Multifunctional balloon catheters of the future

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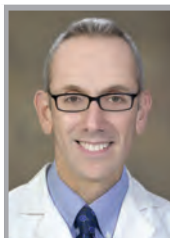

Marvin J Slepian

Sarver Heart Center, University of Arizona, Tucson, AZ 85724, USA

Roozbeh Ghaffari

MC10, Inc., 36 Cameron Ave., Cambridge, MA 02140, USA

John A Rogers

Author for correspondence:
Department of Materials Science and Engineering, Beckman Institute for Advanced Science and Technology, and Frederick Seitz Materials Research Laboratory, University of Illinous at Urbana-Champaign, Urbana, IL 61801, USA
Tel.: +1 217 244 4979
Fax: +1 217 333 2736
jrogers@uiuc.edu

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Cardiovascular medicine has benefited, both diagnostically and therapeutically, from dramatic advances that have occurred in catheter-based techniques. Today, as standard-of-care, we routinely measure pressure and flow in vessels, cardiac chambers and across valves, image the vasculature at high resolution, and therapeutically balloon-dilate and stent arteries and other cardiovascular structures. Despite these capabilities, new catheter-based techniques continue to emerge. Interventional cardiologists are universally excited by the anticipated regulatory approval of percutaneous valve systems and other structural heart technologies. Can we go further? The answer is yes, as a result of significant advances that have occurred in material science and micro/nanoelectronics. Recently, a class of novel materials has been developed: stretchable polymer-electronic composites [1,2]. Utilizing these materials, a new class of catheters has been constructed, containing dense arrays of sensors and therapeutic modules [3,4]. In this article we highlight the present and future status of integrating stretchable electronics with cardiovascular catheter systems.

Why have catheter-based techiques made such a dramatic difference in the practice of cardiology?

Catheters have allowed physicians to safely and sterilely enter and traverse the vascular tree to diagnose and treat anato-pathologic conditions and diseases previously treated medically, often with limited efficacy, or surgically via open invasive procedures. The dramatic shift in the treatment of coronary artery disease (CAD) illustrates this point. Progressive CAD was initially treated medically, with patients being increasingly incapacitated by angina or ischemia-mediated ventricular dysfunction as disease progressed. A major advance occurred with the advent of coronary artery bypass grafting (CABG) allowing redirection of blood flow to ischemic tissue. While highly effective, CABG suffered the limitation of open chest surgery, prolonged recovery, early post-operative physical limitation, infection, bypass pump neurologic risk and limited lifespan for patency of the saphenous veins employed as graft conduits. The world changed in the late 1970s as balloon dilatation catheter technology was developed and percutaneous transluminal coronary angioplasty (PTCA) emerged. Within several years of adoption and growth, PTCA overtook CABG as the standard of care for advanced CAD. This trend has grown at an accelerated pace with the advent of stenting, with percutaneous catheter-based revascularization today being a standard-of-care, performed at a ratio of >4:1, compared with open-CABG surgery.

What do present catheters really do? Catheters deconstructed

Fundamentally, catheters are elongated hollow tubular devices that afford percutaneous measurement or intervention, at a distance within the cardiovascular system. The long catheter shaft allows manual advancement and limited manipulation of the catheter tip from outside the patient to achieve deployment to a specific internal anatomic location. Recently, robotic and magnetic drive systems have been developed facilitating linear advancement, angulation and steering of catheters, although the use of these systems is largely investigational in interventional cardiology. The most basic catheter is a long hollow tube connected to a fluid column allowing pressure determination through the fluid, or angiographic imaging through antegrade injection of a contrast agent. Over the years, balloon technology has been married to catheters, either at the tip, to allow enhanced, blood flow-mediated propulsion (flotation), or over the distal segment to allow co-axial endoluminal dilatation. Balloons are used broadly to dilate stentotic arteries and stenotic valves, to create shunts and even to dilate the pericardium for window creation. Over the past decade, balloons have also been utilized increasingly to expand and deploy stents and stent grafts. While specialty catheters have been developed with enhanced modalities for imaging, for example, intravascular ultrasound (IVUS) or optical coherence tomography (OCT), or for therapeutic use with alternative lesion removal means, for example, atherectomy or laser angioplasty, the bulk of catheters in use today, the 'workhorse' design, are passive tubular devices containing several lumens for fluid infusion and removal. As such, catheters remain largely 'analog' systems, allowing passive measurement of pressure, providing a conveyance for diagnostic or therapeutic agents, and serving as a means of structural dilation or passive expansion of therapeutic devices.

