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Materials for Multifunctional Balloon Catheters With Capabilities in Cardiac Electrophysiological Mapping and Ablation Therapy

Dae-Hyeong Kim^{1,†}, Nanshu Lu^{1,†}, Roozbeh Ghaffari^{2,†}, Yun-Soung Kim¹, Stephen P. Lee², Lizhi Xu¹, Jian Wu³, Rak-Hwan Kim¹, Jizhou Song⁴, Zhuangjian Liu⁵, Jonathan Vimenti⁶, Bassel de Graff², Brian Elolampi², Moussa Mansour⁷, Marvin J. Slepian⁸, Sukwon Hwang¹, Joshua D. Moss⁹, Sang-Min Won¹, Younggang Huang³, Brian Litt^{6,10}, and John A. Rogers^{1,*}

¹ Department of Materials Science and Engineering, Beckman Institute for Advanced Science and Technology, and Frederick Seitz Materials Research Laboratory, University of Illinois at Urbana-Champaign, Urbana, IL 61801 USA

² MC10 Inc., 36 Cameron Avenue, Cambridge, MA 02140 USA

³ Department of Mechanical Engineering and Department of Civil and Environmental Engineering, Northwestern University, Evanston, IL 60208

⁴ Department of Mechanical and Aerospace Engineering, University of Miami, Coral Gables, FL 33146, USA

⁵ Institute of High Performance Computing, 1 Fusionopolis Way, #16-16 Connexis, Singapore 138632

⁶ Department of Bioengineering, University of Pennsylvania, Philadelphia, PA 19104 USA

⁷ Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114 USA

⁸ Sarver Heart Center, University of Arizona, Tucson, AZ 85724 USA

⁹ Department of Cardiology, Hospital of the University of Pennsylvania, 9 Founders Pavilion, 3400 Spruce Street, Philadelphia, PA 19104 USA

¹⁰ Department of Neurology, Hospital of the University of Pennsylvania, 3 West Gates, 3400 Spruce Street, Philadelphia, PA 19104 USA

Abstract

Development of advanced surgical tools for minimally invasive procedures represents an activity of central importance to improvements in human health. A key materials challenge is in the realization of bio-compatible interfaces between the classes of semiconductor and sensor technologies that might be most useful in this context and the soft, curvilinear surfaces of the body. This paper describes a solution based on biocompatible materials and devices that integrate directly with the thin elastic membranes of otherwise conventional balloon catheters, to provide

*To whom correspondence should be addressed. jrogers@uiuc.edu.

†D.-H. Kim, N. Lu and R. Ghaffari contributed equally.

Author contributions

D.-H.K., N.L., R.G. and J.A.R. designed the experiments. D.-H.K., N.L., R.G., Y.-S.K., S.P.L., L.X., J.W., R.-H.K., J.S., Z.L., B.D.G., B.E., M.J.S., S.H., J.V., J.D.M., S.-M.W., Y.H., B.L. and J.A.R. performed experiments and analysis. D.-H.K., N.L., R.G., M.M., M.J.S., J.S., Y.H. and J.A.R. wrote the paper.

Additional information

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multimodal functionality suitable for clinical use. We present sensors for measuring temperature, flow, tactile, optical and electrophysiological data, together with radio frequency (RF) electrodes for controlled, local ablation of tissue. These components connect together in arrayed layouts designed to decouple their operation from large strain deformations associated with deployment and repeated inflation/deflation. Use of such 'instrumented' balloon catheter devices in live animal models and *in vitro* tests illustrates their operation in cardiac ablation therapy. These concepts have the potential for application in surgical systems of the future, not only those based on catheters but also on other platforms, such as surgical gloves.

Inflatable balloon catheters constitute an extremely simple, yet powerful class of medical instrument that can deliver therapy or facilitate diagnosis of biological tissues and intraluminal surfaces through direct, soft mechanical contact. In peripheral or coronary angioplasty, inflation of such a device in a stenotic blood vessel can eliminate blockage and, at the same time, affect the expansion of a stent to maintain an open configuration^{1,2}. In a different procedure, known as septostomy, the balloon plays a related but more forceful role, as an instrument that creates large passages between the right and left atria, to enable shunting for increased blood flow^{3,4}. The balloon catheter device is attractive for these and other procedures because (1) it allows minimally invasive insertion into lumens or other organs of the body through small incisions, due to the miniaturized, cylindrical form of its deflated state, and (2) it can be configured, through controlled inflation, to match requirements on size and shape for its interaction with the tissue, where contact occurs in a soft, conformal manner, capable of accommodating complex, curvilinear and time dynamic surfaces in a completely non-destructive manner. The main disadvantage is that conventional balloons offer minimal utility, due to their construction from uniform sheets of electronically and optically inactive materials, such as polyurethane or silicone.

