An adaptive transfer function for deriving the aortic pressure waveform from a peripheral artery pressure waveform

Gokul Swamy,1 Da Xu,1 N. Bari Olivier,2 and Ramakrishna Mukkamala1

1Department of Electrical and Computer Engineering and 2Department of Small Animal Clinical Sciences, Michigan State University, East Lansing, Michigan

Submitted 17 February 2009; accepted in final form 14 September 2009

An adaptive transfer function for deriving the aortic pressure waveform from a peripheral artery pressure waveform. Am J Physiol Heart Circ Physiol 297: H1956–H1963, 2009. First published September 25, 2009; doi:10.1152/ajpheart.00155.2009.—We developed a new technique to mathematically transform a peripheral artery pressure (PAP) waveform distorted by wave reflections into the physiologically more relevant aortic pressure (AP) waveform. First, a transfer function relating PAP to AP is defined in terms of the unknown parameters of a parallel tube model of pressure and flow in the arterial tree. The parameters are then estimated from the measured PAP waveform along with a one-time measurement of the wave propagation delay time between the aorta and peripheral artery measurement site (which may be accomplished noninvasively) by exploiting preknowledge of aortic flow. Finally, the transfer function with its estimated parameters is applied to the measured waveform so as to derive the AP waveform. Thus, in contrast to the conventional generalized transfer function, the transfer function is able to adapt to the intersubject and temporal variability of the arterial tree. To demonstrate the feasibility of this adaptive transfer function technique, we performed experiments in 6 healthy dogs in which PAP and reference AP waveforms were simultaneously recorded during 12 different hemodynamic interventions. The AP waveforms derived by the technique showed agreement with the measured AP waveforms (overall total waveform, systolic pressure, and pulse pressure root mean square errors of 3.7, 4.3, and 3.4 mmHg, respectively) statistically superior to the unprocessed PAP waveforms (corresponding errors of 8.6, 17.1, and 20.3 mmHg) and the AP waveforms derived by two previously proposed transfer functions developed with a subset of the same canine data (corresponding errors of, on average, 5.0, 6.3, and 6.7 mmHg).

artrial tree; blood pressure; generalized transfer function; model; wave reflection

Since its introduction by O’Rourke and coworkers in 1993 (3), the generalized transfer function has received attention for providing a convenient and safe means for monitoring central aortic pressure (AP) by mathematical transformation of a peripheral artery pressure (PAP) waveform. The basic premise of the transformation is that a single, universal transfer function exists that can faithfully relate the PAP waveform to the AP waveform of all individuals for all time. However, the transfer function linking PAP to AP would ideally be able to adapt to the intersubject and temporal variability of the arterial tree due to, for example, age-related arterial compliance differences, disease-induced peripheral resistance variations, baro- and thermoregulatory modulation of peripheral resistance in response to physiological perturbations, and therapeutic administration of vasoactive agents. To this end, Sugimachi et al. (12) and Westerhof et al. (18) previously proposed a technique to partially adapt the transfer function by defining it through an arterial tube model with a personalized value for a model parameter reflecting the wave propagation delay time and population averages for the remaining parameters. We recently introduced (13, 14) perhaps the first entirely adaptive technique for mathematically deriving the AP waveform by exploiting the commonality in multiple PAP waveforms through the powerful multichannel blind system identification approach. However, the requirement of more than one PAP waveform is a practical disadvantage of this technique.

In this study, we conceived a fully adaptive technique for deriving the AP waveform from only one PAP waveform. The new technique similarly defines the transfer function relating PAP to AP through a parallel tube model of pressure and flow in the arterial tree but then estimates all of its parameters by capitalizing on preknowledge of aortic flow. The parameters are periodically reestimated for each subject so as to yield an adaptive transfer function (ATF). We performed canine experiments in order to test the ATF technique as well as compare it with previous transfer function techniques over a broad array of controlled and significant hemodynamic perturbations. A preliminary version of this study has been reported in abbreviated form (15).

