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Quantification of Wave Reflection in the Human Umbilical Artery from Asynchronous Doppler Ultrasound Measurements

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Abstract

Elevated umbilical artery pulsatility is a widely used biomarker for placental pathology leading to intrauterine growth restriction and, in severe cases, still-birth. It has been hypothesized that placental pathology modifies umbilical artery pulsatility by altering the degree to which the pulse pressure wave, which originates from the fetal heart, is reflected from the placental vasculature to interfere with the incident wave.

Here we present a method for estimating the reflected pulse wave in the umbilical artery of human fetuses using asynchronously acquired Doppler ultrasound measurements from the two ends of the umbilical cord. This approach assumes non-dispersive and loss-less propagation of the waves along the artery and models the reflection process as a linear system with a parameterized impulse response. Model parameters are determined from the measured Doppler waveforms by constrained optimization.

Velocity waveforms were obtained from 142 pregnant volunteers where 123 met data quality criteria in at least one umbilical artery. The reflection model was consistent with the measured

waveforms in 183 of 212 arteries that were analyzed. The analysis method was validated by applying it to simulated datasets and comparing solutions to ground-truth. With measurement noise levels typical of clinical ultrasound, parameters describing the reflected wave were accurately determined.

Index Terms—

Ultrasonic Imaging; Wave Reflection; Placental Pathology

I. Introduction

Human umbilical artery (UA) blood flow pulsatility measured by Doppler ultrasound is a widely used biomarker for the detection of elevated placental vascular resistance. Elevated UA pulsatility, which in the most extreme cases manifests as absent or even reversed end-diastolic velocity, is associated with intrauterine growth restriction (IUGR) and still-birth [1]. Although the causative link between elevated pulsatility and placental pathology is not completely understood, one possible explanation is that elevated placental vascular resistance changes the observed pulsation pattern through elevated reflection of the pulse pressure wave [2], [3]. A reduction in the number, size, and compliance of arterial vessels in the placenta, as well as umbilical cord restriction due to abnormal cord insertion, are known hallmarks of placental pathology that leads to IUGR [4]. Because these factors all lead to an increase in vascular resistance, a number of groups have proposed that reflections that originate from the placenta and travel back towards the fetus interfere with the forward propagating wave generated by the fetal heart and, at least partially, explain the mechanism by which placental pathology modifies UA pulsatility [5], [6].

We have previously applied a non-invasive ultrasound method to detect wave reflections in the mouse UA [7] and have shown that reflection magnitude is sensitive to both acute changes in placental vascular resistance [8] and structural changes in the fetoplacental arterial tree [9]. This method relies on measurement of the time-dependent diameter of the vessel by M-mode ultrasound. However, this approach is impractical for measuring human UA reflections because the spatial resolution of current clinical ultrasound is too low to quantify these small changes in vessel diameter accurately.

Here we present a non-invasive ultrasound method to measure wave reflections in the human UA solely from Doppler blood velocity waveforms. This method takes advantage of the fact that the propagation time along the human umbilical artery is a significant fraction of the cardiac period, which results in spatially-varying interference between the forward moving and reflected waves. We model the observed velocity waveform at different locations along the UA as superpositions of the same forward and reflected waves shifted in time according to position dependent propagation delays. Previous work from our group has demonstrated that reflections are present in the human umbilical artery and have a significant effect on the shape of the observed velocity waveform [3], [10].

Past work has described methods of decomposing the flow or pressure waveform in an elastic tube into two constituent waveforms travelling in opposite directions [11]–[13].

Similar to our present work, by combining three or four measurements of flow, pressure, or tube diameter spaced along the tube, the reflection coefficient was determined analytically. The current work provides novel adaptations to these techniques, making them practical for clinical application in the human UA. Specifically, we overcome limitations related to the unknown distance between measurement sites along the UA, remove the requirement to acquire data from multiple sites simultaneously, and reduce the required number of measurement sites to two.