In this paper, we exploit the balloon catheter as a platform for heterogeneous collections of high performance semiconductor devices, sensors, actuators and other components. The result is a new type of minimally invasive surgical tool that can provide versatile modes of operation inclusive of but far beyond the simple mechanical manipulations involved in angioplasty, septostomy and other standard procedures. Here, we focus on implementation in cardiac ablation therapy, with several modes of sensory feedback control, designed for the treatment of various types of sustained arrhythmias of the heart, like atrial fibrillation⁵⁻⁷. Current procedures use closed or open irrigation layouts with single, point source ablation electrodes that offer limited sensing functionality or array capabilities. The time-intensive nature of surgical work performed with such devices increases the rate of morbidity, and also demands advanced technical skills from the operator⁷. Emerging cryo-, RF, and laser balloon catheters and multi-electrode structures simplify mechanical manoeuvring and ablation but they do not provide critical information about lesion depth, contact pressure, blood flow or localized temperature⁸⁻¹⁷. The systems reported here overcome these limitations and eliminate the need for additional catheters by providing the ability to sense electrical, tactile, optical, temperature and flow properties at the tissue-balloon interface, in real time as the procedure is performed.

Commercially available catheters (8~18 Fr, BARD, USA; Creganna, Ireland) serve as platforms for the devices. Components that integrate with the balloons are formed on semiconductor wafers using adapted versions of planar processing techniques and methods of transfer printing reported elsewhere¹⁸. Wrapping the resulting collections of interconnected devices on the balloon in its deflated state completes the process¹⁹. Encapsulating layers serve as moisture barriers to enable the entire system to operate when completely immersed in bio-fluids. These devices sense physiological signals and stimulate tissue. They are connected and powered through a thin ribbon cable based on an anisotropic

conductive film (ACF) that bonds to the base of the shaft that connects to the balloon, and wraps along the length of the flexible tubing of the catheter. Key steps in the fabrication and assembly appear in Methods section and in Supplementary Information. These procedures add functionality to balloons without significantly altering their mechanical properties or levels of expansion that they can accommodate. The mesh layouts can tolerate tensile strains of up to 200% without fracture, due to optimized configurations guided by quantitative mechanics modelling.

Figures 1a–c provide images of a balloon catheter device with a passive, uniform network mesh, to illustrate the overall construction and mechanics. The strain distributions obtained through analytical and computational modeling capture, quantitatively, the nature of these deformations (inset of Fig. 1c and Figs. S1–3). Active and/or passive devices integrate at the nodes of the mesh, minimizing their mechanical coupling to the strains associated with inflation/deflation of the balloon. Demands on layouts and interconnections for functional systems force local modifications of the simple serpentine geometry of Fig. 1a–c (Fig. S4–5), as illustrated in Fig. 1d. This micrograph corresponds to part of a multifunctional balloon catheter that supports a temperature sensor and an exposed sensing electrode pad. Active semiconductor devices can also be incorporated. Figure 1e shows a completed system, with microscale light emitting diodes²⁰, sensor electrodes, temperature detectors and other components. After multiple inflation and deflation cycles exceeding 100% strain levels^{18,20}, all devices and interconnects undergo little or no performance degradation. Figure 1f presents an x-ray micrograph of a related device, fully deployed in its inflated state within the right atrium. The surface electrodes on the balloon in this case are positioned to record electrical activity near the superior vena cava in a porcine animal model.

We begin by discussing materials and design considerations for various sensors and ablation devices capable of use in cardiac applications. The first is micro-tactile sensors for detecting dynamic mechanical forces exerted on heart tissue. These devices are important for monitoring mechanical interactions during surgery or diagnosis; they must satisfy, simultaneously, two demanding requirements: (1) minimal sensitivity to in-plane forces, to decouple their operation from inflation/deflation or other deformations of the balloon, and (2) high sensitivity to normal forces, in a soft mechanical construction, to allow non-destructive measurements against low modulus tissue. Existing sensor technologies are unsuitable for integration on highly stretchable substrates like balloons^{22–26}. More recent tactile sensors based on electrically conducting rubbers or elastomeric dielectrics also cannot be used because responses to in-plane strains conflate with those from normal strains^{25–26}.

