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EDITORIAL COMMENT

State-of-the-Art Cardiovascular Technology

Taming "Old Physics" for Modern Medical Applications*

Jamshid H. Karimov, MD, PhD, MCH

As we progress further into the 21st century, it is becoming more and more apparent that the future of cardiovascular health—the compensation and repair of lost or altered cardiovascular function—lies in the demands for exceptional clinical expertise and use of unique technological solutions. Presently, technology must accompany each modern-era patient, from early diagnosis to functional or structural recovery and from recovery to long-term rehabilitation and better quality of life. Between each patient and caregiver of the modern era, at any stage or their relationship, there is a medical device.

With great technological leaps and improvements in health care have come an increase in longevity among the global population, especially when considering the acceleration of developments in the last few decades alone. However, even with these advances, among the known pathologies, cardiovascular disease has kept the most overwhelming burden on global morbidity and mortality due to both its high incidence and considerable detrimental effects. That burden has triggered a substantial spike in the exploration of the diagnostic devices, has produced the most appropriate treatment and device solutions, and has boosted translational science endeavors. Thus, these developments are enabling the portfolio of sophisticated clinical and engineering tools to assist that process as clinical representations of cardiac pathology are becoming even more complex and prolonged. In this issue of *JACC: Basic to Translational Science*, Magkoutas et al[1] investigates the effects of continuous monitoring of blood pressure and vascular hemodynamic properties with miniature extravascular Hall sensor-based magnetic sensors, and successfully validated their proof of concept in vitro and in vivo using large animal models to show feasibility and system performance and calibration.[2]

Reliable and timely arterial pressure measurement, hypertension diagnosis, and monitoring changes in hemodynamics are imperative for prevention of and early intervention in hypertension and overall cardiovascular disease prognosis.[3] The proposed Hall sensor-based device (HSBD) solution has become an extravascular sensing system that enables continuous measurement of arterial blood pressure, arterial wall diameter, and arterial circumferential strain.[4] Optimizations have been made that enable signal acquisition from 27- to 36-mm arterial vessels, with potential signal monitoring of smaller vessels. The device comprises a magnetic flux sensor (Hall-effect sensor) and a miniature magnet, both fully encapsulated in 3-dimensional-printed biocompatible housings. Because the elastic interconnection between the Hall-effect sensor and magnet assemblies has been removed, the sensing device not only avoids vascular restriction, but also undesirable sensor drift phenomena. The signal waveform data constitute the basis to further deduce pulse wave velocity, respiration frequency, and duration of the systolic phase of the cardiac cycle, which can offer new capabilities in cardiovascular disease diagnostics and long-term patient monitoring. During early rigorous in vitro testing of up to 7 days, sterilization process (which

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From the Department of Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, USA; and the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, USA.

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had no influence on the operation), dynamic cyclic loading of sensors, as well as robust system performance have been demonstrated. Further testing has continued in large adult porcine models (n = 12), mimicking physiologic and pathologic hemodynamic conditions, verifying intrathoracic implantation of sensors around the aorta, and simulating cardiopulmonary bypass.

Devices were placed around the aorta through a left thoracotomy in fully anesthetized animals. A perivascular transonic flowmeter was used at the base of the ascending aorta to provide reference measurements of cardiac output. Sensor placement consisted of surgical fixation (5-0 polypropylene suture), assuring the position of the HSBD was radial (perpendicular to the longitudinal axis of the aortic wall), allowing the distance between the 2 components to freely follow the pulsatile changes of the wall. The performance of the sensor was assessed under various cardiopulmonary bypass support levels, with and without pharmacological stimulation. The group reported high accuracy in monitoring the arterial blood pressure and the vascular properties in all experimental settings.[1]

Important limitations of this study include the need to establish comprehensive acceptance criteria to evaluate these sensor technologies at the investigational stage, which then may be improved upon with further major device iterations. Based on an operating line with zero misalignment, the resolution of the sensor apparatus was assessed for a linear distance of 1.5 to 2.0 mm between the 2 elements of the system. This distance between elements was defined as optimal, thus a resolution of at least 0.6 V/mm was the criterion to accept the sensor. In a real-world clinical setting, the device may require pretesting calibration and recalibration after fixation on the vascular wall before use, which is feasible.

