

# Application of MR technology to endovascular interventions in an XMR Suite

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Figure 1. ▲

The XMR suite at the University of California – San Francisco. The Integris V5000 catheterization laboratory (foreground) is collinear with an Intera I/T MR scanner (background), permitting easy patient transfer via a floating tabletop. The rooms are separated by an eight-foot wide (2.4 m) pneumatic door, allowing the two systems to be used independently or in combination.

Endovascular interventions provide the opportunity to deliver therapy efficiently, and in a minimally invasive fashion. Traditionally, these procedures have been monitored in a catheterization laboratory, where X-rays are used to visualize the endovascular devices and the vessel lumens.

The latter is typically achieved via the injection of iodinated contrast media, and subtraction techniques are employed to remove overlying bony structures. This methodology has proven to be extremely successful, and currently well over a million inpatient cardiac catheterizations alone are performed on an annual basis in the United States [1].

X-ray procedures, however, suffer from limitations, including their extremely limited ability to visualize soft tissue, and the presence of ionizing radiation. Radiation concerns are paramount for pediatric populations, as lifetime risks associated with such exposures are substantially amplified above

those of middle-aged adults [2]. Such concerns recently instigated the Food and Drug Administration (FDA) of the United States to issue a Public Health Notification, urging hospitals to take steps to reduce dose in pediatric CT exams [3].

Radiation exposure during catheterization ranges widely, but can substantially exceed that received during other procedures [4]. Clearly, these concerns are further heightened in patients requiring multiple procedures or undergoing particularly long or difficult interventions. While the inherent benefits of the performed procedures are likely to well outweigh the radiation risk, the possibility of performing the same or similar procedures as effectively and without ionizing radiation is very appealing. In addition, sensitivity to the cumulative effects of occupational radiation exposure is a growing concern for many clinicians.

Magnetic resonance (MR) technology operates without ionizing radiation, and features many benefits relating to its ability to characterize soft tissue and make functional assessments. These properties open doors for new therapeutic possibilities by directly determining the impact of endovascular interventions via their effect on the end organ.

Historically, MR has not been considered as an alternative imaging modality for catheterizations, primarily due to its relatively slow image acquisition and the closed nature of the magnets. However, the continued development of MR hardware for faster image acquisition and reconstruction rates, along with methodological developments such as SENSE [5] and fully refocused steady state imaging, now makes truly real-time MR imaging both possible and practical. The continuing trend towards shorter and more open magnet technologies is also lowering the barriers towards a role for MR in endovascular therapy.

In 2001, the University of California – San Francisco opened a unique interventional suite (Figure 1) coupling a fully functional X-ray

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catheterization laboratory (Integris V5000) with a 1.5 T short-bore MR system (Intera I/T) [6]. Its hybrid nature, which is termed XMR, permits endovascular procedures to be performed in a conventional fashion but augmented with MR data, or permits part or all of an endovascular procedure to be performed under MR guidance while having the X-ray cath lab as an easy fall-back position. This paper describes the initial application of such a system to endovascular therapy.

## Clinical applications

Initial clinical applications have necessarily focused on therapies that may be augmented by MR data but do not necessarily require direct MR guidance. Direct MR guidance requires endovascular devices that have been customized to be safe and easily visualized in the MR environment. Such devices are still in the developmental stages and are discussed in more detail below in the section on Developmental Applications.

Initial clinical applications have included comparative studies, where MR angiography (MRA) techniques were assessed against diagnostic X-ray procedures, and clinical procedures where MR data enhanced a conventional therapeutic procedure. In the former cases, the MRA data often proved sufficient, obviating the need for a subsequent purely diagnostic catheterization procedure. The following applications are examples where MR data has been integrated into an existing clinical procedure.