To address the aforementioned requirements, we exploit two ideas in mechanics. First, as highlighted in Fig. 1, non-coplanar serpentine mesh layouts with planar nodes experience small strains ($< 1\%$), even for large deformations of the substrate²⁷. Strains at these locations can be reduced further by decreasing the size of the nodes, and by increasing their thickness and modulus²⁸. To exploit these features, we locate our tactile sensors at small nodes on thick (5 μm) layers of a high modulus (~ 4 GPa), photodefinable epoxy (SU8, Microchem Corp). For the second requirement, the stiffness of the sensor in the normal direction must be low and its sensitivity to compression must be high. To this end, we use a pressure sensitive, electrically-conductive silicone rubber (PSR; Elastosil®; LR 3162, Wacker Silicones Corp, USA) with low stiffness (1.8 MPa), configured in a bridge shape, overlying a rectangular feature of a low modulus formulation of poly(dimethylsiloxane) (PDMS; 650 kPa). This structure forces current to flow through the narrow, top layer of the PSR bridge. The soft, underlying PDMS imposes little constraint on compression-induced lateral expansion of the PSR, thereby facilitating associated resistance changes. A thin coating of polyimide (PI) cured at 300 °C for an hour encapsulates the entire structure to

avoid leakage current. This process does not cause device degradation, thereby suggesting that the system is compatible with temperatures used for sterilization.

Figure 2a presents a cross sectional schematic drawing of the sensor (left). The in-plane results of finite element modeling (FEM, right panel) illustrate the ability of the epoxy to reduce strains in the PSR induced by expansion of the supporting balloon substrate. The extent of reduction increases with thickness of the epoxy (Fig. S6a). Figure 2b presents calculated lateral strains in the PSR induced by applying a uniform pressure (1 MPa). With the soft PDMS layer, the bottom of the PSR bridge can expand laterally (orange dotted box). This lateral tensile strain (ϵ_{11}) increases the resistance of the PSR. Without PDMS, the stiff underlying layer of epoxy constrains motion of the PSR, thereby minimizing the lateral expansion strain ϵ_{11} near the interface (pink dotted box).

Figure 2c shows optical micrographs at two stages of the process for fabricating sensors with these designs. For details, see the Methods and SI sections. To test these structures, we used a custom-made micro-compression stage with precision load cell (Methods and Figs S7 and S8). The measured percentage change in resistance ($\Delta R\%$) as a function of normal load appears in Fig. 2d, for sensors with three different thicknesses of PDMS, with a fixed total thickness. The sensitivity increases with PDMS thickness (h), qualitatively consistent with trends in computed values of strain in the PSR bridge (Fig. S6b). We also evaluated changes in resistance associated with full inflation of the balloon substrate (similar to images of Fig. 1; upto 130%) as shown in Fig. 2e.

Temperature sensors, like tactile sensing, demand decoupling of the response from in-plane strains; similar design solutions apply. We used a thin, meandering trace of Pt as a resistance-based detector. In geometries shown in Fig. 1d (50nm Pt), the resistance changes by $1.91 \Omega / ^\circ\text{C}$ (Fig. S9 and S10a). Typical precision in resistance measurements are $\sim 0.003\%$, corresponding to temperature changes of $\sim 0.03^\circ\text{C}$. Strains can also alter the resistance, but the designs reported here reduce these effects to levels that correspond to shifts in temperature of only $\sim 1.5^\circ\text{C}$, even for changes in strain ($\sim 130\%$) associated with transformation from completely deflated to fully inflated states of the balloon (as in Fig. 1; see Fig. S10b). As with the tactile and other resistance based sensors described here, the resistance of interconnects represents a negligible contribution to the measurement.

Temperature is a critical parameter because it provides a way to monitor ablation of aberrant tissue in cardiac arrhythmias treatment. Here, exposed electrode pads (Fig. 2f inset, Fig. S11) provide electrical contact directly to the tissue for the purpose of local RF ablation. Variations in temperature both laterally along the surface of the tissue as well as into its depth determine critical aspects of lesions formed by this ablation process. When combined with quantitative modelling of the ablation process and thermal diffusion, these measurements provide both information. To this end, we developed non-linear models for characterizing electrical and thermal transport, and validated them through comparisons to measurements of in-plane temperature distributions created using a single RF ablation electrode (inset in Fig. 2f) against a piece of tissue from a chicken breast ($\sim 15\text{cm} \times 15\text{cm}$). For calibration, we used a commercial IR imaging system (InfraScope Thermal Imager, QFI Corp., USA) to acquire high resolution temperature maps. A representative measurement appears in Fig. 2f, with an ablation electrode ($290 \times 560 \mu\text{m}$), and an applied voltage oscillating between $+9$ and -9 V in a 450 kHz sinusoidal waveform.

