

# EVALUATION OF PEDIATRIC PULMONARY ARTERY INPUT IMPEDANCE USING WINDKESSEL MODELS AND DOPPLER ULTRASOUND: IN VITRO AND CLINICAL STUDIES

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## INTRODUCTION

The management of children with primary and secondary pulmonary hypertension continues to be a challenge for clinical cardiologists. Several recent advances, especially in the development of chronic therapies for reducing pulmonary vascular resistance, have facilitated the treatment of such patients. A major component of therapeutic evaluation is the assessment of pulmonary vascular reactivity. However, the question of how best to evaluate pulmonary vascular reactivity is still unanswered. The standard technique of relying on quantification of the pulmonary vascular resistance (PVR), defined as the ratio of mean pressure drop across the pulmonary tract to mean pulmonary flow, can be problematic, because changes in hemodynamics may occur due to changes in proximal artery compliance in addition to vascular resistance. PVR only provides estimates of vascular resistance, therefore excluding any arterial compliance information.

In contrast to mean estimates of pulmonary hemodynamics generated through PVR, the arterial input impedance, calculated as the ratio of time-dependent pressure to time-dependent flow and represented as a frequency spectrum, provides information on both resistance and compliance. One method to extract this information from the impedance spectrum is to construct a lumped-parameter model that exhibits an impedance spectrum that matches the clinical case. Significant work has been done with lumped-parameter models that depict the various mechanical parameters of the cardiovascular system using electrical circuit analogs known as Windkessel (WK) models. By extending prior work, we believe that WK models should prove useful for investigation of pediatric pulmonary artery (PA) dynamics and reactivity evaluation.

This investigation evaluates the ability of three different WK models to estimate the input impedance spectrum and physical parameters of resistance, volumetric compliance and PVR in vitro using a mock pediatric PA vasculature. In addition, the use of pulsed wave (PW) Doppler ultrasound is validated as a non-invasive means to

acquire temporal flow for estimation of the input impedance. Finally, data obtained clinically is evaluated to establish the efficacy of this diagnosis technique in the patient-care setting.

## METHODS

An in vitro experimental system was constructed to mimic the essential hemodynamics of the pediatric pulmonary vasculature. Three compliant mock PAs were constructed using silicone elastomers. To simulate *in situ* healthy and hypertensive wall properties, the wall thickness was varied between the tube models. Actual tube compliance was measured using a specialized laser-micrometer-based compliance-testing system for comparison with the WK estimated compliance.

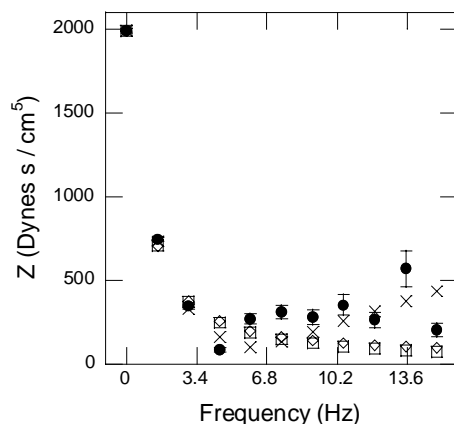
To acquire the in vitro input impedance spectrum, pressure, flow and velocity measurements were performed simultaneously at the entrance of the mock PA. The pressure was measured using a transducer-tipped catheter, instantaneous flow was monitored by a perivascular ultrasonic flow meter and velocity was acquired through PW Doppler ultrasound. All temporal signals were transformed to the frequency domain. The input impedance modulus was calculated as the ratio of the pressure modulus to flow modulus at harmonics of the pumping frequency.

Clinical procedures were performed in the catheterization lab at The Children's Hospital, Denver, CO. Patients undergoing septal and ductus closures and tests for vascular reactivity in the presence of pulmonary hypertension were considered for this study. A fluid filled catheter was used to obtain pressure measurements and blood velocity was obtained through PW Doppler ultrasound at the entrance to the PA.

The three WK models considered to model the input impedance spectrum were a resistor-capacitor (RC) model, an resistor-capacitor-resistor (RCR) model and an inductor-resistor-capacitor-resistor (LRCR) model. To obtain the WK model parameter estimates, a weighted nonlinear least squares regression was applied between the experimental impedance and the analytical expression for the WK model impedance.