II Methods

A. Data Collection

Pregnant women aged between 18 and 45 years with a BMI < 45 kg/m² and no significant maternal co-morbidities were recruited for a fetal ultrasound examination between the 23rd and 37th week of gestation. This cohort was prospectively recruited from general and high-risk pregnancy clinics to obtain a highly heterogeneous cohort with a range of normal appearing and pathological placental phenotypes. Women were scanned by certified sonographers at either Mount Sinai Hospital (Toronto, ON, Canada) or Johns Hopkins Hospital (Baltimore, MD, USA) using either a Philips iU22 (Philips Healthcare, Andover, MA), or GE Voluson e10 (GE Healthcare, Chicago, IL). A subset of this cohort was described previously [3].

For each UA, pulsed Doppler ultrasound was used to obtain blood velocity spectra at both ends of the cord, as well as at a free loop position judged by the sonographer to be roughly midway along the cord. Sonographers were instructed to repeat measurements in cases where fetal cardiac output was poorly resolved (due to signal attenuation or high insonation angle), or unstable (due to motion artefact or variable cardiac output) to ensure the highest quality data reasonably obtainable in a clinical setting.

In-house software written in Python v2.7 was used to extract velocity waveforms from the Doppler spectra. After removing background speckle from the region containing the Doppler spectrum, the maximum velocity envelope was defined by thresholding based on pixel intensity. The onset of systole in each cardiac cycle (i.e. R-wave position) was then detected automatically [14]. Cardiac cycles affected by abrupt motion, irregular cardiac output, or poorly resolved velocity spectra were manually censored from further analysis.

Slowly varying velocity waveform amplitude, likely caused by slowly changing insonation angle, was found to be a common occurrence. A piecewise multiplicative scaling function, with nodes defined at each R-wave position, was used to correct for these slow variations in waveform amplitude. The parameters of this piecewise function were determined by optimization, starting initially from a uniform function and then adjusting the scaling parameters, along with the R-wave positions, in order to minimize the following function:

$$\Omega(R,S) = \frac{\sum_{h=0}^H \sum_{c=1}^C |A_{hc} - \overline{A}_h|^2}{C|\overline{A}_0|^2} \quad (1)$$

where R is a vector of R-wave positions, S is a vector of scaling parameters, A_{hc} is the complex-valued Fourier series coefficient of the scaled velocity waveform indexed by harmonic, h , and cardiac cycle, c . $\overline{A_h}$ is the average of A_{hc} over all cardiac cycles, H is the highest harmonic considered in the Fourier series, and C is the number of acquired cardiac cycles in the velocity waveform. Equation (1), which represents the signal to noise power, was minimized using Powell's method [15] as implemented in SciPy v1.0.0.

B. Wave Reflection Model

We assume that propagation of velocity waves along the umbilical artery is non-dispersive and loss-less such that if an observed UA flow waveform at a location distal to the fetus, $d(t)$, is the superposition of forward propagating and reflected waveforms, respectively $f(t)$ and $b(t)$, then the observed flow waveform at a location proximal to the fetus, $p(t)$, is a superposition of the same two waveforms shifted in time (Fig. 1).

As the measured waveforms are acquired asynchronously and subsequently aligned such that the apparent arrival time of the forward wave is the same between the two measurements, the arrival of the reflected wave at the proximal position has a delay relative to its arrival at the distal measurement site that is twice the UA transit time, τ . We define the time shift needed to synchronize the forward wave at the proximal and distal measurement sites as s . The combined waveforms at the two locations are thus modelled as follows:

$$d(t) = f(t) + b(t) \quad (2)$$

$$p(t + s) = f(t) + b(t - 2\tau) \quad (3)$$

A solution for the forward and reflected waves can be derived in the frequency domain based on a Fourier series expansion of equations (2) and (3). This generates the following unique pair of equations for each harmonic number h :

$$D_h = F_h + B_h \quad (4)$$

$$P_h = F_h e^{-i\omega_0 h s} + B_h e^{-i\omega_0 h (s + 2\tau)} \quad (5)$$

where D_h , P_h , F_h and B_h are the complex Fourier series coefficients of the h^{th} harmonic for the distal, proximal, forward, and reflected waveforms, and ω_0 is the fundamental angular frequency.