Heat released during ablation results from current that flows between the small active electrode and the ground electrode. The distributed Joule heat source q due to this current is given by $q = \sigma(T) \nabla V \cdot \nabla V$, where $\sigma(T)$ is the temperature-dependent electrical conductivity, and the electric potential V , corresponding to the root mean square value of the voltage, is

determined from $\nabla \cdot \sigma(T) = \nabla V = 0$ ²⁹. The quasi-stationary electrical equation is adequate for RF ablation, because the tissue can be considered purely resistive at these frequencies (300 kHz–1 MHz)³⁰. The temperature distribution in the tissue is obtained from the

equation²⁹ $\rho c \frac{\partial T}{\partial t} = \nabla \cdot k \nabla T + \sigma(T) \nabla V \cdot \nabla V - Q_p + Q_m$, where ρ , c and k are the mass density, specific heat and thermal conductivity, respectively. The perfusion heat loss Q_p and metabolic heat generation Q_m are negligible for cardiac ablation²⁹. FEM (ABAQUS) was used to evaluate these coupled, non-linear partial differential equations. For chicken breast, the thermal conductivity $k=0.4683 \text{ W/m}^\circ\text{C}$ ³¹, and electrical conductivity $\sigma=0.80, 1.08, 1.33$, and 1.58 S/m at $20, 40, 60$, and 80°C , respectively³². At steady state, a voltage $V_0=6.1 \text{ V}$ gives a maximum temperature of 70°C and an in-plane distribution (Fig. 2g) that are consistent with experiment (Fig. 2f). Figure 2h shows the temperature distributions along the radial and thickness directions, which can be used to estimate the lesion size and depth. For a representative temperature 45°C ³³, the lesion size (diameter) is 1.6 mm , and lesion depth is 0.8 mm (Fig. 2i). The approximately axisymmetric nature of the system, together with treatment of the tissue as an object of semi-infinite object size, allows an analytical modeling, if we neglect the temperature dependence of the electrical conductivity (See Figs S12–14 and Supplementary Information).

Devices similar to those for temperature sensing can quantify near-surface rates of blood flow. In operation, current that passes through a thin metal film creates a small amount of heat, quantified by measuring the resistance. Any change in the rate of fluid flow over the device (or through tissue contacting the device) changes the steady state temperature and, thus, the resistance. Figure 2j shows a device, with a geometry similar to but larger than that of the temperature sensor of Fig. 2d. The data of Fig. 2k illustrate the response as a function of flow rate when operating in a constant current mode, for three different currents (50, 75 and 100 mA) corresponding to temperatures of 24.9°C , 30.2°C and 35.9°C , respectively (Fig. S10e). The resistance decreases monotonically with increasing flow rate, with a sensitivity that improves with increasing current. For surgical applications, the temperature must not exceed $\sim 40^\circ\text{C}$ ³⁴ to prevent overheating and uncontrolled tissue damage. This consideration suggests that the 50 mA operating condition is most suitable. Devices with layouts identical to those for the temperature sensors (Fig. 1d) show similar responses, as indicated in Fig. S10 c,d.

As previously mentioned, the RF ablation electrodes consist of uniform metal pads at nodes of the mesh (Fig. 2f inset), using the same design configuration as the aforementioned electrophysiological sensors. Successful integration of light emitting diodes onto the same platform (Fig. 1e) demonstrates that active semiconductor devices can also be incorporated. The overall concepts, then, provide a path for integrating nearly any class of sensor or semiconductor device onto the balloon, to match requirements for a variety of envisioned uses in surgery and diagnostics. In the following, we examine cardiac ablation therapy. Although balloon catheters are optimally suited for endocardial modes (Fig. 1f), evaluating the sensor and ablation functionalities is most easily accomplished via epicardial experiments. The results highlight the ability of the electronics to survive clinically-relevant, moist, dynamically changing biological substrates. *In vivo* experiments were performed on rat and rabbit models in which the heart was surgically exposed following a longitudinal sternotomy and pericardiotomy (see Methods). In each experiment, epicardial electrograms³⁵ were recorded from balloon mounted devices with between 2 to 13 bipolar electrodes. The electrodes were typically positioned on the anterior surface of the heart with millimetre placement accuracy using a micromanipulator stage.

