BIOELECTRONIC DEVICES

Catheters gain arrays of sensors and actuators

Flexible multilayer electronic arrays impart endocardial balloon catheters with enhanced sensing and actuation functionality.

Ellen T. Roche

Intracardiac and intravascular catheters are flexible tubes used in a range of minimally invasive therapeutic and diagnostic cardiovascular procedures such as stent placement, valve placement and the acquisition of electrophysiological measurements. Catheter systems can be instrumented with electronic sensing and actuation elements, but the rigidity of the electronics — and thus their lack of conformability to soft tissue — has limited the catheters' functionality[1] and has led to excessive catheter probing and increased procedural times, even when operated by skilled interventionalists. Reporting in *Nature Biomedical Engineering*, John Rogers, Igor Efimov and Yonggang Huang now describe methods for the incorporation of flexible arrays of multilayer electronics onto endocardial balloon catheters[2]. In both in vitro and ex vivo hearts, the devices' conformability to curved tissue enabled the high-resolution spatiotemporal mapping of temperature, pressure and electrocardiogram signals, as well as the use of electrical stimulation for radiofrequency ablation and electroporation.

Rogers and co-authors fabricated the multiplexed arrays (containing up to 160 sensing or actuation elements in each square centimetre) by using extensible serpentine interconnects made of polyimide-coated gold linking a range of sensors, actuators and ancillary electronic elements layered on top of each other via manufacturing techniques commonly used by the semiconductor industry (in particular, the use of temporary silicon wafer substrates and of transfer printing to ultrathin polymer films). Specifically, electrodes for electrophysiology measurements and for electrical stimulation were placed on the tissue-interfacing layer; temperature sensors for precise thermal monitoring were added as an intermediate layer; and pressure sensors for measuring tissue-contact forces were incorporated into the device-interfacing layer (Fig. 1a). The arrays with temperature and pressure sensors contain gold traces configured as resistive elements joined to two connection lines in two different layers, allowing for the selection of particular columns and rows of sensors via a customized circuit. The pressure-sensor arrays were realized by transforming traditional metal cross-shaped strain gauges to three-dimensional mesostructures using compressive buckling, rendering them sensitive to an applied normal force, and were covered with an array of silicone cavities to protect the sensors from mechanical damage during loading. Rigid islands were attached to the base of the arrays to prevent the lateral stretching of the sensors while preserving the overall stretchability of the arrays. The authors show that the arrays can be mounted on clinically used catheters (for example, on a polyurethane cryoablation balloon; Fig. 1b), and that the devices' architecture and the flexible untethered interconnections allow for biaxial extensions greater than 30%, and for at least 10,000 cycles of uniaxial stretching at 20%.

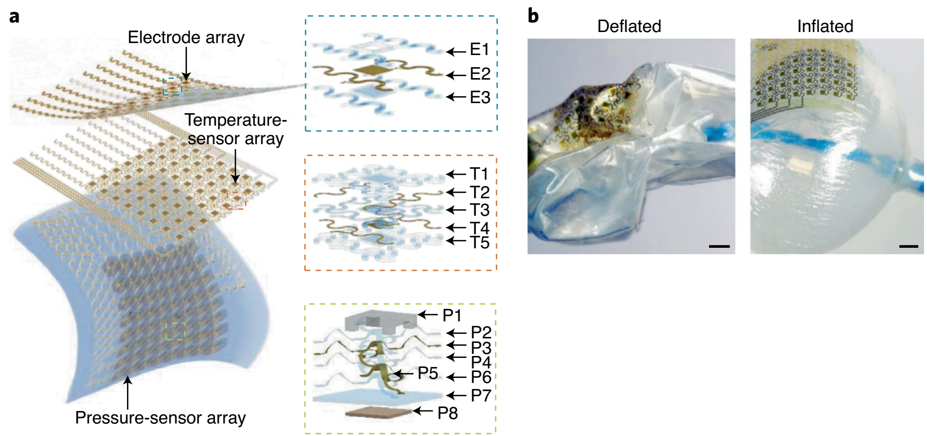

Fig. 1 | Integration of flexible multilayer electronic arrays into cardiac catheters. a, Layers of a multielectrode array. From top to bottom: electrodes and interconnects (E2) interfacing with tissue, temperature sensors (T2), pressure sensors (P3) and rigid gold islands (P8), which interface with the catheter's surface. Layers E1, E3, T1, T3, T5, P2, P4, P6 and P7 are layers of insulting polymers, and layers T2, T4, P3 and P5 include resistive elements that allow for the selection of particular rows of sensors (T2 and P3) or columns of sensors (T4 and P5). P1 is an array of silicon cavities protecting the pressure sensors. **b**, An array of temperature sensors integrated on a polyurethane balloon catheter. Scale bars, 2 mm. Figure reproduced with permission from ref. [2], Springer Nature Ltd.