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What else would be of value? What might we like to know?

Generically, the more information that can be provided as to the material, biochemical and cellular properties of the artery wall, the underlying atherosclerotic lesion or the post-interventional lesion, the better interventionalists would be equipped to make intelligent treatment decisions. For example, if it was clear *a priori* that a lesion had eccentric calcium or rigid fibrous materials that would be non-yielding or have a high likelihood of fracture and dissection, this would be of value in guiding treatment options. Similarly, if one could predict frictional resistance, stent non-passage and edge dissection, this would guide treatment decisions. If one could detect the propensity for restenosis and thrombosis this would be helpful. For instance, if we could identify exuberant proliferation or proinflammatory responders this might help tailor choices as new stents, new drugs on stents and even biodegradable stents emerge. What is needed to accomplish this? The answer lies in the integration of enhanced diagnostic sensors, detectors and analytics on the catheter and potentially on the stent as well.

"*Incorporating enhanced diagnostics, sensing and monitoring may finally get us into the domain of 'see, interrogate and understand (know), treat and be confident'.*"

Stretchable electronics

As with many innovations, breakthroughs occur when there is a marriage of otherwise disparate fields in new and useful ways. The fields of micro- and nanoelectronics and material science have greatly advanced over the past few years. All forms of electronic devices are increasingly becoming smaller, faster and more intelligent. Advances in chip design, processing power and sensor technologies have allowed the development of numerous forms of sensitive microelectronic and micromechanical systems. Micro- and nanosensors exist that can detect mechanical, chemical, optical, electrical, complex analyte, cellular and immunologic signals [3–9]. Similarly, in material science, new advances have occurred, including the development of novel polymer systems, with enhanced mechanical properties, tissue compliance matching [4,5,8,9] and biocompatibility [3,4]. It is the combination of these electronic as well as material advances that has led to the recent breakthrough development of a novel class of materials, stretchable elastomer– nanoelectronic composites, for instance, 'stretchable electronics' [1,2]. These materials allow incorporation of arrays of micro- or nanochip sensors, connected via serpentine elongatable, high fidelity conductive interconnects, in elastomeric stretchable materials. High fidelity digital information may thus be obtained despite stretch-induced deformation, from a material with compliance similar to biological tissue.

Next-generation balloon catheters & stents

Stretchable electronic materials can be incorporated into or be direct structural elements of balloon catheters. Utilizing these active materials will allow local deployment of enhanced diagnostic and therapeutic capabilities at a defined cardiovascular anatomic or pathologic site. These materials afford the potential to convert catheter systems from largely passive or manually activated systems to active, digital, smart systems. Recent proof-of principle of this concept was demonstrated in a series of studies performed by our group [3,4]. As a first step, mechanical strain and force sensors, electrical conductance sensors and temperature sensors were incorporated on an expandable balloon catheter for electrophysiologic mapping and ablation. While initially envisioned for an electrophysiologic application, this demonstration has crossover to interventional cardiology. This study demonstrated the ability to decorate the surface of a catheter expandable balloon with a myriad of microelectronic devices that could provide digital high fidelity, high sensitivity accurate information about the arterial local microenvironment. Similarly, these systems may be incorporated onto the backbone of stents. We have previously described intelligent stents incorporating microelectronic systems for the detection of local pressure, mass or analyte changes that occur within or around the stent that may benefit from stretchable electronics [101].

The more information we can bring to bear on the diagnosis, localized treatment and post-treatment monitoring of endovascular therapeutics, the better we will likely be as far as enhancing long-term interventional treatment efficacy. Presently, we live in an era of 'see, dilate and pray.' Incorporating enhanced diagnostics, sensing and monitoring may finally get us into the domain of 'see, interrogate and understand (know), treat and be confident.' Stretchable polymeric-nanoelectronic composites provide the basis to drive this vision. The limits of this vision at this point remain only those of the imagination.

Financial & competing interests disclosure

Marvin J Slepian, Roozbeh Ghaffari and John A Rogers are cofounders with a company (MC10, Inc.) that is developing catheter-based devices for cardiac therapy. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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