Figure 3a,b show representative recordings ($\sim 1 \text{ mm}$ spacing between electrodes) on the anterior right ventricle (RV) and the left atrium (LA) surfaces. Each electrocardiogram was

obtained by differentiating potential readings from one pair of electrodes. The noise levels were $\sim 10 \mu\text{V}$, corresponding to signal to noise ratios of 60 dB. The electrodes have impedances of $26 \text{ kilohm} \pm 8\%$ at 1 kHz, measured while immersed in normal saline (0.9%) solution. The RV response (Fig. 3a) reveals an S-T segment in an elevated “spike and dome” shape similar to that of monophasic action potentials. In contrast, the recordings from the LA (Fig. 3b) exhibited different electrogram shapes, demonstrating the ability of a high density electrode array on a balloon to capture significant features of epicardial activation from different regions of the heart.

The representative S-T elevation recorded from the RV was found at multiple sites along the anterior RV and across the anterior basal regions of the LV. This feature is likely induced by pressure exerted on the surface of the heart³⁵. The instrumented balloon catheter system thus provides a route for minimizing inflation induced injuries by evaluating S-T elevation recordings from balloon electrodes. This concept can be applied to endocardial measurements in the pulmonary veins where contact pressures exerted during inflation are not well understood. Therefore, we can determine the necessary amount of inflation required to make contact with heart tissue without causing significant damage during inflation using electrical recordings on the balloon surface.

An alternative way to monitor balloon inflation levels and electrical contact is to use tactile sensors on the balloon. These sensors provide accurate feedback about the contact between the heart and the devices (Fig. 3c and d). Fig. 3c shows that the tactile sensors can be used to track clean contact from detachment on a cycle-by-cycle basis without significant hysteresis. In Fig. 3d, the value of $\Delta R\%$ recorded from the tactile sensor (blue) clearly correlates with the electrogram signal (red). When the balloon was in good contact, high quality electrical activation signals were measured, while noisy signals were obtained when the balloon was detached from the heart surface. Because these sensors have sufficient sensitivity for tracking normal sinus rhythm at $\sim 240 \text{ bpm}$, we expect that they can be used to detect onset of tachycardias in humans to evaluate the mechanical heart rhythm. We note that temperature changes associated with motion in and out of contact with the tissue can contribute to the pressure response. Co-located temperature sensors indicated that these differences were $< 1^\circ\text{C}$ for beat rates of $0.5 \sim 2 \text{ Hz}$; from Fig. S9, these changes correspond to resistance variations of $< 0.5\%$ in the tactile sensors.

We also tested the ability of our RF ablation electrodes to create lesions on the heart (Fig. 3e). Ablation using multiple electrodes simultaneously to form larger lesions is also possible (Fig. S11a). These devices were coupled with temperature sensors to monitor the extent of lesion formation (Fig. 3e). The temperature recording shows the same pattern with input RF power change (Fig. 3f). These two devices enable controllable lesion formation. Additional irrigation mechanisms are also possible via microfluidic channel outlets that deliver saline near the ablation electrodes to help avoid charring on the electrodes. In this context and others, flow sensors can be useful. The transmural extent of typical lesions was evaluated using post-operative analysis, which revealed lesion depths spanning $1 \sim 5 \text{ mm}$. We did not observe device degradation due to the presence of biological fluids or mechanical stresses during these ablation or sensing measurements. The PDMS and PI encapsulation layers helped to ensure a robust biocompatible interface, consistent with their use in other contexts described in previous reports^{36,37}.