METHODS

Adaptive transfer function technique. Figure 1 illustrates the major steps of the ATF technique. As shown in Fig. 1A, the arterial tree is modeled as a parallel arrangement of m uniform tubes in series with terminal loads. The ith tube represents the path between the aorta and the ith peripheral artery. Each tube is frictionless and therefore has constant characteristic impedance \[Z_i = \sqrt{(l_i/c_i)},\] where \(l_i\) and \(c_i\) are the tube’s total inerance and compliance and \(l_i/c_i\) is the tube’s characteristic impedance. The waves propagate with constant delay time from one end of the tube to the other \([T_{di} = \sqrt{(l_i/c_i)}]\). Thus, consistent with Poiseuille’s law, mean pressure is identical throughout the tubes. The \(i\)th terminal load signifies the arterial bed distal to the \(i\)th peripheral artery. Like the studies of Sugimachi et al. (12) and Westerhof et al. (18), each terminal load has a frequency-dependent impedance \([Z(\omega)]\), where \(\omega\) is frequency characterized by two parameters that are dependent on the peripheral resistance and compliance \((A_i, B_i, \text{where} \ (0 < A_i < B_i))\) as well as the characteristic impedance of the corresponding tube \((Z_i)\). Thus the wave reflection coefficient at each terminal load is also frequency dependent \([\Gamma_i(\omega) = (Z(\omega)/Z_i)(Z(\omega) + Z_i)]\).

Generally speaking, as shown for the \(m\)th tube and terminal load in Fig. 1A, forward pressure and flow waves [\(p_f(t)\) and \(q_f(t)\)] propagate from left to right along each tube without distortion and are proportional to each other through the tube characteristic impedance. These waves are reflected in the opposite direction at the terminal load with relative magnitude and phase based on the frequency according to the wave reflection coefficient. The resulting backward pressure and flow waves [\(p_b(t)\) and \(q_b(t)\)] likewise travel along the tube without distor-
tion and are proportional to each other. The actual arterial pressure waveform \([p_{at}(t)]\) [or flow waveform \([q_{at}(t)]\)] at any point along a tube may therefore be expressed as the sum (or difference) of the forward and backward pressure (or flow) waves appropriately shifted in time based on the wave propagation delay time between the point and the tube end \((T_{d(i)})\). In this way, the model is able to mimic the well-known progressive distortion that experimental arterial pressure and flow waveforms undergo with increasing distance from the aorta.

Furthermore, from these expressions, a transfer function relating the arterial pressure or flow waveform at any point along a tube to the arterial pressure or flow waveform at any other point along the tube may be established in terms of the model parameters.

More specifically, according to the arterial tree model, a PAP waveform \([p_{at}(t)]\) is related to the AP waveform \([p_{at}(t)]\) through the transfer function shown in Fig. 1B, top (“Pressure \(\rightarrow\) Pressure transfer function”), with unknown model parameters (see detailed derivation in Ref. 11). Thus this transfer function may be applied to a measured PAP waveform so as to derive the AP waveform, if its parameters, namely \(T_{d(i)}, A_i,\) and \(B_i\), could be determined.

To this end, \(T_{d(i)}\), the wave propagation delay time between the aorta and peripheral artery measurement site, is first measured noninvasively (see Discussion). Only one \(T_{d(i)}\) measurement is made for a subject during a period of up to weeks or perhaps even months, as this parameter may not greatly vary over such a time period. That is, although it is well appreciated that \(T_{d(i)}\) and arterial pressure have an inverse relationship, large arterial pressure changes yield only small changes in \(T_{d(i)}\) (see, e.g., Ref. 8). It should be further noted that changes in vasomotor tone should not markedly perturb \(T_{d(i)}\), because the total compliance between the ascending aorta and a peripheral artery is mainly due to the aorta and other large arteries in which smooth muscle is relatively sparse (5).

Thereafter, the three parameters are determined from each 15-s segment of the measured PAP waveform and initial \(T_{d(i)}\) value by exploiting the fact that aortic flow is negligible during each diastolic interval because of aortic valve closure (provided that aortic regurgitation is absent). Thus, as indicated in Fig. 1A, the arterial flow at each tube entrance in the arterial tree model (“arterial entry flow”) may likewise be small during these time intervals. In particular, according
to this model, the PAP waveform is related to the arterial entry flow waveform to the corresponding peripheral artery $[q_{pa}(t)]$ through the transfer function shown in Fig. 1B, bottom ("pressure → flow transfer function") with the same unknown model parameters as the pressure → pressure transfer function. The common parameters are then estimated by finding the pressure → flow transfer function, which when applied to the PAP waveform segment, minimizes the energy (sum of squares) of the arterial entry flow waveform (scaled by $Z_{ci}$) output over its diastolic intervals. In other words, as indicated in Fig. 1B, bottom, the parameters are selected so as to map the PAP waveform to an arterial entry flow of zero during diastole.

