

TREATING PRIMARY ALDOSTERONISM-INDUCED HYPERTENSION VIA MICROWAVE THERMAL THERAPY

PROJECT SUMMARY In this tripartite US-Ireland R&D partnership program R01 research plan, we propose the development, optimization, and evaluation of a minimally-invasive microwave thermal therapy (MWT) system for definitive treatment of primary aldosteronism. Primary aldosteronism (PA) accounts for 5 - 12% of all hypertension and confers a higher risk for cardiovascular and cerebrovascular complications compared to age and blood pressure (BP) matched essential hypertension. Yet PA remains under-diagnosed and under-treated, largely due to the lack of definitive management options for the majority of affected individuals. The current definitive approach to unilateral PA is surgical adrenalectomy, while bilateral disease is managed medically; medical therapy is often poorly tolerated due to off target anti-androgen effects. Only ~30% of all individuals diagnosed with PA undergo surgery, and collateral resection of normal cortex limits the option of surgery to unilateral disease, given the inevitable risk for adrenocortical insufficiency with bilateral adrenalectomy. Therefore, the overall objective of this proposal is the development, optimization, and experimental evaluation of an image-guided approach for sub-ablative MWT of APAs, and for post-treatment assessment of adrenal function. First, we will employ a series of in vitro studies to determine the optimal range of thermal doses for rendering hyperfunctioning adrenal cells defunct, at sub-ablative thermal doses. We will then verify the ability to disrupt adrenal cell function at these thermal doses in an in vivo mouse tumor model, with thermal dose tracked via MRI temperature imaging. Next, we will develop a system employing microwave applicators with precise spatio-temporal control of microwave radiation to deliver MWT to hyperfunctioning adrenal cells. We will develop real-time techniques for identifying the targeted tissue from real-time imaging, informed by pre-procedural PET/CT imaging localizing the hyperfunctioning adrenal cells, in order to guide applicator placement and energy delivery. Finally, we will develop a non-iodinated contrast agent suitable for verifying adrenal cell function, immediately post MWT, thereby providing a means for assessing treatment outcome. The overall system will be evaluated in a large animal model. If successful, and translated to humans in future studies, this approach will, for the first time, extend definitive management of PA to individuals with unilateral and bilateral APAs.

Public Health Relevance Statement:

PROJECT NARRATIVE Primary aldosteronism accounts for up to 12% of all hypertension. Successful completion of this project will lead to the development of a minimally-invasive approach for definitive treatment of hypertensive patients with benign aldosterone producing adenomas in one or both adrenal glands.