4D FLOW DURING PREGNANCY AND AFTER PRETERM BIRTH

Jacob A. Macdonald

Under the supervision of Associate Professor Oliver Wieben

At the University of Wisconsin-Madison

Abstract

4D flow MRI is a powerful imaging technique that allows for the quantification and visualization of blood flow in a three-dimensional vector space over time. With accelerated acquisitions, 4D flow MRI can be performed over large imaging volumes with sub-millimeter resolution in clinically feasible scan times. Such accurate characterization of blood flow patterns is not possible *in vivo* with other imaging modalities. As a result of the utility of these sequences, the last decade has seen the widespread adoption of 4D flow MRI in research settings and increased utility in clinical roles. Typical applications of 4D flow MRI include cardiac, cranial, renal, and hepatic disease. In these anatomical regions, physiologic motion is predictable and well-characterized and vessels-of-interest are typically large relative to the sequence spatial resolution, allowing for quantification of complex flow dynamics.

While 4D flow MRI has proven its value in these settings, there are a variety of previously unexplored applications in which it could represent marked improvement over current clinical techniques. The aim of this dissertation was the development of innovative 4D flow MRI methodology to pioneer comprehensive *in vivo* hemodynamic assessment in two challenging applications: (1) maternal and fetal 4D flow imaging during pregnancy and (2) exercise cardiovascular MR (CMR) with 4D flow imaging during strenuous exercise challenges in preterm adolescents and young adults.

Many pregnancy complications are associated with vascular maladaptation to pregnancy, and thus, the ability to quantify flow in the uteroplacental and fetal vasculature during pregnancy could be a powerful tool for identifying complications in at-risk populations before outward symptoms manifest. Doppler

ultrasound is used clinically for this role but has poor sensitivity early in gestation. The feasibility of 4D flow measurements is demonstrated in a rhesus macaque model, paving the way for future feasibility studies in human subjects.

With regards to the second application, the ability to quantify complex cardiac flow during exercise with MRI is of special interest when studying child and young adult populations with suspected cardiac abnormalities. Exercise challenges are routinely used with ultrasound to elucidate differences in physiological responses between normal subjects and those with pathologies which might be difficult to differentiate at resting conditions. However, exercise studies in the MR bore are challenging and rarely performed. The viability of 4D flow quantification during exercise in adolescents and young adults is demonstrated in this dissertation, including the methodology developments on the unique hardware and software required to overcome challenges associated with exercise CMR. The value of 4D flow exercise CMR is then shown in a small cohort of adolescent and adult subjects born prematurely, a population that may be at an increased risk for cardiovascular disease later in life.

Overall, the techniques implemented in this dissertation offer enhanced capabilities to quantify and characterize the impact of irregular pregnancies on flow over the current clinical standard of Doppler ultrasound, both *in utero* and later in life. These techniques may translate to improved diagnostic and prognostic potential throughout life in affected subjects.