The same concepts that enable instrumentation on balloons can be used with other important platforms of interest such as surgical gloves (Fig. 4a and Fig. S15) for open heart procedures in which concomitant mapping and ablation steps are required. A clinical demonstration is highlighted in Fig. 4b,c in which an induced ischemic injury³⁸ caused by occlusion of the lateral anterior descending (LAD) coronary artery is monitored in real time. The electrogram

waveforms reflect the progression of ischemic injury from the onset (t_0 , t_1) to highly elevated S-T segments³⁵, followed by a shift to an agonal response marked by very slow heart rate (t_2 ; Fig. 4d–f). These measurements were robust and stable to capture epicardial activity at multiple sites prior to, during and post onset of coronary occlusion. Figures 4g,h show epicardial electrical recordings taken concurrently at multiple anterior sites in the rat model. The electrogram signals recorded from the RA and RV indicate that the cardiac rhythm is ectopic and asynchronous. Fig. S15c shows the pressure measurement from a representative tactile sensor on glove (Fig. S15b). Manoeuvring these sensors on the fingertips with natural tactile feedback (from the sense of touch) is also useful for exploring areas of the posterior myocardium, which are out of plain view and consequently difficult to probe during cardiac surgical procedures.

The materials and mechanics concepts introduced here represent a technology foundation for advanced, minimally invasive surgical and diagnostic tools, with demonstrated examples in diagnosing and resolving complex arrhythmogenic disease states of the heart. These devices constitute significant advances over existing balloon and multielectrode catheters in the number of sensing modalities and the spatial density of sensors. Related ideas should also be valuable in other contexts, including atherosclerosis, esophageal and gastrointestinal diseases, endometrial and bladder dysfunction, all of which can be addressed using multifunctional, instrumented balloon catheter systems.

METHODS

Fabrication of stretchable electrode array

The fabrication begins with spin coating of a thin film of polyimide (PI, $\sim 1.2 \mu\text{m}$, Sigma Aldrich, USA) on a sacrificial layer of poly(methylmethacrylate) (PMMA, 100 nm, MicroChem, USA). Metal evaporation (Cr/Au, 5 nm/150 nm), photolithography and wet etching steps define metal electrodes with serpentine-shaped interconnects and rectangular electrodes. Additional PI spin coating, oxygen reactive ion etching (RIE) and metal deposition for contacts completes the array, as shown in Fig. S1a.

Fabrication and compression test of tactile sensors

After patterning serpentine interconnects and electrodes (Cr/Au, 5/150nm) on a uniform thin sheet of PI (1.2 μm thick), casting procedures form a rectangular feature of PDMS (160 $\mu\text{m} \times 220 \mu\text{m}$) between two adjacent Au electrode pads (150 nm thick; left frame, Fig. 2c). Similar steps define a bridge shaped structure of PSR (160 $\mu\text{m} \times 430 \mu\text{m}$) that passes over the PDMS and covers the pads on both sides. Patterned casting procedures form the required features of PDMS and PSR. Here, photolithography first creates trenches in a thick layer of photoresist (AZ P4620, AZ Electronic Materials, USA). Spin-coating PDMS (20:1 mixture of base to curing agent; Sylgard 184, Dow Corning) on top of this resist, curing it at 70°C for 1 hr and then etching back the PDMS removes any residual material from the top surface of the resist. Rinsing with acetone washes away the resist. Next, similarly patterned AZ P4620 defines a structure for the required features of PSR (Elastosil® LR 3162, Wacker Silicones Corp, USA). In this case, placing an excess of this material on top of the resist and then scraping with a razor blade forces it into the trenches and removes it from adjacent areas. Curing at 70°C for 1 hr and then removing the resist yields the desired PSR structure. The tactile sensor is completed by spin-casting a layer of PI for encapsulation.

To calibrate the response, the entire structure is transfer printed onto a 1 mm thick slab of PDMS (30:1 mixture of base to curing agent). A multimeter (SMU2055, Signametrics Corp, USA) measures the change in resistance during compression using a custom assembly of stages and a 25-gram-force GSO load cell (Transducer Techniques, Inc., USA) fixed on a

vibration-isolation table, as shown in Fig. S7. The indentation head mounts on a support designed to cover a single tactile sensor. The tactile sensor attaches to a glass slide that attaches to a vertical translation stage with positioning accuracy of 1 μm . A microscope above the stage facilitates manual alignment. After bringing the device into slight contact with the indentation head, the sample stage moves downward by 30 μm at a speed of 1 $\mu\text{m}/\text{sec}$. For cyclic fatigue testing, speeds were 120 $\mu\text{m}/\text{sec}$. Slight drift in the baseline response can be significantly reduced by several cycles of compression, prior to testing³⁹.

Fabrication of temperature and flow sensors

Thin layers of Ti/Pt (5 nm/50 nm) deposited with an electron beam evaporator serve as the basis for the temperature and flow sensors (Fig. 1d). A lift-off process defines the meandering electrode patterns. Surface treatment of the PI with oxygen plasma or deposition of a thin silicon dioxide (SiO_2) layer (~50 nm) on top of the PI improves the adhesion of the Pt. Patterning gold interconnects, encapsulating with a layer of PI and etching to define the mesh completes the fabrication.

