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● *Original Contribution*

TOWARD NONINVASIVE BLOOD PRESSURE ASSESSMENT IN ARTERIES BY USING ULTRASOUND

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Abstract—A new method has been developed to measure local pressure waveforms in large arteries by using ultrasound. The method is based on a simultaneous estimation of distension waveforms and velocity profiles from a single noninvasive perpendicular ultrasound B-mode measurement. Velocity vectors were measured by applying a cross-correlation based technique to ultrasound radio-frequency (RF) data. From the ratio between changes in flow and changes in cross-sectional area of the vessel, the local pulse wave velocity (PWV) was estimated. This PWV value was used to convert the distension waveforms into pressure waveforms. The method was validated in a phantom set-up. Physiologically relevant pulsating flows were considered, employing a fluid which mimics both the acoustic and rheologic properties of blood. A linear array probe attached to a commercially available ultrasound scanner was positioned parallel to the vessel wall. Since no steering was used, the beam was perpendicular to the flow. The noninvasively estimated pressure waveforms showed a good agreement with the reference pressure waveforms. Pressure values were predicted with a precision of 0.2 kPa (1.5 mm Hg). An accurate beat to beat pressure estimation could be obtained, indicating that a noninvasive pressure assessment in large arteries by means of ultrasound is feasible. (E-mail: n.bijnens@tue.nl) © 2011 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Local pressure estimation, Pulse wave velocity, Cardiovascular disease, Cross-correlation.**

INTRODUCTION

For several decades, noninvasive local blood pressure assessment in arteries has been a challenge with numerous clinical applications in diagnostics as well as in monitoring treatment of the cardiovascular system. Absolute local blood pressure waveforms would be extremely valuable before and after peripheral vascular bypass surgery. Presurgical planning of arteriovenous shunts in hemodialysis patients could benefit from accurate local pressure and flow waveforms. Furthermore, it is known that aortic pulse pressure and carotid pressure are better indicators of cardiovascular mortality and morbidity than brachial systolic blood pressure (Mitchell et al. 1997; Waddell et al. 2001). In a clinical study, Boutouyrie et al. (1999) showed that carotid pulse pressure was a strong independent determinant of carotid artery enlargement and wall thickening, whereas mean blood pressure and brachial pulse pressure were not. Additionally, accurate estimates of vascular impedance (transfer function between pressure and blood flow in the artery) characterizes the properties of the vascular bed downstream and is of particular value in studies on heart load, vascular circulation and distal vascular bed vasomotricity (Brands et al. 1996). Studies of arterial impedance in humans, however, are hampered by the lack of reliable noninvasive techniques to simultaneously record volume flow and pressure waveforms locally as a function of time. Local pressure assessment together with flow assessment in arteries has great potential for improving the ability to diagnose and monitor cardiovascular disease (CVD).

In clinical practice, ultrasound is frequently applied to noninvasively assess blood velocity, blood volume flow and blood vessel wall properties such as vessel wall thickness and vessel diameter waveforms (Hoeks et al. 1990, 1997; Brands et al. 1999). These properties can be converted into relevant biomechanical properties that

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are related to CVD, such as elastic modulus and compliance of the vessel wall (Reneman and Hoeks 2000; Meinders et al. 2000; Wilson et al. 1995), if local pressure is assessed simultaneously. In many works, the pulse wave velocity (PWV) is measured (Brands et al. 1998; Rabben et al. 2004; Zhang and Greenleaf 2006; Hermeling et al. 2007); Hoctor et al. 2007) to estimate the local relevant biomechanical properties corrected for prevailing pressure, without the necessity of knowing pulse pressure locally. The PWV, widely used for estimating the stiffness of an artery, is preferably assessed over a short segment of an artery, thus, allowing estimation of local instead of average material properties. Precise local PWV assessment is hampered by the presence of reflections in the arterial tree. Recently, it has been shown that the influence of reflections can be minimized by looking at characteristic points in the waveform, which are not largely influenced by reflections, *e.g.*, the systolic foot (McDonald 1974; Hermeling et al. 2007). Rabben et al. (2004), proposed the flow-area (QA) method, in which the local PWV in the artery is estimated during a reflection free period of the cardiac cycle as the ratio between the change in flow and the change in cross-sectional area. The reflection free period can be easily identified as a linear section in the QA-loop. In the study by Rabben et al. (2002, 2004), the cross-sectional area was estimated from M-mode data by assuming an axi-symmetric geometry. The flow was determined from a Doppler ultrasound velocity measurement, acquired at the same position as the M-mode data, by application of Womersley theory for pulsatile flow in straight tubes (Womersley 1955). Vessel diameter and blood velocity were acquired subsequently and several cardiac cycles were averaged to obtain smooth diameter and flow waveforms. As a result, temporal misalignment between the area and flow curves can result in errors in the PWV estimate. Williams et al. (2005, 2007) estimated both flow and diameter waveforms from color flow coded B-mode images, circumventing temporal misalignment errors. However, the assessed flow waveforms were scaled afterwards using an additional Doppler measurement. Additionally, the determination of the vessel area, which also influences the flow, was affected by the insonification angle.

