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MR Angiography and Development: Review of Clinical Applications

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1. Introduction

Contrast-enhanced Magnetic Resonance Angiography (CR-MRA) is remarkable technique to image the vascular system from head to toe in diagnostic imaging armory. Computed tomography is still an adequate imaging method of choice in few applications such as in follow-up studies in neuro-vascular pathologies, even then MRA is getting an equal share with tremendous improvements in spatial and temporal resolution. Current clinical indications for MRA of the supra-aortic vessels in head and neck include evaluation of steno-occlusive disease, assessment of AV-malformations in cerebral vessels, aneurysms, atherosclerotic disease and dissections. Moreover, as with other imaging applications, limiting contrast dose is a major issue, particularly with the increased risk of development of Nephrogenic Systemic Fibrosis (NSF) with higher doses of contrast agent [1] [2]. Therefore, contrast agents with higher relaxivity or higher concentration (1M), for which lower doses may be used, are beneficial for dynamic MRA studies.

The critical advantages of Gd-contrast agent for MRA of the vessels are: increased signal-to-noise ratio and greater vessel conspicuity. In this chapter we will discuss in detail the benefits and limitations of currently available gadolinium contrast agents for MRA with respect to its clinical indications. We will focus on gadofosveset [3;4] as well, it is relatively a new contrast available in clinical applications and would be nice to compare its benefits and limitations with other Gadolinium contrast agents which have been used for long in clinical environment.

2. Conventional technique of magnetic resonance imaging angiography

MR imaging depends on the relaxation times (T1, T2 and T2*) and proton density in the tissue of interest. MRI is very sensitive to flow and motions originating during image acquisition. The motions induced by flow can be responsible for number of artefacts which can drastically impair the diagnostic image value but on other hand sometime these flow effects are of vital interest to image the vascular anatomy. The MRA can be classified to time of flight (TOF) and phase contrast MRA [5]. In TOF MRA the blood flow is assumed to be perpendicular to the plane of acquisition. For repetition time (TR) shorter than the longitudinal T1 relaxation of the stationary proton spins in the imaging slice, the signal will be reduced due to partial saturation effect (saturating RF pulse). Inflow blood in the vessel

will move the spins from outside of the slice into the imaging plane; these spins have not been subjected to the spatially selective RF pulse. These unsaturated spins upon entering the slice will produce a much stronger signal than stationary spins assuming the gradient echo sequence is applied. This effect is called “entry slice phenomenon” or “inflow enhancement” or “flow related enhancement”. The amount of inflow enhancement will depend on various factors like tissue properties (T1), sequence parameters (flip angle and TR) and geometrical parameters (slice thickness, orientation and flow velocity). TOF is based on fundamental principle that any vessels segment can be imaged by cutting through the vessel perpendicular to the flow direction [5]. With this repetitive method applied at each slice a complete three dimensional data of vascular tree can be acquired. Various multiple 3D reformatting algorithms are available with the post processing unit (Maximum Intensity Projection) which can help radiologist visualise the complex vascular anatomy with appropriate precision [5]. The image acquisition can be 2D or 3D (as other MRI sequences). Both techniques are currently used in clinic with specific applications. The 2D techniques offers a higher vessels/background contrast hence can be used in slow flow zone but 3D method is limited to fast flow situations. Another aspect of choice among two is the spatial resolution. In 2D technique the inplane resolution depends on the FOV and matrix size resulting in an anisotropic volume where slice thickness is usually higher than inplane resolution. Whereas the isotropic resolution can be achieved with 3D techniques up to sub-millimetre scale, in addition offers a better signal to noise ratio due to averaging effect of the phase encoding in slab direction.

Phase contrast Angiography: This class of MRA is based on the changes in the phase of transverse magnetization [5]. The phase shifts occur when the spins move along a magnetic field gradient. The flow induced phase shift has a linear relationship with the moving velocity. Hence flow induced phase shift can be used for flow quantification. The phase contrast MRA is acquired as two data sets with different flow sensitivity. The first data (S1) is acquired with flow compensation (no flow sensitivity), whereas the second (S2) is acquired with flow sensitivity. The amount of sensitivity is controlled by gradient strength. The length of the complex difference between S1 and S2 is dependent on the phase shift. An image with signal intensity of difference represents the velocity of the spins within the field of view.