Figure 2 illustrates the detailed steps of the technique through a flowchart. First, since the mean or DC value of $p_{pa}(t)$ is already known [i.e., approximated as the corresponding value of $p_{pa}(t)$ due to Poiseuille’s law], the DC value of $p_{pa}(t)$ is removed in order to focus the mapping on the unknown zero-mean or AC components. AC $q_{pa}(t)$ is then calculated to within a $1/Z_{ci}$ scale factor by applying the pressure → flow transfer function to AC $p_{pa}(t)$ for a set of $A_i$ and $B_i$ values over a physiological range with the $T_{di}$ value as measured. Next, the end of each diastolic interval in each candidate AC proportional $q_{pa}(t)$ is determined by identifying the minimum preceding the peak amplitude of a cardiac cycle, and the start of each corresponding diastolic interval is approximated based on Malik’s formula (4) relating the cardiac cycle length to the systolic interval length. Then the values of $A_i$ and $B_i$ are selected that provide the minimum variance of AC proportional $q_{pa}(t)$ over its diastolic intervals among those values yielding physiologically reasonable pressure and flow waveforms [i.e., AC proportional $q_{pa}(t)$ exhibits an undershoot during diastole as

Fig. 2. Flowchart of the detailed steps of the ATF technique. MAP, mean arterial pressure; Δ, small fraction of $T_{di}$. 
typically seen in experimental waveforms (6), and \( p(t) \), computed as described below, does not reveal double peaks). In the event that none of the \( A_i \) and \( B_i \) values in the set results in physiologically reasonable waveforms, \( T_{ua} \) is successively incremented until mean pressure decreases relative to the \( T_{ua} \) measurement period or decremented when mean pressure increases relative to this period until the criterion is satisfied. Finally, the pressure \( \rightarrow \) pressure transfer function, with the selected values for \( A_i \), \( B_i \), and \( T_{ua} \), is applied to \( p(t) \) (including its DC value) so as to derive \( p(t) \). [Note that the DC value of proportional \( q(t) \) may be determined by shifting the diastolic intervals of the AC waveform to zero amplitude.]

**Data collection.** Data were collected from six healthy adult beagles (10–12 kg) under an experimental protocol approved by the Michigan State University All-University Committee on Animal Use and Care. For each dog, general anesthesia was induced by an intravenous injection of propofol (2.2–6.6 mg/kg) and maintained with an inhaled mixture of oxygen and isoflurane (1.5–2.5%). A micromanometer-tipped catheter (Millar Instruments, Houston, TX) was placed in a femoral artery for the PAP waveform for analysis. A similar catheter was inserted in the opposite femoral artery or a carotid artery and positioned in the ascending aorta for the reference AP waveform. A catheter was also placed in a cephalic vein for drug and isotonic fluid administration, and electrodes were positioned for standard ECG measurements. In the fifth dog, a bipolar electrode catheter (EP Technologies, Boston Scientific, Sunnyvale, CA) was inserted into a jugular vein and advanced to the right atrium for high-rate pacing with an external pulse generator (Medtronic, Minneapolis, MN). In the sixth dog, a quadrupolar ablation catheter (EP Technologies) was inserted into a femoral vein and positioned to ablate the atrioventricular (AV) node and to then apply bipolar electrical stimulation to the His bundle as previously described (10) for low-rate pacing with the external pulse generator. (Additional instrumentation was also installed in the fifth and sixth dogs to address different specific aims.) Placement of all central catheters was accomplished by guidance with a single-plane lateral projection fluoroscopic imaging unit (GE, Milwaukee, WI). The analog transducer outputs were interfaced to a personal computer via an analog-to-digital conversion system (DataQ Instruments, Akron, OH). The arterial pressure waveforms and ECG measurements were recorded at a sampling rate of 1,000 Hz during a baseline period and after infusions of phenylephrine and nitroglycerin in the first dog; dobutamine and esmolol in the second dog; norepinephrine and xylazine in the third dog; saline and progressive hemorrhage in the fourth dog; verapamil and high-rate pacing in the fifth dog; and vasopressin (before AV node ablation) and low-rate pacing in the sixth dog. Several infusion and pacing rates were employed, followed by recovery periods.