Tortoli et al. (2006) avoided the problem of the insonification angle by using two ultrasound transducers, one set at optimal angle for wall motion measurements and the other for blood velocity profile measurements. In this way, a simultaneous assessment of wall shear rate and wall distension in carotid arteries was possible. However, for impedance assessment, a single simultaneous measurement of flow and pressure (distension) waveforms is preferred. In 2004, Meinders and Hoeks (2004) derived pressure waveforms in carotid arteries from diameter waveforms as assessed by ultrasound. They combined the diameter-derived pulse pressure method (van Bortel et al. 2001) and the exponential relationship between arterial cross-section and pressure (Powalowski and Pensko 1988). However, the mean arterial pressure was estimated from measured systolic and diastolic brachial pressures that may be inaccurate in individuals. The aim of current work is to offer a noninvasive local blood pressure assessment that can be incorporated in routine echo scans of large arteries extending these scans to a patient specific functional measurement of local and global cardiovascular condition for early detection and treatment monitoring of CVD. This work is based on a recently validated new ultrasound velocity assessment technique which in contrary to the commonly used Doppler technique estimates two-dimensional (2-D) velocity vectors and, hence, also the velocity components perpendicular to the transducer scan line (Beulen et al. 2010a). The new method described below allows an accurate and simultaneous estimation of both flow and pressure waveforms in large arteries as well as the local PWV. The method was validated in a phantom set-up, employing a fluid that mimics the acoustic and rheologic properties of blood. The estimated pressure and flow waveforms and the PWV are compared with reference measurements.

METHODS AND MATERIALS

The new method to determine local pressure waveforms in arteries from ultrasound data is based on a recently validated ultrasound velocity assessment technique (Beulen et al. 2010a) which will be referred as perpendicular ultrasound velocimetry (PUV). In PUV, a commercially available ultrasound scanner is used at high frame rate and particle image velocimetry (PIV) analysis techniques are applied to raw radio-frequency (RF)-data frames. In contrary to the commonly used Doppler method where only a single component of the blood velocity along the transducer scan line is obtained, 2-D velocity vectors are assessed with high precision. Resulting velocity profiles are integrated to flow by using the cosθ-integration model (Verkaik et al. 2009; Beulen et al. 2010b). Additionally, due to the applied perpendicular insonification of the ultrasound beam, the vessel diameter changes can be accurately assessed simultaneously from the same measurement. Based on the QA method (Rabben et al. 2004), the local PWV in the artery can be estimated during a reflection free period of the cardiac cycle as the ratio between the change in flow and the change in cross-sectional area. The reflection free period can be identified as a linear section in the QA-loop. The PWV, c, is related to the Young's modulus E, compliance C, and distensibility D by the well-known

Moens-Korteweg (first terms) and Bramwell-Hill equations (last terms):

$$c=\sqrt{\frac{Eh}{\rho d}}=\sqrt{\frac{A_0}{\rho}\frac{\mathrm{d}P}{\mathrm{d}A}}=\sqrt{\frac{A_0}{\rho}\frac{1}{C}}=\sqrt{\frac{1}{\rho D}} \tag{1}$$

in which h is the thickness of the wall, ρ is the density of blood, d is the vessel diameter, P the local pressure, A the cross-sectional area of the artery and A_0 is the cross-sectional area of the artery at end-diastolic pressure. This expression can be derived from Newton's second law with the assumption of linear elastic thin-walled ($h<<d$) vessels and using an inviscid fluid.

Equation (1) can be used to estimate the compliance, C, of the vessel or, since C = $\mathrm{d}A/\mathrm{d}P$, to estimate the local pressure, $P(t)$, with respect to $P(0)$, by:

$$P(t)-P(0)=\int_{A(0)}^{A(t)}\frac{1}{C}\,\mathrm{d}A=\int_{A(0)}^{A(t)}\frac{\rho c^2}{A_0}\,\mathrm{d}A, \tag{2}$$

From which follows that once the PWV is known, local pulse pressure waveforms can be estimated from the distension waveforms. Since it is convenient to take the cross-sectional area A at t = 0 equal to A_0, the cross-sectional area at end-diastolic pressure, $P(0)$ will be the end diastolic pressure P_0. In the *in vitro* set-up, P_0 as measured with the pressure wires can be taken. *In vivo* P_0 can be measured with a cuff since diastolic blood pressure is assumed the same throughout the major arteries. In this way, absolute local pressure values result from eqn (2).

Phantom set-up

In a phantom set-up (Fig. 1), a shear thinning blood mimicking fluid (BMF) with both acoustical and mechanical properties similar to blood was pumped through a phantom vessel (Beulen et al. 2010a). For this, a polyurethane tube with a radius, a, of 12.5 mm, a wall thickness of 0.1 mm and a length of 1.5 m was used. The phantom vessel was fully submerged in a reservoir filled with water to prevent the vessel from deforming under influence of gravity. Additionally, the water acted as a conductor of sound.

