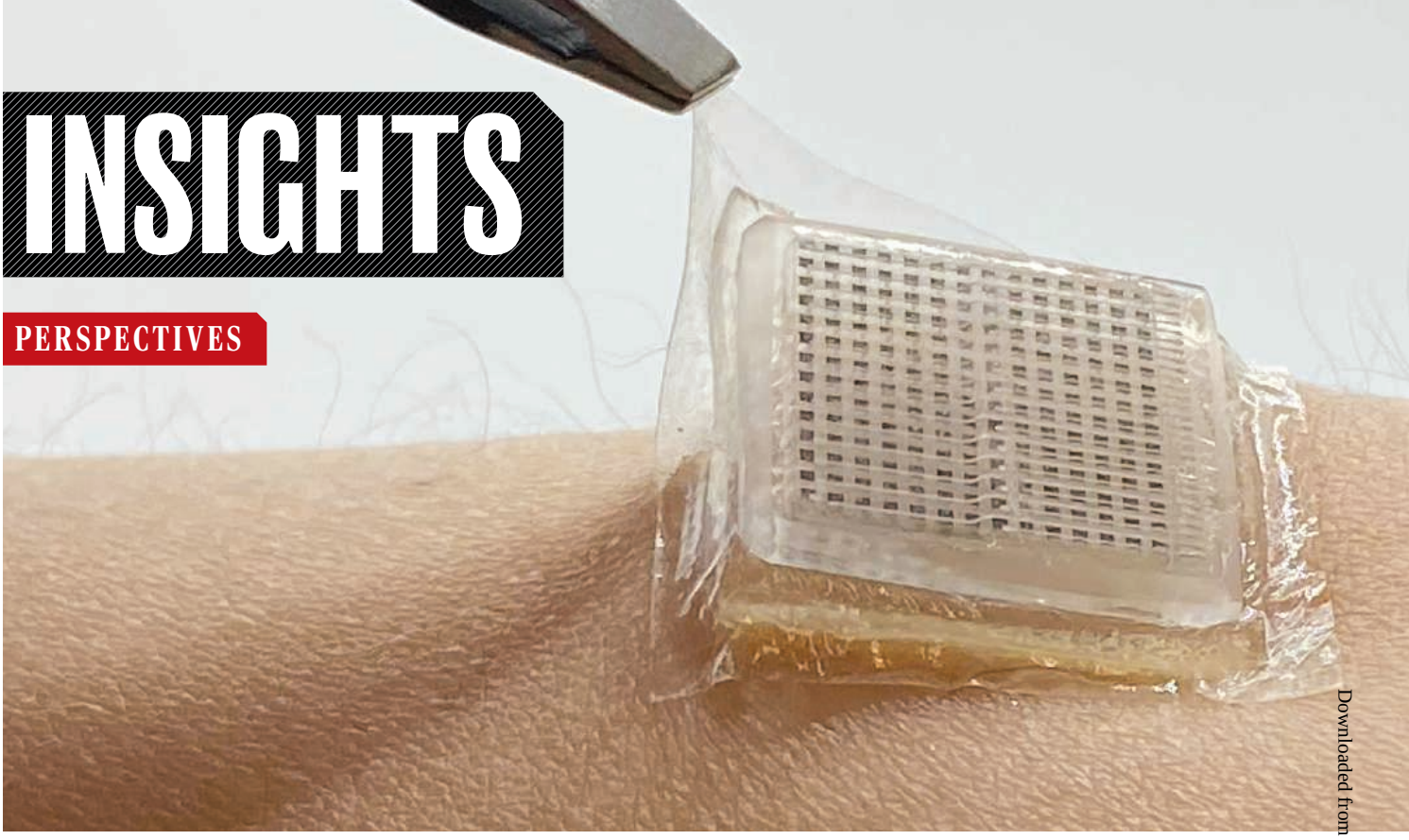
INSIGHTS

PERSPECTIVES



MEDICAL IMAGING

Seeing inside a body in motion

Adhesive ultrasound patches can provide medical imaging for patients on the go

By **Philip Tan**[1] *and* **Nanshu Lu**[1,2,3,4,5]

Ultrasonic imaging is one of the most powerful and commonplace medical tools for noninvasive visualization of soft tissues inside the body. However, ultrasonography requires highly trained sonographers to position and orient the transducer on the surface of the patient's body, and image quality is highly dependent on the steadiness of the operator's hand. Because of this, ultrasonic imaging has been largely limited to short and static sessions not only for logistical reasons but also because of the very real threat of musculoskeletal injuries for sonographers from repetitive motions associated with transducer manipulation (*1*). Coincidentally, there has also been a sonographer shortage worldwide over the past decade, and the demanding and specialized training required for certifying sonographers does not help alleviate this problem (*2*). On page 517 of this issue, Wang *et al.* (*3*) introduce a bioadhesive ultrasound (BAUS) patch with the potential to overcome many of these outstanding challenges.

Over the past few years, several wearable ultrasound patches have been developed (*4*–*7*). Although there have been improvements in transducer thinness and softness, none satisfy all the patch-tissue-interface requirements for high-quality ultrasonic imaging. To be ready for real-world applications, the patch must have stable adhesion to the body, the acoustic energy from the transducer must be transmitted efficiently into the body, and the device must not cause skin irritation. In a standard ultrasound exam, liquid gel is the de facto couplant, that is, a material that improves acoustic transmission at the transducer-tissue interface. However, conventional ultrasonic gel is only suitable for short imaging sessions because it dries out or drips down over time. Conversely, elastomer (*4*, *5*, *8*) and hydrogel (*8*) couplants have been explored but tend to have less-than-desirable transmissivity or usable time, respectively.

