Vascular bleeding is currently resolved through invasive surgical repair or cauterization. An alternative is endovascular embolization, a procedure that uses a catheter to inject a material through the target vessel, which lacks refined precision to reach the target. No one procedure is ideal, but, based on surgeon preference, they represent the current state of the art. What if there was another way, a way that could save the vessel from these invasive techniques and ensure precision in reaching the target location? An investigational electroactive hydrogel was developed by a group of scientists and clinicians at Universities of Leuven and Ghent to achieve a non-invasive endovascular repair [occlusion]. Their effort is part of a larger drive towards developing electroactive polymers for treatment of cardiovascular disorders, supported through the effort of the European Union Seventh Framework Program [Heart-e-Gel Project].

So, there is a clear problem – bleeding must be stopped, while the current techniques are lacking effectiveness. Any solution requires a method of plugging the bleeding site, and the product should be able to conform to the required shape at the target location leading to a permanent seal. Further it should be easily delivered at location without loss of integrity or function.

Hydrogels have been considered strong candidates for developing such a product. Their swelling capacity in aqueous environments could render them ideal to achieving local occlusion. They are compact, which benefits their delivery at location. However, depending on the target location, if the hydrogel interfaces with fluids [such as blood], it instantly starts swelling. This could be a significant problem when extended time is required to reach a target site, as the process of swelling in route to location would render the hydrogel unusable. As a result, the Heart-e-Gel group investigated the development of an electroactive hydrogel that would conform to shape at location, and would employ an electrical stimulus responsible for decelerating expansion. The in vivo findings were reported in their publication entitled “An electro-responsive hydrogel for endovascular applications: an in vitro and in vivo evaluation” which is available as a free access article on our Journal’s website.

This elegant solution instigated a number of questions that the Heart-e-Gel group kindly agreed to address.

The era of “smart” hydrogels was ushered in some time ago. Various types of stimuli can be “paired” with monomeric recipes that would render the hydrogel responsive to pH, temperature, electric field, etc. Why was electro-responsiveness considered in this case? Dr. Verbrugghe clarified that electrical stimulation leads to several advantages in the hydrogel behavior in situ. Endovascular occlusion requires fine hydrogel shape adjustments. To achieve outcomes that require selective changes, a controlled stimulus is needed – control over electrical field can be achieved significantly more precisely compared to control over pH or temperature. A potential advantage addresses the need to achieve a controlled drug eluting profile if the hydrogel doubles as a drug delivery system. The electrical field could control the size of the exiting pores, thereby predictably controlling the drug release. As the field of sensor miniaturization expands, these capabilities could be embedded into the electroactive hydrogel to support healing/therapy at location by pairing the electroactive capabilities of the hydrogel to the function of the miniaturized system.

For colleagues who had a chance to read my latest Editorial on the state of translational research published in the October issue of our Journal, the next aspect I was curious to understand comes as no surprise – the choice of animal model. The authors selected an ovine model. Because of the endovascular occlusion application, the ovine model provided a closer understanding of how the electroactive hydrogel would respond in humans, especially due to the similarity in vessel size, and resemblance to the human coagulation system. Before the in vivo evaluation was performed, “in vitro testing of the swelling characteristics in a custom build mock circulatory system showed that the hydrogel was able to occlude arteries and resist pressure higher then physiological arterial blood pressure”.

Endovascular occlusion by electroactive hydrogels: the era of the “go happy” cauterization is coming to an end

Gabriela Voskerician, PhD
Further, I wondered about the “thin” toxicity evaluations that were performed by the Heart-e-Gel group. This work was reported as a preliminary study. Therefore, *in vitro* fibroblast cytotoxicity was the only biocompatibility evaluation reported.

The Heart-e-Gel group had recognized that cytotoxic evaluation of the hydrogel “building blocks” does not render the ready-to-implant product biocompatible. It was recognized that the size, charge, hydrophobicity, permeability and surface functionality will contribute to the overall biocompatibility. Previous work had qualified some of these hydrogel recipes cytotoxic right after polymerization, possibly due to unreacted monomers, oligomers and initiators after polymerization. This early finding was resolved through the implementation of a rinsing protocol post-polymerization.

The Heart-e-Gel group was elusive in terms of next steps in evaluating biocompatibility. Clearly, the current product development requires further refinement of several parameters that will impact the biocompatibility validation direction. I hope that this very talented group of scientists and surgeons realizes that it is never too early to determine the biocompatibility validation general plan to ensure accelerated translation of a solution that has tremendous practical clinical usability.

Returning to the science, Dr. Verbrugghe shared that the endovascular occlusion application represents only the first step. In this case, electroactivation was used to control swelling of the hydrogel en route to the target location. The electrical activation was achieved with a previously described solution of integrated electrodes. This technology could be extended to other applications such as aneurysm sac filling, sealing of paravalvular leakage, and theoretically any application requiring the “bulking” of an intravascular space. The pairing of miniaturized sensing/therapeutic systems with hydrogel electroactivation will create in the not so distant future an *in situ* “one stop shop” healing and therapeutic solution.

This work highlights the critical need in understanding the problem that is being solved – endovascular bleeding requires a system that plugs the rupture therefore stopping the bleeding. The value of understanding the premise onto which a solution is developed leads [usually] to a practical and adoptable application rather than the proverbial “square peg in a round hole” forced approach that ends up being clinically inapplicable. I would like to thank Dr. Verbrugghe and his colleagues for kindly agreeing to discuss their team’s findings beyond the confines of the published scientific work.

To our readers: I am looking forward to your comments that can be sent to gabriela.voskerician@case.edu using the heading “Editors’ Choice”. We hope to develop this feature into a dynamic forum think-tank.