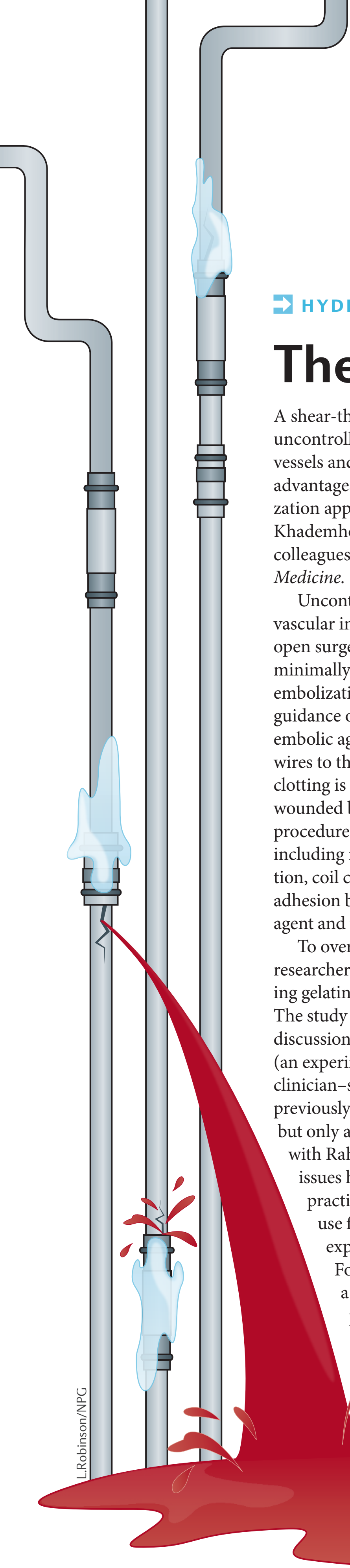

HYDROGELS

The blood stops here

A shear-thinning hydrogel stops uncontrolled bleeding in blood vessels and conveys several advantages over existing embolization approaches, report Ali Khademhosseini, Rahmi Oklu and colleagues in *Science Translational Medicine*.

Uncontrolled bleeding due to vascular injury is treated either with open surgery or, more recently, with minimally invasive endovascular embolization. The latter involves guidance of metallic coils or liquid embolic agents with catheters and wires to the site of bleeding, where clotting is induced to occlude the wounded blood vessel. However, this procedure comes with certain risks, including recanalization, coil migration, coil compaction or toxicity, and adhesion between the liquid embolic agent and the catheter.

To overcome such problems, the researchers used a hydrogel, comprising gelatin and silicate nanoplatelets. The study was conceived upon discussion between Khademhosseini (an experimentalist) and Oklu (a clinician–scientist). “My lab had previously developed the biomaterial, but only after initiating interactions with Rahmi and trying to solve the issues he has seen in his clinical practice, we realized its potential use for internal bleeding,” explains Khademhosseini. For Oklu, this research is a successful example of patient-inspired bioengineering: “We developed a biomaterial not just for the bench or for use in animal models, but tailored it so that it could be used with tools, imaging technology and with the needs of the end user (that is, the physician) in mind.”

Two salient features of their hydrogel render it suitable for endovascular embolization: the nanoplatelets can mimic platelet cells to induce blood clotting and the gel exhibits shear-thinning behavior (that is, the viscosity decreases under shear strain). This rheological behaviour allows the gel to flow through the catheter under mechanical pressure applied through a syringe. Once administered at the site of bleeding, the modulus recovers (that is, the material solidifies) owing to the reduced pressure, and a tight seal is created.

After fine-tuning the viscoelastic and gelation properties to allow delivery with standard catheters and needles, the researchers first tested their shear-thinning biomaterial *in vitro*. The gel was mechanically stable under physiological pressures and exhibited similar clotting to, and higher hemocompatibility times than metal coils. A particular advantage of the gel is that — unlike metal coils — it does not require intrinsic thrombosis, which is beneficial for patients suffering from clotting disorders or who are taking anticoagulation medication.

The shear-thinning materials were then tested *in vivo* in both small (murine) and large (porcine) models. Upon direct injection into the femoral artery, full occlusion occurred — revealed by computed tomography imaging — with the gel remaining at the site of injection. Having validated the effective embolization of the shear-thinning biomaterial, the researchers then successfully administered the material through catheters into the arterial vasculature and forelimb venous vasculature. Again, full occlusion of the target vessels was achieved, further demonstrating the translational potential of this biomaterial.

The fate of the biomaterial and the injured vessel after embolization are also important considerations. Histological analysis of embolized vessels revealed that remodelling of the vessel occurs in concert with clearance of the biomaterial, which is thought to be mediated by phagocytic cells. Consequently, there is a low risk of recanalization or fragmentation of the gel. Moreover, the authors suggest that this process of remodelling and biomaterial clearance provides the opportunity to incorporate stimuli to, for example, control angiogenesis.

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Given the success of this proof of concept, the authors now intend to take their biomaterial into clinical trials. “We have shown that the material works in pre-clinical models; in particular, it seems to work in cases where existing therapies do not,” says Khademhosseini. “Now, we aim to demonstrate the ultimate utility of the material in the clinic.”

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ORIGINAL ARTICLE Avery, R. K. *et al.* An injectable shear-thinning biomaterial for endovascular embolization. *Sci. Transl. Med.* http://dx.doi.org/10.1126/scitranslmed.aah5533 (2016)
FURTHER READING Gaharwar, A. K. *et al.* Shear-thinning nanocomposite hydrogels for the treatment of hemorrhage. *ACS Nano* **8**, 9833–9842 (2014)