

Integrating X-ray angiography and MRI for endovascular interventions

MRI and X-ray angio will be integrated in the same facility.

Installation of a novel interventional radiology facility at the University of California Medical Center, San Francisco, is planned for the latter part of the year 2000. The facility will integrate magnetic resonance imaging (MRI) and X-ray fluoroscopy. The design is intended to provide a no-compromise solution for endovascular interventions, combining the excellent angiographic quality of conventional X-ray technology with the physiologic, soft-tissue contrast of MRI. The new facility is based on a Philips Gyroscan Intera 1.5 T MRI system, used in combination with a Philips Integris V 5000 X-ray angiography system. Both of these systems represent the state of the art in their respective imaging modalities. Together they offer exciting opportunities to explore new fields of interactive and interventional imaging.

MRI offers exquisite soft-tissue contrast, without ionizing radiation.

In current clinical practice, digital subtraction angiography (DSA), based on conventional X-ray projections, is the modality of choice for many diagnostic vascular imaging procedures, as well as for monitoring endovascular interventions. The speed and resolution of the X-ray technique are, however, offset by the poor soft-tissue information, the high radiation exposure (especially during fluoroscopy) and the limitations of two-dimensional projection imaging. On the other hand, many (non-vascular) diagnostic imaging studies are performed with MRI, which offers exquisite and physiologically relevant soft tissue contrast, with no exposure to ionizing radiation. MRI allows cross-sectional and three-dimensional image acquisition, but generally suffers from 'intermediate' spatial resolution and limited temporal resolution. Thus, with their somewhat distinct constraints, the two techniques have so far found different areas of application.

With technical advances, however, the spatial resolution of MRI is continually improving. In MR angiography, for example, it allows the

delineation of small vessels, and currently challenges X-ray angiography for diagnostic imaging of the vasculature in several body areas. The increasing temporal resolution of ultra-fast MRI has seen image frame rates approach the figure of 30/second, offering an alternative for real-time monitoring of interventional processes. However, such fast scans have limited spatial resolution. This, together with the demands of MR compatibility for interventional devices, has slowed the adoption of MR for clinical interventional radiology.

The differences in spatial and temporal resolution of the two imaging modalities, as described above, can in fact be viewed as complementary: where X-ray DSA defines the vasculature, MR describes the surrounding tissue. During an intervention, DSA can be used to monitor the vascular therapy, while MRI can monitor the consequences in the tissue. The possibilities offered by the combination of the two modalities are expected to provide exciting new opportunities and advances in vascular imaging in general, and endovascular interventional radiology in particular.

Physically, the MRI and X-ray angiography components will be installed in two separate bays (Fig. 1), separated by a sliding door lined with



Fig. 1a. The combined MRI/X-ray angio suite. The diagram illustrates the 'two-room' concept: the MR and angio bays are separated by a sliding door allowing them to be used independently or together. For mixed modality imaging, the tabletop carrying the patient can be slid in-line through the open door between the two rooms of the suite.

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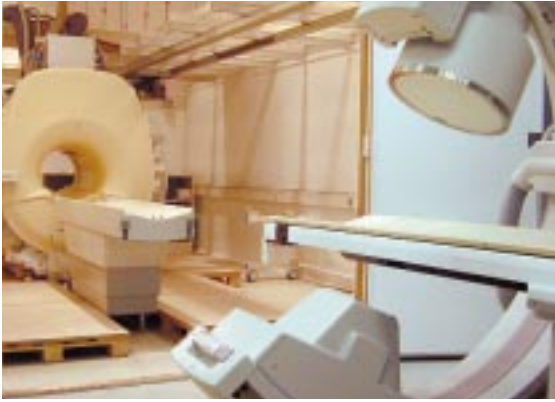


Fig. 1b. The combined MRI/X-ray angio suite. (Photograph taken at the Philips Medical Systems facility in Best during production and assembly).

lead and copper shielding, for X-ray and MR respectively. When the door is closed, both rooms may be used independently. When a procedure calls for mixed modality imaging, the tabletop carrying the patient can be slid in-line through the open door between the two rooms of the suite, allowing reproducible imaging with minimal patient movement and time delay.

