Gadofosveset is a new MR contrast agent with an intravascular half-life of about 28 minutes, which allows steady-state contrast-enhanced MR angiography for up to 1 hour after administration of the contrast material.

Contrast-enhanced MRA with gadofosveset allows the acquisition of high-resolution images of the vasculature in any part of the body, comparable to those from CTA.

Contrast-enhanced MRA with gadofosveset is valuable for the evaluation of the entire vasculature with adequate differentiation of arteries and veins.

Because gadofosveset has high relaxivity and high MR signal, the dose needed is approximately one-third that of commonly-used MR contrast agents.

**Figure 1.** (A) MRA using gadopentate digluimine (Magnevist®) at a dose of 0.1 mmol/kg. (B) MRA images of same patient, who returned for follow-up imaging one year later, using gadofosveset (Ablavar®) at a dose of 0.03 mmol/kg. Note the brighter contrast and improved detail in small blood vessels (arrows), seen in B.

Although there are a number of long-established methods of imaging the vasculature, all of these methods have some drawbacks. Catheter-based digital subtraction angiography (DSA) is regarded as the gold standard, although it is invasive and has largely been replaced by less invasive methods. CT angiography (CTA) provides high resolution images but involves radiation exposure and use of iodinated contrast materials, which can cause allergic...
reactions in some patients and are not well-suited to patients with poor renal function. MR angiography (MRA) does not necessarily require contrast but contrast-enhanced MRA (CE MRA) is more commonly used because it is faster and it is less dependent on blood flow. A major limitation of CTA and CE MRA is that the standard contrast materials readily pass through the walls of the vasculature (except in the brain) and, therefore, images must be acquired during the first pass of the contrast material through the circulatory system. Timing of image acquisition can be a major challenge in those with vascular disease or cardiac dysfunction. Given the short intra-vascular presence of these contrast materials and the limited time window to obtain high quality images, the dose of the most commonly used contrast material for CE-MRA, gadopentate diglumine (Magnevist), is often two to three times higher than that used for non-vascular applications of contrast-enhanced MRI.

Gadofosveset trisodium (Ablavar) is a new contrast material (originally developed in the MGH NMR Center by Randall Lauffer, PhD) that was approved for MR angiography in Europe in 2005 and by the FDA in 2010. Gadofosveset reversibly binds to serum albumin, forming a complex that remains within blood vessels, thereby increasing the time window for image acquisition. In addition, the large molecular size of the complex increases the magnetic resonance relaxivity and, therefore, results in higher signal strength. For this reason, the dose of gadofosveset needed for contrast enhancement (0.12 mL/kg body weight or 0.03 mmol/kg of body weight) is one-third of that standard MR contrast materials in non-MRA applications or 11-33% of that used in CE MRA (Figure 1). Gadofosveset is excreted at a comparable rate to gadopentate diglumine, primarily by the kidneys, with 94% excreted in the first 72 hours after administration.

The combination of high signal strength and long circulation time is particularly advantageous for assessing vascular disease because it is possible to image the vasculature during the steady-state phase, obviating the need to time image acquisition precisely to the expected arrival of the contrast in the blood vessels of interest. The time window for image acquisition is longer, which allows for acquisition of high-resolution isotropic images of 1 mm³ or less, comparable to those obtained by CTA. Moreover, gadofosveset-enhanced MRA images are not marred by calcium-containing plaque, which can pose problems for CTA, nor is there any exposure to radiation. Imaging acquisition is generally performed in the coronal plane and reformatted to obtain high quality images of other planes. The ability to achieve isotopic imaging avoids the problem of superimposed arterial and venous structures on mean intensity projections, which can occur with lower resolution MRA images.

Figure 2. Gadofosveset-enhanced arterial MRA of lower extremities in a patient with symptoms of claudication. MIP reconstruction of dynamic first pass imaging using gadofosveset demonstrates occlusion of the right tibioperonal trunk.
Note that the regular contraindications to MRI apply (see MRI Safety, RadRounds, February 2005). Although no cases of nephrogenic systemic fibrosis have been linked to gadofosveset, its use is contraindicated in patients with poor renal function (eGFR < 30 mL/min/1.73m²) unless the diagnostic information is essential and not available with non-contrast enhanced MRI or other modalities.