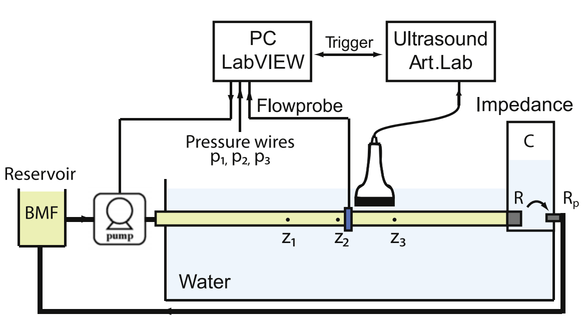

Fig. 1. Schematic overview of the experimental set-up.

At the inlet of the phantom vessel, a pulsatile flow waveform with a cycle time of 1 s, a mean of 0.7 L/min and a peak flow of 8 L/min was generated by means of a servo-actuator operated piston pump (home developed), from which the trajectory was computer controlled using LabView software (National Instruments, Austin, TX, USA). The Womersley number, α, was calculated:

$$\alpha=a\sqrt{\frac{\omega\rho}{\eta}}, \tag{3}$$

with the viscosity at a characteristic shear rate, $\eta=\eta(\dot{\gamma}_{char})=\eta(2\overline{Q}/\pi a^3)$. ρ is the density of the BMF, $\overline{Q}$ the volume flow rate through the vessel and a the radius of the vessel. The characteristic shear rate was based on a Poiseuille profile (Gijsen et al. 1999). For the first harmonic, the Womersley number, α, was approximately equal to 10, from which it can be concluded that for pressure waves traveling through the phantom set-up, the PWV is approximately equal to the Moens-Korteweg wave speed (Womersley 1957) and, hence, eqn (1) can be used to relate the PWV to the distensibility of the vessel.

The vessel was terminated by an impedance from which the BMF flows back through a reservoir to the inlet of the pump. For the terminal impedance, a Windkessel model was applied (Noordergraaf 1963). The viscous dissipation in the distal vessel, R, and the viscous dissipation in the distal capillary bed R_p, were modelled by local narrowing. The compliance of the arterial system, C, was modelled by an air-chamber. The impedance was set such that the maximum wall distension of the polyurethane tube was 0.5 mm.

The ultrasound probe was positioned at 0.75 m from the inlet of the tube, perpendicular to the tube lumen, with the mechanical acoustic focus (2 cm) at the centre to the vessel. At 1 cm upstream of the ultrasound probe, an ultrasonic flow probe (10PAA; Transonic, NY, USA) was positioned to measure the flow through the tube. Three pressure wires (PressureWire; Radi, Uppsala, Sweden) were positioned at different axial positions (z_1, z_2 and z_3) inside the vessel. The data from the flow probe and pressure wires measurements were acquired simultaneously with the data from the ultrasound scanner using a common trigger signal generated by a PC, using LabVIEW data acquisition software (National Instruments, Austin, TX, USA).

Data acquisition

The commercially available Picus Art.Lab ultrasound system (ESAOTE Europe, Maastricht, The Netherlands) was used to collect raw RF-data for offline processing. The system was equipped with a 7.5 MHz 40 mm long linear array transducer, consisting of 128 elements. This results in a transducer pitch, δz_p, equal to 0.3125 mm. A bipolar transmission signal was used. The RF data were sampled at 33 MHz (f_s) and had an approximate centre frequency of 6.8 MHz and a bandwidth of 4 MHz.

For the PUV technique, the ultrasound system was operated in fast B-mode, also called multiple M-line mode. In this mode, 14 M-mode lines are produced composing a single frame. The distance between the M-lines is equidistant and was set at the transducer pitch (0.3125 mm). To maximize the signal level at the focal point, the electrical focus was set equal to the mechanical focus, which is fixed at 2 cm from the transducer surface. The spatial resolution along the ultrasound beam (axial direction), determined by the ultrasound wavelength of 0.3 mm, is higher than the resolution in perpendicular direction (lateral resolution), which is approximately 1 mm at focal point. The frame rate of the ultrasound system is determined by the number of M-lines and the pulse repetition frequency, which depends on the depth setting. In this study, the depth was set to 50 mm, which resulted in a pulse repetition frequency $f_{pr,}$ of 10211 Hz and a frame rate f, of 730 Hz. The maximum measurement time is hardware limited to 3.8 s. The RF data matrix obtained from the system is a three-dimensional (3-D) function of depth (r), time (t) and position along the probe (z).

Data processing

The RF data were processed on a PC using MatlabR2007b (The MathWorks, Natick, MA, USA). After removal of the DC component of the RF signals, a 4th order Butterworth band pass filter (4.2 MHz and 12.5 MHz) was applied according to the quality factor (the center frequency divided by the band width) of the ultrasound beam. A 4th order Butterworth high pass filter with a cutoff frequency of 20 Hz was applied in the temporal direction to suppress static and slow moving objects (*e.g.*, wall reverberations).