3. Contrast enhanced MRA

The paramagnetic extracellular contrast agent (Gd chelates) increases the blood signal by shortening the T1 relaxation time of the blood. Thus the blood produces the highest signal compared to tissue; hence vessel lumen can be demarcated with maximum intensity projections. There are various Gd- contrast agents available with different properties and relaxivities (table 1) [6-8]. Each one has different relaxivity at different field strength (table 2) [6-9] which is very important to know for practical applications. The details of various gadolinium contrast agent [10;11] properties are beyond the scope of this chapter, we will focus on the application of these contrast agents in various clinical conditions.

4. Magnetic resonance angiography of head and neck

The information provided by magnetic resonance imaging (MRI) in evaluation of brain lesions is critical for accurate diagnosis, therapeutic intervention and prognosis [12]. Contrast enhanced MR neuroimaging using gadolinium (Gd) contrast agents depicts blood-

Agent	Trade name	Manufacturer	Concentration (mol/l)	Protein-binding	r1*	r2*
Gadobenate dimeglumine	MultiHance®	Bracco Diagnostics	0.5	Weak	9.7–10.8	12.2–12.5
Gadodiamide	Omniscan™	GE Healthcare	0.5	None	4.8	5.1
Gadopentetate dimeglumine	Magnevist®	Bayer Schering Pharma AG	0.5	None	4.9–5.0	5.4–6.3
Gadoteridol	ProHance®	Bracco Diagnostics	0.5	None	4.6	5.3
Gadoversetamide	OptiMARK®	Mallinckrodt	0.5	None	NA	NA
Gadoterate meglumine	Dotarem®	Guerbet	0.5	None	4.3	5.0
Gadobutrol	Gadovist®	Bayer Schering Pharma AG	1.0	None	5.6 [41]	NA
Gadofosveset	Vasovist®	Bayer Schering Pharma AG	0.25	Strong	33.4 to 45.7 mM-1 s-1 (0.47 T)	NA

*Measured at 0.47 T in human serum or plasma

Table 1. Gadolinium contrast agents used in MR Imaging [6-8].

Field strength	Source	Gd-BOPTA		Gd-DTPA	
		r1 (l/mmol ⁻¹ ·s ⁻¹)	r2 (l/mmol ⁻¹ ·s ⁻¹)	r1 (l/mmol ⁻¹ ·s ⁻¹)	r2 (l/mmol ⁻¹ ·s ⁻¹)
0.2 T	Pintaske ^a	10.9	18.9	5.7	9.2
0.47 T	de Haën ^b	9.7	12.5	4.9 ^d	6.3 ^d
	Rohrer ^c	9.2	12.9	3.8	4.1
1.5 T	Pintaske ^a	7.9	18.9	3.9	5.3
	Rohrer ^c	6.3	8.7	4.1	4.6
3.0 T	Pintaske ^a	5.9	17.5	3.9	5.2
	Rohrer ^c	5.5	11.0	3.7	5.2

Gd-BOPTA=gadobenate dimeglumine; Gd-DTPA=gadopentetate dimeglumine

(a) In human plasma at 37°C

(b) In heparinised human plasma at 39°C

(c) In bovine plasma at 40°C

(d) In heparinised human plasma

Table 2. Relaxivities of Gadobenate dimeglumine and gadopentetate dimeglumine at varying magnetic field strengths [6-9].

brain barrier disruption, thereby demonstrating the location and extent of the disease by depicting the increased EES contrast concentration in these areas. Simple contrast-enhanced morphologic imaging, however, is limited in accurately predicting tumor aggressiveness [13]. Adding dynamic contrast-enhanced and perfusion weighted imaging [14] can solve this problem by providing physiological information (hemodynamic and neoangiogenic status) in addition to pure lesion morphology [15-17].

Most of available Gd-contrast agents differ in their T1 and T2 relaxivities, but have a comparable tissue enhancing properties. The exceptions are gadobenate, gadoxetate and gadofosveset [4], all of which have transient protein binding capability that is responsible for up to twice (and more) the R1 and R2 relaxivity as compared to the other agents at all magnetic field strengths [8] [18;19]. In this section, we summarize the current clinical applications of gadolinium contrast agents in neuroimaging.