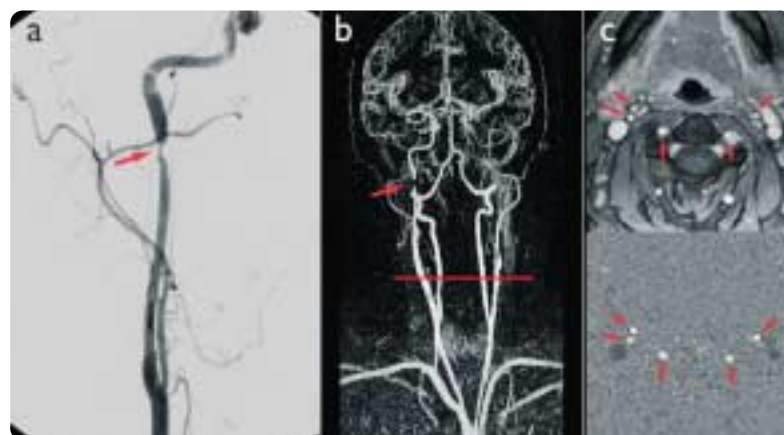
### Carotid stenting

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Stenting of the carotid artery is becoming an increasingly popular alternative to carotid endarterectomy as a therapy for moderate to severe atherosclerotic disease [7, 8, 9, 10]. In many cases, stenting is the only viable alternative because the lesion cannot be accessed from an operative approach.

Concerns remain regarding the effect of such therapy, most notably the release of microemboli to distal brain tissue. MR can potentially augment such procedures with information on the status of

the plaque, flow conditions within neck vessels, and the presence or absence of regions of distal ischemia. Correlation of this data with the eventual outcome of the procedure may provide key insights regarding what circumstances are most amenable to stenting over endarterectomy.



▲ **Figure 2.** Baseline scans performed on a patient with a focal narrowing of the internal carotid artery (arrow in a and b). Correspondence between X-ray angiography (a) and MR angiography (b) was very good, but with MR tending to overestimate the degree of stenosis. Quantitative flow measurements were acquired at several different levels prior to and following stenting. Shown are the magnitude (c, top) and phase (c, bottom) images taken just superior to the right carotid bifurcation (level marked on b). The carotid and vertebral feeding vessels are marked on these two images (arrows).

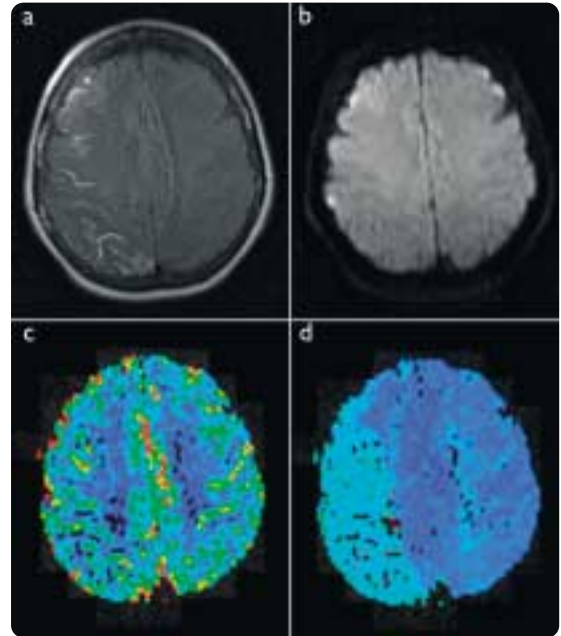
To date, eight patients with disease of the internal carotid artery (ICA) have undergone carotid stenting augmented with MR data (Figure 2). Prior to and immediately following therapy, MR flow assessment of carotid and vertebral arteries was performed, along with brain perfusion, atheroma assessments and diffusion imaging. CE-MRA was also acquired and compared to 3D rotational X-ray angiography (3DRA), which was performed at the time of intervention. Stent (Smart Stent, Cordis, Warren NJ) delivery was performed in a conventional fashion under X-ray guidance.

When severe stenosis was present in the ICA, stenting of the lesion resulted in a substantial increase in flow (from  $1.4 \pm 0.9$  ml/heart-beat to  $4.6 \pm 8$  ml/heart-beat) as demonstrated by quantitative MR flow data. Two of the patients were treated for other conditions (fibromuscular dysplasia, dissection) and exhibited little volumetric flow change. Perfusion and diffusion assessments did not reveal foci of acute ischemia immediately following therapy in any of these patients. CE-MRA was found to reliably reflect the location and extent of stenotic disease, although it tended to overestimate the severity of stenosis and underestimate vessel diameters.