If τ and s are known, determination of each F_h and B_h is straight-forward. However, in the context of clinical data acquired consecutively with a single transducer, these time-shift parameters need to be estimated from the data. As this problem is underdetermined, additional constraints must be applied to yield a unique solution for t and s . An earlier implementation of this technique, which was the basis for the results presented in [3], and described in detail in [10], constrained the problem by forcing the wave reflection model to be consistent with a third blood flow waveform measured near the middle of the UA. In the

current work, these constraints are generated by modeling the placenta as a linear time-invariant system and restricting the functional form of the impulse response function (IRF) that relates the reflected wave to the forward wave. Under the assumption that the system is causal and that reflections are generated within the placenta, even reflections from the most distant site of reflection within the placenta should arrive at the distal measurement site with only a short delay. We propose a functional form for this impulse response as follows:

$$\gamma(t) = \Gamma_e \delta(t) + \Gamma_d \lambda e^{-\lambda t} u(t) \quad (6)$$

where $\delta(t)$ and $u(t)$ respectively represent the Dirac-delta function and the Heaviside function. Free parameters Γ_e and Γ_d set the area under each arithmetic term, and λ controls the width of the decaying exponential.

The first term represents a reflected pulse that is generated at the entrance to the placenta and that returns immediately to the distal measurement site, while the second represents reflections generated from a diffuse set of sites deeper within the placenta. Based on estimated ranges for the distance traveled in the placenta ($\lesssim 10$ cm [16]) and assuming a pulse wave velocity near 5 m/s, the time for a pulse to exit the placenta after a single reflection should be at most a few tens of milliseconds and would be nearly indistinguishable from a reflected pulse originating from the entrance to the placenta. However, we hypothesize that if reflections are generated within the placenta, reflected energy will emerge from the placenta over a delayed period due to the phenomenon of wave trapping [17] whereby the total distance traveled is extended by partial re-reflection of the reverse travelling waves. Wave trapping occurs because vascular networks (such as the placenta) that have evolved to transmit pressure waves efficiently in one direction will transmit them inefficiently in the opposite direction. As a result, when a reflected wave travels backward through the placenta, only a small fraction of its energy will pass through each bifurcation. The remaining energy is again sent forward, traveling toward the same downstream reflection sites. Assuming the wave amplitude is attenuated by the same fraction after each reflection, an exponentially decaying wave is a plausible model for the waveform that emerges in response to an impulse.

Enforcing that the IRF is described by (6) results in the following equality constraint in the frequency domain for each harmonic number h :

$$B_h = F_h \left(\Gamma_e + \Gamma_d \frac{1}{1 + i\omega_o h / \lambda} \right) \quad (7)$$

The reflection coefficient, which is the Fourier transform of the IRF, naturally cannot have a magnitude greater than unity. This leads to the following inequality constraints for each harmonic number h :

$$\left| \Gamma_e + \Gamma_d \frac{1}{1 + i\omega_o h / \lambda} \right| \leq 1 \quad (8)$$

$$|\Gamma_e| \leq 1 \quad (9)$$

$$|\Gamma_d| \leq 1 \quad (10)$$

For values of τ where the factor $e^{i2\omega_0 h \tau}$ approaches unity, equations (4) and (5) become ill-conditioned, allowing for solutions with unrealistically large values of F_h and B_h that cancel when summed. To exclude these solutions, the estimate of $f(t)$ is constrained to be well-behaved by enforcing its Fourier series coefficients to decrease in magnitude with increasing harmonic number. This is expressed as the following inequality constraint for each harmonic number h .

$$|F_h| \leq |F_{h-1}| \quad (11)$$

Finally, values for τ , s , and λ were constrained based on physical plausibility arguments, as follows:

