Modify, simplify, apply: Do we need preclinical models for surgical innovation?

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Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication July 6, 2018; accepted for publication July 9, 2018; available ahead of print Aug 8, 2018.

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J Thorac Cardiovasc Surg 2018;156:1869-70

0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2018.07.024>

The contemporary practice of cardiothoracic surgery is safe, effective, and proven. We owe a great debt to the surgical innovators of the past.¹ Blalock and Vivien Thomas developed a model of pulmonary hypertension using an animal model. The knowledge gained was applied as a novel shunt for congenital cardiac malformations. This innovation is widely recognized as the catalyst for the dawn of modern heart surgery. Not long after, Wilfred Bigelow performed seminal laboratory experiments in animals to establish the use of hypothermia to facilitate open heart surgery. Denton Cooley, a legendary innovator, espoused his motto that defined translation in surgery—modify, simplify, apply. This pragmatic approach leveraged use of animal models when cardiac surgery was just a bold vision. Preclinical animal models used in laboratory-based translational research still remain a foundation and touchstone to enable surgical innovation.

The translational landscape for animal models has changed from large preclinical organ physiology experiments toward more complex cellular and molecular biology techniques with genetically altered small animal models. We now have a rich toolbox in the modern laboratory to help validate and translate our boldest surgical visions. The value proposition for surgeons to innovate outside the operating room within a laboratory environment using preclinical models remains high.² However, appropriate financial and time resources to allow surgeons to innovate in a translational laboratory are a persistent threat. In addition, the robustness of many current animal models and their relative effectiveness for translation to enhance clinical outcomes has been disappointing.^{3,4} There is a convincing body of evidence that supports a profound impact for animal models to shape preclinical research and inform human studies.⁵ Simultaneously there is growing concern over the value of our animal models and a strong collective voice for improved model development and validation.⁶ We need to modify, simplify, and apply the best models.

Wilfred Bigelow used preclinical animal models to establish the first successful “cold” open heart surgery in 1950 at the University of Toronto. (Photo courtesy of Pixie Bigelow Currie.)

Central Message

Rigorous preclinical studies using animal models of human disease will continue to play a pivotal role in shaping the evolution of cardiothoracic surgery. Model development and validation should be supported and encouraged to safely and effectively translate surgical innovations to clinical practice.

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In this issue of the *Journal*, Ruaengsri and colleagues⁷ offer a new large preclinical model to better elucidate the interplay between left atrial volume and electrophysiological aberrancies, specifically atrial fibrillation. The authors use strong scientific methodology to validate a novel and robust animal model that can be leveraged in future studies to inform our understanding of atrial volume and cardiac arrhythmias in the setting of mitral valve disease. The clinical relevance for cardiac surgeons is obvious. The model appears to mimic the clinical presentations of mitral regurgitation and atrial fibrillation in humans. Surgeons should be encouraged and supported to perform studies like that of Ruaengsri and colleagues,⁷ who set an example of research excellence.⁸ The importance of surgeons developing preclinical models to inform surgical practice is proven by our rich history and similarly, it is critical for our future. We should congratulate this research team for their efforts in developing a new model and providing a foundation for future work. We must also acknowledge the leadership of the *Journal* for providing a forum willing to highlight the arduous work of animal model development as a valued and useful academic enterprise worth reporting.

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