**MR's ability to characterize soft tissue offers new therapeutic possibilities.**

Figure 3. ▶

MR assessment of a patient with an aneurysm of the right internal carotid artery. Contrast enhanced turbo-FLAIR (a), diffusion (b), perfusion cerebral blood volume (c) and time-to-peak (d) images were all evaluated before and during test occlusion of the right internal carotid. Enhancement of the right hemisphere in the watershed territory occurred only during occlusion (a). No changes were detected in diffusion images or CBV maps. TTP arrival delays in the affected hemisphere averaged 1–2 seconds during occlusion, which was slightly shorter than when the aneurysmal vessel was patent.



The balloon test shows whether there is sufficient collateral circulation.

### Balloon test occlusion of the carotid artery

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Patients with pathology (tumor, aneurysm etc.) intimately associated with their carotid artery may need to have the artery sacrificed as part of their therapy. Under such circumstances it is necessary to determine whether they have sufficient collateral circulation to tolerate arterial sacrifice, or whether a surgical extracranial to intracranial (EC/IC) bypass must be performed. To test this, a temporary occlusion of the carotid artery is achieved by endovascular inflation of a balloon in the affected artery [11]. Typically, these patients are monitored for neurological performance over a 30–60 minute examination period to determine their tolerance for loss of this vessel.

MR may be a valuable tool for detecting subclinical ischemia during temporary occlusion of the carotid artery [12]. We have been performing baseline perfusion, diffusion, post-contrast turbo-FLAIR and flow measurements prior to occlusion and then repeating these measures during balloon inflation (Figure 3). Conventional diffusion-weighted scans ( $b = 1000 \text{ s/mm}^2$ ) have not demonstrated perceptible changes during inflation: an effect that was unlikely considering the short time scales associated

with test occlusions. Post-contrast turbo-FLAIR acquisitions, however, have demonstrated pial enhancement in brain parenchyma distal to the occluded carotid artery in some instances. First-pass perfusion imaging further allows quantification of perfusion delays associated with collateral perfusion, as well as elucidating hemispherical differences in blood volume and flow levels. The combination of these acquisitions may eventually provide additional parameters from which an improved determination of tolerance to carotid occlusion may be assessed.

### Localized chemotherapy delivery

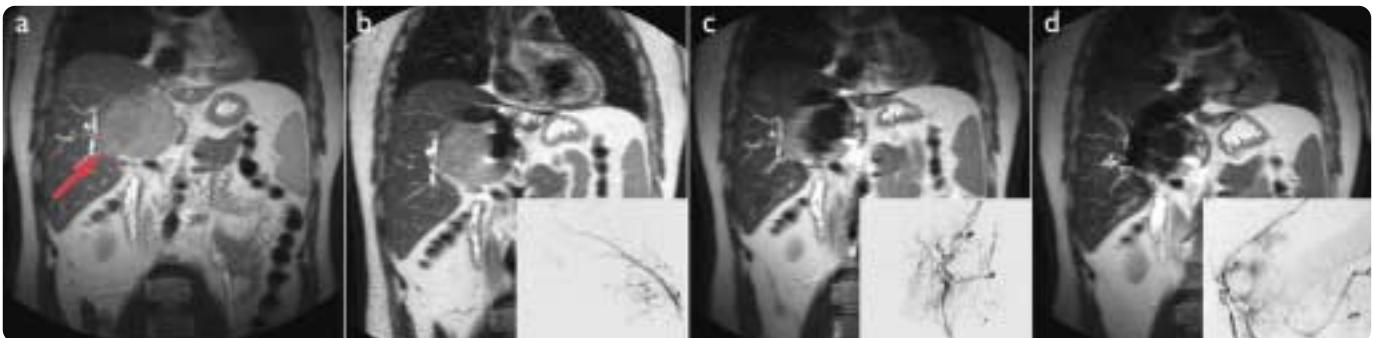
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Localized delivery of drug therapy offers substantial potential benefits over systemic delivery, including more effective local therapy and the potential for fewer or less severe side effects. For optimal transcatheter endovascular delivery, however, one must be able to appreciate both the vascular structure and the soft tissue in which it sits. An XMR envir-

MR can show the distribution territory of endovascular chemotherapy.

