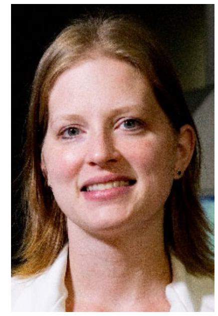
THE HARTWELL FOUNDATION

2021 Individual Biomedical Research Award

Katherine A. Kutney, MD

Assistant Professor
Departments of Pediatrics

Case Western Reserve University



Monitoring the Progression of Diabetic Kidney Disease with Multimodal Magnetic Resonance Imaging

Diabetic kidney disease (DKD) manifests as a result of organ damage caused by chronically high levels of blood sugar in type 2 diabetes, a metabolic disorder characterized by insulin resistance, insufficient insulin production and an inability to convert glucose into energy. Early-stage kidney disease usually has no symptoms, but the effect of elevated blood sugar can cause permanent damage to the eyes, blood vessels, heart, nerves, and kidneys. Sadly, between 10-30% of children will already have signs of kidney damage at type 2 diabetes diagnosis; and more than half will manifest chronic DKD within 15 years. Unfortunately, currently available screening tests do not accurately detect early kidney disease or predict which patients will progress rapidly to kidney failure. Type 2 diabetes was once known as adult-onset diabetes but now commonly impacts children and adolescents due to the epidemic of obesity plaguing western societies. The exact cause is not known, but contributing factors include obesity, sedentary lifestyle, and chronic stress. Up to 5,000 US children and adolescents are diagnosed with type 2 diabetes each year and the rate is increasing by approximately 5% per year, placing thousands of children at risk for DKD. Fortunately, new diabetes medications that inhibit reabsorption of glucose in the kidney to lower blood sugar may help slow the progression of DKD. However, despite their renal-protective effects, the inhibitors carry a risk of necrotizing genitourinary infections and life-threatening diabetic-induced metabolic complications (ketoacidosis), so it is critical they be used only in the subset of children who are at most risk for progressive DKD. To identify those children at risk, I propose to use magnetic resonance imaging (MRI) to noninvasively identify the structural, metabolic, hemodynamic and functional changes in the kidney that are associated with DKD. Evaluating three promising renal MRI measures (multi-modal), rather than selecting a single technique increases the likelihood of capturing the relevant physiologic features of DKD. This multimodal approach is enabled by state-of-the-art *magnetic resonance fingerprinting* that can simultaneously acquire quantitative measures of kidney blood flow (arterial spin labelling), blood oxygenation (blood oxygen level dependent), and structural damage (diffusion tensor imaging), in a reasonable timeframe without the use of intravenous contrast media. The MRI technique uses a machine learning approach to enable quantification of multiple inherently spatially registered maps of tissue properties. If I am successful, clinical translation of multimodal renal MRI will make it possible to accurately monitor and differentiate the clinical stages of DKD over time (typical healthy, type 2 diabetes without kidney disease, and type 2 diabetes with kidney disease). Risk stratification of children for renal-protective therapies or renal transplant will thus significantly improve the quality of life for children affected by type 2 diabetes.