Buelmann et.al [20] conducted a study comparing equal single doses of gadobenate dimeglumine and gadopentetate dimeglumine for CE-MRA of the supra-aortic vessels at 3T in 12 healthy volunteers. Qualitative image analysis revealed significantly higher ($p=0.031$) values in all the examinations with a gadobenate dimeglumine [7;21]. The overall score for vessel delineation was also significantly ($p=0.005$) higher and in general a significant ($p\leq 0.026$) preference for gadobenate dimeglumine was noted as well as specifically for assessments of the extracranial arteries, Circle of Willis and vessels distal to the Circle of Willis. In addition, gadobenate dimeglumine use demonstrated significantly ($p\leq 0.021$)

greater rCNR (relative contrast to noise ratio) for the internal carotid, middle cerebral and basilar arteries [22].

The 1M formulation of gadobutrol permits a 50% reduction in the bolus injection volume, thus it has been hypothesised that this reduced volume along with a faster injection rate would facilitate a sharper peak in the contrast bolus, therefore a better first-pass MRA signal [23;24]. However, the results from few clinical studies have been in disagreement with the hypothesis. In a small intraindividual study (N=12); patients received a single dose of 1M gadobutrol and a double dose of 0.5M gadopentetate dimeglumine, a significantly higher SNR and CNR, and better delineation of arterial morphology, was observed with the 1M agent [25;26]. However, in another volunteer study, 5 healthy volunteers underwent 4 consecutive MRA examinations with: a single dose of 1M gadobutrol, a single dose of 1M gadobutrol diluted to twice the volume, and single doses of gadopentetate dimeglumine and gadobenate dimeglumine for which the volume and flow rate were doubled to match the diluted gadobutrol volume and concentration. Quantitatively, the SNR and CNR for gadobenate dimeglumine and both standard and diluted forms of gadobutrol were significantly ($p < 0.02$) higher than gadopentetate dimeglumine [27;28], yet no significant difference between either form of gadobutrol and gadobenate dimeglumine was reported [12]. Overall, it seems that 1M gadobutrol may or may not be advantageous for MRA of supra aortic vessels, depending on the vascular territory being examined but it has never demonstrated benefit beyond the higher relaxivity agents for CE-MRA [20;27-29]. But it has been proved that gadobutrol is beneficial in brain perfusion imaging than gadopentetate dimeglumine (Figure 1 courtesy) [23].

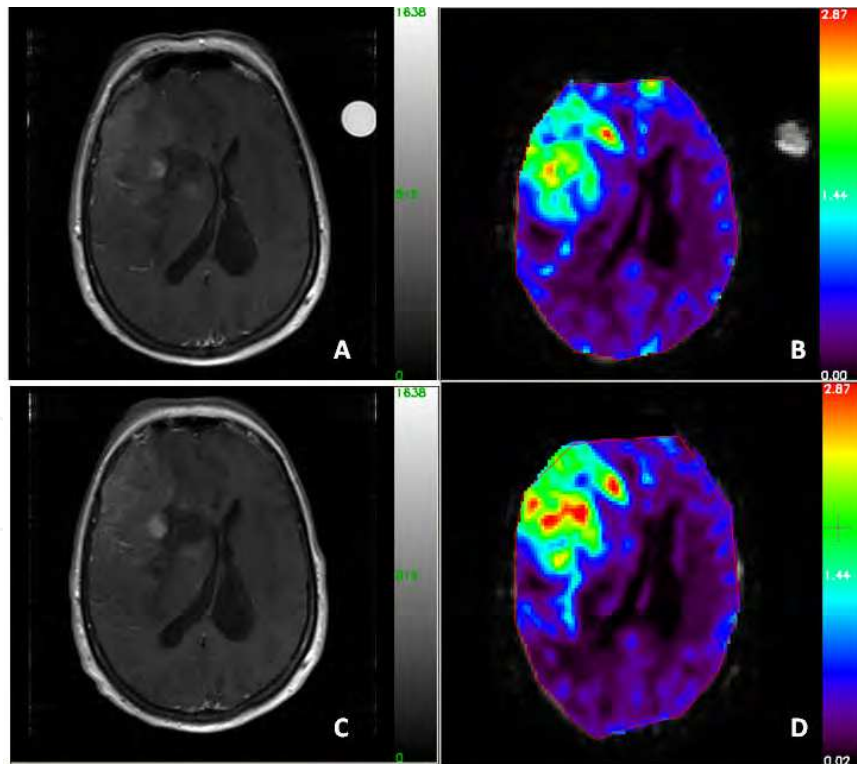


Fig. 1. Intraaxial tumor: T1-weighted image (A) with Gd-DTPA showing a brain tumor in the frontal lobe of the right hemisphere; maximum concentration color map for perfusion-weighted image with Gd-DTPA (B). T1-weighted image with gadobutrol (C); maximum concentration color map for perfusion-weighted image with gadobutrol (D).

