Stem cells build new blood vessels to treat peripheral arterial disease

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Bone marrow stem cells suspended in X-ray-visible microbubbles dramatically improve the body's ability to build new blood vessels in the upper leg—providing a potential future treatment for those with peripheral arterial disease or PAD, say researchers at the Society of Interventional Radiology's 35th Annual Scientific Meeting in Tampa, Fla.

"Bone marrow stem cells, which have the ability to renew themselves, could unlock the door to treat peripheral arterial disease (PAD) with cell-based methods. They offer a future novel method to help PAD patients by increasing the number of blood vessels to replace or augment those choked off by plaque buildup," said Frank Wacker, M.D., an interventional radiologist at Johns Hopkins School of Medicine in Baltimore, Md. "The future hope is to use adult stem cells extracted from a healthy donor's bone marrow and inject the cells into the patients' legs where circulation problems exist, stimulating the growth of new or more blood vessels in the leg, thus improving circulation," noted veterinary radiologist Dara L. Kraitchman, V.M.D., Ph.D. "Using an animal model, we found that stem cells in X-ray-visible microbubbles dramatically improve the ability to build new blood vessels when a blood vessel in the upper leg has been suddenly closed or occluded," said Kraitchman, an associate professor at Johns Hopkins School of Medicine. "With this treatment, the body was able to provide a more normal blood supply to the toes—possibly offering the hope of dramatically reducing—or avoiding—amputation. Treatment could also be personalized for individual patients," she added. Using X-ray

techniques performed by interventional radiologists, researchers viewed the new blood vessels and validated their results by examining the new vessels that formed via microscope, she said.

PAD, which affects about 10 million (mostly older) Americans, is a chronic disease that progressively restricts blood flow causing poor blood circulation (generally in the legs) and—if left untreated—can lead to serious medical complications, including heart attack, stroke, amputation and death. Many people can manage the symptoms of PAD and stop its progression through lifestyle changes. If lifestyle changes are not enough, additional medical treatment may be needed, including prescribed medicine to prevent blood clots, lower blood pressure and cholesterol and control pain. Interventional radiologists treat severe cases of PAD with minimally invasive treatments, including angioplasty and insertion of stents. "About 10 percent of the PAD patients cannot be treated with typical methods to reopen the arteries, such as angioplasty or stents," said Wacker.

Because many treatments like stenting are done using X-rays, this microbubble stem cell treatment could be performed when an interventional radiologist is performing a dye study to look at a patient's arteries. Since an interventional radiologist can see where he or she puts the stem cells and whether they remain in the leg, the stem cells could be administered potentially where they can do the most good. The treatment could be repeated, if needed.

Hopkins researchers used a technique that encloses stem cells derived from bone marrow (not embryonic stem cells) in an alginate capsule or microbubble made from seaweed that contains stem cells to create factors to recruit the building of new vessels along with an X-ray-visible contrast agent. Tested in a rabbit model, the bubble prevents the body's immune system from reaching and attacking the transplanted cells. They not only made the stem cells X-ray visible, but they also made the stem

cells themselves visible much like the way a firefly's light is visible at night, said Kraitchman. Because the microbubble protects the stem cells from being destroyed even if they come from another person's bone marrow, there is the potential to provide this therapy similar to blood transfusions. Like blood transfusions, one cannot anticipate which PAD patient will need stem cells, so there may not be time to harvest a person's own stem cells in advance for treatment, said Kraitchman.

"We are continuing to test the treatment in animals and attempting to perfect methods using non-invasive imaging, such as magnetic resonance imaging (MRI), ultrasound and blood pressure measurements, which could be used to follow up patients without exposing them to X-rays or needing to enter a blood vessel to inject dye to see the newly formed vessels," said Kraitchman. "We are also fusing the X-ray imaging results with other imaging techniques like MRI to provide a better picture of where to place the stem cells," she added.

Provided by Society of Interventional Radiology