The overall footprint of the sensor build is relatively small (total weight = 1.38 ± 0.02 g; height = 3.22 ± 0.01 mm; footprint on vascular surface = longitudinal length × circumferential length = 7 ± 0.02 mm × 8 ± 0.4 mm). However, the tissue encapsulation of the elements of the sensor apparatus and the extent of tissue reaction to foreign materials may impact overall tissue-device dimensions. Compared to other implantable devices, the sensor footprint is relatively modest and should not create any particular issues after fixation. Potential device dehiscence from the fixation bed or migration to other locations would be excluded by properly selecting device location, avoiding potential rubbing or interaction with adjacent mobile anatomical structures (ie, pulmonary artery or pericardium). Finally, concerns remain regarding the long-term biocompatibility of such devices, which will likely be further investigated in future studies.

A key element for this technology would remain both the stability of the alignment of HSBD elements during implantation, as well as the preservation of the fixation boundaries along the selected anatomical landmarks. In their experimental setup, Magkoutas et al[1] compared HSBD resolution to the resolution that was acquired during the calibration before the experiment. A deviation >10% of the preoperative and postoperative resolution resulted in disqualification of the sensor. Further research and development might surround additional device attachment to standardize the element measurement and fixation before clinical use.

At first glance, the elements of simplicity to this invasive approach are all desirable and deliverable features. However, there should be a balance between both the amount and the sophistication of the objective hemodynamic data that can be obtained with this approach that may subsequently affect system accuracy. The real surgical case scenario may differ because healthy tissue is present in an animal model's chest. Reoperations, tissue adhesions, malformations, and variable quality, stiffness, and compliance of the vascular wall could affect HSBD fixation. Any issues caused by misalignment would inevitably affect the accuracy of the sensor apparatus, and thus affect technology adoption.

Treatment of patients with cardiovascular disease is complex and highly demanding. Continuous monitoring of the patient's hemodynamics necessitates timely decision-making and effective intervention. Hemodynamic parameters, such as pressure, volume, and flow, are either measured intermittently or continuously based on invasive recordings, thus limiting patient mobility. New technologies, such as implantable or integrated sensor systems, pave the way to continuous patient monitoring even in remote settings. Based on sensor apparatus registration, the prolonged telemetric readouts for longer-term patient monitoring and control of medical devices seem feasible. The rigid geometries that were previously incompatible with tissues and organs are now flexible and stretchable to conform to organ curvatures, and local device architectures are able to accommodate variability in tissue compliance, anatomical representation and location.[5] Continuous monitoring of patient hemodynamics, or the flow and pressure of blood, gives incredibly valuable insights into the mechanical pumping function of the heart. Because electrical excitation and mechanical contraction are closely coupled in the heart, an understanding of a

patient's hemodynamics provides insight into the health of their entire cardiovascular system. These hemodynamic monitors are typically implanted into the body, which renders the procedure invasive, but no better alternatives exist in bridging the sampling environment, such as vascular lumen, with the sensing device.

Modern bioelectronic systems are available to monitor the human body to collect information about health status. These wearable or implantable devices collect data such as blood pressure, electrocardiograms, electroencephalograms, body temperature, heart rate, and much more. Future devices would be able to wirelessly connect to enable a more interconnected, aggregate understanding of the body's condition in real time. Information collected by this network of bioelectronic sensors would enable early detection, help make decisions in critical situations, and provide a pathway for more personalized medical diagnosis and treatment.[5]

In their effort, Magkoutas et al[1] successfully show how taming old physics fundamentals combined with rapid technology prototyping techniques using biocompatible materials and advanced engineering could generate powerful patient-centered solutions. The arduously crafted experimental protocol and early data look encouraging, and addressing existing safety concerns could bring this promising technology closer to the desired translational pipeline. Additional trials are necessary to establish the long-term clinical benefits of implantable continuous hemodynamic monitor-guided care in patients with cardiovascular disease in modern era.

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ADDRESS FOR CORRESPONDENCE: Dr Jamshid H. Karimov, Department of Biomedical Engineering/ND20, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Lerner Research Institute, Cleveland Clinic, 9500 Euclid Avenue, ND20, Cleveland, Ohio 44195, USA. E-mail: karimoj@ccf.org.

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