1. Upper and lower limits for τ were chosen to exclude unrealistically low and high pulse wave velocities, respectively. Based on published UA lengths of 25–70 cm [18] and pulse wave velocities of 10–15 m/s [19], [20], τ was constrained to 20–85 ms. Although the upper bound on cord length and lower bound on pulse wave velocity imply an upper bound of 70 ms on transit time, the limit was relaxed to 85 ms to accommodate a multitude of solutions best fit by a higher transit time.
2. The value of s was limited to be a small fraction of the cardiac period, because it represents a short delay used to correct for residual misalignment between forward waves in the already aligned distal and proximal waveforms, s was constrained to be between –20 to 20 ms.
3. An upper bound on λ was chosen to prevent degeneration of the IRF into opposing delta function, with highly correlated values for Γ_e and Γ_d . This bound was chosen to ensure the IRF decayed to no less than 25% of its initial value by one twelfth of the cardiac period ($\lambda < 16.6f_0$, where f_0 is the fundamental frequency in Hz).
4. A lower bound of λ was chosen to avoid an implausibly long decay of the IRF. This bound was set to $2f_0$ which results in the exponential term decaying to less than 14% of its initial value after one cardiac period.

C. Solution Method

The model parameters that best match the model to the observed measurements can be found using a constrained non-linear regression technique. In our implementation, a cost function defined in frequency space is minimized using the Sequential Least Squares Quadratic Programming (SLSQP) algorithm [21] as implemented in the Python package PyOpt v1.2.0 [22], applying equations (7) to (11) as constraints. This algorithm makes successive quadratic approximations of the cost function and linear approximations of the constraints,

hence converting the problem to an ordinary quadratic programming problem. The Lagrangian of the problem is minimized along the search direction appropriate to the corresponding quadratic programming problem.

Multiple minima may exist in the cost function owing to its non-linearity with respect to τ and s . To ensure that the global minimum is found, the search is first initialized with τ and s held constant with values chosen from a coarse grid spanning their respective domains. With τ and s removed from the cost function, the cost function becomes quadratic with respect to all other variables, so its optimization is especially well-suited to SLSQP. The solution found at each grid point in the space of τ and s is then used to initialize another search where τ and s are free to vary. The lowest cost position in the cost-landscape found after these multiple initializations is assumed to be the global minimum. A solution was deemed valid when its root mean square error (RMSE), relative to the corresponding measurements, was less than 1.5% of the mean velocity.

Because the human umbilical cord contains two umbilical arteries and sonographers cannot keep track of which UA is which, there are two scenarios for how proximal-end waveforms can be paired with distal-end waveforms. Solutions are found for both scenarios. The scenario which yields the highest number of valid solutions (i.e. 0, 1, or 2 arteries fitting the model) is assumed correct. When both scenarios yield an equal number of valid solutions, the one with the lowest average RMSE is assumed correct.

D. Validation

Monte Carlo simulations were performed to test the accuracy and precision of the proposed analysis using waveforms based on the wave reflection model, with realistic measurement noise added. For each simulation, the parameters describing the shape of the forward wave were copied from one of six template forward waves found to fit our clinical data. Noise characteristics, including noise power distribution as a function of harmonic number, correlation between real and imaginary components of noise, and number of cardiac cycles measured at each UA site, were copied from one of 212 waveform pairs available from our clinical data. The Monte Carlo simulation and testing procedure consisted of the following steps:

1. One IRF parameter (Γ_e , Γ_d , or λ) was held constant while the values of the remaining two were chosen randomly from a uniform distribution over an allowed domain.
2. The forward wave was defined by random selection of one of six template forward waves, each defined by a set of six Fourier coefficients, F_h .
3. τ and s were randomly chosen from uniform distributions; 45 to 65 ms for τ and -10 to 10 ms for s .
4. The parameters of the backward wave, B_h , were set according to equation (7).
5. The Fourier coefficients of measured waveforms were generated according to equations (4) and (5).