The twin-bay combined MRI/X-ray angio suite at UCSF will provide an environment for exploring the integration of MRI and X-ray angiography facilities, each independently representing the state-of-the-art in technological performance. Three broad concepts will provide the framework for planned studies:

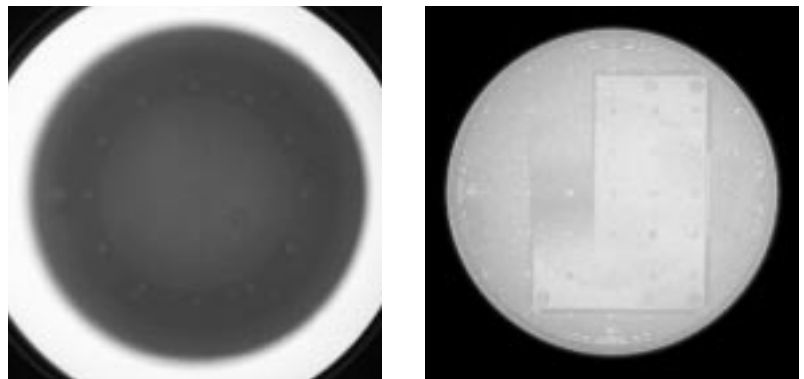
- Correlative/comparative studies between diagnostic X-ray angiography and MRA (e.g. intra-arterial contrast-enhanced MR digital subtraction angiography)
- MR-assisted angiography (i.e. combining tissue information from MR and X-ray fluoroscopy)
- Defining the opportunities, requirements and limitations of 'interventional MR', thus finding the range of interventional applications which can be performed under MR guidance alone, without compromising efficacy.

One of the major technical requirements of the facility is the ability to integrate information from either imaging modality into the monitoring display of the other device. For example, the 'anatomic background' could be added to the display of X-ray fluoroscopic images, setting the vascular definition in a tissue context.

Using an integrated MRI/X-ray angio system will offer many advantages to the patient undergoing radiologic intervention. To maximize this benefit, strategies will be developed to appropriately fuse the information from one modality with that of the other, allowing an integrated display of soft tissue (MRI) and vascular (X-ray angio) structures.

Because MRI is a volumetric technique, while X-ray angiography is a two-dimensional projection method, appropriate algorithms for registering (i.e. matching and superimposing) the images will be investigated. The registered images will allow the interventional radiologist to visualize the vasculature during the X-ray angio procedure, within the anatomic context of the surrounding soft tissue provided by a previously acquired MRI scan. Similarly, physiologic tissue information derived from MRI will be interpreted in the light of information on the feeding blood vessels.

Not only will MR images and X-ray angiographic projections be registered to provide combined images for interventional practitioners, but parametric maps, or synthesized images, derived from multiple MR images and directly reflecting physiological parameters (such as tissue blood volume) will be registered and displayed in both X-ray angio and MR environments.



Some of the hurdles still to be overcome in image fusion are shown in Figure 2. These images were acquired at the Philips Medical System facility in Best prior to shipping the MRI and X-ray systems.

A plastic test phantom, filled with GdDTPA-doped water, was imaged successively using both modalities, mimicking a typical combined clinical imaging procedure. While the 'field of view' and acquisition plane was prescribed to be similar, a number of observations can be made:

X-ray vascular images are related to the soft-tissue MRI images.

Fig. 2. A plastic test phantom, filled with GdDTPA-doped water, was imaged successively using both modalities, mimicking a typical combined clinical imaging procedure.

The projection X-ray image (left) and the MR image (right) demonstrate a number of obstacles to effective image registration and comparison, notably X-ray image magnification, different image contrast and the 2D v. 3D acquisition.

Fig. 3: Unenhanced MRA on the Gyroscan Intera (Release 7). Fig. 3a. MRA of Circle of Willis of a healthy volunteer. 512x512 matrix, interpolated to 1024x1024. Maximum intensity projection.