**Data analysis.** The ATF technique was applied to 260 min of recorded PAP waveforms resampled to 250 Hz, with \( T_{ua} \) measured for each dog as the time interval between the onsets of upstroke of the AP and PAP waveforms during the initial beats of the baseline period. The resulting derived AP waveforms were low-pass filtered with a cutoff frequency of 15 Hz as previously justified (2) and then quantitatively evaluated against the (unfiltered) reference AP waveforms in terms of the sample-to-sample (total waveform, TW), beat-to-beat systolic pressure (SP), and beat-to-beat pulse pressure (PP) root mean square errors (RMSEs) for each experimental condition and overall. The unprocessed PAP waveforms were likewise assessed with respect to the reference AP waveforms after time aligning the two waveforms to eliminate error due merely to the wave-propagation delay.

For further comparison, AP waveforms were also derived by an autoregressive exogenous input-based generalized transfer function (GTF\(_{ARX}\)) technique (2) (which was shown to be the most accurate among 3 generalized transfer function techniques) and the tube model-based partially adaptive transfer function (PATF\(_{tube}\)) technique (12, 18) (i.e., the transfer function shown in Fig. 1B, top, with \( T_{ua} \) measured for each dog as described above and the same values for the \( A_i \) and \( B_i \) parameters for all dogs). More specifically, the two previous transfer functions were established by averaging over a set of transfer functions computed from each 15-s segment of the PAP and AP waveforms of one of the dogs and then applied to the PAP waveforms of the remaining dogs (see DISCUSSION). The resulting derived AP waveforms were then similarly low-pass filtered and evaluated. This procedure was repeated for each dog in order to avoid any bias, and the results were averaged.

Finally, the TW, SP, and PP RMSEs in the AP waveforms derived by the ATF technique were statistically compared with the corresponding errors in the time-aligned PAP waveforms and the AP waveforms derived by the GTF\(_{ARX}\) and PATF\(_{tube}\) techniques over all the experimental conditions. In particular, paired \( t \)-tests were performed after log transformation to make the data more normally distributed. A \( P \) value of <0.05 was considered statistically significant.

**RESULTS**

Table 1 illustrates the AP and heart rate (HR) levels during each of the experimental conditions. Table 2 shows the TW, SP, and PP RMSEs in the PAP waveforms after time alignment and the AP waveforms derived by the new ATF technique as well as the previous GTF\(_{ARX}\) and PATF\(_{tube}\) techniques for each condition and overall along with \( P \) values indicating statistically significant differences. Figure 3 provides visual examples of the measured AP and PAP waveform segments and the corresponding derived AP waveform segments during five different conditions.

**AP and HR levels (means ± SD) varied widely over the various experimental conditions. Mean arterial pressure (MAP) ranged from 62 ± 3 to 134 ± 15 mmHg, SP from 78 ± 8 to 162 ± 22 mmHg, PP from 18 ± 1 to 55 ± 11 mmHg, and HR from 73 ± 20 to 197 ± 16 beats/min.**

On the whole, the PAP waveforms were markedly different from the reference AP waveforms, especially in terms of SP and PP. The overall TW, SP, and PP RMSEs in the time-aligned waveforms were 8.6, 17.1, and 20.3 mmHg, respectively. The level of discrepancy between the unprocessed PAP and reference AP waveforms likewise varied over the different experimental conditions. The TW, SP, and PP RMSEs were by far the smallest during the nitroglycerin condition (3.2, 2.0, and 2.2 mmHg) and largest during the norepinephrine condition (14.0, 30.9, and 35.2 mmHg).