6. Random noise was added to the Fourier coefficients generated in step 5, where the noise characteristics were copied from one of 212 waveform pairs chosen randomly from clinical data.
7. These simulated measurements were fed into the solution method described in the previous section (section II.C).
8. Steps 1 to 7 were repeated 2000 times. The mean and standard deviation of the given IRF parameter in these 2000 solutions were recorded to characterize the bias and precision of the estimation procedure.
9. Step 8 was repeated with Γ_e held constant at -50% , -30% , -10% , 10% , 30% , or 50% .
10. Step 8 was repeated with Γ_d held constant at -50% , -30% , -10% , 10% , 30% , or 50% .
11. Step 8 was repeated with λ held constant at $5f_0$, $8f_0$, $11f_0$, and $14f_0$.
12. Steps 9 to 11 were repeated with the noise power spectrum scaled to yield a noise power fraction of 0.000% , 0.025% , 0.050% , 0.075% , or 0.100% of the signal power.
13. Steps 9 to 11 were repeated with the noise power spectrum scaled to maintain the original noise power fraction of the clinical measurement from which the noise characteristics were copied (hereby called *natural noise conditions*).

The allowed domains for Γ_e and Γ_d (in step 1, above) were set to -50% to 50% rather than -100% to 100% because we typically have not seen such high values of Γ_e and Γ_d that fit measured data. The allowed range of λ was set to the same range used to constrain the solution ($2f_0$ to $16.6f_0$).

III. Results

A. Analysis of Clinical Datasets

Doppler sonograms were collected from a total of 142 pregnant volunteers. Nine volunteers had a single UA. From the 275 measurement pairs that could be used to measure wave reflections, 63 were discarded due to irregular cardiac output, motion artefact, and/or variable heart rate (defined as heart rate variability greater than 10 beats per minute between measurement sites). 123 of the 142 datasets had at least one pair of measurements that were suitable for analysis.

Velocity waveforms were extracted from all sonograms where the data quality was suitable for analysis using the method described in section II.A. We observed that signal power decreased rapidly with increasing harmonic number. The highest harmonic number considered when applying equation (1) was the sixth, above which the Fourier coefficients were dominated by noise. On average, 99.87% of the signal power was accounted for in the first six harmonics. Fig. 2a shows an example sonogram with the waveform trace (yellow/blue before/after scaling) and automatically identified R-wave positions (red/green before/after refinement). A three-cycle region of the sonogram was manually identified and

censored where the amplitude of the waveform had changed abruptly, likely due to subject motion. Also shown in magenta is the piece-wise linear velocity scaling function used to maximize consistency between the individual cardiac cycles based on equation (1). Fig. 2c shows the overlaid traces in the time domain after R-wave positions were adjusted and motion corrected, clearly showing improved alignment compared to Fig. 2b. which shows overlaid traced before alignment.

Of the 212 measurement pairs analyzed, 183 yielded valid solutions using the method proposed in section II.C. Two representative examples of wave decomposition are shown in Fig. 3. Portions of the Doppler spectra acquired from each end of the UA are shown in the top row. The middle and bottom rows show the same forward and reflected waves that, when added together with different temporal shifts, closely reproduce the measurements at the proximal (middle row) and distal measurement sites (bottom row). The residual difference between the measurements and model is shown multiplied by 10 and shifted down by 50 mm/s to aid visibility.

The distribution of impulse response function parameters Γ_e and Γ_d for the 183 measurement pairs that fit the wave reflection model are presented in Fig. 4 as a scatter plot. The two examples from Fig. 3 are plotted with empty circles. The magnitude of reflections observed in our cohort is diverse, ranging from very little reflection (points near the origin) to very large reflections. Γ_e with a mean and standard deviation of 11.1% and 19.9% tends to take positive values (71% of solutions), while Γ_d with a mean and standard deviation of -42.9% and 33.4% tends to take negative values (92% of solutions).

B. Validation

Fig. 5 shows the distribution of noise power as a fraction of signal power from 212 pairs of experimental UA waveforms, demonstrating that the majority were below 0.10%. This observation motivated the range of simulated noise powers investigated during validation of the proposed analysis (step 12 of section II.D). Simulations with natural noise levels had noise power sampled from this distribution.

Results of the numerical validation are presented in Fig. 6, showing the mean and standard deviation of the IRF fit parameters as a function of noise level, including natural noise. The mean and standard deviation of the estimated values of Γ_e and Γ_d under natural noise conditions are summarized in Table I.