Blood pool agents such as gadofosveset (Vasovist®) remain in the circulation for an extended time and thus might be potentially useful for imaging of the vasculature [8]. Benefits of steady state MRA imaging of the head and neck with blood pool agents are anticipated because of its high relaxivity and the extended imaging time associated with its use. CE-MRA with gadofosveset, the only blood pool agent approved for use, has demonstrated improvements in sensitivity, specificity and accuracy compared with non-contrast time-of-flight MRA. However, the benefit of gadofosveset compared with other Gd-contrast agents has been more difficult to establish [4]. Studies have shown that gadofosveset is superior to gadoterate meglumine (Dotarem®) and gadopentetate dimeglumine for MRA of the hand and whole body [3], respectively. While for MRA of the peripheral arteries, gadobenate dimeglumine significantly more specific ($p < 0.0001$) and gadofosveset was found to be significantly more sensitive ($p = 0.011$) [3].

5. Magnetic resonance angiography of pulmonary vessels

Selective visualization of the pulmonary arteries and veins in high spatial resolution has been the domain of conventional digital subtraction angiography. Drawbacks of the technique were its invasiveness, the use of nephrotoxic contrast media, and long exposure to ionizing radiation. The traditional MRA techniques (including time-of-flight and phase-contrast angiography), with long acquisition times, were substantially limited by motion artifacts, inplane saturation, and intravoxel dephasing. In particular, this affected visualization of small pulmonary vessel details.

With the introduction of three-dimensional gadolinium-enhanced MRA (3D-Gd-MRA), the limitations of non-enhanced MRA were overcome. The high-resolution pulmonary angiograms could be acquired in a single breath hold without use of nephrotoxic contrast media and radiation exposure [30;31]. CE-MRA has already been established as a safe and reliable technique for the detection of pulmonary embolism. However, overlay of arteries and veins in single-phase acquisitions with scan times of over 20 seconds affects the diagnostic reliability, particularly if assessed by the maximum intensity projection (MIP) algorithm. Several clinical scenarios require a dedicated selective assessment of pulmonary arteries and veins. In 30% of young patients with cerebrovascular accident (CVA), no underlying etiology is found. In these patients, pulmonary venous thrombosis has been suspected as the source of emboli, which was confirmed by autopsy later in some cases [32-34]. For accurate surgical pre-planning in patients with pulmonary arterio-venous malformations or bronchial carcinoma, a detailed analysis of the arterial and venous pulmonary vasculature is mandatory. Multiphase angiography with very short acquisition times in each of the single time-resolved phases has produced pure arterio- and venograms of the lungs at the cost of substantially lower spatial resolution and anatomic coverage [35].

The image quality of 3D-Gd-MRA has remarkably improved within the last few years up to a point at which vascular pathologies are detected with accuracy similar to that by the conventional digital subtraction angiography [36]. This is primarily possible by the faster sequences, which allow higher resolution scans within a single breath-hold acquisition. In addition, optimized strategies for bolus timing and acquisition during maximum arterial gadolinium concentrations have substantially contributed to consistently high image quality. However, the problem remained of imaging structures separately with rapid sequential enhancement. This includes imaging of pulmonary arteries without overlay of

veins or renal arteries without overlay of renal parenchyma [37]. It is expected to improve with faster acquisition sequences and further improvement in MRA technology.

In short we can say that the diagnostic workup of many pulmonary diseases has improved tremendously by the non-invasive, safe technique of CE-MRA. Surgical planning could benefit from the selective 3D visualization of arteries and veins compressed or invaded by centrally growing tumors. The different components of arteriovenous malformations including feeding and draining vessels could be selectively visualized, and the rate of contrast fill-in and transit could be assessed. This also includes monitoring of the lesion after interventional embolization. Selective venograms are particularly useful to assess the pulmonary venous system for thrombi.

