Title
Cardiac Desynchronization/Resynchronization – A New Heart Therapy

Abstract
In patients with long standing electromechanical conduction delay and depressed cardiac function, electrical stimulation from both sides of the heart – termed cardiac resynchronization therapy (CRT) – can improve function, energetic efficiency, clinical symptoms, and long-term clinical outcome. Our initial understanding of the mechanisms of CRT derived almost entirely from human data, which meant that the data were based on intact heart and cardiovascular physiological measurements. We learned that CRT improves systolic function and enhances cardiac work, but does so without an energetic cost, improving the mechano-efficiency of the heart. Over the past decade, our laboratory has systematically explored the basic cellular and molecular mechanisms that result from CRT. This work has revealed profound improvement in cell survival signaling, calcium homeostasis, beta-adrenergic receptor function and coupling, mitochondrial function, and myofilament sensitivity. We also revealed that the resynchronized heart is uniquely better than one that was never dyssynchronous in the first place. This intriguing observation has led us to explore the value of purposefully making failing hearts temporarily dyssynchronous, to leverage the benefits of resynchronization. In this talk, I will review our recent mechanism studies, and explore some new concepts that may provide a therapeutic option for heart failure patients who do not have underlying dyssynchrony.