For simulations without noise, the method converged to the ground truth within numerical precision. Under natural noise conditions, the standard deviations of the estimated value of Γ_e and Γ_d were small (ranging from 4.1% to 11.4%) compared to the range of values shown in Fig. 4. With increasing noise, uncertainty in these fit parameters grew. Even with noise levels near the maximum of what we observed from our clinical data, the standard deviation remained on the order of 10% to 15%, which is significantly smaller than the biological distribution of these parameters indicated in Fig. 4. Similarly, the bias in these estimates was small compared to the observed biological distribution of Γ_e and Γ_d .

Fig. 6c shows that the standard deviation in the estimate of λ is very large compared to its allowed range. This is largely driven by cases where Γ_d takes values near zero, resulting in the value of λ having very little impact on the model. Detailed inspection of simulation results shows that exclusion of cases with Γ_d near zero reduces the standard deviation of the estimate of λ . Fig. 6c shows a clear pattern of bias toward the center to the allowed range of λ . Inspection of simulation results show that this is due to estimates of λ falling at the upper and lower limits of this parameter a large fraction of the time, especially under high noise levels.

IV. Discussion and Conclusion

We have presented here a new technique to measure wave reflections using velocity waveforms recorded at two positions along the human UA. The technique does not require synchronized acquisitions, making it applicable to Doppler ultrasound recordings obtained during conventional clinical assessment. 183 out of 212 clinical datasets (each consisting of waveform measurements at either end of the UA) were found to be consistent with the wave reflection model and the proposed impulse response function constraints.

Through simulations it was shown that if the measured data is consistent with the wave reflection and impulse response model, this technique provides an accurate measurement of the counter propagating waveforms that add in super-position to form the observed measurements. Furthermore, it was shown that this technique performs well in the presence of noise levels typical of clinical ultrasound measurements.

In the experimental data, there was a large range in magnitude of the impulse response function parameters (as shown in Fig. 4). In most cases, the reflection at the entrance to the placenta, Γ_e was positive, consistent with an expansion wave, while the reflection coming from within the placenta, Γ_d , was negative, consistent with a compression wave. A change in vessel wall properties such as an increase in compliance at the entrance to the placenta could explain a positive Γ_e , although we are not aware of any biomechanical studies of placental vessels that could support this observation. The observation that in most instances Γ_d is negative is interesting because a negative reflection (that is, one with a 180° phase shift at the reflection site) will arise where the wave encounters a site of high mechanical impedance. While it is not clear where this could arise in the placenta, a likely candidate is the capillaries within the terminal villi. This association, if established, could make this parameter a useful biomarker of placentas where the villous structure is maldeveloped.

Estimates of the fit parameters that are likely of most interest for placental assessment (Γ_e and Γ_d) showed some susceptibility to bias on the order of a few percent under natural noise conditions. Increasing levels of noise translated to increasing bias and uncertainty in fit parameters (Fig. 6). Therefore, efforts must be made to reduce error in velocity measurements. In this study, sonographers were trained to retake measurements when data quality was affected by motion artefacts and poor signal to noise ratio (for example, from a high insonation angle). By retaking measurements and applying the correction techniques described in section II.C, noise was reduced sufficiently to produce values of Γ_e and Γ_d with standard deviations under 10%.

The results of the simulation analysis assume that measurements are consistent with the wave reflection model. In practice, other factors unrelated to wave reflections from the placenta could partially explain waveform variation along the UA, such as attenuation of the pulse wave due to viscous energy loss in the blood and non-elastic forces in the vessel walls. However, a large subset of cases (such as the low reflection example in Fig. 3) show very little to no difference in waveform shape between the two ends of the cord, indicating that energy loss due to these factors is negligible. We have previously shown that the patterns of waveform variation are not consistent with attenuation along the cord [3]. It should be noted that cord abnormalities or temporary compression of the UA may generate reflections along the cord, which cannot be accounted for by the wave reflection model. A difficulty with non-simultaneous ultrasound acquisitions from each end of the UA is the possibility that cardiac output changes between measurements, therefore invalidating the wave reflection model. Efforts can be taken to mitigate this, such as scanning during periods of fetal quiescence or rejecting measurement pairs with significant heart rate variation.

