exposed to avulsion hazards that they have never experienced before.

Avulsions are the ultimate delta process. They operate at the largest time and space scales of a delta system—happening over centuries to millennia and covering the entire delta landscape up to thousands of square kilometers. River avulsions have extremely positive and negative effects on the landscape and its communities. They distribute sediment widely across the entire deltaic region, building and maintaining delta plains. For example, coastal Louisiana was shaped and built through multiple switches in the course of the Mississippi River over millennia (*6*). However, avulsions also present an obvious hazard to communities living near rivers. Hundreds of millions of people living in coastal areas around the world are at risk of powerful flooding resulting from sudden and catastrophic avulsions, in addition to the constant threat of sea-level rise and other climate crises. The infrequent nature of avulsions, compared to more frequent extreme weather events and the continuous effect of sea-level rise, makes avulsions a less-discussed topic despite their catastrophic effects.

The dichotomy between the dynamics required by river systems to be sustainable and the stability desired by communities living on these systems is the grand challenge for delta management (*7*). Human civilizations have established themselves in proximity to water, which in turn exposes communities to a combination of acute (e.g., flooding events, avulsions) and chronic (e.g., river migration, sea-level rise) stresses (*8*). For centuries, societies have implemented various engineering interventions to protect communities and their livelihoods (*9*), such as building 2500 km of levees along the Mississippi River and extensive embankments that create the low-lying lands on the Ganges-Brahmaputra-Meghna delta. However, as impressive as these engineering feats are, human-scale interventions provide only local and temporary stability relative to the temporal and spatial scale of avulsions. This can contribute to a false sense of protection (*10, 11*) and even amplify degradation at the system scale by limiting natural sediment dispersal (*12–14*).

Can engineering interventions be designed to address sustainability at the delta system scale while simultaneously providing protection to the communities living on the landscape? Here lies the conflict between the temporal and spatial scales needed for landscape sustainability versus those that are important for human-scale stability. Designing for immediate stability provides short-lived protection over local spatial scales, but these local interventions tend to not achieve landscape sustainability. Interventions to achieve long-term system-scale sustainability should include river diversions that approximate the sediment dispersal achieved by large spatial- and temporal-scale avulsions.

"Interventions… should include river diversions that approximate the sediment dispersal achieved by… avulsions."

Effective placing of river diversions requires a comprehensive understanding of natural avulsion timing and location. The ability to predict avulsions is improving and moving toward providing robust predictions that governments and decision-makers can use to implement interventions at the system scale. Researchers must focus on integrating process models and remotely sensed global patterns to provide actionable predictions of landscape change over the coming decades. Moreover, river diversion placement must account for the socioeconomic aspects of these interventions and consider how community needs can be integrated with the large spatial and temporal scales of avulsions (*15*). Only through such an approach will we be able to find a compromise between the human desire for stability and the dynamics that are needed for a landscape to be sustainable over time. ■

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MEDICINE

Remote control of the heart and beyond

A resorbable closed-loop sensor-actuator implant can temporarily control heart rate

By **Wolfram-Hubertus Zimmermann**[1,2,3,4,5,6]

External and internal electrical pacing of the heart are fundamental interventions in patients with cardiovascular disease (*1*). Recently, wearables, such as the Apple Watch and Fitbit devices, have been introduced to the consumer market to monitor key bodily functions such as heart rate and rhythm, blood oxygenation, blood pressure, and body temperature (*2*). On page 1006 of this issue, Choi *et al.* (*3*) go beyond sensing by reporting a resorbable closed-loop sensor-actuator (see the figure), with the eventual aim of controlling heart function in patients with a postsurgical risk of bradycardia (slow heart rate). This technology is wireless, circumventing common shortcomings of implanted devices, such as drive-line infections or the need for surgical procedures to remove or replace, for example, pacemaker leads or batteries. The demonstrated cardiac application of this technology in rats, dogs, and ex vivo human heart preparations could improve outpatient surveillance, allowing for earlier release from the hospital and remote monitoring of patients living in medically underserved areas.

Choi *et al.* made use of a previously introduced design strategy, comprising water soluble metals (molybdenum and silicon) and degradable polymers [polyurethane and poly(lactic-co-glycolic acid)], to fabricate resorbable devices (*4*). In addition to providing preclinical proof of concept