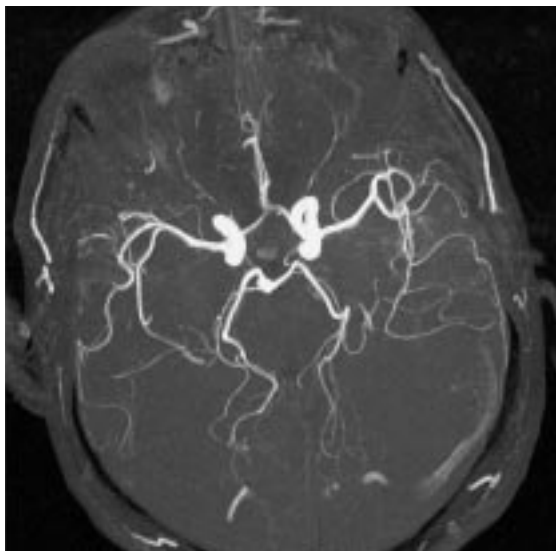


Fig. 3b. Coronary MRA: navigator-corrected T2-prepped 3D image revealing separate origins of a non-dominant RCA and conus artery with relatively high spatial resolution (Image acquired in collaboration with Prof. De Roos and colleagues at Leiden University Medical Center, Leiden, the Netherlands).



Applications include stroke, angioplasty and intra-arterial therapy.

- Contrast in the two images is very different and, in fact, almost complementary. The X-ray beam is attenuated by the plastic structures of the phantom, while the MR signal arises from the fluid within.
- While the spatial resolution of the MR image is defined by the image matrix and the 'field of view', the X-ray image is subject to a magnification factor.
- The X-ray image is a projection of the entire object, while the MR acquisition allows a 3D data set to be derived, which could be interrogated post-hoc along arbitrary viewing planes. In the example shown, a maximum intensity projection through the MR data set has been made in order to achieve the closest approximation to the X-ray image.

The first goal of the integrated suite is to offer the possibility of optimizing comparisons between the continually advancing techniques of MRA, with X-ray DSA as the gold standard. Increasing spatial resolution and enhancement with intravenously-administered contrast media have increased the clinical applicability of MRA technology. One example is high-resolution MRA of the Circle of Willis (Fig 3a). However, despite the advances, application in some areas, such as the coronary circulation, remains challenging (Fig. 3b). The combined facility offers the possibility of intra-arterial administration of contrast agent, which may further improve the quality of MR angiograms.

Another intriguing development is the future availability of advanced 'blood-pool' contrast agents, which are currently only available for experimental studies. Due to their persistence in the vascular system, blood pool contrast agents, in combination with appropriate motion compensation tools, offer the possibility of further increasing the spatial resolution of the MRA technique, as well as avoiding the limitations of current approaches in situations of slow blood flow.

The second goal will be that of integrating MRI and X-ray angiography, while the third goal will be that of defining the requirements, limitations and opportunities for interventional procedures to be performed under MR guidance alone.

Applications

The application procedures described below illustrate some of the approaches being considered for the second goal of integrated MRI and X-ray angiography. In general, these applications will progress through experimental validation stages as well as protocol optimization for clinical implementation as 'integrated' procedures. The examples are not intended to be exhaustive, but rather to illuminate the concepts of MR-assisted angiography and the augmentation of fluoroscopic and intra-arterial catheterization procedures with morphological and functional information obtained by MRI

Evaluation and therapy of acute stroke

In this era of thrombolytic therapy for acute stroke patient management, the optimal evaluation of a patient with acute cerebral infarction includes

screening for the existence of hemorrhage, identifying the occluded vessel, and characterizing the ischemic penumbra (tissue at risk). Hemorrhage, which is an exclusion criterion for thrombolysis, is generally identified on non-contrast CT. Powerful physiological insights are offered by diffusion and perfusion MR imaging, which may be performed in conjunction with determination of the site of vessel occlusion using angiography (Fig. 4).

Currently, these imaging procedures are accomplished in a time-inefficient fashion, largely due to the different modalities (CT, MR, Angiography) required to accomplish the various tasks. Furthermore, the ischemic penumbra (as indicated by differences between diffusion and perfusion MR imaging) is not generally characterized in a dynamic fashion immediately during or following intra-arterial thrombolysis. Ideally, intra-arterial thrombolysis should be halted at the time of adequate perfusion of the hemisphere in question, in order to decrease the chances of hemorrhagic conversion.

The dual MR/X-ray angio facility provides a unique opportunity for prompt diagnosis, assessment, therapy, and monitoring of that therapy using both angiographic and MR techniques. In addition, documenting more precisely the effect of thrombolysis on the perfusion of the ischemic cerebral hemisphere may result in less drug administration and reduced risk of hemorrhage.