Radiofrequency ablation — the use of electrical currents to heat adjacent tissue — and irreversible electroporation — the use of pulsed electrical fields to increase cell permeability, causing localized cell death — are widely used to treat arrhythmias. Rogers and co-authors show, in rabbit Langendorff hearts, that the multilayer electronic arrays can be used to perform programmable radiofrequency ablation (by selectively powering two out of 64 electrodes in contact with tissue without moving the catheter tip, and with temperature sensing on the epicardial surface providing spatiotemporal feedback during the procedure), as well as multifocal ablation and programmable irreversible electroporation. They can also be used to detect atrial and ventricular excitation as well as ventricular relaxation (by comparing electrograms and voltage maps from the electrode array during pacing and arrhythmia). Pressure-sensing data show that electrogram measurements are more sensitive when contact between the array and the tissue is more intimate. Moreover, by using ventricular tissue segments from a human heart ex vivo, the authors show that the arrays offer better

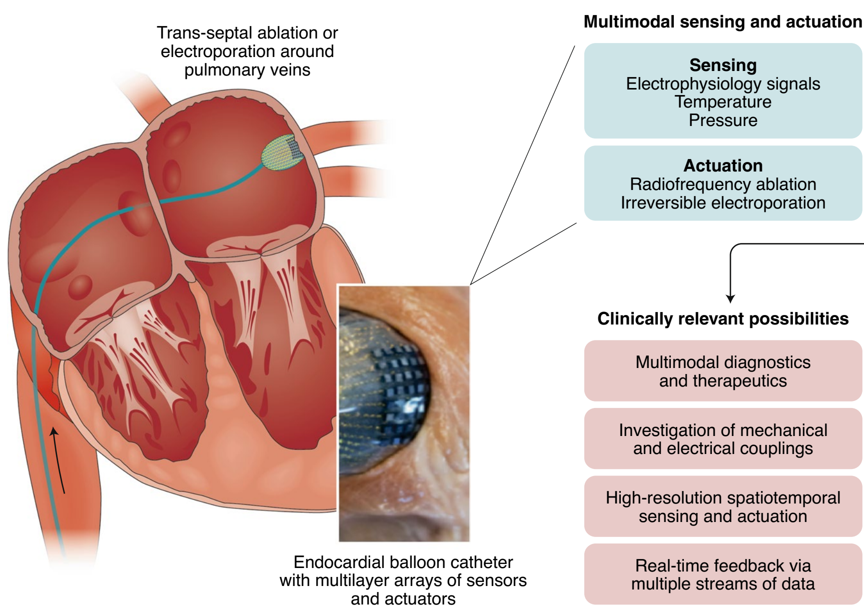

Fig. 2 | A balloon catheter instrumented with multilayer flexible electronic arrays with sensing and actuation functionality would offer clinically relevant advantages. The schematic shows an endocardial balloon during trans-septal ablation or electroporation around the pulmonary veins. Photograph of the balloon catheter reproduced with permission from ref. [2], Springer Nature Ltd.

control over the location of the ablated tissue than traditional tip or ring electrodes for ablation.

By integrating multimodal and multiplexing capabilities into minimally invasive surgical instruments, Rogers and colleagues' flexible electronic arrays may lead to improved surgical outcomes, particularly in applications requiring high spatiotemporal resolution, as is the case with radiofrequency ablation and irreversible electroporation (Fig. 2). Catheters that use intracardiac balloons at each side of the septum to stabilize an adhesive patch during photoactivation of the adhesive for intracardiac defect closure[3], and other such technologies currently in the research phase, may also benefit from instrumented balloons. In this case, pressure sensors integrated into the balloon could quantify the amount and distribution of contact and the pressure applied by each balloon to the septum, and temperature sensors could detect the photoactivation energy delivered to the adhesive. The pressure map would help to ensure adequate device conformability and thus adhesion of the activated adhesive to the tissue. Such intraprocedural monitoring of critical parameters would be useful in the translational development of the devices and during clinical use.

Blood flow (particularly when turbulent) and dynamically moving tissue in intracardiac in vivo environments should put the robustness and performance of Rogers and colleagues' devices to the test. Also, folding, loading and inflating instrumented balloon catheters can lead to high shear stresses and could thus damage the electronics in the arrays or their protective coatings. In particular, arrays mounted on a compliant Foley catheter (the most common indwelling urinary catheter) in the deflated state may be vulnerable to biaxial stretching greater than 30% when the balloons are fully inflated. Also, the devices' multifunctionality may make validation work particularly extensive. Yet the integration of high-density multimodal mapping with customizable layouts that can be readily integrated into existing catheter systems offers exciting clinically relevant possibilities: the measurement of maps of thermal conductivity (by adding a separate layer of thermal actuators), which could be useful in blood-flow analysis, tissue perfusion and hydration; closed-loop control; the study of correlations between different physiological and pathological parameters (between mechanical and electrical perturbations, for example); and access to multiple data streams in real time during intravascular, gastrointestinal and urogenital procedures. ❐

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Competing interests

E.T.R. is a consultant for Holistick Medical, and holds equity in the company.