Gadofosveset-enhanced MRA is suitable for all vascular imaging and has specific advantages in certain applications. Generally, images are acquired during the first pass of the contrast material when the contrast material is in the arteries only, followed by steady-state imaging 5-10 minutes after contrast material administration. If technical problems occur or if patient motion results in poor quality images, steady state imaging may be repeated. The following are a few examples of vascular imaging using gadofosveset that illustrate its advantages over other imaging techniques.

**Peripheral Vascular Disease**

Whole body MRA using standard contrast materials has been accepted as an alternative to digital subtraction angiography for treatment planning in patients with peripheral arterial disease. During whole body MRA, images are acquired at several stations, covering the thoracic and supra-aortic vessels, the abdomen and pelvis, and the lower extremities. However, timing is crucial if standard contrast materials are used because images must be acquired during the first pass of contrast through the vasculature; if acquisition is too early, it causes artifacts, and if too late, it results in venous contamination and poor arterial visualization.

CE MRA with gadofosveset provides a solution to such problems because it is possible to image in the vasculature through a technique called steady-state imaging after a single injection of gadofosveset. Because of the longer time period available for imaging, high-resolution images can be acquired which allow the separate visualization of arteries and veins (Figure 2). This is possible, even when the vessels are of small caliber, by imaging with voxels of 0.50.7 mm. For example, in one study that compared the sensitivity and specificity of gadofosveset-enhanced whole body MRA with DSA, the sensitivity of combined first pass and steady-state imaging of the lower leg was 0.81 (CI 0.60.93) compared to 0.42 (CI 0.230.63) with first-pass imaging alone. The specificity of both techniques was comparable at 0.94.98.

**In-stent Restenosis**

Although the symptoms of peripheral artery disease can be alleviated with stenting, it is a progressive disease. If symptoms reappear, it is essential to differentiate between in-stent restenosis and de novo lesions. Although CTA has been shown to be accurate for this purpose, markers at the proximal and distal ends of the stent can cause blooming artifacts and impaired visualization in some cases. MRA using gadofosveset has very high accuracy, especially for large non-ferromagnetic stents, compared with DSA and is has limited vulnerability to susceptibility artifacts caused by stents.

**Arteriovenous Malformations**

The long intravascular half-life and high contrast-enhancement of gadofosveset makes it well-suited for time-resolved imaging of blood flow, which is advantageous for evaluating lesions such as arteriovenous malformations (AVMs) especially during therapy planning. First pass imaging using time resolved MRA technique helps to distinguish simple and complex AVMs as well as slow arterial flow and high flow vascular malformations (Figure 3). Late dynamic and steady-state imaging can show the complexity of venous drainage of the vascular malformation.
Varicosities
In some cases, extremity varicose veins may persist despite adequate therapy with radiofrequency or laser ablation of the saphenous veins. Multiple factors may contribute to the treatment failure, for example, incompetent dilated perforator veins that allow reversed blood flow, filling the varicosities. Perforator veins may not be easily detected by ultrasound. However, they can be readily visualized by gadofosveset-enhanced MRA (Figure 4).

Conclusion
Gadofosveset has been available for clinical use for a short period of time and has only bee in use at the MGH since July 2011. Therefore, the potential applications of this new contrast material are yet to be fully explored. These examples given above are just a few of the possible uses. Several other vascular imaging applications have been explored and may be superior to currently accepted practice. Other applications, such as perfusion imaging of tumors are currently experimental and may prove to be valuable.

Further Information
For more information about contrast enhanced MR angiography, please contact George Oliveira, MD, or Sanjeeva Kalva MD, FSIR, Vascular Radiology, Mass General Hospital, at 617-726-8315.

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References


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