For assessment of vessel wall position, the vessel-lumen interface was identified by means of a sustain attack filter (Meinders and Hoeks 2004). The sustain attack filter is an automatic edge detector based on constructing a reference signal, decaying as a function of depth. The filter works on the envelope of the RF-data. Subsequently, the RF domain complex cross-correlation model (C3M) estimator (Brands et al. 1997) was applied to assess the anterior and posterior wall movement. Since the C3M is an unbiased mean frequency estimator, it can be used for summation of time-dependent velocities to obtain tissue displacement. Subsequently recorded RF lines are cross-correlated, resulting in high precision wall tracking. The dimensions of the data window for the C3M estimator had a temporal size of 7 ms at an overlap of 5 ms and a size in depth equal to 330 μm.

To determine the axial velocity distribution of the flow through the tube, subsequent RF data frames were correlated according to the PUV technique (Beulen et al. 2010a): 50%overlapping data windows were applied to the lumen of the vessel. Because of the high spatial resolution along the ultrasound beam, data windows have a small width of 0.2 mm (corresponding to eight samples) in the radial direction (r) and a rather large width of 4.4 mm (corresponding to 14 M-mode lines) in the axial direction (z) of the vessel. The shift between two corresponding data windows from subsequent frames was calculated by performing a 2- cross-correlation in the time domain on the filtered RF data. To gather sub-pixel information, a three-point Gaussian-fit estimator (Westerweel 1993) was applied for determining the peak position in the cross-correlation plane. Resulting velocity profiles were integrated to flow by using the cosθ-integration model (Verkaik et al. 2009; Beulen et al. 2010b).

PWV assessment

To obtain a reference value for the PWV, the PWV was estimated by generating a steep pressure pulse and measuring the transit time over a long section of the polyurethane tube. Because the polyurethane tube has uniform mechanical properties and neither wall thickness nor tube radius varied, the local PWV corresponded with the global PWV. For the assessment of the transit time, the first pressure wire was positioned near the inlet of the tube ($z_1 = 0$ m), the second 0.15 m downstream ($z_2 = 0.15$ m) and the third pressure near the outlet of the tube ($z_3 = 1.28$) m (see Fig. 1).

To obtain PWV by means of the QA-method, the ultrasound system was operated in fast B-mode, employing 14 M-lines, generated at the minimum pitch Δz_p=0.3125 mm. The distance between the employed M-lines was minimized since for the cross-correlation based velocity estimation an increased pitch results in de-correlation, deteriorating the velocity estimation. The fast B-mode RF-data were processed as described in (Beulen et al. 2010a). This resulted in 2816 estimations of the vessel diameter, $d(t)$, and the instantaneous velocity profile, $v(r,t)$waveforms, sampled at 730 Hz. A median filter with a temporal and spatial window size of respectively, 4×10^{-3} s and 6.9×10^{-5} m, was used to remove outliers from the velocity measurement. The velocity profiles were integrated to obtain flow, $Q(t)$, by using the cosθ-integration method (Verkaik et al. 2009; Beulen et al. 2010b); the velocity profile is split into two equal parts at the centreline. Subsequently, each part of the profile is integrated over half of the surface of the tube. To suppress high frequency noise, a low pass Butterworth filter with a cutoff frequency of 20 Hz was applied, both to the diameter and to the resulting flow waveforms. For application of the QA-method, it was assumed that the cross-sectional area of the vessel was circular. Consequently, the area waveform, $A(t)$was determined from the diameter waveform, by $A(t)=\pi d^2(t)/4$.

Local pressure estimation

Local pressure was estimated from the simultaneous assessment of the PWV and the cross-sectional area waveform by means of eqn (2). However, the integral was replaced by a cumulative sum, since the diameter waveform, as assessed by means of ultrasound, was a discrete function:

$$P_n=P_0+\frac{\rho c^2}{A_0}\sum_{i=1}^{n}\Delta A_i with \Delta A_n=A_n-A_{n-1}, \qquad (4)$$

in which, P_0 is the end diastolic pressure, $p_n=p(n\Delta t)$and $A_n=A(n\Delta t)$, with $\Delta t=f^{-1}$ and $n=0,1,2,\ldots,N-1,N$, N = 2816. For c, the PWV obtained from the QA-measurement was used.

RESULTS

The pressure signals as assessed simultaneously by means of the pressure wires are presented in Figure 2 (top). For each signal, the time point corresponding to the global maximum is determined and subsequently plotted as a function of pressure wire position (Fig. 2, bottom). The PWV is assessed by performing a least squares linear fit. The PWV, which is equal to the slope of the linear fit, is found to be: c = 9.4 ± 0.1 ms^{-1}.

Velocities were estimated by using the PUV correlation method. Velocities were integrated as indicated above. Figure 3 shows the flow waveforms as obtained from the Transonic flowprobe (solid line) and the flow assessed by the PUV method (dashed line).

