Visible hydrogels for rapid hemorrhage control and monitoring

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Credit: Terasaki Institute for Biomedical Innovation

There are many different events which may lead to excessive and uncontrolled bleeding within the body. This can occur as a result of inflammation and ulcerations, abnormalities in the blood vessels or trauma-related injuries. Individuals with predisposing conditions, such as cardiac patients, are at particular risk of internal bleeding due to the anticoagulants they are often prescribed as a preventive measure. They are also prone to gastrointestinal bleeds, affecting 40% of patients who are on cardiac assistance devices. In addition to the need for an effective treatment for these conditions, there are also indications for controlling the blood flow that contribute to aneurysms and tumor cell vascularization.

An ideal treatment method would quickly and effectively block the break in the affected blood vessels to stop the bleeding and allow the vessel wall to heal. Then the blocking material would eventually degrade enough to allow the blood to flow again normally.

Current treatments involve both solid and liquid materials as blocking agents. Coils made of braided platinum or stainless steel wires are commonly used. They come in a variety of lengths, shapes and thicknesses and are placed into blood vessels using a special catheter. There are also liquid blocking agents that are injected into the blood vessels and solidify after injection.

But there are many difficulties in using the current methods. Because coils need special catheters for insertion and specialized equipment to detach and place them, the procedure is difficult and requires intensive training by the physician. Also, there are times when multiple coils need to be placed in order to be effective, and there are other times where the coils migrate or compact, necessitating repeat procedures. Liquid agents often leak during injections, resulting in inaccurate placement, toxic effects on the surrounding tissues and the necessity for additional attempts. These problems raise the potential for added time and cost.

In addition, neither of these methods have the ability to accurately view the procedures by conventional CT, MRI, X-ray and fluoroscopic methods. Successful imaging would greatly help to guide placement and to monitor the blood vessel block over time.

A previous study by the authors has used inexpensive, gelatinous materials called hydrogels in an attempt to produce an effective material for controlling hemorrhage. In addition to having superior biocompatibility and tunable elastic and mechanical properties, hydrogels also exhibit sheer-thinning capabilities—the ability to deform upon injection and then quickly self-recover and mold itself to fit the desired space; this allows delivery to be made using standard catheters without specialized equipment. Silicate nanoplatelet discs were mixed into the hydrogel to mimic the clotting ability of platelet cells, and the resultant composite proved to be highly effective at sealing off damaged veins.

A collaborative team of clinical intervention radiology specialist and bioengineering researchers has taken this project a step further by adding imaging particles made from tantalum hydrogel mixture. Tantalum, a highly biocompatible metal, has been shown to be safe to use in biomedical applications and is excreted in the urine.

The team made of scientists from the Terasaki Institute and Mayo Clinic performed various tests to determine the optimum tantalum particle size and quantity to use and their effect on the mechanical properties of the hydrogel composite. They also established the optimum formulation for the three components of their new composite gel. Their experiments determined that the tantalum particles dispersed well into the hydrogel composite, did not affect its mechanical properties and retained their sterility over time.

Another ambitious goal of the project was to perform their hemorrhage control experiments on arteries something that had not been done with hydrogels before. This effort posed additional challenges, due to the higher blood flow and pressure in arteries, their wide size variation and their potential fragility.

After various experiments conducted on the arterial vessels of live anticoagulated porcine models, the team obtained positive results with their new tantalum-laced composite hydrogel. They were able to create an effective seal against bleeding in the pigs' arteries, with a deployment time that was 40 times faster than with coils. The arterial block also exhibited stability and durability, staying in position without migration for four weeks before degrading naturally and being replaced by connective tissue repair of the vessel.

Due to the tantalum component in the gel the animal models' arterial procedures and monitoring were performed with clear, real-time visualization using CT, X-ray fluoroscopy and ultrasound.

"The experimental results that were observed in our tantalum-loaded gel clearly demonstrate its effectiveness and versatility", said HanJun Kim, a member of the Terasaki Institute's team. "We were able to meet our goals of being able to visualize and accurately place a stable block in an arterial vessel to rapidly treat uncontrolled intravascular hemorrhage."

The team went on to conduct additional experiments to test the reversibility of the new hydrogel's arterial placement and found that their solidified arterial plug could easily be removed using an aspirational catheter. They were also able to obtain successful arterial blockage by applying their hydrogel composite to coils that had been placed in the vessels and had failed to achieve or sustain blockage.

The use of this tantalum-loaded gel to control bleeding exhibits many unique advantages over current methods. It is a safe, easy-to-use, and cost effective method which demonstrates optimum effectiveness, precision and versatility for a variety of potential medical applications.

"The treatment method developed here are a vast improvement over current methods and it has the potential to affect many lives," said Ali Khademhosseini, Ph.D., director and CEO for the Terasaki Institute. "It is one of many examples of the innovative and impactful work that we do at our institute."

More information: Hassan Albadawi et al, Nanocomposite Hydrogel with Tantalum Microparticles for Rapid Endovascular Hemostasis, *Advanced Science* (2020). [DOI: 10.1002/advs.202003327](https://dx.doi.org/10.1002/advs.202003327)

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