6. Magnetic resonance angiography of heart and coronary arteries

Magnetic Resonance Angiography is the most attractive of angiography procedures for Coronary arteries because of its widespread clinical availability and the absence of ionizing radiations. Kim et al [38] performed a multicentre trial in which coronary magnetic resonance angiography revealed left main or three-vessel disease with a sensitivity of 100% and a specificity of 85%. Coronary MRA is still undergoing rapid improvement, aimed to increase its accuracy for visualizing the distal coronary artery segments and to reduce the number of uninterpretable images. The key issue in coronary MRA to improve the image quality remains a trade-offs selection between various options to acquisition time, spatial resolution, CNR and correction of cardiac and respiratory motion. Parallel image encoding is one of the techniques to improve the acquisition speed. Multiple parallel imaging coil elements are used to simultaneously obtain the signal from region of interest. Each coil has a known specific sensitivity which needs to be mapped beforehand to calculate signal share by each coil. Parallel image encoding can be combined with common coronary MRA approaches like gradient echo and echo planar imaging. Potential disadvantages of parallel image encoding are the extended computation power, the requirement for pre-scanning (to create the sensitivity map), the signal-to-noise penalty that comes with this technique, and potential inaccuracies in reconstruction. The preliminary works demonstrated the feasibility of parallel imaging for coronary MRA and ability to cut down the acquisition time by half when using three-dimensional coronary MRA combined with respiratory navigator motion correction and parallel imaging as compared to a conventional approach. In summary, the main rationale for the application of parallel-image encoding techniques is the improved data acquisition speed, which in turn may allow achieve higher spatial resolution, lower temporal resolution, or larger three-dimensional volumes.

Spiral coronary MRA is another way to improve the image acquisition speed, in which the k-space is sampled more efficiently and faster. Spiral k-space sampling offers number of advantages [39;40]: 1) reduced acquisition speed by faster sampling, 2) enhanced contrast as sampling starts from the centre of the k-space, 3) acquisition are insensitive to flow artefacts. There are certain drawbacks with spiral MRS: 1) reduced SNR because of faster acquisition, 2) it is sensitive to main field inhomogeneity.

Steady State Free Precession (SSFP) in the sequence to improve the image contrast for coronary angiography [39;40]. It gives an excellent image contrast between blood and myocardium. SSFP is characterized by an alternating phase of excitation pulse combined

with the application of time balanced gradients for all gradient directions. SSFP provides high signal intensity for tissues with a high T2/T1 ratio (blood) independent of TR and flow artefacts. SSFP is of special interest in cardiac functional analysis. SSFP has been compared with GRE, and improved endocardial border delineation was reported for the SSFP images which in turn facilitated automated edge detection during cardiac functional analysis. The potential use of SSFP for coronary MRA has recently been shown by Deshpande et al. in a study comparing conventional FLASH (fast low-angle shot) to three-dimensional true-FISP (Fast Imaging with Steady-state free Precession)[39]. The SNR and CNR were improved with 55% and 178% respectively for the SSFP acquisitions. McCarthy et al. used SSFP for the evaluation of coronary artery stenosis in 17 patients, with x-ray angiography as standard of reference. In this work, it was shown that hemodynamically significant stenoses could be detected with a sensitivity of 70% and a specificity of 88%.

Coronary MRA using a static magnetic field strength of 3 Tesla improves the signal-to-noise ratio, which in turn can be employed to increase the in-plane resolution, reduce the slice thickness, reduce the overall acquisition time, or to compensate for the signal-to-noise penalty that comes with several fast acquisition techniques such as echo planar imaging (EPI) or spiral imaging due to high sampling bandwidths. The increased field strength may also cause various side effects, especially when subjects move through the static field while entering the bore of the magnet leading to vertigo and nausea.