For three cycles, the cross-sectional area and flow were determined from the velocity and diameter estimation obtained from the RF-data. The resulting area and flow waveforms and the flow vs. area loop are presented in Figure 4. The straight part of the loop corresponds to the reflection-free period of the cycle. By means of a least squares linear fit of the straight section, which was manually identified, the slope was found to be 9.38 ± 0.05 m/s. Several measurements with the same flow pulse were performed and analyzed from which a mean PWV value of 9.4 m/s with a standard deviation of 0.3 m/s resulted. This PWV estimate was combined with the vessel wall diameter waveform to calculate the local pressure estimate by means of eqn (4). The resulting pressure waveform is presented in Figure 5. The shaded area illustrates a standard deviation of 0.3 m/s on the PWV

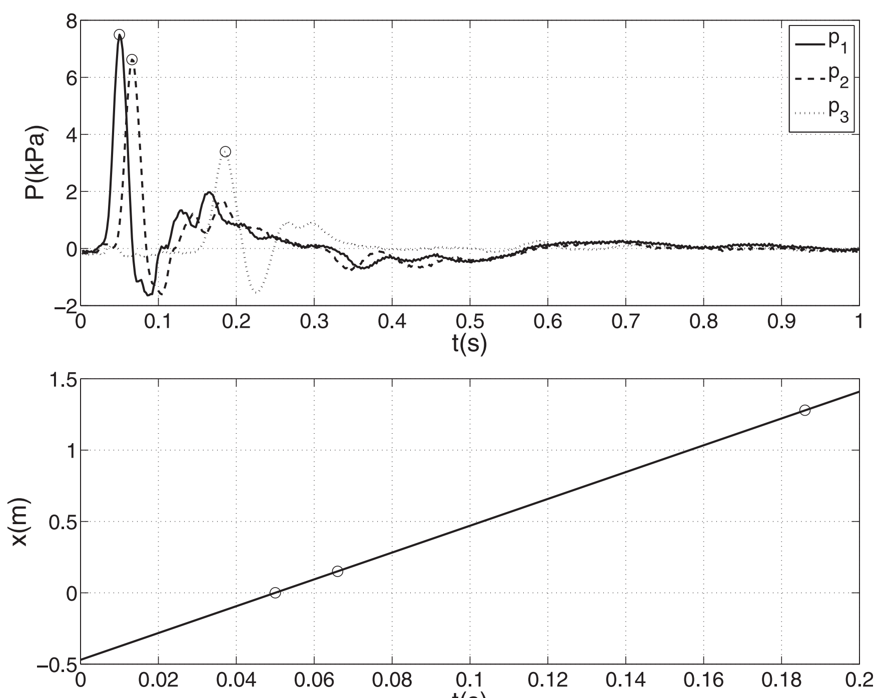

Fig. 2. In the upper graph, the pressure signals [$p_1 = p(z_1,t)$, $p_2 = p(z_2,t)$ and $p_3 = p(z_3,t)$] assessed by means of the pressure wires are presented. For each signal, the global maximum is indicated by ○. In the lower graph, the time point corresponding to the global maximum in each pressure signal is plotted as a function of the measurement position, z_1, z_2 and z_3. The solid line indicates a least squares linear fit.

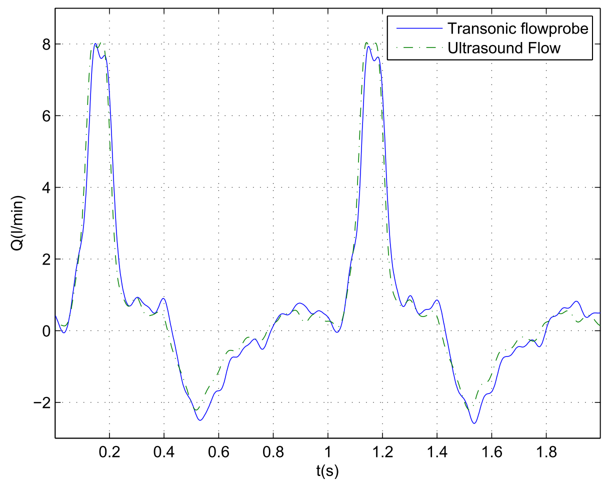

Fig. 3. Flow waveforms as obtained from the transonic flowprobe (solid line) and the flow estimated from the ultrasound radio-frequency (RF)-data by using the perpendicular ultrasound velocimetry (PUV) correlation method (dashed line).

value. As a reference, the pressure assessed by the pressure wire was added. Systolic and diastolic peak values are estimated accurately, showing differences of less than 0.2 kPa with respect to the pressure wire measurement.