Figure 4. ▼

Prior to catheterization, baseline T2-weighted MR images (a) delineate the extent of this hepatic lesion (arrow). An initial feeding vessel was selected under X-ray fluoroscopy (inset in b), the agent was injected, and the patient was then returned to MR to determine its distribution volume (b). The procedure was repeated twice (c, d), producing near complete coverage of the lesion.



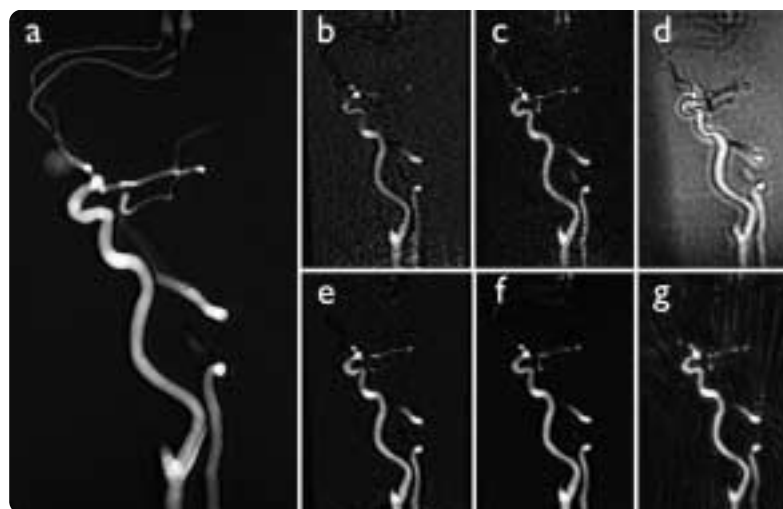
onment is ideal for such procedures, and we have been exploring the delivery of an iron-tagged chemotherapeutic agent (MTC-DOX, FeRx Inc, San Diego, CA) in patients with liver carcinoma. The iron content of this agent creates a susceptibility artifact that manifests as a region of signal loss on MR images.

Patients in this study receive a pre-procedure MR examination (axial and coronal single-shot T2-weighted TSE, post-contrast T1-weighted TSE spin echo) and are then moved to the Integris V5000 for catheter placement. A vessel feeding the tumor is selected and used to deliver a portion of the chemotherapeutic agent. The patient is then immediately returned to the MR. The T2-weighted TSE sequences are repeated, and the distribution territory of the agent can be directly inferred. By iteratively delivering the chemotherapeutic agent under X-ray angiography, and assessing its distribution territory with MR (Figure 4), it has proven possible to optimally deliver the agent to the tumor while minimizing its exposure to healthy liver parenchyma. In the XMR suite this is possible within a single procedure.

## Developmental applications

There remains considerable work before MR can move from the role of augmenting endovascular interventions to being used to directly guide all aspects of the therapy. The endovascular device industry has developed numerous sophisticated devices for transcatheter delivery of therapy under X-ray guidance. Unfortunately, ferrous components and long conductor lengths, both of which pose safety and imaging problems with MR, limit the direct application of these devices to the MR environment [13].

In order for MR to be considered as a practical clinical alternative, it is imperative that these devices be adjusted to optimize their safety and utility in an MR environment. Such steps, however, must be motivated by the demonstrable abilities and benefits of MR. Accordingly, investigational studies aimed at performing endovascular interventions with MR, and utilizing early prototypes of MR compatible devices, are currently being undertaken in animal models. The following is a brief overview of some of these projects currently underway at UCSF.



▲ **Figure 5.** MR fluoroscopy performed on an anthropomorphic phantom of cerebral circulation containing saline or a 1 % Gd-DTPA solution. A high-resolution reference image (a, 30 s acquisition FFE) is shown for comparison. Fluoroscopic acquisitions (b–g) all featured a 100 ms acquisition time but varied in scan technique, resolution etc. Shown are the results for an FFE (b), FFE-EPI (c) and spiral (d) acquisition in saline and a T1-FFE (e), b-FFE (f), and radial b-FFE (g) acquisition in a 1 % Gd-DTPA saline solution.