Cardiac motion correction is one major concern which captures much attention in cardiac MRA. Cardiac motion occurs in both systole and diastole, but is said to be minimal in mid-diastole (at diastasis). Cardiac motion correction is therefore usually achieved by timing the acquisition to the mid-diastolic phase of the cardiac cycle. There is considerable variation of motion patterns, motion ranges and motion velocities for coronary artery segments among individual patients. On average, the right coronary artery has greater movement and greater velocity as compared with the other coronary arteries, up to a factor of two for the proximal segments. But, in spite of all movements, the coronary arteries return to the same location from heartbeat to heartbeat during the rest period, which is an absolute requirement to perform a quality coronary MRA.

In addition to cardiac motion, heart is subjected to respiratory motions as well. Heart sits on the diaphragm, it translates during each respiratory cycle in a supero-inferior direction. These motion artefacts can be corrected and presently there are two approaches in clinical settings: 1) breath holding and 2) free-breathing navigator gating. During navigator gating approach, the position of the right hemi-diaphragm is deduced in real time from a navigator pencil beam acquisition. The image data that is acquired only while diaphragm position is within acceptable window are used for filling the k-space. The gating window is usually chosen as the end expiratory respiratory phase. Navigator implies that only a fraction of total imaging time is used for actual data acquisition. The lead to an overall imaging time prolonged by a factor of two using gating for motion correction. Patient compliance is very important in this aspect, an average navigator efficacy is 40-60% but it drops to 20%-30% when patient is in-compliant or very sick to maintain a regular breathing. The problem is sometime addressed with motion adapted gating (stringent acceptance window for low frequencies of k-space but wider window while acquiring higher frequencies).

Coronary MRA is practically used for all cardiac assessment protocols. Anomalous coronary arteries, coronary stenosis, bypass grafting and assessment of relative perfusion and vascular integrity are some of the commonest indications for cardiac MRA.

In conclusion, today's technical achievements for three-dimensional coronary MRA are able to provide excellent high-resolution images. However, MRA is still hampered by poor sensitivity and specificity for diagnosing coronary artery disease in distal segments even though it is the best non-invasive technique for evaluation of the proximal arteries. As coronary plaque imaging is still very challenging with MRA therefore CT Angiography benefits from high contrast of plaque compared to adjacent tissue even in the distal part of the coronary artery. However, with metal stents the major drawback in CT is, that the metal artifacts make image interpretation impossible.

7. Magnetic resonance angiography of the abdomen and pelvic arteries

Contrast enhancer MRA is now very well accepted as a reliable technique in assessment of abdominal vascular system (Figure 2 courtesy) [62]. In recent investigations, multiphase 3D CE-MRA has been shown advantageous in several respects [41;42]. The acquisition of multiple phases during contrast media transit guarantees the arterial contrast with no venous contamination [43;44]. In recent investigations with a more technical focus, multiphase 3D-Gd-MRA has been shown advantageous in several respects [45]. It is also shown that Time-resolved CE-MRA performed at 3 T with a 32-channel volume coil can be improved using the high-relaxivity agent, which increases quality and quantity of vessel enhancement (Figure 3 courtesy) [46].