To overcome these weaknesses, Wang *et al.* combined the strengths of both elastomers and hydrogels by encapsulating a soft hydrogel in a thin elastomer membrane and coating it with a bioadhesive material. This hydrogel-elastomer hybrid, which they named the BAUS couplant, enables more than 48 hours of adhesion to the skin and sustained transmissivity. The soft and adhesive BAUS couplant also alleviates the stiffness of a rigid transducer array, making it more comfortable to wear. The rigid transducer array allows for a high transducer density, with 400 transducers per square centimeter.

The BAUS patch opens exciting opportunities for increasing accessibility to ultrasound exams. Although, at present, the patch still needs to be attached to a nonportable data acquisition system for processing the images, it could provide immediate relief for sonographers, for example, during sessions when a patient is undergoing anes-

PHOTO: WANG ET AL. (3)

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Wang *et al*. created a hydrogel-elastomer adhesive that can be used as a conductive medium for an ultrasound transducer, which provides the flexibility needed for a wearable ultrasound imaging device.

thesia and constant monitoring of cerebral blood flow is required (*9*). In this scenario, the BAUS patch can simply be stuck to a patient's temple and provide stable blood flow imaging. The patch also opens opportunities for long-term, dynamic, high-resolution imaging of internal organs. For example, discreet monitoring of bladder volume could help people who suffer from urinary dysfunction. The inability to sense bladder fullness is a cause of urinary incontinence, leading to physiological and psychological injury, and a portable ultrasonic device for measuring bladder fullness can provide private alerts for these individuals to relieve themselves (*10*). For managing cardiovascular disease, stress echocardiograms provide valuable insights into cardiac functions, including valvular regurgitation, valve gradients, chamber volume, and myocardial strain tracking (*11*). However, the difficulty of maintaining the transducer probe during motion puts substantial logistical limits on these exams.

Thanks to excellent coupling to the tissue, the BAUS patch can capture high-quality images during a wide range of motions (see the figure). Muscular imaging enables quantification of muscle contraction, which enhances athletic training and rehabilitation of neuromuscular disorders (*12*). Also, ultrasonic imaging of the lungs has been a powerful tool for screening for respiratory diseases such as COVID-19 (*13*). A "set-and-forget" ultrasonic patch would allow for continuous monitoring of contagious patients with minimal exposure risk to the medical staff.

However, there do exist several limitations of the BAUS patch that will require future improvement. Wang *et al.* introduced a plug-and-play snap connector system that could link to several dozen transducers. However, three-dimensional ultrasonic imaging will require thousands of transducers to provide sufficient resolution. Controlling thousands of transducers requires extensive circuitry and hardware, which will limit maneuverability and mobility. Forming interconnects between transducers and the circuitry becomes more challenging with more transducers involved. Research into "ultrasound on a chip" will offer the much-desired integration of transducers with requisite analog and digital processing circuitry. The BAUS couplant has the potential to improve the long-term wearability of these systems, despite differing transducer array fabrication approaches.

To make ultrasound completely user-friendly for the average patient, artificial intelligence technology may also be needed to assist with placement and beam steering. Researchers have demonstrated an interactive application using a deep-learning model that guides the operator to manipulate the transducer to produce the best image of a target anatomy (*14*). Moving forward, automated image analysis and interpretation will be just as important as image acquisition. The road to providing universal accessibility for mobile ultrasonic imaging will require concerted efforts in diverse fields of engineering, science, and medicine. ■

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CANCER

Targeting brain cancer

A new drug is designed to hit an old target with increased precision

By **Roger Reddel** *and* **Adel Aref**

Glioblastoma (GBM) is the most common form of malignant tumor originating in the brain and is one of the most lethal cancers, with only 1 in 20 patients surviving for 5 years after diagnosis (*1*). The relentless growth of cancers such as GBMs results from DNA mutations and epigenetic changes, but these also create opportunities for targeted therapies. On page 502 of this issue, Lin *et al.* (*2*) describe a new approach to killing GBM cells that targets a well-known molecular change in GBMs: the decreased expression of the DNA repair enzyme O^6-methylguanine methyltransferase (MGMT). The authors develop a new agent that exploits this reduced DNA repair capacity and propose that their approach could be generalized to other cancers with defective DNA repair.

The expression of the *MGMT* gene is repressed by DNA methylation of its promoter. This occurs in ~50% of GBMs and >70% of lower-grade gliomas (grades II and III), and less frequently in other cancers (*3*). How this change contributes to oncogenesis is unclear, but MGMT interacts with the p21 and proliferating cell nuclear antigen (PCNA) cell cycle proteins (*4*), so lack of MGMT protein presumably contributes to unrestrained cell proliferation. What is much clearer is that MGMT provides a critical function in maintaining the integrity of DNA, with its primary function being to repair O^6-methylguanine DNA adducts, which cause base-pairing with thymine rather than cytosine and thus can introduce mutations during DNA replication. MGMT repairs these adducts through a "suicide" mechanism in which it transfers the methyl group from damaged DNA to the sulfur group in its internal acceptor site, inactivating itself (*3*).

One of the few therapeutic interventions that has well-documented benefit in GBM

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