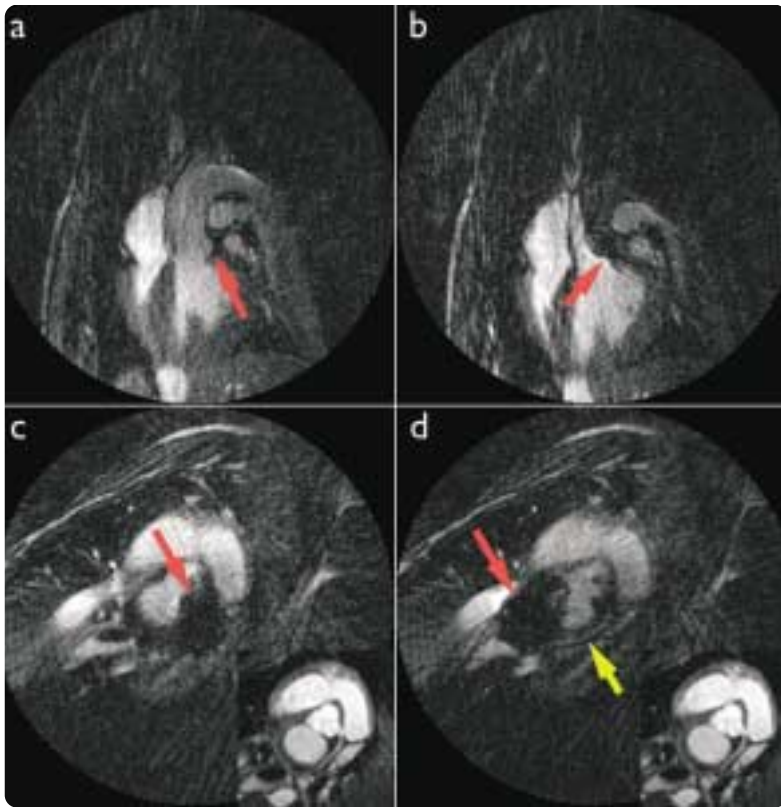
## MR fluoroscopy

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Real time imaging (> 10 fps) is mandatory for guiding most vascular interventions. In addition to temporal resolution, this imaging must achieve sufficient resolution, signal and contrast to accurately depict the anatomy of interest. We evaluated a number of different MR protocols, including spoiled and unspoiled gradient echoes, gradient echo EPI, steady-state techniques, and radial and spiral acquisition schemes, for their suitability for MR fluoroscopy of the vasculature. All acquisition schemes were optimized for a 100 ms acquisition time, and utilized a SENSE factor of two where possible (Cartesian acquisitions). The protocols were evaluated on an anthropomorphic phantom of the cerebral circulation, in which the vessels were filled with either saline or a 1 % Gd-DTPA saline solution. The results of this study (Figure 5) indicated the superiority of steady-state acquisitions (balanced FFE) independent of the presence of contrast, while reinforcing the need for contrast with rapid gradient echo imaging. Contrast had a strongly negative impact on EPI and spiral acquisitions. While contrast did not substantially affect image quality for balanced sequences, the presence of contrast was found to be necessary for adequately tracking interventional devices, which may produce localized disturbances in the steady state [14]. The presence of T1-shortening contrast provided a more immediate return to the steady

**Protocols for MR fluoroscopy were evaluated with a cerebral circulation phantom.**

**T1-shortening contrast improves the tracking of interventional devices.**



**Figure 6. ▲**

The introduction of a guidewire into the circumflex artery of a canine. A guiding catheter is initially introduced via a femoral puncture and pushed over the aortic arch (a) towards the left coronary artery ostium (arrow). Once engaged with the ostium (b, arrow), a guidewire can be inserted through the guiding catheter into the coronary artery. The distal tip of the guidewire produced a substantial artifact that could be tracked through the coronary artery (red arrows in c, d). Inset in c and d is a conventional MR angiogram of the circumflex artery in the same scan plane as the fluoroscopic acquisition. The circumflex artery can also be seen in the last fluoroscopic view (yellow arrow).