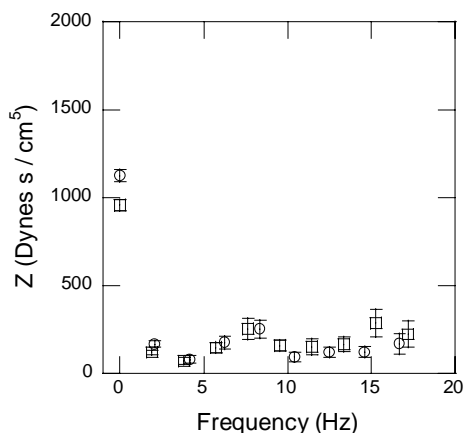
## RESULTS

**In Vitro Study:** The in vitro model reproduced the hemodynamic features of the proximal pediatric pulmonary arteries during moderate and severe hypertensive conditions. Excellent correlation was seen between the WK estimated PVR and the actual PVR by both flow measurement methods (Flow meter: WK PVR =  $1.07 \times \text{actual PVR} - 0.33$ ,  $r^2 = 0.98$ ; PW Doppler: WK PVR =  $1.03 \times \text{actual PVR} - 0.24$ ,  $r^2 = 0.98$ ). WK models were not able to predict the actual compliance measured by the laser micrometer system. However, differences among each of the three tube models were discernable through the RC and RCR model results. The results of the LRCR model demonstrated differences between the most compliant and two least compliant tubes only. No differences could be determined between the two least compliant tubes by the LRCR model results. Figure 1 shows the ability of each WK model to predict the experimental impedance spectrum throughout 10 harmonics. The error bars represent the uncertainty in the impedance modulus.



**Figure 1. Comparison in vitro input impedance modulus (●), Z, against the impedance spectra generated by the RC (□), RCR (◇) and LRCR (×) WK models.**

When the impedance spectrum calculated by the flow meter based data was compared to the PW Doppler based data, the impedance modulus agreed below 7 Hz. Above this frequency, deviation was seen between the two estimated impedance moduli.



**Figure 2. Impedance modulus, Z, of a patient breathing room air, (○), and oxygen, (□).**

**Clinical Study:** Data was obtained from patients undergoing closure of atrial septal defects and patent ductus arteriosus, in addition to patients undergoing reactivity evaluation associated with pulmonary hypertension. Figure 2 shows the pulmonary input impedance from a 6 year old child undergoing reactivity testing. It can be seen that the pulmonary resistance dropped significantly (the zero frequency of the impedance spectrum) but no significant change is reflected by oxygen treatment within the frequencies above 3 Hz.

## DISCUSSION

In this project, we constructed an in vitro model of the pediatric pulmonary vasculature to simulate the healthy and hypertensive hemodynamics. RC, RCR and LRCR Windkessel models were constructed to predict the experimental and clinical input impedance spectrum and estimate the physical parameters of resistance, compliance and PVR.

WK estimated PVR correlated to the actual PVR within the in vitro system. The use of the laser micrometer based compliance system provided an independent means to determine the actual volumetric compliance for comparison with the WK estimated capacitance. Though notable differences between the measured compliance and WK estimated C were demonstrated for all tubes, WK models may still be useful for assessment of pulmonary reactivity and general pulmonary artery health. A change in reactivity would modify mean pressure, which in turn would change volumetric compliance. Any change in compliance is reflected within the impedance spectrum by the rate of decay over the first few harmonics. Thus, hemodynamic changes from baseline (essentially the definition of reactivity) can be examined and quantified more accurately due to the inclusion of compliance variations that are identifiable by WK models.

This study also served to validate PW Doppler for use in estimation of pulmonary arterial impedance. Prior clinical investigations have utilized a perivascular flow probe to acquire the temporal flow rate; however, the invasive nature of these probes precludes them from routine clinical use, especially in the pediatric setting. Input impedance obtained from PW Doppler derived flow values agreed well with those obtained using the flow meter method at frequencies below 7 Hz. Above this frequency, differences between the two techniques varied between agreement and an overestimation by the PW Doppler.

Preliminary clinical data acquired on patients undergoing catheterization procedures show promise of this technique and illustrate the feasibility of PW Doppler to estimate arterial blood flow in quantification of the pulmonary input impedance modulus.

## CONCLUSIONS

Windkessel modeling was shown capable of providing estimates of PVR from experimental data; however the estimates of capacitance did not correlate to volumetric compliance. The RC and RCR Windkessel models did successfully discern trends in compliance between the three experimental tube models with both the perivascular flow meter and PW Doppler flow data. PW Doppler ultrasound was demonstrated in vitro as a viable means to noninvasively obtain temporal flow for use in estimation of arterial impedance. Finally, preliminary clinical studies show promise for Windkessel modeling as an additional diagnostic tool for clinicians in the study of the pediatric pulmonary artery health.

## ACKNOWLEDGEMENTS

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