Connector fabrication and integration

The connector consists of an array of metal lines (Cr/Au, 5 nm/150 nm) on a commercial PI film (Kapton, Dupont, USA). Another top coating of PI (~1.2 μm) helps to prevent breakage or delamination of the metal during integration. The stretchable electrode array and one side of the connector are interconnected with an anisotropic conductive film (ACF), connected through application of heat (~150°C) and pressure with conventional binder clips for ~10 min, as shown in Fig. S5b. The opposite side of the connector connects through the ACF to a circuit board that interfaces to a analog to digital converter for data acquisition.

Animal Experiments

Experiments used rat ($n = 4$; 390–500 g) and rabbit ($n = 4$; 3.5–4.0 kg) models. All rats were anesthetized with an initial dose of 0.45 mL sodium pentobarbital (Nembutal; 50 mg/mL) supplemented with 0.15 mL (25 mg/mL) booster doses at ~1 hr intervals. Rabbits were anesthetized with a 0.5 mL/kg mixture of ketamine (30 mg/kg), xylazine (7 mg/kg), and acepromazine (3.5 mg/kg), and were then intubated and maintained with 2% isoflurane at room temperature. A median sternotomy and pericardiotomy were performed to gain access to the epicardium. Next, the parietal pericardium was removed to allow balloon- and sheet-based devices to come in direct contact with the heart. A micromanipulator stage with micrometer scale accuracy was used to position the balloon catheter surface in contact with the anterior surface of the heart. Ringer's solution was used to keep the epicardial surface moist during experiments. Measurements were taken at multiple sites along the LA, RA, RV, and LV surfaces to differentiate local excitation across the different chambers of the heart. During ischemic injury experiments (Fig. 4), a suture ligature was used to occlude the LAD coronary artery. Electrocardiograms were recorded with multifunctional devices to capture the onset and development of injury at multiple sites on the heart. All animal experiments were approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Arizona. Endocardial measurements using femoral vein access into the porcine heart (Fig. 1f) were performed to capture x-ray images using previously published procedures¹⁴. These experiments were approved by the Massachusetts General Hospital Center for Comparative Medicine (CCM).

Data Acquisition Systems

The data acquisition system consists of a pressure sensing module and an electrophysiological mapping module (Fig. S16a). The pressure sensing circuit sends a controlled programmable current across the tactile pressure sensor's terminals. The AD8671

op amp generates the constant current. A switch toggles between two current ranges (Fig. S16b). Voltage changes across the tactile pressure sensor are monitored by an NI PXI-6289 and PXIe-10731 data acquisition (DAQ) board.

The electrophysiological signals detected by the stretchable electrode array are conditioned with the Intan RHA1016, a multiplexed biopotential amplifier array. The RHA1016 provides common-mode rejection, gain, low-pass filtering at 5 kHz and multiplexing. A Ripple Grapevine system converts the multiplexed analog signal from the RHA1016 to digital output. It samples the RHA1016's output at 300ksps and decimates the signal to 1ksps. In addition, it applies a digital 50/60 Hz notch filter to the signal. The data is recorded in the Cyberkinetics NEV2.2 NS2 format. The data is then viewed with custom Matlab software.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Multifunctional inflatable balloon catheters

a, Optical image of a stretchable, interconnected passive network mesh integrated on a balloon catheter (deflated) showing the overall construction, including connectors and ACF metal traces on the proximal side of the balloon and its wrapping configuration along the length of the catheter shaft. **b**, Optical image of the balloon inflated by ~130% relative to its deflated state (inset). **c**, Magnified view of non-coplanar serpentine interconnects on the balloon in its inflated state. This region corresponds to the area defined by the green dotted line in **b**. The spacings between the islands and the configurations of the serpentine interconnects compare well with simulation results (inset, purple dotted area from Fig. S2). **d**, Magnified image of a temperature sensor and gold lines used to apply positive and negative bias voltages. Electrodes for simultaneous electrogram mapping are also shown. **e**, Optical image of a multi-functional balloon catheter in deflated and inflated states. The image shows arrays of temperature sensors (anterior), microscale light emitting diodes (posterior) and tactile sensors (facing downward). **f**, X-ray angiography image of an instrumented balloon catheter deployed in the heart (right atrium) of a pig for *in vivo* recording of electrophysiology near the superior vena cava. The balloon was filled with contrast dye to facilitate imaging.