All three techniques were able to derive the AP waveform with considerably greater accuracy than merely time aligning

<table>
<thead>
<tr>
<th>Table 1. <strong>AP and HR levels</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Condition</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Phenytoin</td>
</tr>
<tr>
<td>Nitroglycerin</td>
</tr>
<tr>
<td>Dobutamine</td>
</tr>
<tr>
<td>Esmolol</td>
</tr>
<tr>
<td>Norepinephrine</td>
</tr>
<tr>
<td>Xylazine</td>
</tr>
<tr>
<td>Saline</td>
</tr>
<tr>
<td>Hemorrhage</td>
</tr>
<tr>
<td>Verapamil</td>
</tr>
<tr>
<td>High-rate pacing</td>
</tr>
<tr>
<td>Vasopressin</td>
</tr>
<tr>
<td>Low-rate pacing</td>
</tr>
</tbody>
</table>

Quantities are expressed as means ± SD. AP, aortic pressure; MAP, mean arterial pressure; SP, systolic pressure; PP, pulse pressure; HR, heart rate; bpm, beats per minute.
the PAP waveform. The TW, SP, and PP RMSEs in the derived waveforms were markedly reduced relative to those in the unprocessed waveforms for almost all of the individual experimental conditions. The notable exception was the norepinephrine condition, in which processing of the PAP waveforms by each technique actually increased the RMSEs, because these waveforms were already in close agreement with the AP waveforms. In addition, the GTFARX technique provided no or only modest reductions in the RMSEs during the dobutamine condition. As a result, the TW, SP, and PP RMSE reductions achieved by the three techniques easily reached statistical significance over all conditions (P values not shown for the GTFARX and PATFtube techniques).

The ATF technique was the most accurate over all the experimental conditions. The overall TW, SP, and PP RMSEs in the AP waveforms derived by this technique were 3.7, 4.3, and 3.4 mmHg, respectively. The corresponding RMSEs of the GTFARX and PATFtube techniques were similar to each other and, on average, 5.0, 6.3, and 6.7 mmHg. The TW, SP, and PP RMSEs of the ATF technique were statistically smaller over all the conditions than their counterparts for both previous techniques, except for the SP error of the GTFARX technique.

The ATF technique attained its largest improvements in accuracy over the two previous techniques during the conditions of dobutamine (reduction in TW, SP, and PP RMSEs by 2.6, 5.4, and 8.0 mmHg, respectively, on average), norepinephrine (4.3, 3.3, and 3.9 mmHg), saline (0.7, 4.5, and 5.8 mmHg), and phenylephrine (4.0, 2.9, and 2.8 mmHg). However, this technique was less accurate than the GTFARX technique during the baseline condition (increase in TW, SP, and PP RMSEs by 1.0, 3.5, and 1.1 mmHg, respectively) and the xylazine condition to a small extent (−0.7, 1.3, and 0.8 mmHg).

### DISCUSSION

Pressure waveforms simultaneously measured from the central aorta and a peripheral artery show striking differences in both morphology and level (see, e.g., Fig. 3). Most importantly from a clinical point of view, peripherally measured SP and PP are generally larger than their centrally measured counterparts. This counterintuitive amplification of the pressure waveform with increasing distance from the central aorta arises from wave reflections in the arterial tree. It is therefore the pressure in the central aorta that truly indicates cardiac afterload and myocardial perfusion. Perhaps as a consequence, previous studies have shown that centrally measured arterial pressure can offer clinical information superior to more distally measured pressure (9, 17). Even so, the PAP waveform is much more commonly measured in practice because of the relative ease and safety of its measurement.

In this study, we developed a technique to mathematically transform a PAP waveform so as to obtain the AP waveform conveniently and safely. The technique was inspired by the following investigators: 1) Stergiopulos et al. (11), who proposed a physical basis for the transfer function relating PAP to AP through an arterial tube model; 2) Sugimachi et al. (12) and Westerhof et al. (18), who employed the tube model to establish a partially adaptive transfer function for deriving the AP waveform; and 3) Cohen, who thought to compute the total aortic flow waveform from a PAP waveform by finding a black box, rather than physical model-based, transfer function that maps the PAP waveform to zero during diastole (personal communication in 2000 and now described in Ref. 1 as a result of this study). Our technique similarly defines the transfer function relating PAP to AP through a tube model and then estimates the unknown model parameters from the PAP waveform as well as a one-time noninvasive measurement of the wave propagation delay time between the aorta and peripheral artery measurement site by likewise exploiting the fact that aortic flow is negligible during diastole (see Figs. 1 and 2). In this way, in contrast to the conventional generalized transfer function and perhaps all other previous techniques for mathematically deriving the AP waveform, the new technique is able to fully adapt to the intersubject and temporal variability of the arterial tree with only a single PAP waveform available for analysis.
To demonstrate feasibility of the new ATF technique, we measured a PAP waveform from a femoral artery and the reference AP waveform from the ascending aorta of 6 healthy beagles of similar size during 12 different hemodynamic interventions (see Table 1). Thus, unlike most previous related efforts, we were able to assess the efficacy of the technique over a diverse set of significant perturbations of known effect. On the other hand, our measurements did not allow us to investigate the technique in the context of a varying population of subjects.