The dual facility will be used to selectively catheterize the middle cerebral artery for administration of thrombolytic drugs and for documenting perfusion and diffusion deficits in the cerebral hemisphere. In a patient presenting with an acute stroke, an MR exam will first be obtained and will include echo-planar diffusion weighted imaging (DWI), T2-weighted images, gadolinium bolus perfusion weighted imaging with a calculation of perfusion deficit, and MRA. The patient will then be moved to the X-ray suite where catheter angiography will be performed to document the site of thrombus. If thrombolytic therapy is performed, the patient will remain in the angiography suite for the first sixty minutes.

At sixty minutes, a repeat MRI (including diffusion and perfusion sequences) will be performed. The patient will then be moved back to the X-ray suite for documentation at 120 minutes follow-

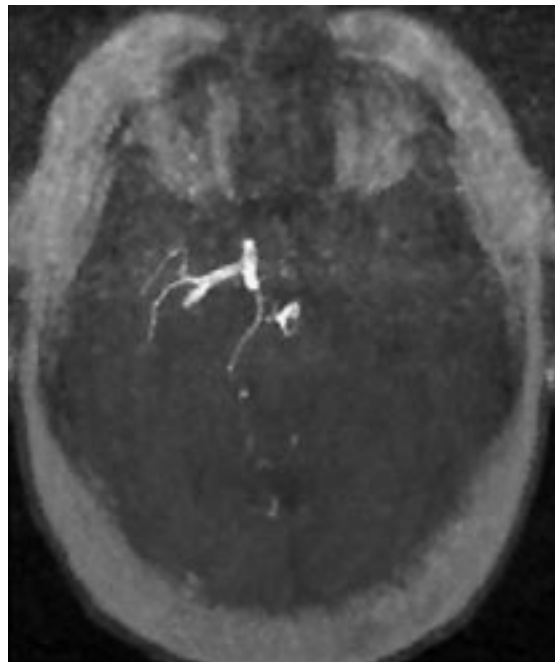
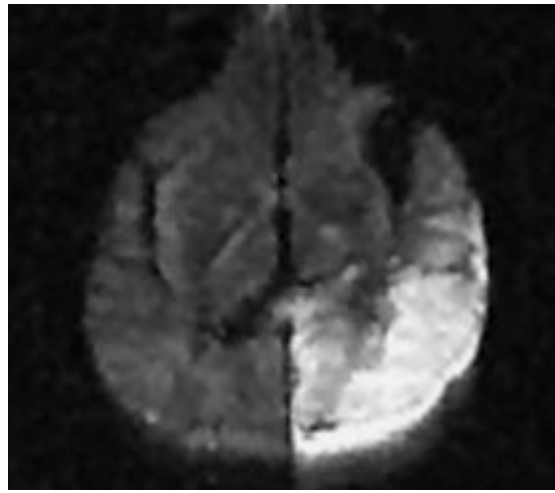


Fig. 4. The tissue consequences of vascular occlusion: acute ischemic stroke. Diffusion weighted images (top) reveal a large region of acute infarction involving the left occipital, posterior parietal and posterior temporal lobes. The findings are consistent with the left carotid occlusion which is also identified on the MRA (below).

ing thrombolytic therapy. At the end of the procedure the patient will once again be moved to the MRI suite for a final diffusion and perfusion examination as well as a T2-weighted image. Calculation of perfusion deficit and volume of diffusion abnormality will be compared before, during, and after thrombolytic therapy. It is anticipated that these results will establish whether a suite of this sort can refine the patient population to be treated and refine the indications for such treatment.

Rapid calculation of diffusion and perfusion maps of the brain will be required. It is anticipated that

The facility provides a unique opportunity for prompt diagnosis and treatment.

The effect of thrombolysis can be precisely documented.

these will be reconstructed on the EasyVision workstation, or using the Research Workstation with direct (and, ultimately, real-time) access to the MR scanner image database. Algorithms for reconstruction of diffusion-weighted images, maps of attenuation factor, apparent diffusion coefficient, tensor trace and a variety of anisotropy indices are under continual development. Similarly for perfusion, parameter maps will be generated reflecting rCBV, transit time, time to peak and wash-out characteristics. Other parameters reflecting other physiologic entities (perhaps reflecting autoregulation, CMRO₂, CBF etc.) are likely to become required during the course of these studies and algorithms for their generation could be implemented similarly.

