PET Imaging of Myocardial Viability Defect Using the Novel Voltage Sensor 18F-FBnTP

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Mitochondrial dysfunction, expressed by the decline of membrane potential (delta psi m), is a hallmark of heart failure. Yet, a clinically relevant and effective non-invasive method to quantify mitochondrial dysfunction is not available. In an effort to address this need, we characterized the efficacy of the novel PET imaging voltage sensor 18F-flurobenzyl tryphenyl phosphonium (FBnTP), developed in our laboratory, in animal models of cardiomyopathy. The coupling of FBnTP myocardial distribution with critical checkpoints of cardiomyopathy, including oxidative stress, apoptotic cell loss and ventricular wall contractility was investigated using dynamic PET imaging.

Myocardial Aging: FBnTP PET was acquired in 4 age groups (6 - 24 mo) of Fisher rats. Oxidative stress was measured using aconitase assay. FBnTP demonstrated an age-dependent progressive decrease of uptake in the free wall. Strong inverse spatial and quantitative correlation was found between FBnTP distribution and oxidative stress, but not with blood flow measured using 13N-ammonia PET.

Heart Failure: Dynamic and gated FBnTP PET scans were acquired in 9 mongrel dogs before and after 4 wks of rapid pacing (210-240 bpm). LV wall motion was measured on CT images. Extent of apoptosis was measured by immunostaining of caspase-3 cleavage. Pre-pacing images demonstrated highly uniform distribution of FBnTP in the LV wall. Rapid pacing resulted in a global and area-specific decreased of FBnTP uptake. Localization and extent of focal decrease varied between animals, and may depend on the site of the pacing lead electrode. A strong inverse quantitative and spatial coupling was found between regional FBnTP myocardial distribution and segmental impaired wall motion and regional apoptotic index, but not with microsphere blood flow.

Conclusions: 18F-FBnTP PET is an effective and accurate non-invasive technology to quantify and localize the extent and propagation of mitochondrial damage - a key mechanism of heart failure.