The method was also tested for more physiological flow profiles. Figure 6 shows QA cycles for a typical carotid artery flow pulse in the same set-up. The flow pulse as estimated from the ultrasound PUV method is shown in the lower right panel. The estimated area waveforms are shown in the upper left panel. The resulting QA loops were much larger as compared with the loops from steep flow pulses in the same set-up. By means of a least squares linear fit on the first straight section of the first loop, a slope of 9.43 m/s was found in agreement with previous measurements. As can be seen in the right upper panel, 33 data points were used for the fit, corresponding to a time scale of 45 ms. The resulting pressure waveform is presented in Figure 7. The shaded area results from a variation of 0.3 m/s on the PWV value. As a reference, the pressure assessed by the pressure wire was added. Systolic and diastolic peak values showed differences of less than 0.2 kPa with respect to the pressure wire measurement.

DISCUSSION

For deducing biomechanical parameters and haemodynamic variables that are related to the development of CVD, such as compliance and vascular impedance, the assessment of geometry and blood velocity solely is not sufficient. A simultaneous and noninvasive assessment of blood flow and blood pressure is required. This can only be obtained by an accurate and simultaneous measurement of the blood velocity distribution and wall motion, which is not feasible with the commonly used Doppler technique. In general, current noninvasive pressure estimation methods consist of the assessment of a waveform closely related to pressure, which is

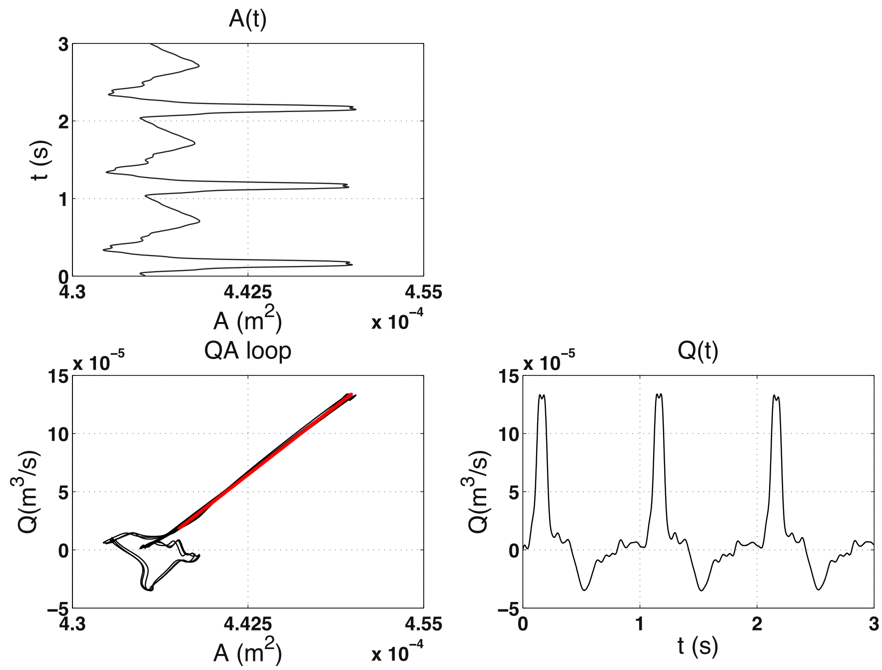

Fig. 4. Estimated cross-sectional area, $A(t)$, flow, $Q(t)$, and flow vs. cross-sectional area loop for three cycles. The thick solid line indicated in the QA-loop represents a linear fit to the straight part of the loop.

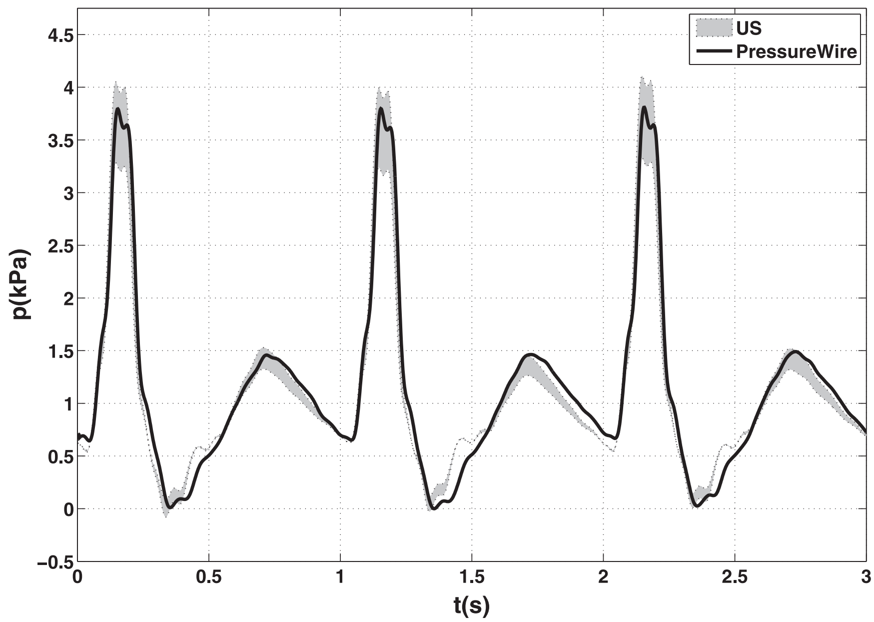

Fig. 5. Local pressure for a steep flow pulse, as estimated by means of a pressure wire measurement (solid line) and as estimated from a simultaneous assessment of diameter waveform and pulse wave velocity (PWV). The shaded area illustrates a standard deviation of 0.3 m/s on the PWV value.

