

# What lessons can we learn from the translational research model?



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## COMMENT & ANALYSIS

Although heart disease remains a major cause of morbidity and mortality worldwide, age-adjusted mortality in the Western world has reduced by nearly half since the 1960s. The gains in cardiovascular health have been achieved through the introduction of highly effective therapies including statins, beta adrenergic antagonists, calcium channel blockers, angiotensin-converting enzyme inhibitors, and interventional and surgical technologies including percutaneous balloon angioplasty, drug-eluting stents (DES), implantable cardioverter-defibrillators, heart valves, and percutaneous mitral valve repair. Notably, the translation of interventional cardiology has progressed rapidly from an experimental stage to patient care.

The impact of translational research (TR) that begins after discovery at the laboratory bench and transcends to patients outcomes (T1) and then to community development (T2) is demonstrated in saved lives, improved quality of life and socioeconomic benefits. So there is much to celebrate.

It is, however, equally important to recognise the challenges and the lessons that warrant consideration for future bench-to-bedside research as we move into the age of stem cell, gene and nano therapies. Numerous bench discoveries never reach the patient. The translation has been slow, complex, arduous, over-regulated and expensive. From Virchow's observation of a yellowish fatty material, later termed atheroma, in patients dying of myocardial occlusion, to the establishment of cholesterol as a culprit in heart disease, the unravelling cholesterol biosynthesis pathway (1960s) and finally the availability of lovastatin (1987), required a long and complex journey of T1 translation. Furthermore, for T2 translation, the

controversy of statin efficacy remained until the completion of the 4S trial in 1994 and the Heart Protection Study in 2002.

The rapid development of DES based on the initial experiment of Andreas Gruentzig in 1977 to metal stents (1986) and then DES (2001) is another example. Here, investigators worked

closely with multiple disciplines involving engineering, biomaterials, pharmacology, vascular biology and histopathology. The efficient iterations using the data from clinic to lab and back, rapidly produced DES that dramatically reduced restenosis.

Although, the recent National Institutes of Health (NIH) initiatives are



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creating greater appreciation of the critical need for efficient and effective TR organisations, significant impediments exist. These include, inadequate faculty for TR, recognition for TR contributions to tenure, transferable skills, training, research funding, intellectual property and barriers to collaborations with industry. Efficient and effective translational research will require appropriate infrastructure, multidisciplinary teams, incentivising through funding and faculty positions, greater collaboration with industry and reduction of intellectual property barriers. My recent experience with an open-source interdisciplinary model at St. Joseph's Translational Research Institute has been transformational in comparison to the closed pharma model. The institute has created a translational research focused platform for clinicians, scientists, biomedical engineers, biopolymer chemists, pharmacologists, veterinary staff, and the collaborators from industry and academe to work under one organisation. Co-ordinated implementation of multiple translational projects including cardiovascular devices, tissues, engineered grafts, biopolymer drug delivery, cells and protein therapy is efficiently achieved by multidisciplinary teams. The model is exemplified by the recruitment of Todd McAllister, a cardiovascular tissue engineering specialist who successfully translated early research in cell-based therapies to the clinic. Similarly, we have partnered with researchers such as Mark Poznansky at Harvard to help translate basic research in inflammation into clinically relevant therapies. This approach was very intriguing to many national and international visitors who toured the facility during ACC. In the words of Tom Eagen, a pulmonary cardiothoracic surgeon and navigator of TR at the University of North Carolina, "The model is very interesting and free of barriers commonly found in academic institutions." These issues were highlighted by industry and academic leaders at a recent meeting called by the Clinical Research Translation Award (CSTA) and the director of NIH. We believe the model is worthy of consideration by CSTA which is targeting funding for 60 centres around the country of \$500 million annually.

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## New connector system for cardiac devices

Boston Scientific Corporation has announced that its new cardiac rhythm management connector system is now available commercially in European. The system consists of the Endotak Reliance 4-Site defibrillation lead and compatible cognis cardiac resynchronisation therapy defibrillators (CRT-Ds) and Teligen implantable cardioverter defibrillators (ICDs). The system is designed to simplify the implant procedure by combining three terminals into one integrated connector, further reducing the volume of the world's smallest and thinnest high-energy CRT-Ds and ICDs. The Company announced CE Mark and first implant of

this system in May 2009.

"Boston Scientific commissioned a prospective, multi-center observational clinical study involving more than 400 patients to extensively evaluate the 4-Site system and to demonstrate appropriate clinical performance before making it broadly available in Europe," said Poul Erik Bloch Thomsen, Gentofte University Hospital, Copenhagen, Denmark. "The study examined both shocking and pacing performances and showed that the 4-Site system increased the simplicity and overall efficiency of the implant procedure, and further reduced the already low

likelihood of complications arising from connections being reversed."

"The launch of the Endotak Reliance 4-Site lead system is another significant milestone for our Company, which spans from the first human implant of the ICD 30 years ago to manufacturing the smallest, thinnest high energy devices today," said Fred Hrkac, President of Europe, Middle East and Africa (EMEA) for Boston Scientific. "This system represents the next advance for the Endotak Reliance lead family, which has demonstrated reliability in more than 400,000 implants worldwide."