**MR-guided coronary stenting offers substantial benefits.**

state, substantially improving the visualization of these devices during movement or in the presence of flow.

Sliding window reconstruction can also be very useful for fluoroscopic applications. In fluoroscopy, the same data set is repetitively acquired, and conventional reconstruction calls for an image update after each complete data set is filled. It is possible, however, to reconstruct more frequently by combining data from a previous image with the partially acquired data for the current image. This methodology permits a real-time 'feel' in terms of image display, even when true image acquisition rate is in the 3–5 fps range. This approach is particularly effective with radial and spiral acquisitions, where the center of k-space is updated on each readout. Our experimental applications routinely speed up the reconstruction by a factor of two to three with this sliding window approach. Images featuring rapidly changing objects produce easily identifiable image artifacts that provide the neces-

sary feedback to slow down or wait for a clearer image. Further refinement of parallel imaging technology is also likely to provide additional temporal benefits.

### Coronary stenting

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The coronary arteries represent a substantial challenge for MR, due to their small caliber and the degree to which they move during cardiac and respiratory motion. Accordingly, stenting of the coronaries demands a combination of high spatial and temporal resolution that has only recently become achievable [15]. The use of MR to guide coronary stenting has some substantial benefits that will only be enhanced with the continued development of drug-eluting stent designs [16]. Notably, MR may be able to depict regions of significant atherosclerosis, independently of whether or not the plaque has created substantial narrowing of the lumen. Such information may provide a more appropriate target for placement of stents that attempt not only to improve vessel patency, but also administer localized drug therapy.

Coronary stent placement has been performed in three dogs (Figure 6). MR fluoroscopy was achieved within the interactive viewer with a radial balanced FFE acquisition with a true temporal resolution of 5 fps and a reconstruction rate of 10 fps. Three scan plane geometries, corresponding to the aortic arch, the plane of the aortic valve and the circumflex artery, were stored and used to subsequently monitor the procedure. It was possible to guide a catheter to the plane of the aortic valve and position it at the ostium of the left coronary artery (Figure 6b). Positioning was confirmed by puffs of dilute Gd solutions, whose path was visualized on T1-weighted real-time acquisitions. A guidewire was then introduced in the circumflex artery and visualized via its stainless steel (SS) tip, which produced a relatively strong artifact (Figure 6c, d). The nitinol body of this guidewire could not be visualized in this case, so the passage of the SS tip was visualized in orthogonal planes along the coronary artery to assure its position prior to stent deployment. This study affirmed the possibility of using real-time MR scanning to deliver stents even to the most difficult anatomical locations, but reinforced the need for substantial improvements in optimizing the MR visibility of endovascular devices.

## Myocardial injection

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New therapeutic frontiers in the fields of drug and gene therapy hold great promise and will need an appropriate means of delivery and monitoring. The treatment of ischemic portions of the myocardium with angiogenesis growth factors (AGF) is an excellent early example of this emerging field [17]. MR is an ideal means of delivering such therapy, as it can delineate the ischemic territory, as well as guide and monitor the injection of AGF into only the diseased portions of the myocardium.

MR guidance of myocardial injections requires that the distribution volume of AGF correspond well with the MR detected volume. Tagging of therapeutic agents with MR-sensitive agents such as Gd-DTPA permits optimal visualization of the injectate's distribution pattern. To confirm that the MR-indicated distribution volume corresponds to the true area of delivery, we have been studying injections of dilute Gd contrast and blue dye, which have similar atomic weights. It has proved possible to guide catheters into the left ventricle and to monitor transcatheter injection of these agents into the myocardium (Figure 7). While substantial improvements in the delivery system of these agents is also required, there has been a good correspondence between the distribution volumes indicated by MR and the histologically determined distribution volumes, with less than a 10 % discrepancy between the two. Further studies for injection of MR tagged therapeutic agents in animals with myocardial ischemia are planned.

