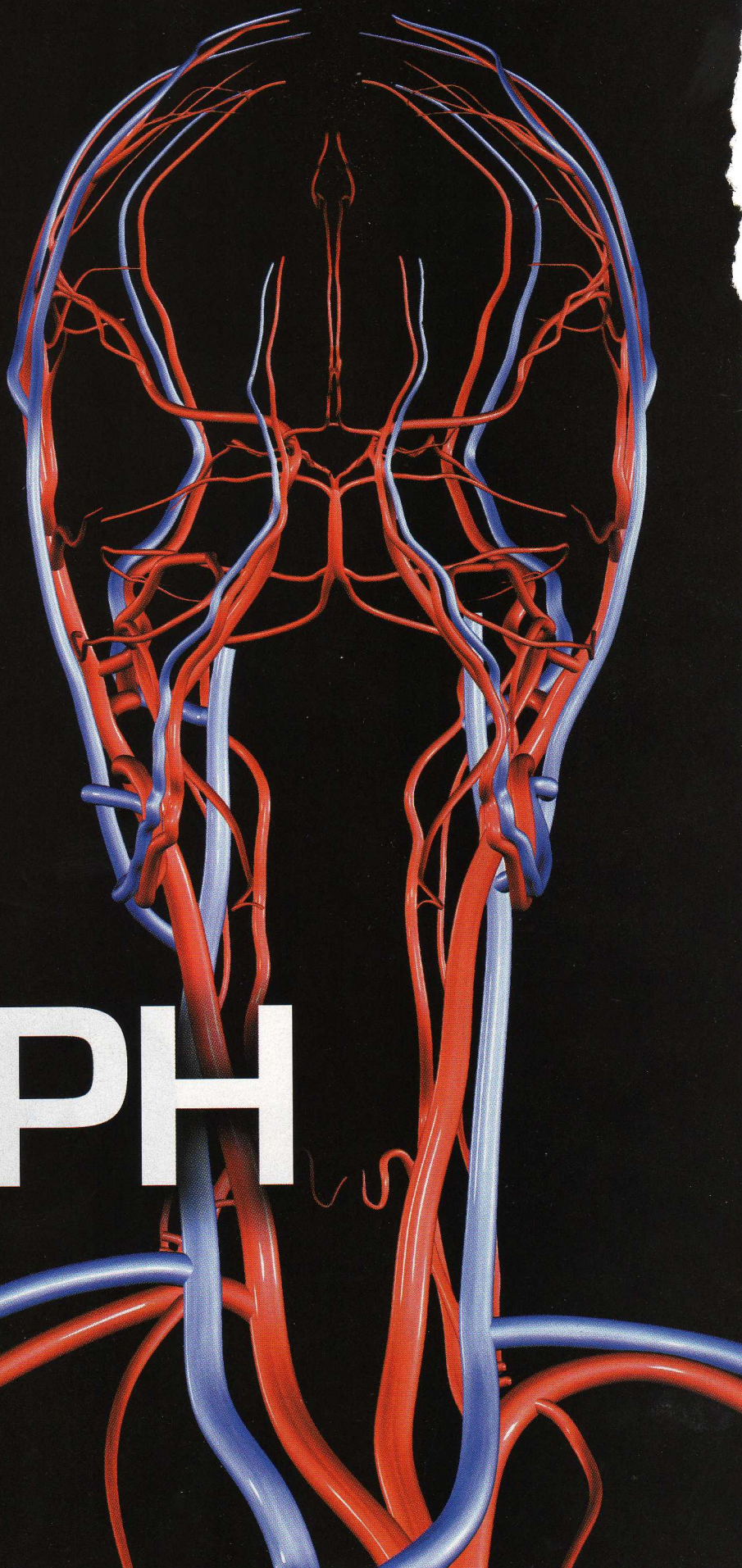


It may look like a license plate number, but 3D MRIPH may someday provide a new vascular imaging tool to predict and prevent stroke and heart attack.

3D MRIPH

New Vehicle for
Vascular Imaging



Organic entities function with a strong will to survive, a biologic pattern evident in the human body. But the manifestation of this law isn't restricted to larger complex entities, nor is it always considered positive, as in the case of cancer tumors forming in the body that can develop life-sustaining vascularity, a capability that often complicates a cure.

Recent medical research has revealed that the same process is present within the atherosclerotic plaque that arises from vessel wall damage. This discovery has profound significance and implications. Vessel wall damage that occurs over time, fostered by factors such as smoking, high cholesterol, and diabetes, and within certain sites (eg, in places of turbulent flow and bifurcation, as in the carotid and coronary vessels) can lead to worst-case scenarios such as strokes and heart attacks.