Endovascular balloon angioplasty and stenting

It is estimated that there are 50 000 patients per year in the USA with abdominal aortic aneurysms or severe peripheral artery disease. Endovascular interventional procedures, ranging from balloon angioplasty to stent graft placement, may benefit from the combined imaging opportunity.

Algorithms for generating a wide variety of physiologic data are under development.

One scenario that might be considered involves insertion of the balloon catheter under X-ray guidance, with acquisition of an X-ray DSA angiogram. The patient would then be transferred to MR. Upon clinical availability, MRA could then be performed with a blood-pool contrast agent, to define the vascular space even in situations of slow flow. Such contrast agents remain in the blood vessels for several hours, allowing MR angiography to be done before and after the interventional procedure. Morphometric analysis of the blood vessels will be possible, because the MR angiography sequences are not time-limited, and can therefore have high spatial resolution, and they are not flow-dependent, so that even vessels with slow, or turbulent flow, for example near stenoses, will be accurately depicted. The balloon angioplasty could then be performed under MR visualization and technical success could be documented with increased volume filling of contrast agent. Furthermore, a quantitative assessment of efficacy could be obtained by blood flow determination after angioplasty using velocity encoded cine MR.

Pulmonary arterial stents in congenital heart disease

Transcatheter stent placement is effective in the

treatment of pulmonary artery stenosis and stenosis of pulmonary conduits. Fluoroscopic guidance of endovascular procedures carry high radiation exposure, leading to increased incidence of malignancy in children who have undergone repeated cardiac catheterization and X-ray angiography. Hence there is considerable incentive to explore an alternative for endovascular therapy of congenital heart disease that does not involve the use of ionizing radiation. The combination of MR and X-ray facilities offers the immediate possibility of using MR to quantify the morphological and functional results of endovascular stent procedures (e.g. by the documentation of arterial flow rates, using velocity encoding) as well as providing an environment where the possibility of guiding the stent placement and deployment under MR 'fluoroscopic' imaging can be evaluated.

Intra-arterial therapy (angiogenesis growth factor)

Improvements in coronary collateral flow, and in the overall vascularity in the myocardial perfusion bed served by obstructed coronary arteries, have been reported following treatment with various angiogenesis growth factors (AGF).

Various methods have been used for delivery of AGF to the coronary circulation (e.g. intravenous injection, direct myocardial injection). The use of AGF appears to be a promising regimen for the treatment of end stage ischemic heart disease.

A proposed sequence, or workflow, would include selective coronary catheterization under X-ray guidance, followed by coronary angiography to document coronary arterial anatomy. The patient would then be transferred to MR, where intra-coronary artery MR contrast injection would be followed by rapid T1-weighted imaging to quantify the mass of enhanced myocardium (perfusion bed of injected artery). The patient would then be removed to X-ray for placement of the catheter in another coronary artery. MR would subsequently be repeated. Total flow to the LV myocardium would also be assessed using velocity-encoded cine MR of the coronary sinus. Since we can measure LV mass, it is possible to express myocardial flow in units of ml/min/g myocardium. It is expected that the myocardial flow will increase post-AGF.

In all these examples, the catheter placement could be performed under X-ray guidance, as is current clinical practice. MR would be used as an immediate adjunct to characterize the therapeutic

efficacy, either on a vascular level (e.g. by establishing vessel patency, diameter and indeed flow) or by assessing tissue consequences of the therapy (e.g. reversal of diffusion weighted hyperintensity upon reperfusion in acute stroke).

The benefits of the two modalities could be combined to improve both the technical success and the functional outcome of the interventional procedure.

Dynamic MRI and catheter tracking

For the third goal, the definition of requirements, limitations and opportunities for interventional procedures to be performed under MR guidance alone, there are a few minimum prerequisites.

These are:

- MR-compatible catheters and other devices
- MR-visible materials for tracking
- Real-time imaging with pseudo-fluoroscopic display.

The technical advances incorporated in the Gyroscan Intera (Release 7) offer realistic perspectives for real-time dynamic imaging (Fig. 5).

Development of MR interventional devices.

The opportunity of using MR to guide interventional procedures offers a number of advantages for the patient. However, it also necessitates the

development of interventional and surgical tools which are:

- MR-safe
- MR compatible (i.e. free from intolerable image artifacts)
- MR visible

It is anticipated that dedicated catheters, biopsy needles, scalpels and other devices will be designed and constructed, optimized for MR suitability.

