Adhesive hydrogel coating prevents scarring around medical implants, prolongs lifespan of such devices

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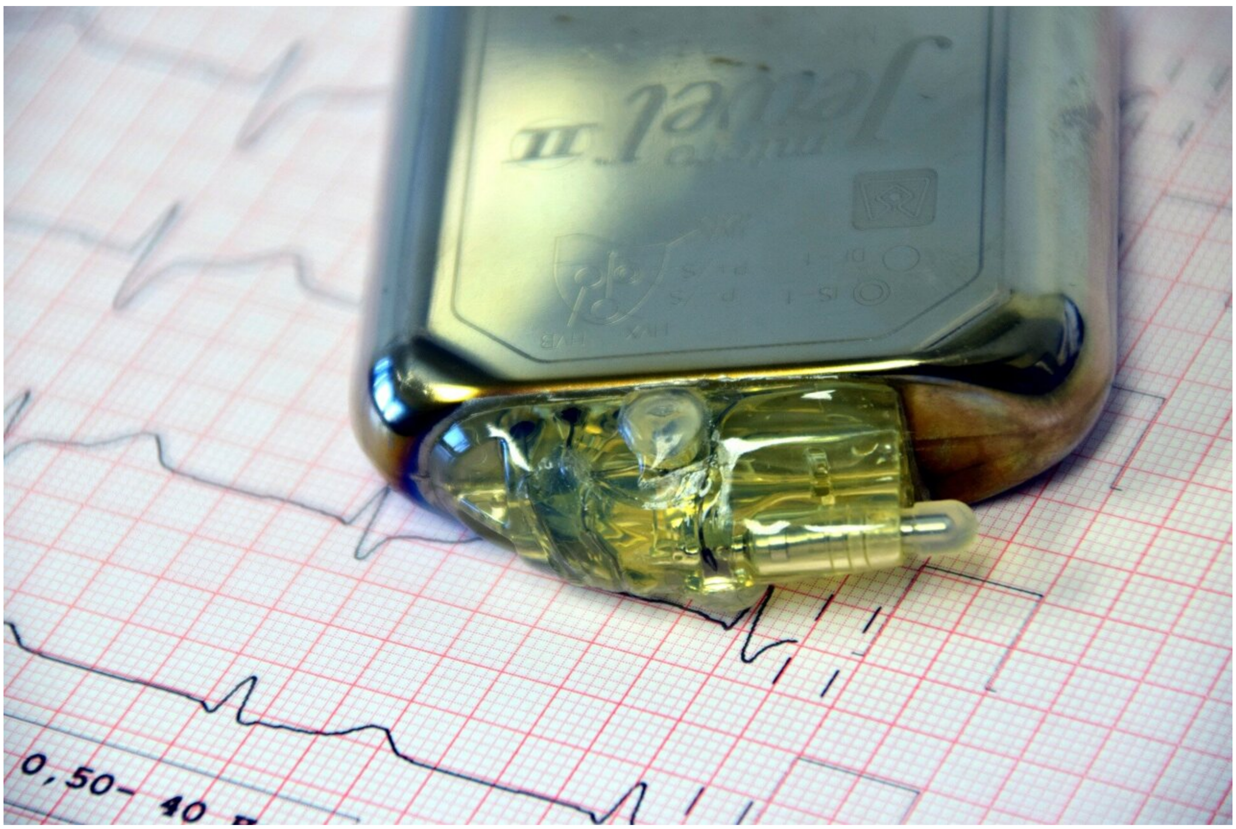

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When medical devices such as pacemakers are implanted in the body, they usually provoke an immune response that leads to buildup of scar tissue around the implant. This scarring, known as fibrosis, can interfere with the devices' function and may require them to be removed.

In an advance that could prevent that kind of device failure, MIT engineers have found a simple and general way to eliminate fibrosis by coating devices with a hydrogel adhesive. This adhesive binds the devices to tissue and prevents the immune system from attacking it.