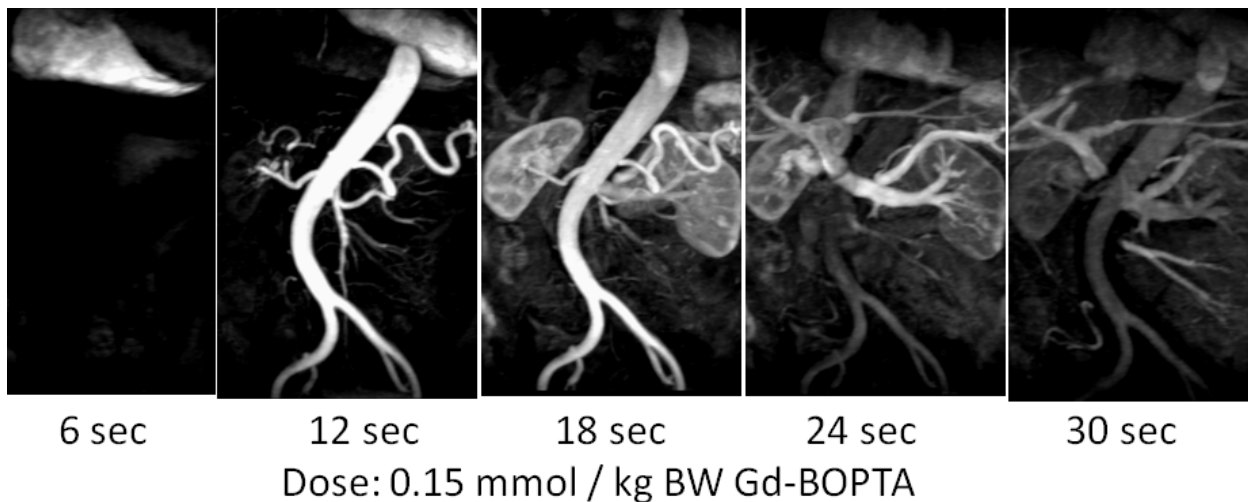
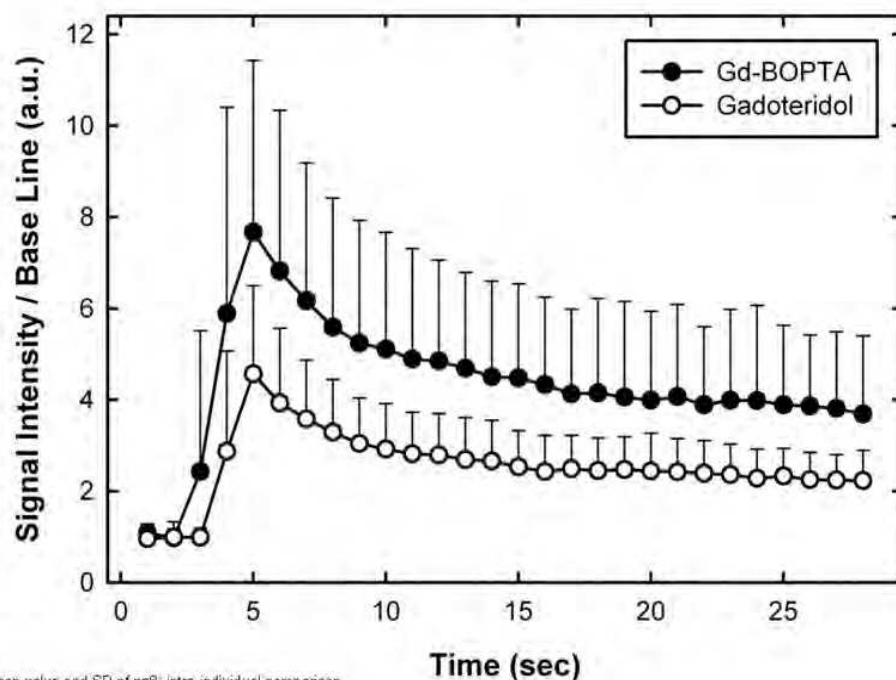
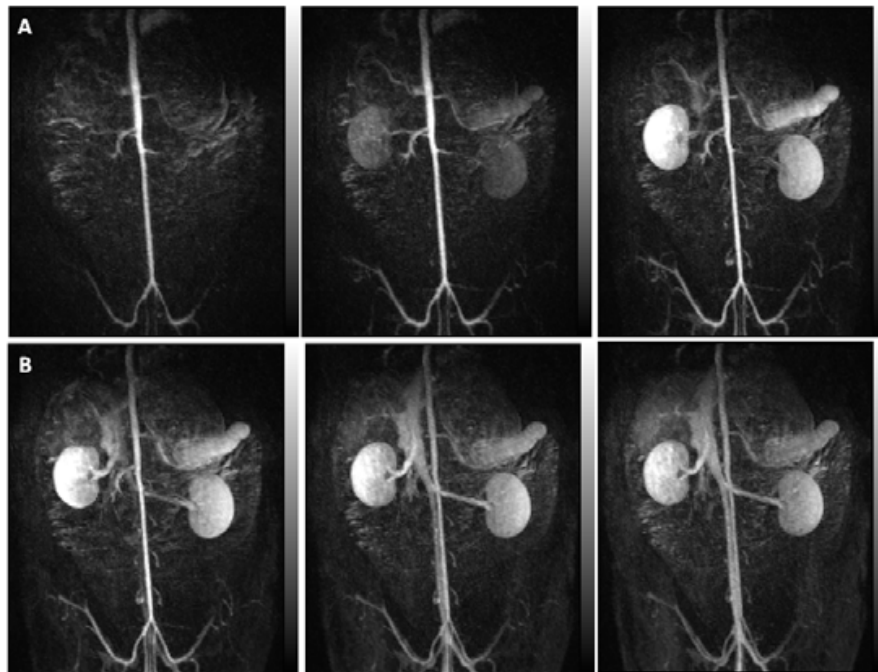


Fig. 2. Multiphase MRA of abdominal aorta after injection of MR contrast Gd-BOPTA, showing arterial, parenchymal and venous phase with respect to time (sec).



