Stents disrupt blood flow

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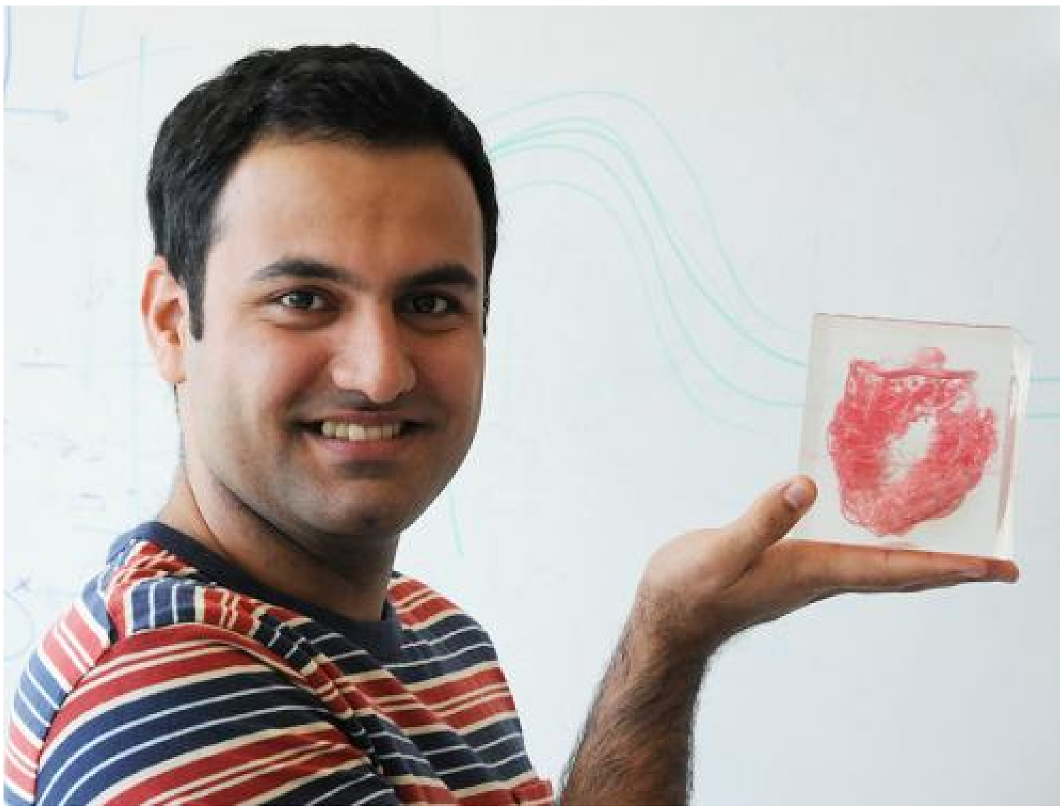

On the basis of such a model of a real pig's heart, Farhad Rikhtegar simulated how blood flows through an artery containing a vasodilatory stent. Credit: Peter Rüegg / ETH Zurich

(Medical Xpress)—A researcher at ETH Zurich is designing a realistic artery model with an implanted stent and is using a computer to simulate the blood flow through the stent. In doing so he is uncovering weaknesses in this common form of therapy for atherosclerosis and paving the way for the development of optimized stents.

Coronary arteries are susceptible to plaque that can lead to illness, a phenomenon known informally as a "hardening" of the arteries. The effect of this is narrowing of blood vessels. If a clot detaches itself in another blood vessel and does not flow through the constricted section, this prevents blood supply to the heart and can be dangerous or even fatal in some cases. The disease-induced narrowing of coronary vessels and related heart attacks are one of the most common causes of death in industrial nations.

Cardiologists use what are referred to as stents to open the closed-up vessels. Stents are tiny mesh tubes that are inserted into the bloodstream via the artery in the groin and placed in the constricted section. The doctors use a balloon catheter to expand the tube. This expands the blood vessel and the blood can flow through freely again. This method has saved the lives of many heart patients, but it does also have one disadvantage: in two of five patients, plaque and growths – referred to as "restenosis" – accumulate again at the place where the stent is located in the blood vessel, leading to a narrowing of the arteries once again.

Arteries on the screen

In order to understand the processes and the effects of stents in arteries better, Farhad Rikhtegar, a doctoral student from Professor Dimos Poulikakos' group at ETH Zurich has implanted a stent in a porcine coronary artery in a laboratory, rendered the real internal surface of the artery including the stent in visual form and in mathematical terms and reproduced it exactly. He also created a computer model of the blood flow in the region of the stent. The paper relating to this work was recently published in the journal *PloS One*.