Our results (see Table 2 and Fig. 3) showed that the overall TW, SP, and PP RMSEs in the AP waveforms derived by the ATF technique were, respectively, 3.7, 4.3, and 3.4 mmHg. These errors effectively amounted to 75% reduction in wave distortion in the PAP waveforms. The corresponding RMSEs of the GTF_{ARX} and PATF_{tube} techniques were, on average, 34%, 47%, and 96% higher than the new technique. Indeed, the RMSE reductions achieved by the new technique were, in general, statistically significant over all of the experimental conditions. It is important to recognize that, unlike the previous techniques, the ATF technique was not given crucial information, namely training data comprising a subset of the canine AP waveforms. Even with this handicap, the new technique was able to outperform the previous techniques.

The improved accuracy afforded by the ATF technique over the previous techniques was especially pronounced during the dobutamine, norepinephrine, saline, and phenylephrine conditions. During the first condition, the transfer function relating PAP to AP was altered to a relatively large degree. Evidently, intense vasodilation occurred during this positive inotropic condition, as centrally measured PP and HR markedly increased from the baseline condition without a change in MAP (see Table 1). During the latter three conditions, the ATF technique was comparatively more effective. On the other hand, this technique was ineffective during the nitroglycerin condition, although better than the previous techniques, and relatively less efficacious during the baseline condition. However, it should be noted that a statistical assessment of the relative accuracy of the techniques during the individual conditions was not feasible, because we employed two different
To obtain the above results, we developed the GTF\textsubscript{ARX} and PATF\textsubscript{tube} techniques using one-sixth of the canine data and tested them on the remaining data. Even under the ideal scenario for the previous techniques in which all of the data were utilized for both development and testing, these techniques were still not able to derive the AP waveform with greater accuracy than the ATF technique. However, as indicated in Table 3, the gap between the overall TW, SP, and PP RMSEs of the two previous techniques and the new technique were reduced from 34%, 47%, and 96% to 15%, 33%, and 74%, respectively, and over half of the statistically significant RMSE differences were lost. It should be noted that, in contrast to this ideal scenario, a generalized transfer function does not represent a perfect estimate of the population average transfer function in practice. The reason stems from the high level of invasiveness needed to obtain the requisite AP waveforms, which limits the number of subjects (usually to <100) and the class of subjects (usually to cardiac catheterization patients) available for transfer function derivation. Thus a real-world generalized transfer function suffers from nonnegligible standard error and population bias. We therefore believe that the results of comparing the ATF technique to the previous techniques as developed with one-sixth of the data better indicate, and perhaps even underestimate, what the relative accuracy of the techniques would be when applied to the diverse population of patients seen in clinical practice.

The parallel tube model on which the ATF technique is based (see Fig. 1A) neglects arterial tapering and stiffening, as the dominant wave reflection sites appear to be at the arterial terminations because of their high resistance (6, 19). The model also ignores the inerterance of the distal arterial bed, since it is well appreciated that inertial work is small compared with viscous work in the high-pressure systemic arterial tree. Nevertheless, such modeling inaccuracies as well as imperfect parameter estimation represent the sources of error of the technique. To determine the relative contributions of the modeling and parameter estimation errors to the derived AP waveform error, we first found the “actual” parameter values, using the measured PAP and AP waveforms. We specifically established the actual parameter values for each individual segment of analysis by finding the pressure → pressure transfer function (see Fig. 1B, top), which when applied to the PAP waveform segment, best fits the measured AP waveform segment in the least-squares sense. We then applied the transfer function with the actual parameter values to the PAP waveform segment so as to derive the AP waveform segment. The overall TW RMSE in the derived AP waveforms, which represents the lower bound for the ATF technique due only to its modeling error, was 2.8 mmHg. Thus most (76%) of the corresponding RMSE of the ATF technique was due to modeling inaccuracies. As a related comment, it should be noted that the GTF\textsubscript{ARX} and PATF\textsubscript{tube} techniques derived the AP waveform with similar average overall RMSEs (see, e.g., Table 2), perhaps as a result of the modeling error offsetting the partial individualization of the latter tube model-based technique.