This work builds on previous work that made no assumptions about the shape of the IRF to constrain the wave reflection model [3], [10]. Instead, the wave reflection model was assumed to be consistent with a third measurement near the middle of the UA. In doing so, the parameters of the wave reflection model became over-determined and were solved using non-linear regression, similar to what was done in this work. By removing the need to include a third measured waveform, the chances of the wave reflection model becoming invalidated due to changing cardiac output during the exam have been greatly reduced. This is reflected in the larger fraction of datasets that fit the wave reflection model. 86.3% of measurement pairs analyzed in this work fit the wave reflection model, while only 66.7% of the measurement triplets analyzed in [10] fit the model.

In conclusion, we have presented here a novel analysis technique to measure wave reflections in the human UA that utilizes blood velocity waveforms measured at either end of the UA. In this work, we measured these velocity waveforms in a cohort of 142 pregnant volunteers using Doppler ultrasound. From this cohort, we applied our analysis technique to 212 waveform pairs. 183 of these measurement pairs yielded a valid solution to the wave reflection model that was consistent with the proposed placental impulse response. The analysis technique was validated using Monte Carlo simulations. These simulations showed that when the measured data is consistent with the wave reflection model, the proposed technique converges on the correct solution. Increasing levels of measurement noise decrease the precision by which the parameters of the forward and backward propagating waves can be estimated. Under noise levels typical of clinical ultrasound, the most relevant parameters of the wave reflection model (Γ_e and Γ_d) could still be estimated with high precision and low bias, relative to their estimated biological distribution.

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Fig. 1.

Illustration of the wave reflection model. A velocity wave propagates from the fetal heart toward the placenta, and a fraction of this wave's energy reflects from the placenta and travels back toward the fetus. Because of the time it takes for a wave to propagate along the length of the cord, counter-propagating waves add with different temporal shifts at each end of the cord, resulting in different observable waveforms

Fig. 2.

Illustration of waveform extraction and refinement from Doppler sonograms, a) shows the sonogram with the original waveform trace, original R-wave positions, the scaled trace, the refined R-wave positions, and the scaling function shown. Extracted traces, separated by cardiac cycle, are shown in b) and c) respectively before and after being scaled and aligned

Fig. 3. Illustrative wave decomposition examples with large (a) and small (b) reflections, (a, b) Portions of Doppler spectra sonograms measured at either end of the UA. (c-f) Forward and reflected waveforms that, when added, closely reproduce the measurements at the proximal (c, d) and distal UA sites (e, f). Note that residuals are scaled by a factor of 10 and offset vertically for visualization

Fig. 4.

Distribution of IRF fit parameters for the 183 measurement pairs that fit the wave reflection model. Points corresponding to the examples in Fig. 3 are shown as empty circles.

Fig. 5.

Histogram of noise power, as a fraction of waveform power, for 212 waveform pairs measured in a clinical setting.

Fig.6. Convergence properties of IRF parameters about their ground truth values, showing virtually no error or bias with zero added noise.

TABLE I

Convergence Properties of IRF Parameters

Γ_e (%)			Γ_d (%)		
Ground Truth	mean $\pm$ SE	SD	Ground Truth	mean $\pm$ SE	SD
-50	-49.9 $\pm$ 0.1	4.1	-50	-50.3 $\pm$ 0.2	6.8
-30	-29.9 $\pm$ 0.1	4.3	-30	-30.8 $\pm$ 0.1	6.3
-10	-9.9 $\pm$ 0.1	4.8	-10	-10.9 $\pm$ 0.2	5.9
10	10.0 $\pm$ 0.1	5.8	10	12.7 $\pm$ 0.2	8.8
30	29.3 $\pm$ 0.2	7.8	30	32.5 $\pm$ 0.2	10.4
50	49.3 $\pm$ 0.2	9.0	50	51.2 $\pm$ 0.3	11.4

SE=Standard Error, SD=Standard Deviation