Materials science offers a number of non-metallic materials with appropriate physical properties (e.g. tensile strength, flexibility) based on ceramic and plastic technologies. During the guidance of endovascular catheters for patients undergoing interventional procedures, it is of pivotal importance to visualize the precise *location* and *orientation* of the catheter tip, in real time, and with reference to the tissue background.

Two strategies will be developed for visualizing the catheters: '*passive tracking*' and '*active tracking*'. Both require rapid acquisition with 'real-time' image reconstruction and display. For the passive approach, catheters may be labeled with materials that will show up in appropriately weighted MR imaging sequences. For the active approach, a coil carrying a small electric current will be incorporated in the catheter, and this will transmit a signal to the MR detector coil.

Endovascular interventions may benefit from combined imaging.

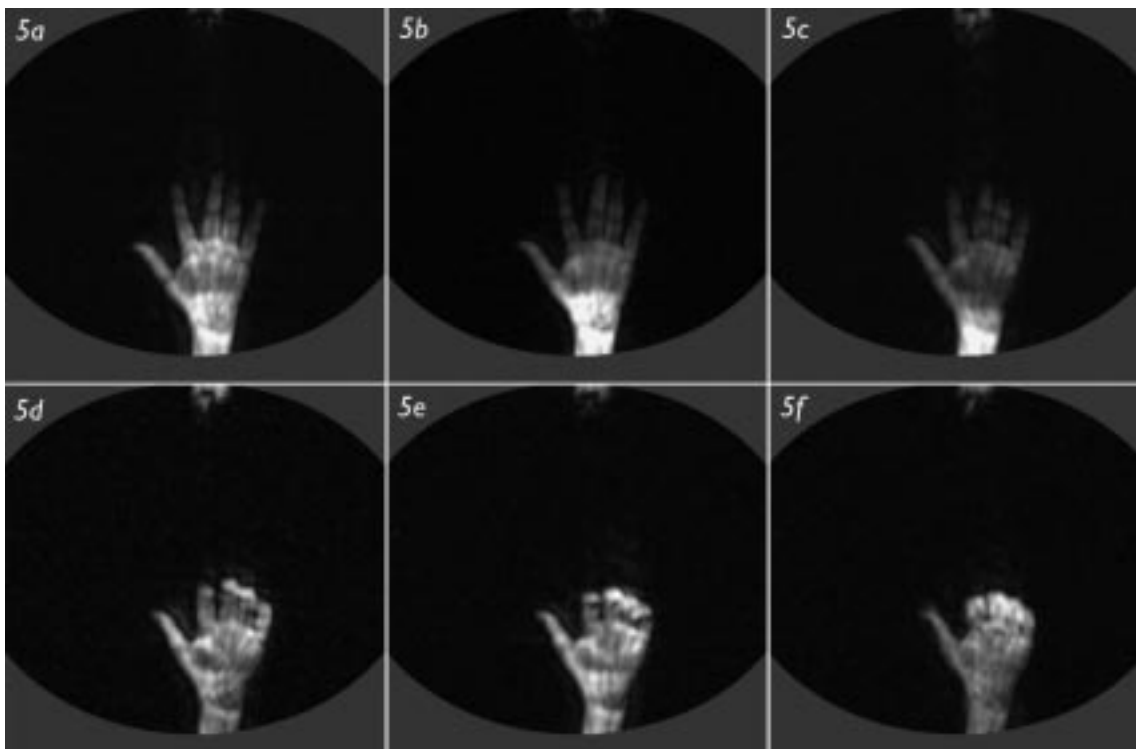


Fig. 5. Dynamic imaging at approx. 10 frames/second, performed on a Philips Gyroscan Intera (Release 7.1.2) 1.5 T MR scanner at the Philips Medical Systems facility in Best. These dynamic images were acquired during free hand movement in the bore of the magnet. Image acquisition was performed using a thick-slice 2D FFE sequence in 'interactive' mode.