Rikhtegar's computer models are realistic and achieve a level of detail that has never been seen before. Older models depicted blood vessels in a simplified manner and took into account only very simple clinical scenarios. However, the simulations by the ETH Zurich researcher are more complex and are based on real-life materials: porcine coronary arteries scanned at high resolution in which stents were implanted.

Stents eliminate shear stress

The simulations make clear that the tiny mesh-like strut connectors of a stent that lie against the wall of the blood vessel slow down the blood flow along these struts considerably. They also show that the blood in the tunnels formed by the stent struts can be "trapped" in vortices, which also reduces the speed of the blood flow in the vicinity of the stent.

Because of the slower blood flow, the shear stress that the blood flow exerts on the wall of the blood vessel decreases. Endothelial cells that cover the blood vessel can only carry out their function properly if the blood flow and thus the shear stress acting on them reach a certain average value. If this stress is too low, they allow more and more bad cholesterol into the vessel wall. This in turn leads to infections that result in atherosclerosis once again. It can happen that the artery narrows once again in the region of the stent.

Blind spots create a higher risk of restenosis

The simulations also show what can happen if a stent is poorly positioned and does not lie flat against the vessel wall. In such a case, "blind spots" occur between the stent and the blood vessel wall where the speed of the blood flow is also severely reduced, increasing the risk of restenosis.

Rikhtegar created further models where two stents, partially overlapping, were inserted into porcine arteries. The risk of restenosis is even greater when stents overlap than in the case of one individual stent. Evaluation of this data is not yet complete, however, and the doctoral student would like to publish the results in another paper.

Intricate methodology

Farhad Rikhtegar had to be quite creative with ideas on how to create the experiments and the related simulations. He created real-life conditions for the subsequent digitalization process using porcine hearts from the slaughterhouse. In collaboration with cardiologists from the University Hospital Zurich, he implanted the stents into the largest coronary artery. The ETH Zurich doctoral student then prepared the blood vessels by injecting them with resin. After the resin had hardened, he removed the tissue and thus obtained a three-dimensional sculpture of the blood vessels in the porcine heart.

This preparation method is not new. However, Rikhtegar optimized the method by developing a pump that pressed the resin into the veins using physiological pressure. He explained that he was still injecting the resin by hand in the first trials. But he exerted too much pressure when using this method, destroying the fine capillaries in the vessels. By contrast, automated injection of the resin into the heart vessels ensured that the detailed meshing of even the finest capillaries was retained.

Rikhtegar scanned this resin cast at high resolution with a micro-computed tomographer (CT) from Professor Ralph Müller's group. This gave him a precise digital presentation of the artery in the vicinity of the stent, through which he was able to allow blood to flow in computer simulations. Normal computed tomography used in clinics and hospitals does not have a sufficient resolution to depict the struts of the stent, which are just 100 micrometres thick. However, micro-computed tomography can provide resolutions for structures of just a few micrometres in size. This allowed Rikhtegar to also present the deformation of the blood vessel wall in a vertical and horizontal direction and to show the position of unfavourably positioned stents. Using the geometry of the vein area containing the stent as calculated by the micro CT images, the ETH Zurich doctoral student was able to carry out simulations for almost any scenario.

From aeronautics to medical applications

Rikhtegar explains that the work was quite a challenge. There was a specific method for each individual sub-step. In cooperation with the respective experts in the field, the aim was to optimize each of these sub-steps. "That took a lot of time", says Rikhtegar, who is originally an aeronautical engineer. For his dissertation, he had to acquire specific medical knowledge and learn the corresponding methods. "Now I can even insert stents into coronary arteries – it's not really that difficult", he grins. In order to carry out his work, he used around 80 porcine hearts that he was able to get from the slaughterhouse. He used these to test and optimize the different work steps. He then had 15 hearts for the scans and the simulations.

The method he has developed is a unique tool that allows for research into the relationship between hemodynamic factors and vascular biology. But the simulation can also be used to optimize the use of stents or to develop new forms of stents and test these on a computer.

More information: Rikhtegar F, Pacheco F, Wyss C, Stok KS, Ge H, et al. (2013) Compound Ex Vivo and In Silico Method for Hemodynamic Analysis of Stented Arteries. *PLoS ONE* 8(3): e58147. doi:10.1371/journal.pone.0058147

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