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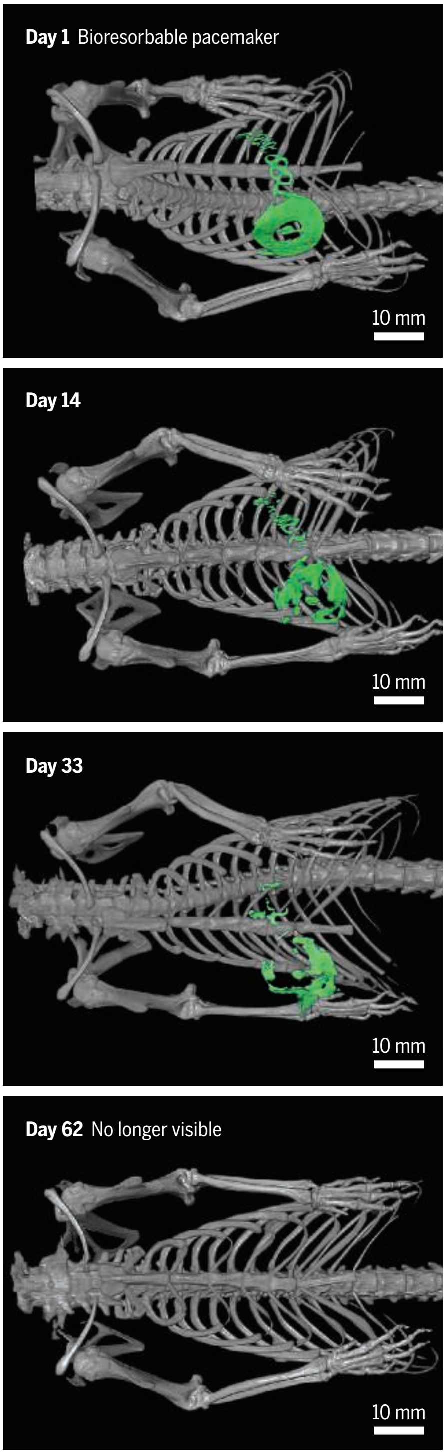
for their use in monitoring and pacing the heart, the authors demonstrated important additional features of their device such as magnetic resonance imaging (MRI) compatibility, mechanical robustness, rechargeability, rate-adapted pacing capabilities, and secure data processing.

Triggering electrical pulsing in response to sensing defined biosignals adds a new layer of complexity to human-machine interfacing. But is such a disruptive technology ready to be deployed in clinical practice? There are a number of key issues that need to be addressed: the degree to which the obtained data are reliable, how safety and effectiveness can be ensured, and how misuse can be prevented.

The spectrum of wearable devices is growing rapidly, with the promise that close monitoring of fundamental bodily functions can support lifestyle changes. Whether such devices can be used beyond the consumer market to sustain a healthy lifestyle and, ultimately, to inform life-saving medical interventions remains to be determined by well-controlled clinical investigations with confirmation of safety and effectiveness. Implantable pacemakers, defibrillators, and electrocardiogram (ECG) monitors have been in broad clinical use for decades. More recent developments allow telemonitoring of heart rate and rhythm as well as pulmonary artery pressure by permanently implanted microelectromechanical systems (MEMS) with documented clinical utility in preventing sudden cardiac death and reducing hospitalization for worsening of heart failure (*5*, *6*).

Whether transient devices, made from degradable materials, will obtain similarly reliable data for exploitation as clinical biomarkers while also allowing autonomous organ control will need to be documented in patients. The required information goes beyond what is necessary for the clearance of consumer market wearables as class I and II medical devices by the US Food and Drug Administration (FDA) or CE marking by the European Medicines Agency (EMA). Most notably, clinically obtained evidence for safe and efficacious use in a designated indication, such as bradycardia, will be required for premarket approval of implantable closed-loop recorders, which will be considered class III medical devices.

In the case of using closed-loop sensor-actuator systems with pacemaker functions in patients, risks of inaccurate pacing will have to be determined and minimized (*7*). This is not a trivial task because such devices must be able to make highly accurate ECG recordings for a clear dissection of signal from noise (a common problem in contemporary pacers and defibrillators) and appropriately manage pacing. It remains to be determined in clinical trials whether the resorption of the implant, foreign body reactions, patient-specific anatomical features of the heart (such as hypertrophy, dilation, scarring, fibrosis, fat deposition), or the presence of other implants will have an impact on real-life ECG signal recordings. Local steroid administration, introduction of improved materials, and the implementation of explainable artificial intelligence algorithms may help to further improve relevant signal recovery.



Computed tomography images show resorption of the pacemaker device in rats over the course of 9 weeks.

Implanted sensors will collect highly personalized data, which could be misused or even manipulated. Patients need to be made aware of the related risks and countermeasures in case of, for example, an unwanted loss of control of the actuator component of the autonomically acting closed-loop device. Moreover, designated data protection measures need to be established that restrict access to recorded information to dedicated and trained medical staff.

The technology described by Choi *et al.* could have broad applications in sensing and controlling the function not only of the heart but also of other excitable organs or tissue. In some cases, transient support will be desirable and sufficient, such as in patients with transient paralysis. There may be other scenarios where chronic or even permanent use may be of interest, such as in patients with a dysfunctional pacing function of the sinus node (sick sinus syndrome) or permanent paralysis after, for example, traumatic denervation.

Although the use of closed-loop sensor actuators can be readily envisioned as a bridge to recovery, as in the proposed case of postsurgical recovery from bradycardia, additional biological repair may be required to overcome the need for extended electrical support. Support of endogenous and exogeneous tissue regeneration and repair of the heart has been an intense topic of research, and a first clinical trial on sustainable remuscularization of the failing heart is underway (i.e., the BioVAT-HF-DZHK20 trial: NCT04396899). By combining electrical and tissue engineering, it seems plausible that electromechanical activity of engrafted cells or tissue may, in the future, be controllable to facilitate electromechanical integration. Similar applications may be envisioned in other diseases caused by the dysfunction of electrically excitable cells. ■

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