Simulation of Asthma Attack and Inhaler Actuation using the Pulse Physiology Engine

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Introduction: Models of drugs and medical devices that can be used to simulate function, patient response, and/or train for use are key to the future of medical device development. The Pulse Physiology Engine is a set of integrated open source computational physiology models comprised of lumped-parameter models that represent the different physiologic systems of the body and a limited number of medical devices, including a pressurized metered dose inhaler (pDMI). The whole-body computational models were designed to model the body's response to trauma and treatment to provide accurate and consistent results that are well-validated. The Pulse Physiology Engine models an asthma attack and treatment via a pDMI and can be used to simulate proper vs improper use of an inhaler.

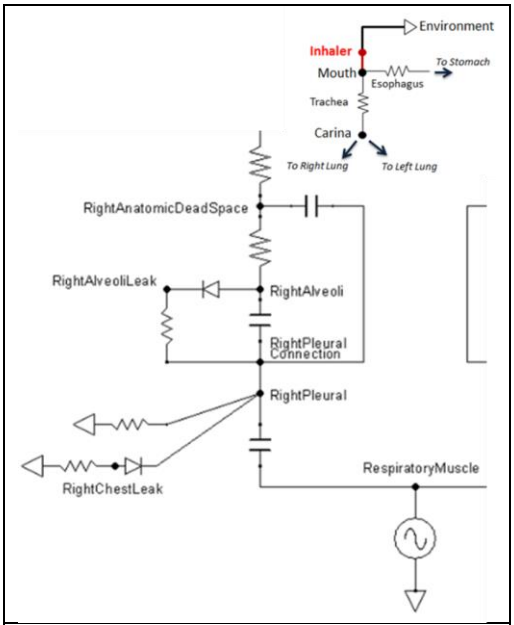

Figure 1. Lumped-parameter models of the Pulse Physiology Engine respiratory and inhaler circuits.

Materials and Methods: An acute asthma attack is simulated by increasing the airway resistance in the respiratory system (Figure 1). The inspiratory/expiratory (I/E) ratio is also modified to represent the extended exhalation time associated with asthma. The pDMI is modeled by adding an inhaler node to the respiratory circuit (Figure1). When the inhaler is actuated, the drug dose is added to the air mixture at the inhaler node. Conscious breathing behavior is coordinated with inhaler actuation to represent a deep breath and/or breath hold. A fraction of the drug is removed from the trachea to represent onopharynx deposition. The drug is modeled as an aerosol with particle deposition and retention dependent on particle size and the circuit dynamics. The deposition fractions are calculated based on particle diameter using the formulation in [1]. The plasma drug concentration, calculated via the Pulse PK/PD model [2], is used to reverse the effects of asthma.

Results and Discussion: As expected during an asthma attack, the Pulse simulation shows an I/E ratio and tidal volume decrease, a respiration rate and blood carbon dioxide level increase, and an oxygen saturation drop. The inhaler actuation simulation was performed for both correct and incorrect use of the inhaler. For the well-timed inhaler actuation, it was expected that 47-65% [3] of the albuterol dose would reach the alveoli and for the poorly-timed actuation, 0-12% [4] would reach the alveoli. The Pulse simulation produces a near zero albuterol deposition for the poorly timed case and a near 66% deposition for the well-timed actuation. The Pulse Physiology simulation shows good agreement with the experimental data.

Translational Impact: The ability to simulate a patient's physiology in conjunction with the function of medical devices is important for medical device development and testing. This work is one example of the potential for simulation in medical training. One limitation of the model is the assumption of a constant droplet diameter, but pDMIs typically generate a polydisperse aerosol. By pairing patient physiology models with drug and medical device models, treatment protocols and devices can be tested for reduced cost. Pulse has also been paired with high fidelity models for virtual surgery simulation and medical device hardware for closed loop algorithm analysis. Future work includes addressing the current limitations of the inhaler model, creating patient-specific configurations for the patient physiology, and developing a population of patients for testing these technologies.

Disclosure Statement: The authors have no known conflicts of interest.

Acknowledgements: Funding provided by US Army MRMC, Fort Detrick, MD (co. no. W81XWH-13-2-0068).

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