Catecholaminergic polymorphic ventricular tachycardia (CPVT) is characterized by an arrhythmogenic mechanism involving disruption of calcium handling. This genetic disease can result in arrhythmia leading to sudden death in children and young adults during physical exercise or emotional stress. Prior CPVT studies have focused on calcium handling, but structure of the contractile apparatus and mechanical functionality have rarely been investigated. Using a patient iPSC line with RyR2-H2464D mutation and control line from the patient’s mother, we evaluated the structure-function relationship between sarcomere organization and contractile strain. We hypothesized that variation in sarcomere organization and contractile strain can be utilized as a quantitative indicator of cardiomyocyte functionality in CPVT. In this study we use a validated human stem cell derived cardiomyocyte culture technique developed in our lab. The experimental platform is created by microcontact printing extracellular matrix (ECM) proteins onto PDMS substrates of varying Young’s modulus spanning the range of healthy to diseased myocardium. The use of substrates with patterned ECM better recapitulate the sarcomere organization found in native tissue. This culture platform also bridges the gap between single-cell and tissue studies, by measuring contraction between multiple cells while including the structural detail of individual cells. Sarcomere alignment is quantified using Scanning Gradient Fourier Transform software and the strain field is evaluated across the sample measured using digital image correlation. This analysis expands our understanding of cardiomyocyte activity in CPVT patients, and the quantitative analysis techniques can be applied to exploring other diseases, as well as pharmacological intervention.

Figure 1. CPVT Stem Cell Derived Cardiomyocytes cultured on a pattern created with matrigel coated stamps on (A-B, E-F) 5kPa and (C-D, G-H) 10kPa PDMS. An iPSC line with RyR2-H2464D mutation (A-D) and control line (E-H) were compared. (A,C,E,G) Brightfield images taken 5 days post seeding. Scale bar: 100 µm. (B,D,F,H) Fluorescent microscopy image of portion of sample taken at 40x magnification. Samples were fixed 15 days post seeding. The nuclei are stained with DAPI (blue) and the proteins n-cadherin (white) and α-actinin (green). Scale bar: 50 µm