For many years, scientists and clinicians working in the cardiovascular and neurovascular arenas believed that blood vessel stenosis was the main cause of thromboembolic events leading to the aforementioned conditions. However, it's a bit more complicated. Ongoing research indicates that it is the plaque composition, rather than the stenosis, that leads to these life-threatening events.

"We now understand that vessel wall disease and resulting atherosclerotic plaque, in a sense, works like a minitumor," says radiologist Alan R. Moody, FRCR, FRCP. "That is, once disease starts to grow and the vessel wall thickens, plaque begins developing its own internal blood supply in the form of microvessels. As within a tumor environment, new and fragile vessels develop."

As these developing vessels are frail, they're vulnerable to leakage. "In other words, they can bleed," says Moody, radiologist-in-chief in the medical imaging department at Sunnybrook Health Sciences Centre in Toronto.

This bleeding leads to substantial problems: The proatherogenic process promotes the progression of atherosclerosis. "When bleeding occurs, a number of things can happen. First, the blood is very inflammatory, which compounds the entire inflammation process occurring within the plaque," Moody explains. "In turn, this causes plaque progression and leads to more acute problems like stroke and heart attack."

Problematic Composition

Medical research and advanced imaging technology not only reveal these circumstances but also contribute to greater understanding of the specific issues involved. "Now, we realize that composition can better predict future events than the degree of vessel stenosis," says Moody.

Of course, stenosis is a major factor in stroke

occurrence, but Moody points out that strokes occur when lesser degrees of stenosis are present. "That told us that something else must be going on that triggers the thromboembolic event that causes the stroke," he says. "In the last five to 10 years, researchers have determined that it is something within the plaque itself, and this ties in with the idea of composition and vulnerable plaque."

Composition relates to plaque characterization that can include ulcerations of a vessel's surface, blood clots, and wall bleeding. The microhemorrhaging present in the vessels can lead to plaque rupture, which emits an unhealthy discharge of microscopic debris into the bloodstream. These discharges can lead to clots that could position themselves in precarious locations, such as in a vessel that supplies blood to the brain—a blockage that likely results in a stroke.

Imaging technology not only unmasked the problem; it also provided an effective tool for dealing with the critical circumstances. This was underscored by a recent study conducted by Moody and colleagues at the Sunnybrook Health Sciences Centre. They used an advanced MRI technique that accurately depicts hemorrhages within the walls of compromised arteries. The technique is called 3D MRIPH, an acronym that specifically indicates 3D MR imaging applied to intraplaque hemorrhage (IPH), a condition common in advanced coronary atherosclerotic lesions.

Exported Expertise

Moody developed the technique while working in England, and he exported it to Canada when he transferred to the Sunnybrook facility. The technique, he points out, can detect disease within a blood vessel before significant stenosis develops, and it reveals the plaque danger level and the vulnerability of plaque rupture. Essentially, by bringing the technique to North America, Moody provided a new set of clinicians with a new cache of information they never had.

"The original publication about the technique came out in about 2003, and it involved a 3D, T1-weighted, fat-suppressed technique similar to what we now use," says Moody. "However, we have taken the technique to a higher resolution level that allows us to more effectively localize the IPH."

Now, the technique's high-spatial resolution 3D sequence depicts complicated plaque in carotid arteries, and its wide-ranging field of view helps physicians accurately measure the full extent of the disease. More specifically, 3D MRIPH generates 3D images of the artery and reveals bright signals in blood vessel areas where there are hemorrhages in plaque deposits.

In addition, the technique is easy to use and interpret. Further, it helps clinicians detect artery wall bleeds. In the future, it may

be used to screen patients at high risk for stroke, as well as monitor the impact of interventions deployed to slow progression of atherosclerotic disease.

The aforementioned study, published in the October issue of *Radiology* ("In Vivo 3D High-Spatial-Resolution MR Imaging of Intraplaque Hemorrhage"), applied 3D MRIPH to image carotid arteries of 11 patients (ranging in age from 69 to 81). The researchers also compared the results of 3D MRIPH with those of microscopic analysis.

Histologic Comparison

The purpose of the study was to apply 3D MRIPH and compare it with histologic analysis "as the reference standard to detect the T1 hyperintense intraplaque signal and to test the hypothesis that T1 hyperintense material represents blood products (methemoglobin)," wrote Moody, the lead researcher and primary author.

The study's 11 patients were undergoing carotid endarterectomy, surgery to remove plaque from the lining of a carotid artery that had thickened or suffered damage and to restore blood flow. The patients were referred for the evaluation of symptomatic or asymptomatic carotid artery stenosis. They also had undamaged endarterectomy specimens (ie, specimens that were circumferentially removed with the plaque remaining as one piece and that could be sliced), according to researchers.