While modeling inaccuracies represent a cost of the new technique, it should be noted that the benefit of basing the technique on a model extends beyond the realization of a fully adaptive transfer function. In particular, unlike conventional black box techniques such as the GTF\textsubscript{ARX} technique, the parameters of the model on which the ATF technique is based carry physiological meaning (e.g., peripheral resistance and compliance) and may be utilized to calculate additional physiological quantities (e.g., wave reflection coefficient) (12, 18). Thus, by periodically reestimating these parameters, our model-based technique may offer expanded physiological monitoring capabilities over the conventional techniques.

For this demonstration study, we obtained the single measurement of the wave propagation delay time between the aorta and the peripheral artery measurement site \((T_d)\) for each dog by using a few beats of the measured AP and PAP waveforms during the baseline period. In practice, \(T_d\) may be measured noninvasively by, for example, placing a handheld tonometer on the carotid artery and determining the time between the onsets of upstroke of the waveform that it measures and the recorded PAP waveform (12). For long-term monitoring applications, such an operator-required measurement would likely need to be made periodically (e.g., every few weeks). Alternatively, \(T_d\) may be continuously approximated through, for example, a simultaneously recorded ECG or phonocardiogram.

It is claimed that a generalized transfer function is justified when applied to a PAP waveform from the upper limb but not the lower limb (7). Despite this claim, we measured the PAP waveform from a femoral artery in this study because of experimental convenience, the observation that this waveform appears significantly different from the AP waveform (see Fig. 3), and the fact that this peripheral artery is commonly cannulated in clinical practice. Our study may therefore be among the first, if not the first, studies demonstrating the feasibility of mathematically transforming a PAP waveform from a lower limb to the AP waveform. Because of its ability to adapt to arterial tree changes, our technique should be applicable to pressure waveforms obtained from any peripheral artery including the readily accessible radial artery (but excluding distal arteries in the coronary circulation for which arterial entry flow is significant during diastole). However, while we believe that our technique will also reveal improved accuracy over generalized transfer function techniques when applied to a PAP waveform from the upper limb, we do acknowledge the possibility that the overall difference in accuracy may not be as significant.

In summary, we have developed perhaps the first fully adaptive technique for mathematically deriving the AP waveform from one PAP waveform and have demonstrated its feasibility in animals over a wide range of physiological conditions. In the future, it would be worthwhile to explore refinements to the parallel tube model on which the technique is based (e.g., the inclusion of additional parameters to more...
accurately represent the terminal loads) as well as continuous approximation of the wave propagation delay time from simultaneously recorded noninvasive measurements. In addition, further testing of the technique is needed to establish its relative efficacy during different experimental conditions and to assess its applicability to PAP waveforms measured noninvasively, from the upper limb, and from humans. Such testing should involve side-by-side comparisons with the previous transfer function techniques in terms of not only AP waveform derivation accuracy but also cardiovascular risk stratification capabilities (see, e.g., Refs. 9, 17) in order to convincingly demonstrate the added value of the new technique. If such follow-up studies prove successful, then the technique could be employed for more precise arterial pressure monitoring, titration of therapy, and cardiovascular risk stratification in intensive care and surgical units in which PAP catheters are routinely inserted and other clinical environments such as outpatient clinics and home in conjunction with noninvasive PAP devices. Finally, subsequent combination of the technique with an AP waveform analysis technique that we have also recently developed (16) may ultimately permit continuous monitoring of cardiac output and left ventricular ejection fraction in addition to AP from just a single PAP waveform.

ACKNOWLEDGMENTS

The authors thank Thoralf Hoelzer-Maddox for his technical contributions to the data collection.

GRANTS

This work was supported by the National Science Foundation CAREER Grant 0643477 and an award from the American Heart Association.

REFERENCES