Artificial blood vessel lets researchers better assess clot removal devices

April 17 2015

Researchers at the University of California, San Diego School of Medicine have created an in vitro, live-cell artificial vessel that can be used to study both the application and effects of devices used to extract life-threatening blood clots in the brain. The artificial vessel could have significant implications for future development of endovascular technologies, including reducing the need for animal models to test new devices or approaches.

The findings are published in the current online issue of the journal *Stroke*.

Cerebrovascular disease covers a group of dysfunctions related to blood vessels supplying the brain. Risk factors include hypertension, diabetes, smoking and ischemic heart disease. More than 6 million American adults are affected, with the number steadily growing.

When blood supply to the brain is significantly diminished or blocked, an acute stroke may result, requiring quick medical intervention to avoid permanent brain damage or death. More than 795,000 Americans experience a stroke each year; 130,000 die.

"Timely restoration of normal blood flow is absolutely critical," said Alexander Khalessi, MD, director of endovascular neurosurgery and surgical director of neurocritical care at UC San Diego Health System. "Clot-dissolving drugs like tPA (tissue plasminogen activator) help, but might not work sufficiently fast or fully in some situations. In those

cases, doctors must perform endovascular thrombectomies where they mechanically remove the emboli or clots."

The rate of endovascular thrombectomies is rising, but the approach, which typically involves running a catheter to the site of the blockage and using one of several marketed devices to remove the clot, can be improved, said Khalessi. For example, some patients experience negative consequences caused by either the mechanical removal of the emboli or by the restoration of blood flow, called reperfusion, specifically to the endothelial cells (ECs) that form the lining of blood vessels.

Current pre-clinical analyses of new therapeutic approaches or devices is limited to either in vitro glass or plastic tubing testing intended to mimic biological counterparts or by using animal models, such as pigs.

"Both of these have significant drawbacks. Although transparent and thus easier to study, glass and plastic tubing does not recapitulate blood vessel biology," said Khalessi. "In vivo animal models are more realistic, but we cannot directly observe the interaction between devices and ECs. Plus animals are not perfect models of humans and they are expensive to use."

Khalessi, along with co-author Shu Chien, MD, PhD, director of UC San Diego's Institute of Engineering in Medicine, and colleagues developed a novel in vitro live-cell platform that allows direct visual characterization of effects and injury patterns to ECs. Bovine artery ECs were perfused into optically clear, biocompatible tubular silicone with a thickness of 0.25 millimeters and inner diameters of 2.5, 3.5 and 4.5 millimeters.

The researchers then introduced porcine blood clots into the platform, allowing the clots to integrate, tested various clot-retrieval devices and examined the post-removal effects.

"We found that the in vitro platform permitted high-resolution quantification and characterization of the pattern and timing of EC injury with various thrombectomy devices and vessel diameters. The devices each displayed different effects."

The researchers subsequently validated their in vitro findings with in vivo testing.

"This work offers significant promise going forward," said Khalessi. "The live-cell artificial vessel enabled us to conduct detailed studies of the endothelium after thrombectomy, which may contribute to future device design. Animal studies confirmed the relevance of the platform, which suggests the artificial model could represent a practical, scalable and physiological alternative to existing technologies."

Provided by University of California - San Diego