As part of their workup, the patients underwent MR direct thrombus imaging performed with GE Healthcare's 1.5T TwinSpeed MR unit and USA Instrument's eight-channel neurovascular phased-array coil.

The imaging technique's high spatial resolution enabled the researchers to noninvasively analyze tissues within the artery wall and to identify small hemorrhages present in rupture-vulnerable plaques that could have placed patients at risk for future events such as stroke, Moody says. For the MR imaging of hemorrhage, researchers used a free-breathing, 3D, T1-weighted, fat-suppressed spoiled gradient-echo sequence, which allowed them to identify patients with complicated plaques (ie, plaques with hyperintense T1 signal and presumptive IPH).

Complicated plaques found in diseased arteries were then surgically removed for microscopic analysis. Subsequently, the researchers observed a strong concurrence between lesions identified by MRI as complicated plaques and the histologic analysis of tissue samples. In other words, areas revealed by the MRI technique corresponded with areas of plaque buildup when surgeons performed carotid endarterectomy.

Moody and colleagues concluded that the study resulted in successful application of a "high-spatial-resolution 3D MR sequence specifically designed to depict complicated plaque in the carotid arteries, as compared with a histologic reference standard, thereby confirming its ability to depict T1 hyperintense IPH, as compared with a histologic reference standard."

Further, "The combination of a 3D high-spatial resolution acquisition and extended coverage [allowed] full assessment

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of complicated carotid plaque." This noninvasive assessment, they continued, provides a technique that can be used in the longitudinal study of high-risk atherosclerotic disease of the carotid arteries.

"What we've done so far strongly suggest that 3D MRIPH indicates future events," says Moody.

Patient Care Implications

As far as the healthcare implications, 3D MRIPH provides clinicians with a good deal more information about diseased arteries—enough information to potentially offer a new imaging standard.

Also, along with making it easier to noninvasively identify those patients with high-risk carotid atherosclerotic disease, the 3D MRIPH application can play an important role in clinician intervention, as well as stabilizing atherosclerotic plaques, as the paper relates.

"Up until recently, the primary biomarker for predicting stroke, focusing on the carotid vessels, was stenosis. Patients needed to have a 70% stenosis before they could be considered a candidate for surgery. But vascular biology has also revealed that a huge amount of disease occurs before someone reaches that 70%, which is why a lot of people end up with strokes or heart attacks. Simply stated, visualizing the lumen is a very insensitive way of looking at the disease. We needed to look at the vessel wall itself," explains Moody.

Future Research Directions

Of course, the Sunnybrook study was restricted to one site and a small patient cohort, but the researchers will be collaborating with other scientists and clinicians through a recently established network.

"We've created the Canadian Atherosclerosis Imaging Network, which encompasses about 20 sites around Canada,"



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explains Moody. “As the name suggests, we will now be studying atherosclerosis throughout Canada, specifically within two vascular beds: the coronary and the carotid. Within that network, we’re setting up a site that allows for the exchange of images and patient recruitment, among other things. We will also perform multicenter studies that involve as many as 250 to 300 patients over the next several years.”

Future studies may entail 3D MRIPH to evaluate the natural history of hemorrhage within the plaque. Also, according to the researchers, MR imaging of IPH potentially could be used to acquire IPH volumes and total atheroma burden measurements more accurately, “with the potential to monitor the effects of interventions on atherosclerotic plaques.” They also indicate that differences in the location of IPH among patients with a symptomatic carotid artery and those with an asymptomatic carotid artery “may allow a better understanding of why a plaque becomes symptomatic.”

In addition, imaging the same patients at different times would enable evaluation of the reproducibility of this technique to image IPH, the researchers point out.

Moody says the Sunnybrook study will be placed as one of the first studies entered into the network. Researchers in subsequent studies will look to reproduce, in larger context, the results of the Sunnybrook study, particularly as far as outcome and predictability related to IPH. This will help provide answers to ongoing questions about risks of stroke in patients with the complicated plaques and the need for surgery.

As the researchers move forward, they will be better able to determine how 3D MRIPH can be used in clinical practice. “In the clinical setting, it has the potential to be a valuable tool to further improve stroke prevention,” says Moody.

He adds that researchers will also try to translate the same technology for the coronary artery. “That’s assuming that the coronary artery has similar pathobiology with IPH, which we know is the case,” says Moody. “But as it will take us from the carotid, which is a large vessel, that is superficial and standing still, to the coronary vessel, which is small, deep, and moving around, there will be technical challenges. But, as we’ve seen with cardiac MR, such challenges can be overcome, and this is an area of particular interest for us.”

— Dan Harvey is a freelance writer based in Wilmington, Del., and a frequent contributor to *Radiology Today*.