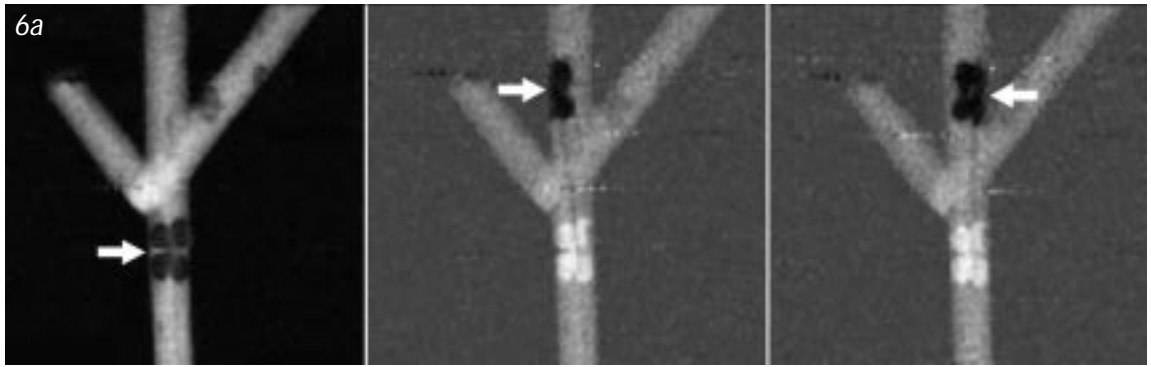


Fig. 6. MR visibility.

Fig. 6a. Catheter steering and tracking.

Left: Catheter tip can be visualized in a trifurcation phantom by the field disturbance and signal void associated with 30mA DC current applied to microcoil wound at the catheter tip. Advancing the catheter with current applied to the coil (and thus catheter tip) causes deflection in a direction defined by the coil's magnetic moment and the steady magnetic field of the MR magnet.

Center; right: Altering the DC current polarity or the choice of 3 axis coils at the tip allows arbitrary catheter tip deflection. Visualization can be improved by subtracting a baseline template image.

MR angiography sequences are not limited by time or flow.

Passive tracking

Gadolinium, iron or dysprosium-labeled catheters lead to local signal loss, due to magnetic susceptibility effects. The geometry of the 'labels' will be selected in such a way as to cause orientation-specific signal loss patterns. Catheters will be evaluated with various geometric arrangements of magnetic susceptibility labels, including:

- Thin rings (diameter-thickness)
- Extended cylindrical coatings (length > diameter)
- Longitudinal 'stripes' (Fig. 6b).

MR requires safe and compatible tools.

After appropriate optimization of catheter labeling geometry and fast imaging strategy, catheters will be evaluated in animal models of endovascular procedures. For such studies, blood pool contrast agents will be identified to positively enhance the vascular background and improve the conspicuity of the catheter labels. By incorporating multiple 'labels' into the catheter, a sense of catheter orientation will be established. From this, interactive control of scan parameters is anticipated, providing such options as 'automated plane selection from two points and target', 'centering of FOV to catheter tip' and 'long range and short range views'.

Active tracking

In addition to the passive labeling of catheters, active methods will be evaluated. While these impose some additional safety considerations, they offer benefits of control and selectivity of visualization. In general, the catheter tip will include an electrical coil. Current flowing in the coil will

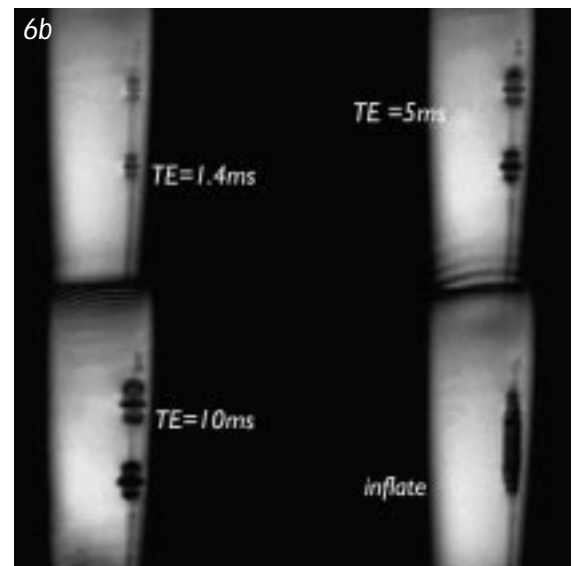


Fig. 6b. A balloon catheter (Cordis, Roden, the Netherlands) with dysprosium labels at the proximal and distal ends. The labels produce field disturbances and signal voids. Imaging sensitivity can be adjusted with the echo time, TE. Once positioned, balloon deployment can be visualized by MRI.

