Advancing our understanding of the pathophysiology of cardiac disease using in vivo assessment of heart structure and function in rodent models

Introduction

Advancing our understanding of the pathophysiology of cardiac disease using *in vivo* assessment of heart structure and function in rodent models

Integrative mammalian biology is the study of how genes influence body function. The value of integrating scientific research data collected at the molecular and cellular level with whole-animal physiology is increasingly recognized as a prerequisite in order to provide new therapeutic strategies to treat both human and animal diseases.

In the field of cardiovascular research, the animals that are predominately used are rodents. The use of laboratory mice and rats provides several advantages, including the following: (i) similarities in the cardiovascular physiology of rodents with humans; (ii) a relatively fast reproduction rate, enabling the use of genetic alteration; and (iii) ease of animal handling. Furthermore, the cost and logistics associated with housing these smaller animals in highly controlled environments is lower and often simpler when compared with the use of larger species. Whilst these important benefits exist, the small size and fast heart rate of rodents are two main disadvantages that become apparent when phenotyping these species in cardiovascular research. Fortunately, in the last 5–10 years there have been many technological advances that have been developed in order to overcome the complicating influences of these two drawbacks.

On 5 July 2012, at the annual meeting of The Physiological Society, a group of world-leading experts on *in vivo* assessment of cardiac function in rodents were brought together in Edinburgh for a symposium entitled *Advancing our understanding of the pathophysiology of cardiac disease using* in vivo *assessment of heart structure and function in rodent models* to share their first-hand experience of developing and using these new technologies. The reports that make up these symposium proceedings summarize the speakers' presentations that day.

Passing on first-hand knowledge is undoubtedly fundamental to the successful establishment of these techniques in other laboratories. Communication of the pitfalls and limitations of a technique can save months or years of valuable time. More importantly, such dissemination of knowledge through symposium publications can help to ensure the replacement, refinement and reduction of use of animals in research, as well as optimization of the husbandry, care and welfare of these laboratory animals.

Symposium presentations

Stephan Lehnart (Goettingen) used his own research on sarcoplasmic reticulum-mediated Ca^{2+} release in cardiomyocytes to demonstrate elegantly how the latest super-resolution imaging can provide insights from the intact animal to the subcellular level. In comparison, ultrasound and magnetic resonance imaging are already well established for preclinical imaging. In this symposium, we heard from Carmel Moran (Edinburgh) on how new developments in high-resolution ultrasound are now allowing more rapid and detailed assessment of cardiac structure and function *in utero*, as well as in adult mice. Craig Lygate shared with us the expertise gained by the Oxford team in using magnetic resonance imaging for assessment of myocardial metabolic pathways, leading to identification of potential new therapeutic targets during the development of heart failure. Functional assessment is key in physiological and pathophysiological studies of the heart, and James Clark (King's College London) focused on the pros and cons of intraventricular catheterization to achieve this in the mouse. The latter refers to the talks after the break included discussion of the challenges of imaging mice after myocardial infarction. This theme was continued

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by Adelaide Greco (Naples), who showed that positron emission tomography, now available for preclinical imaging, can provide an effective means of assessing infarct size, particularly when combined with computed tomography. Gillian Gray (Edinburgh) demonstrated that fluorescence molecular tomography now permits interrogation of inflammatory processes *in vivo* during infarct healing, adding to the structural and functional information gained from magnetic resonance imaging and high-resolution ultrasound.

Summary

It is clear from these symposium proceedings that a step increase in technology has been made over the last 5–10 years. This advance has substantially overcome many of the difficulties associated with assessing *in vivo* cardiovascular function in rodent disease models. The wide range of innovative techniques presented is enabling the cardiovascular research community to characterize cardiac structure and function with unprecedented accuracy. These techniques, when combined with the relevant models of cardiac disease, can ultimately put into context the impact of specific molecular changes on whole-heart function, and many of our existing questions on cardiovascular function can be investigated and answered. However, it is also clear that with an enhanced ability to dissect the intricacies of *in vivo* heart function many new questions will arise and additional experiments will be required. Ultimately, this technology-driven positive feedback loop can only advance our knowledge on the pathophysiology of cardiovascular disease.

Call for comments

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References

Clark JE & Marber MS (2013). Advancements in pressure–volume catheter technology – stress remodelling after infarction. *Exp Physiol* **98**, 614–621.

Gray GA, White CI, Thomson A, Kozak A, Moran C & Jansen MA (2013). Imaging the healing murine myocardial infarct *in vivo*: ultrasound, magnetic resonance imaging and fluorescence molecular tomography. *Exp Physiol* **98**, 606–613.

Greco A, Fiumara G, Gargiulo S, Gramanzini M, Brunetti A & Cuocolo A (2013). High-resolution positron emission tomography/computed tomography imaging of the mouse heart. *Exp Physiol* **98**, 645–651.

Lehnart SE (2013). Understanding the physiology of heart failure through cellular and *in vivo* models towards targeting of complex mechanisms. *Exp Physiol* **98**, 622–628.

Lygate CA, Schneider JE & Neubauer S (2013). Investigating cardiac energetics in heart failure. *Exp Physiol* **98**, 601–605.

Moran CM, Thomson AJW, Rog-Zielinska E & Gray GA (2013). High-resolution echocardiography in the assessment of cardiac physiology and disease in preclinical models. *Exp Physiol* **98**, 629–644.