MODEL BASED ASSESSMENT OF SYSTEMIC AND UTERINE CIRCULATION CONTRIBUTION TO AN ABNORMAL UTERINE ARTERY DOPPLER

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INTRODUCTION
In present day obstetrics, the Uterine Artery Doppler (UAD) is a noninvasive sonography method used to measure the uterine artery blood flow in pregnant women with the goal of characterizing the state of placentation and fetal blood supply. UAD generates waveforms to monitor the velocity of blood flowing through the uterine artery. An abnormal UAD waveform, representing the failure of proper gestational adaptations, is associated with high-risk for pregnancy complications or adverse fetal outcome such as preeclampsia or fetal growth restriction (FGR) [1].

In normal pregnancy, vascular adaptations occur in the maternal body to help accommodate the placenta and fetus. Blood volume, heart rate, and cardiac output increase, while the vascular resistance decreases. Within the uterine circulation, the endovascular extravillous and interstitial trophoblast cells migrate to help convert the highly coiled spiral arteries to handle the increased blood flow. The spiral arteries lose their smooth muscle in the vessel walls and their elastic lamina. The terminal ends of the spiral arteries undergo vast changes in the diameter than in their original coiled state [2].

Abnormal UADs are typically quantified in terms of characteristic changes in the morphology of uterine artery blood velocity waveform. For example, the resistance index is derived by dividing the systolic peak velocity by the sum of diastolic and systolic peak velocities. A value greater than 0.58 is considered abnormal. However, due to high false-positive rates in considering just the resistance index alone, the presence of a ‘notch’ in the beginning of diastolic portion of the waveform is also considered. The deeper the ‘notch,’ the higher the risk for adverse pregnancy outcome for the patient. Abnormal UADs are traditionally thought to occur from failure in spiral artery adoptions which raises the downstream impedance in the uteroplacental flow. However, theoretical considerations suggest that this may not be the full picture, especially since only 40% of abnormal UAD at early pregnancy went on to develop preeclampsia [1]. Because there are significant changes in the entire maternal systemic arterial circulation during pregnancy, an abnormal UAD may be a combination of deficiencies in both uteroplacental and maternal systemic arterial circulations. In-vivo experimental testing is not possible because we cannot produce isolated changes in maternal systemic arterial and uteroplacental circulations. Therefore, we are required to use a mathematical modeling-based approach.

HYPOTHESIS/SUCCESS CRITERIA
We hypothesize that aberrant uteroplacental circulation properties are not the sole determinants of an abnormal UAD waveform; the generalized maternal systemic arterial dysfunction may play a significant role. The first success criterion for this project is to develop a baseline model that produces physiologically realistic pressure and flow waveforms at different systemic arterial locations. For example, the average pressure that we expect to see in the ascending aorta and femoral artery is around 97 mmHg, while the average flow in the ascending aorta and femoral artery is 83 and 4 ml/s, respectively. We will strive to have our model-based outputs within 5% of the physiological values obtained from the literature.

METHODS
The baseline model was built using Matlab/Simulink and PLECS simulation software, and it is based on several validated models of the human circulatory system. First, it utilizes a left ventricle (LV) model developed by Dr. Sanjeev Shroff that consists of a time-varying elastance and pressure-dependent internal resistance [3-6]. This LV model is connected to the rest of the systemic arterial circulation (SAC), generating pressures and flows in the coupled LV-SAC system. The SAC portion of the coupled model was developed by Dr. Alberto Avolio, which utilizes the distributed, or ‘branched,’ concept that divides the arterial system into 128 smaller elements, each having its own characteristic impedance and propagation coefficient [3]. Each arterial segment is represented in terms of an equivalent electrical analog, wherein a capacitor represents vascular compliance, a resistor represents vascular hydraulic resistance, and an inductor represents the inertia of blood [3].

A previous student investigator, Jake Bosin, incorporated the LV and SAC models together to create the baseline model, and proposed the segmental layout for the additional elements to create the uterine circulation. The baseline model produced lower than expected values for pressures and flows. Therefore, we first focused on diagnosing the cause of this model deficiency by checking on LV and SAC model parameter values and the numerical calculations associated with the LV model. We used a simpler coupled LV-SAC model that produced realistic aortic pressure and flow to help refine our baseline model. SAC in the simpler coupled model was represented by a 3-element Windkessel model wherein the entire systemic arterial circulation was a single chamber (segment), as opposed to 128 segments in the current baseline model. In parallel to correcting the baseline model, the uterine circulation circuit structure proposed by Jake Bosin was incorporated in the baseline model. Specifically, connecting to the abdominal aorta and the internal iliac artery, the uterine circulation added an additional 44 segments to the original 128-segment SAC. The parameter
values for the electrical components associated with these new 44 segments are derived using formulas that are developed to convert vascular vessel properties into the electrical analogs. The arterial vessel properties are gathered through physiological data from literature, and model parameters will be refined until expected pressure and flow patterns are produced for the spiral arteries.

RESULTS

![Pressure and Flow Waveforms](image.png)

Figure 1: Pressure (top) and flow (bottom) waveforms for one cardiac cycle at two systemic arterial circulation sites (ascending aorta (blue) and femoral artery (orange)) produced by the model.

After adjusting the initial parameters of the LV and SAC models and debugging the numerical calculations to allow the model to run at a faster heart rate (67 beats per minute), the baseline coupled model produced more physiological values. Figure 1 shows the resulting waveforms after making the proper adjustments. The mean ascending aortic pressure was 98 mmHg, while the mean femoral artery pressure was 97 mmHg. For the arterial flows, the ascending aorta had an average flow of 80 ml/s, while the femoral flow as 3.7 ml/s. All of these pressure and flow values are within 5% of the physiological values mentioned above. For efforts for incorporating the uterine circulation, all 44 elements have been added to the baseline arterial system, however the parameter values for the branch components are still being researched.

DISCUSSION

The revised baseline coupled model meets the success criteria by producing outputs with errors less than 5% of the expected averages for mean pressures and flows. The biggest difference was observed for the ascending aortic flow, which had a 3.6% error. However, there is still much work that needs to be done before the coupled model is ready to test the stated hypothesis. First, the uteroplacental circulation must be fully incorporated. It was difficult to search for literature values of vessel properties, such as vessel diameter and wall thickness, for some of the lesser known arteries of the uterine circulation (e.g., basal and arcuate artery). Some modeling efforts for the uterine circulation of animals exist, but it is not possible to simply scale the measurements from an animal and use them for a human model. This added uteroplacental circulation model will have to be validated based on the match between model-based blood flows at various sites (e.g., uterine artery, spiral arteries) and known physiological data. Second, model parameters will have to be adjusted to simulate the normal pregnancy condition. This will be done by matching model-based pressures and flows to known normal pregnancy-associated physiological data.

If the hypothesis is rejected then the current interpretation of an abnormal UAD as an indicator of aberrant placentation will be validated. On the other hand, if we fail to reject the hypothesis then additional model-based investigation will be necessary to explore ways in which one can remove the confounding effects of the maternal systemic arterial circulation.

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REFERENCES