serve to identify the tip (by field disturbance, or by beacon-like imaging). The coordinates of such a localization will typically then be registered to a previously acquired image ('roadmap') for real-time updating of the tip position. Initial studies will be performed in phantoms and will serve to evaluate the feasibility of active tip-tracking approaches. An approach involving two orthogonal projections (for determination of x- and y-coordinates respectively) will be developed, as well as a transmit/receive 'beacon-imaging' approach (in which the coil is used to excite and detect an MR signal). Because the coil has a poor distance sensitivity, by virtue of its size, only signal from the immediate environment is detected. In both cases overlay on a roadmap image is required, but the acquisition can be interleaved with the

(slower) roadmap acquisition, reducing problems associated with subject motion and image registration errors.

The 'beacon imaging' strategy will also be compared to the 'DC-field disturbance subtraction' technique, in which a DC-current applied to the catheter tip coil creates a magnetic field disturbance, and signal loss, similar to the passive tracking approach. If images are acquired with and without the DC-current, the catheter tip can be identified by subtraction.

The development of catheter visualization and tip tracking will be of paramount significance to all endovascular procedures attempted under MR guidance. The additional features of interaction of the catheter visualization with subsequent scan acquisition parameters (e.g. FOV centering, auto-plane selection etc.) may offer potential utility not currently enjoyed in conventional X-ray fluoroscopy.

Steering catheter tips

One of the challenges of endovascular interventional procedures is to direct the remote catheter tip into tiny blood vessel branches such as those in the brain or heart. Conventional approaches to this problem have involved development of catheter materials, tip geometries and the 'hands-on' exact skill of the interventional practitioner. While these procedures are generally performed under image guidance of X-ray fluoroscopy (with considerable radiation exposure), initiatives to use MRI for guidance of such endovascular interventions are being developed. Interventional MRI has many pros and cons when compared with traditional imaging approaches; however, it also affords a special opportunity for remote orienting of the catheter, exploiting the ambient strong magnetic field. Current research at UCSF is seeking to exploit this opportunity and to develop a device for remotely controlling the orientation of the catheter tip.

The device consists of a minute electrical coil or series of coils wound around the tip of the catheter. When an electric current is passed through the coil, a magnetic moment (and small magnetic field) is generated. In the presence of a strong external magnetic field, this magnetic moment (and thus the coil, and catheter tip) experiences a turning force,

or 'torque', tending to align the magnetic moment with the external field of the MR scanner.

Depending on the polarity of the applied current, the coil will tend to align, or anti-align, with the magnetic field, deflecting the catheter tip either 'upwards', or 'downwards'. With 3-axis coils, under independent control, the tip can then be oriented in 3D space, under remote control (Fig. 6).

Conclusion

The primary goal of the dual-bay integrated MRI/X-ray angio suite is to explore and improve the field of endovascular interventional radiology. The second goal will be that of integrating MRI and X-ray angiography. Applications will benefit from the synergistic information provided by the soft-tissue and physiologically-relevant contrast of MR, in combination with the vascular definition of X-ray DSA. MRI will also provide a means of rapidly evaluating both the technical and clinical success of interventional procedures. Blood flow quantification using velocity-encoded MRI will provide an additional measure of confirming reperfusion, along with definition of vessel patency and assessment of vessel diameter.

The third goal will be that of defining the requirements, limitations and opportunities for interventional procedures to be performed under MR guidance alone. Advancing MR technology should be capable of providing the necessary spatial and temporal resolution, along with appropriate contrast, to offer an alternative to X-ray guidance in certain applications. Guidelines will be generated to ensure no compromise in procedure performance and patient care.

This combined facility offers abundant opportunities for the comparison and integration of the two imaging modalities, and thus for the optimization of endovascular diagnostic and interventional radiology as a whole.

Acknowledgements

The authors would like to thank the Lucille Packard Foundation and Philips Medical Systems for support of this program. Drs Joop van Vaals, Roy Gordon, Mark Wilson, Randy Higashida and Bill Hassenzahl are gratefully acknowledged for many insightful discussions.

Special strategies are required for catheter tracking.

Magnetic susceptibility labels can be used for passive tracking.