A cardiac troponin I mutation that causes familial dilated cardiomyopathy

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Introduction: Spontaneous oscillatory contraction (SPOC) has been known for decades but only recently has it been used to measure contractile function. Using <5 mg of human heart muscle tissue SPOCs auto-oscillate between contraction and relaxation following ADP-induced activation. It displays characteristic saw-tooth type activation defined by rapid lengthening (relaxation) and slow shortening (contraction) phases. This characteristic is ideal for measuring three parameters of interest: (1) SPOC amplitude (equivalent to fractional shortening); (2) the times spent contracting (systole) and relaxing (diastole); and (3) the rates of contraction (systole) and relaxation (diastole). These measurements identify the quintessential characteristics of cardiomyocyte contractility and provide a guide to functional defects in human cardiomyopathies.

Caridiomyopathy is a common disease that weakens the heart muscle. Familial dilated cardiomyopathy (FDCM) is characterised by left ventricular (LV) dilatation and cardiomyocyte enlargement. As the LV dilates and its wall thins, contraction is impaired resulting in reduced LV ejection fraction (LVEF). This study compares SPOC parameters for four patients with FDCM with four aged-matched donors. Two patients have LVEFs between 15-30% and two with LVEFs <15%. One patient in the latter category has a known TNNI3 gene mutation.

Results: One-way ANOVA comparing LVEF to donors reveals significant differences in SPOC parameters. Compared to donors, patients with LVEF<30% exhibit higher SPOC amplitudes (equivalent to fractional shortening) and faster lengthening and shortening rates while those with LVEF<15% display longer periods of shortening and lengthening, and slower rates of shortening and lengthening.

Conclusion: SPOC parameters from FDCM patients differ significantly from donors, consistent with their clinical phenotypes. This suggests that SPOC is a sensitive measure of contractile function in heart failure.