subsequently scaled by an additional pressure measurement to gain the pressure estimate. The PWV based method evaluated in this study, however, allows local pulse pressure estimation from a single B-mode measurement; a simultaneous assessment of the motion of the vessel and the volume blood flow through the vessel. Current methods for local PWV estimation, *e.g.*, by means of cross-correlation based estimation methods (Struijk et al. 1992; Eriksson et al. 2002), are affected by reflections. Although the impact of reflections can be minimized by looking at characteristic points that are not too influenced by reflections, *e.g.*, the systolic

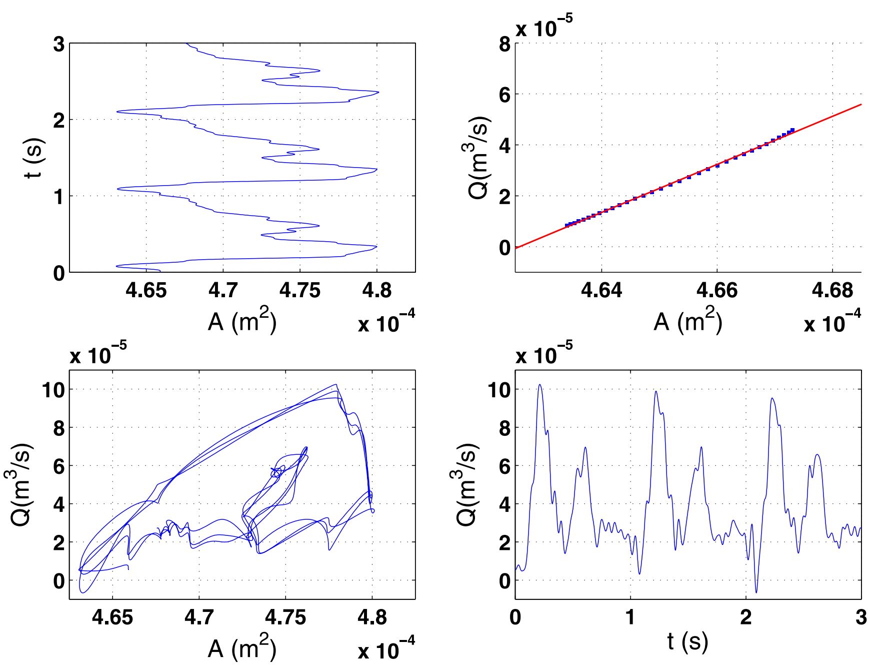

Fig. 6. Estimated cross-sectional area, $A(t)$, flow, $Q(t)$, and flow vs. cross-sectional area loop for three cycles. The upper right panel indicates the linear fit on the first part in the first QA-loop.

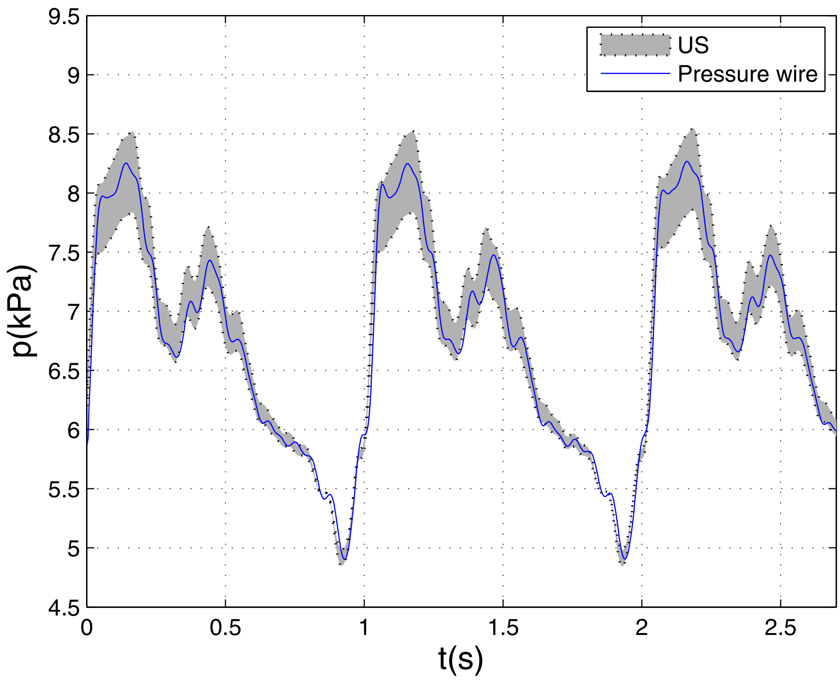

Fig. 7. Local pressure for a carotid artery flow pulse, as estimated by means of a pressure wire measurement and as estimated from a simultaneous assessment of diameter waveform and pulse wave velocity (PWV). The shaded area illustrates a variation of 0.3 m/s on the PWV value.

foot in the distension waveform (McDonald 1974; Hermeling et al. 2007), this requires an unambiguous approach for identifying these characteristic points. Besides, only a single point of the available distension waveform is employed, whereas an entire waveform is available.

