels were investigated with an SNR of 5 dB (two lower panels).

Figure 6 Demonstrating the potential of applying the *ST-PE* method in-vivo. 2D flow estimates from the *ST-PE* method are superimposed on the color flow images of a carotid artery of a healthy volunteer. Two frames (systole and diastole) and both imaging setups (2 and 4 kHz) are shown.

Figure 7 Analysis of the in-vivo flow angle (mean and standard deviation) is shown in the left panels. The right panels show a similar analysis but derived from the simulated flow estimates. All four 2D flow estimators are compared and the solid black line indicates the reference flow angle.

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