## Discussion

MR-guided endovascular therapy holds great promise, but is currently in its infancy. By combining a suite having the full capabilities of a catheterization laboratory with a state-of-the-art MR scanner, it has been possible to start exploring the possible role of MR in therapeutic endovascular procedures. MR's ability to perform angiography and quantify flow is interesting for applications where vascular stenosis is treated. A routine role for MR in these therapies, however, is likely limited to applications where dose is a particular concern or where additional information on plaque composition and distribution are particularly important.



▲ **Figure 7.** MR-guided injection of a saline solution containing 10 % Gd-DTPA and dilute blue dye into the myocardium of a canine. The catheter (arrow) was introduced into the left ventricle via a femoral puncture (a) under real time b-FFE imaging. A needle was then inserted into the apex of the heart and 2 ml of the solution were injected. T1-weighted black blood TSE images reveal the distribution territory of the agent 3 minutes after injection (b, arrow) and compared well with the distribution pattern seen ex vivo (c) following sacrifice at 5 minutes post injection.

Routine angioplasty and stenting are quickly and efficiently performed with existing X-ray techniques, and this is unlikely to change unless a fundamental paradigm shift in therapy occurs and MR becomes as easy to use as a cath lab.

MR's more important role in endovascular interventions will most probably be associated with interventions where the tissue's response is important, or where the distribution and activity of a therapeutic agent is crucial to the clinical outcome. The confluence of capabilities that an MR platform brings to the therapeutic environment may be mandatory for these therapies. Our experience with the delivery of an iron-tagged chemotherapeutic agent to liver lesions is a nice example of the visualization benefits that MR offers. Stroke therapy also remains an immediate application where MR's abilities may provide crucial information for optimal therapy in the hyperacute stages. By providing information not only on the patency of blood vessels, but also on the status of the tissue through perfusion, diffusion and quantitative flow assessments, it may be possible to expand and improve the selection of patients who may benefit from thrombolytic therapy. It may simultaneously be possible to improve the monitoring of the therapy to assure the minimum necessary dose is delivered to realize maximal revascularization. The primary barriers to performing this work remain logistical, with the need for both timely delivery of patients thought to be suffering a hyperacute stroke and priority access to an XMR-type suite on an emergency basis.

For MR to completely remove the need for an adjacent X-ray cath lab, significant improvements in endovascular devices and the MR environment

**MR can show tissue status and drug distribution.**

**Improved monitoring could ensure the minimum dose for maximum revascularization.**

**Significant improvements in endovascular devices still have to be realized.**

**Advances improve the outlook for MR-guided vascular interventions.**

still have to be realized. Current versions of MR-compatible devices are relatively crude and do not provide accurate localization of, for example, the tip of a catheter or guidewire. Moreover, delineating the location and shape of endovascular devices within a substantial background of signal from tissue remains extremely challenging. Sufficient fluoroscopic image quality has been realized for passive visualization systems (i.e. susceptibility markers) to be practical. However, safe active devices may realize substantial additional benefits.

Automatic scan plane positioning, as determined from microcoils integrated into endovascular devices, is a tremendous and unique capability of MR. It enables the use of thinner scan planes and thereby limits the information content in the image to that of tissue near the device. This approach can make image interpretation and device tracking much simpler and faster. Continuous tracking of the microcoil position is further possible even when not acquiring images, permitting a 'roadmapping' approach to interventions. In such a methodology, the position of the device

is continuously superimposed on a high-quality image which is acquired relatively slowly. This approach has already been implemented within the interactive viewer. However, appropriately constructed interventional devices have not yet become available.

Physical access to the groin while the target tissue is near the isocenter is currently possible but often uncomfortable. This fact, coupled with the acoustic noise produced by rapid acquisition schemes, still makes the MR environment relatively unpleasant for the interventionalist. Moreover, additional improvements in the rate of image acquisition, reconstruction and display still have to be realized before MR fluoroscopy begins to rival its X-ray counterpart. Advances in these areas continue to be made and further improve the outlook for MR-guided endovascular interventions.

*Further information on the XMR suite at the University of California – San Francisco can be obtained from the web site:  
<http://xmr.ucsfmedicalcenter.org>.*

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