In this study, the QA-method was evaluated, enabling a straightforward method for measuring the local PWV. As for current methods, the applicability of the QA-method is restricted to reflection-free periods of the cardiac cycle, however, it is more appropriate for practical application since this method allows a simple identification of the reflection free periods, by finding linear sections in the QA-loop. Contrary to previous studies (Rabben et al. 2004; Williams et al. 2005; Tortoli et al. 2006), in the present study, the vessel diameter and velocity profile were acquired simultaneously in a single ultrasound B-mode measurement with perpendicular insonification. The recently validated PUV-correlation method (Beulen et al. 2010a, 2010b) was used to estimate the flow in the vessel. As shown in Figure 3, accurate flow waveforms can be deduced without additional scaling or velocity profile approximations. The distension waveforms were obtained from a commercially available wall tracking method applied on the same RF-data set. This resulted in an accurate and simultaneous estimate of volume flow and cross-sectional area (see Fig. 4). For steep pulses, a long straight part in the QA-loop resulted in a mean PWV estimate of 9.4 ± 0.3 ms^{-1}, which accurately corresponded with the reference value as assessed using the peak to peak transit time measurement (9.4 ± 0.1 ms^{-1}). For more carotid artery like pulses (see Fig. 6), the straight parts in the QA loops were less clear. Only the first 45 ms of the straight part in the loops showed a good agreement with previous PWV measurement. Possibly reflections from previous pulses have an effect on the "linear part" of the loops and only this first part in the first loop is reflection free.

It should be noted that for the experimental set-up, even for the carotid artery flow pulse, the "straight part" in the QA loop is relatively long. It is known, however, that in most humans, only the early systolic wave is reflection free (Li 2004), which lasts approximately 50 ms (Rabben et al. 2004). Although this is a short time period, the high sample rate (730 Hz) of the measurement technique applied in this study allows to estimate 35 sample points in the early systolic wave. This should be sufficient to adequately estimate the slope of the linear section in the QA-loop. Still, the presence and the length of the reflection free period depend on the measurement location in the arterial system. In the periphery, the reflection free period might be significantly shorter. Furthermore, it should be noted that the knowledge of the wavespeed can be used to separate the pressure and flow waveforms into their forward and backward components, which can help clarify the pattern of waves in the arteries throughout the cardiac cycle (Khir et al. 2001).

The combination of ultrasound based local PWV estimation and the distension waveforms, as obtained from the wall tracking algorithm, resulted in accurate local pressure waveforms. As illustrated in Figures 5 and 7, for various applied flow pulses, a good agreement was found between the pressure waveforms as obtained from the ultrasound measurement and the reference pressure waveforms. With the knowledge of the end-diastolic pressure (P_0), absolute pressure values were predicted with a precision of 0.2 kPa (1.5 mm Hg). For *in vivo* applications this could be done with a simple standard pressure measurement since diastolic blood pressure is assumed the same throughout the major arteries.

Errors in pressure estimation can be introduced due to nonuniform tissue properties surrounding the vessel and nonlinear material properties of the vessel wall. Noncircular areas of the vessel will introduce errors when the velocity profile is integrated for flow estimation. The Bramwell-Hill equation can not be used for nonlinear material properties. It should also be noted that the cross-correlation PUV flow detection technique is limited due to the limited frame-rate of the ultrasound system. In current setting, only axial velocity values lower than 0.8 m/s can be measured accurately. This will limit the application of the method to arteries where velocities are not too high.

Perpendicular insonification, as described here, places higher demands on the computational subsystem compared with the currently used Doppler methods. For the accurate discrimination of the backscatter part of the signal, new approaches will have to be invented. The algorithms can be based on linear algebraic, wavelet methods and complex cross-correlation. The real-time postprocessing of the RF-data may be done on a standard desktop PC with a powerful graphical processing unit (GPU). A pilot study has already shown the feasibility of this approach: the processing time could be reduced to 100 microseconds per frame.

CONCLUSION

In conclusion, the QA method was found to allow an accurate and precise estimation of the PWV. Based on the QA-method derived PWV and vessel diameter measurement, an accurate beat to beat local pressure waveform could be obtained, indicating that a noninvasive pressure assessment by means of ultrasound is feasible. The introduced method enables an improved assessment of the condition of the vascular system, which in the future can be applied to identify parameters that are characteristic for the development of CVD and to monitor the effect of therapeutic interventions.

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