Title: Exploring the Effects of Hemodialysis on Renal and Hepatic Blood Flow and Function using CT Perfusion Imaging

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Structured Abstract:

Hemodialysis (HD) is the most common form of kidney replacement therapy for end-stage renal disease patients. While HD is a life-saving therapy, patients develop a wide range of complications, including cardio- and cerebrovascular disease. Previous work used multimodal imaging to characterize the mechanisms behind these complications and evaluate potential therapeutic interventions. In most HD patients, intradialytic hypotension, exacerbated by aggressive ultrafiltration and increased circulating endotoxin, results in significant circulatory stress and development of pathologies.

My PhD focuses on using CT perfusion (CTP) imaging to address several questions related to end-stage renal disease and HD:
- Residual renal function (RRF) is linked to improved clinical outcomes, yet characteristically declines upon HD initiation. Are recurrent renal ischemic insults responsible for RRF loss?
- Although the liver normally clears endotoxin, increased circulating endotoxin levels have been found in HD patients. Does HD disrupt liver hemodynamics and perpetuate endotoxemia?
- Dialysate cooling (DC) is a low-cost, feasible intervention that ameliorates HD-induced circulatory stress. How does DC affect renal and hepatic hemodynamics during HD?
- If it was possible to accurately assess glomerular filtration rate (GFR) in HD patients, HD prescriptions could be adjusted in accordance with RRF and potentially result in better outcomes. Can CTP be used to accurately measure GFR in HD patients?

To address these questions, HD patients were randomized to receive standard (36.5°C dialysate temperature) or cooled (35.0°C) HD first in a 2-visit crossover study. CTP imaging was performed before, during and after HD without any interruption to treatment. Imaging was done without breath-hold for 2 min immediately following a bolus injection of contrast agent. Renal and hepatic perfusion maps were generated from registered CT images.

We determined that renal perfusion significantly decreases during HD, which represents the first step towards pathophysiologically characterizing HD-mediated RRF loss, and that DC mitigated these effects. In addition, we showed that concurrent hepatic perfusion redistribution and decreased liver function during HD are likely responsible for increased circulating toxin levels, and that DC ameliorates these effects. Lastly, our CTP-based GFR quantification methodology yielded physiologically realistic renal function values, demonstrating the feasibility of this approach in terms of reliability and accuracy.

These findings help explain RRF loss and endotoxemia in HD patients, important yet poorly understood phenomena, while providing preliminary data to support DC as a simple and effective therapeutic intervention for these complications. In addition, this work demonstrates the benefit of using CTP and other functional imaging techniques to further characterize and evaluate therapies for end-stage renal disease pathologies in patients.