"The dream of many research groups and companies is to implant something into the body that over the long term the body will not see, and the device can provide therapeutic or diagnostic functionality. Now we have such an 'invisibility cloak,' and this is very general: There's no need for a drug, no need for a special polymer," says Xuanhe Zhao, an MIT professor of mechanical engineering and of civil and environmental engineering.

The adhesive that the researchers used in this study is made from cross-linked polymers called hydrogels, and is similar to a surgical tape they previously developed to help seal internal wounds. Other types of hydrogel adhesives can also protect against fibrosis, the researchers found, and they believe this approach could be used for not only pacemakers but also sensors or devices that deliver drugs or therapeutic cells.

Zhao and Hyunwoo Yuk, a former MIT research scientist who is now the chief technology officer at SanaHeal, are the senior authors of the study, which appears in *Nature*. MIT postdoc Jingjing Wu is the lead author of the paper.

Preventing fibrosis

In recent years, Zhao's lab has developed adhesives for a variety of medical applications, including double-sided and single-sided tapes that could be used to heal surgical incisions or internal injuries.

These adhesives work by rapidly absorbing water from wet tissues, using polyacrylic acid, an absorbent material used in diapers. Once the water is cleared, chemical groups called NHS esters embedded in the polyacrylic acid form strong bonds with proteins at the tissue surface. This process takes about five seconds.

Several years ago, Zhao and Yuk began exploring whether this kind of adhesive could also help keep medical implants in place and prevent fibrosis from occurring.

To test this idea, Wu coated polyurethane devices with their adhesive and implanted them on the abdominal wall, colon, stomach, lung, or heart of rats. Weeks later, they removed the device and found that there was no visible scar tissue. Additional tests with other animal models showed the same thing: Wherever the adhesive-coated devices were implanted, fibrosis did not occur for up to three months.

"This work really has identified a very general strategy, not only for one animal model, one organ, or one application," Wu says. "Across all of these animal models, we have consistent, reproducible results without any observable fibrotic capsule."

Using bulk RNA sequencing and fluorescent imaging, the researchers analyzed the animals' immune response and found that when devices with adhesive coatings were first implanted, immune cells such as neutrophils began to infiltrate the area. However, the attacks quickly quenched out before any scar tissue could form.

"For the adhered devices, there is an acute inflammatory response because it is a foreign material," Yuk says. "However, very quickly that inflammatory response decayed, and then from that point you do not have this fibrosis formation."

One application for this adhesive could be coatings for epicardial pacemakers—devices that are placed on the heart to help control the heart rate. The wires that contact the heart often become fibrotic, but the MIT team found that when they implanted adhesive-coated wires in rats, they remained functional for at least three months, with no scar tissue formation.

Mechanical cues

The researchers also tested a hydrogel adhesive that includes chitosan, a naturally-occurring polysaccharide, and found that this adhesive also eliminated fibrosis in animal studies. However, two commercially-available tissue adhesives that they tested did not show this antifibrotic effect because the commercially-available adhesives eventually detached from the tissue and allowed the immune system to attack.

In another experiment, the researchers coated implants in hydrogel adhesives but then soaked them in a solution that removed the polymers' adhesive properties, while keeping their overall chemical structure the same.

After being implanted in the body, where they were held in place by sutures, fibrotic scarring occurred. This suggests that there is something about the mechanical interaction between the adhesive and the tissue that prevents the immune system from attacking, the researchers say.

"Previous research in immunology has been focused on chemistry and biochemistry, but mechanics and physics may play equivalent roles, and we should pay attention to those mechanical and physical cues in immunological responses," says Zhao, who now plans to further investigate how those mechanical cues affect the immune system.

Yuk, Zhao, and others have started a company called SanaHeal, which is now working on further developing tissue adhesives for medical applications.

"As a team, we are interested in reporting this to the community and sparking speculation and imagination as to where this can go," Yuk says. "There are so many scenarios in which people want to interface with foreign or manmade material in the body, like implantable devices, drug depots, or cell depots."

More information: Jingjing Wu et al, Adhesive anti-fibrotic interfaces on diverse organs, *Nature* (2024). DOI: 10.1038/s41586-024-07426-9.
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