Figure 2. Fabrication, characterization and analysis of tactile and temperature sensors and RF ablation electrodes for multifunctional balloon catheter devices

a, Schematic cross-sectional drawing of a tactile sensor (left) and calculated distributions of strain (right) at the base of the PSR due to inflation of the balloon substrate, for cases with and without an underlying layer of epoxy. **b**, Calculated deformations and distributions of strain in the PSR across the cross section of a sensor with layout illustrated in **a**, induced by uniform compression (black arrows). The two top frames show cases with (top) and without (bottom) a PDMS layer (white). The bottom two frames show magnified views of the strains in the top part of the PSR bridge. **c**, Optical image of a rectangular feature of PDMS between two electrode pads (left). A fully-integrated tactile sensor (right) containing a PSR layer formed on top of the PDMS. The red dashed line indicates the position of the cross-sectional view depicted in **a**. **d**, Percent change in resistance ($\Delta R\%$) vs. applied pressure for sensors with three different PDMS thicknesses (**h**). **e**, Plot of $\Delta R\%$ as a function of time during several cycles of inflating and deflating the balloon substrate. **f**, IR camera image of the distribution of temperature in tissue created by activation of an RF ablation electrode (inset). The highest measured temperatures ($\sim 70^\circ\text{C}$) coincide with the location of the electrode. **g**, Temperature distributions determined by coupled thermal and electrical modelling of the ablation process. **h**, Modelling results for thermal distributions along the radial (r) and transverse (normal; z) directions. **i**, Distributions in both radial and transverse directions for the cross sectional plane indicated by the blue dashed line in **g**. **j**, Optical image of a flow sensor. **k**, Plot of $\Delta R\%$, as a function of flow rate in water, at three different constant current measurement modes.

Figure 3. *In-vivo* epicardial recordings of cardiac electrophysiological, tactile and temperature data, and RF ablation in a rabbit heart

a, Epicardial activation map of the right ventricle (RV). ‘Spike and dome’ configuration indicates elevated S-T segments with ~ 25 ms duration. **b**, Electrical mapping of left atrium (LA) activity. **c**, Optical image of an instrumented balloon catheter in its inflated state, showing an array of tactile (white dashed boxes) and electrogram sensors positioned in direct contact with the surface of the RV. The inset shows a magnified view of a tactile sensor. **d**, Simultaneous recordings of electrical activation and mechanical contact measured on the surface of the beating heart. **e**, Optical image of epicardial ablation lesions (white discoloration) created by two pairs of RF ablation electrodes. The yellow line denotes the region of temperature sensing. The inset shows an image of representative RF electrodes co-located with temperature sensors. **f**, Temperature monitoring before, during and after RF ablation. The time constants for the temperature rise and the absolute temperatures achieved during ablation are comparable to those associated with conventional cardiac ablation catheters.

Figure 4. *In-vivo* epicardial mapping of electrophysiology using an instrumented surgical glove during ischemic injury

a, Optical image of smart surgical glove in close proximity to the beating heart. **b**, Series of images documenting the progression of ischemic injury induced by surgical occlusion of the later anterior descending (LAD) coronary artery with a suture in a rabbit heart.

Hemorrhaging was followed by myocyte apoptosis and necrotic cell death ~15–20 minutes later. The heart became visibly enlarged, indicating significant fluid retention, swelling of cardiac myocytes and edema, particularly in the ischemic region. A simultaneous reduction in cardiac output was observed.

c, Optical image showing effects of ischemic injury in a rat heart using the same approach. **d**, Electrogram of epicardial activation near the RV

immediately following LAD occlusion (t_1). **e**, S-T elevation was noticeable at $t_2 = \sim 5$ min with slight increase in sinus rhythm pace (~ 260 bpm). At $t_2 = \sim 15$ min, the shape of electrical activation was consistent with ventricular tachycardia (VT). The large dome shapes indicate S-T segment elevation beyond levels in Fig. 1d. **f**, Electrogram showing the heart in agonal phase, marked by very slow erratic beating ($t_2 = \sim 30$ min). **g**, Atrial

fibrillation was also apparent, marked by erratic p- and t-wave behaviour between QRS complexes. **h**, Surface activation from the RV and the LA were detected simultaneously using array of sensors on surgical glove.