

## **SPontaneous Oscillatory Contraction (SPOC): Quantifying contractile performance in isolated human cardiomyocytes under partial activation**

*J.E. Robinson,<sup>1</sup> R. Whan,<sup>2</sup> F. Braet,<sup>2</sup> Y. Su,<sup>2</sup> S. Ishiwata,<sup>3</sup> M. Yamane,<sup>3</sup> T. Kagemoto,<sup>3</sup> N. Fukuda,<sup>4</sup> J. Hughes,<sup>1</sup> T. Kraft,<sup>5</sup> J. van der Velden,<sup>6</sup> S.B. Marston,<sup>7</sup> M. Steenman,<sup>8</sup> P.S. Macdonald<sup>9</sup> and C.G. dos Remedios,<sup>1</sup> <sup>1</sup>Muscle Research Unit, Bosch Institute, Department of Anatomy and Histology, University of Sydney, NSW 2006, Australia, <sup>2</sup>Australian Centre for Microscopy and Microanalysis, University of Sydney, NSW 2006, Australia, <sup>3</sup>Department of Physics, Faculty of Science and Engineering, Waseda University, Tokyo, Japan, <sup>4</sup>Department of Cell Physiology, School of Medicine, Jikei University, Tokyo, Japan, <sup>5</sup>Molecular and Cellular Physiology, Medical School Hanover, Hanover, Germany, <sup>6</sup>Laboratory for Physiology, Institute for Cardiovascular Research, VU University Medical Centre, Amsterdam, The Netherlands, <sup>7</sup>National Heart and Lung Institute, Imperial College London, London, United Kingdom, <sup>8</sup>Institut du Thorax, Université de Nantes, Nantes, France and <sup>9</sup>Heart and Lung Transplant Unit, St Vincent's Hospital, Darlinghurst, Australia.*

Under conditions of partial activation, striated muscle fibres exhibit repetitive, cyclic auto-oscillation between rapid-lengthening (relaxation) and slow-shortening (contraction) phases. This phenomenon is termed SPontaneous Oscillatory Contraction (SPOC), and represents a third state of muscle that exists intermediate to contraction and relaxation. The cardiac SPOC period and shortening velocity have been correlated with heart rate in various animals. Thus, SPOC is likely to reflect the physiology of the heart as it functioned in life. Small bundles of skinned, immobilised human cardiomyocytes suspended by adhesive tape were exposed to precise ionic conditions to induce SPOC, and recorded at high spatial and temporal resolution using live cell microscopy. Quantitative analysis allows us to draw conclusions about how the SPOC parameters, including total SPOC period and rates of shortening and lengthening, change with age in non-failing human heart samples, from 3 weeks to 65 years. Further, we look at SPOC as a technique for demonstrating and quantifying a functional defect in cardiomyectomy samples from patients diagnosed with hypertrophic cardiomyopathy (HCM), where a causal genetic mutation has been identified. SPOC might be applied in future as a tool to assist with the diagnosis and risk stratification of HCM patients.