Mean value and SD of n=8; intra-individual comparison
(paired t-Test $p < 0.001$)
(T value 13.34; Degrees of Freedom 28)

Fig. 3. Multiphasic time resolved CE-MRA allowed high spatial resolution imaging of the abdominal aorta. The first three phases present the early and late arterial phase while the lower row shows the early and late venous phase. The hepato-biliary pathway can be depicted nicely by Gd-BOPTA (a), while Gadoteridol is mainly excreted via the kidney (b). c) Relative signal time curve of both contrast media (SI [aorta] / SI [baseline]). Significantly ($p < 0.001$; paired t-test) greater signal intensity enhancement was noted for Gd-BOPTA at all time-points after the peak signal enhancement is attained.

The acquisition of multiple phases during contrast media transit almost guarantees high arterial contrast with absent venous enhancement. In addition, the technique can show vessel segments with substantially delayed enhancement on successive scans. This is particularly important in cases of aortic dissection, aneurysm, or occlusion with variably delayed fill-in of the arteries downstream [47]. During a typical abdominal aorta imaging, in the early arterial phase, the distal and intrarenal arteries are visualized without substantial overlay from enhanced renal parenchyma [37]. In addition, vessels structures with delayed enhancement can be detected in later phases of the scan [48] [49]. It has been observed that the results from the renal arteries and common iliac arteries were somewhat better than those from the external iliac vessels and further distal segments [50]. This is most likely related to the three issues. First, the external iliac arteries curve fairly anteriorly and thus are often located in the margins of the 3D slab where the signal is typically inhomogeneous due to the poor slice profile of the fast 3D GRE sequences. Second, stenoses in this vessel's segments might be already located at the margin of the field-of-view where the magnetic field is not linear any more, resulting in image distortions [51;52]. Third, the spatial resolution of MRA sequence occasionally limits accurate evaluation of very small external iliac arteries [53]. In literature it has been reported that the acquisition of multiple phases is helpful for depicting vessel segments with substantially altered enhancement kinetics or delayed contrast fill-in [42;54]. Multiphase MRA is a robust technique with reproducible accuracy [31;43]. It can therefore be recommended for screening of atherosclerotic abdominal and pelvic arterial disease. Higher resolution MRA techniques may be preferred for staging of very small vessels, presurgical evaluation or fibromuscular disease.

8. Magnetic resonance angiography of vascular run-off

Contrast-Enhanced Magnetic Resonance Angiography is rapidly gaining acceptance as the method of choice for diagnostic imaging of the run-off vessels [55] [56] (Figure 4 courtesy [55]).

Compared with time-of-flight imaging, CE-MRA is significantly faster and far less prone to flow, saturation, and motion artefacts. Recent studies have shown CE-MRA with gadolinium contrast agents to be equivalent to conventional angiography for diagnostic imaging of the peripheral vasculature [57;58]. However, a problem inherent to CE-MRA of the run-off vessels is the large vascular territory to be imaged [56]. While technological improvements such as moving bed and dedicated lower extremity coils have contributed towards advances, satisfactory imaging of the run-off vessels is still highly dependent on the spatial resolution attainable. Unfortunately, spatial resolution in the peripheral arteries often is restricted by insufficient signal-to-noise (SNR) and contrast-to-noise (CNR) in the more distal parts of the field of view (FOV). In looking to overcome problems associated with insufficient SNR and CNR, various authors have advocated either single injections of high-dose contrast agents or cumulative dosing with injections at two or more stations along the vascular territory. Drawbacks of these approaches, however, include increased costs for contrast agents and, when multiple dosing protocols are used, problems associated with degraded image quality following the second injection due to residual gadolinium from the first injection and the high dose related Nephrogenic Systemic Fibrosis. An alternative approach to increasing SNR and CNR with standard doses of gadolinium without further

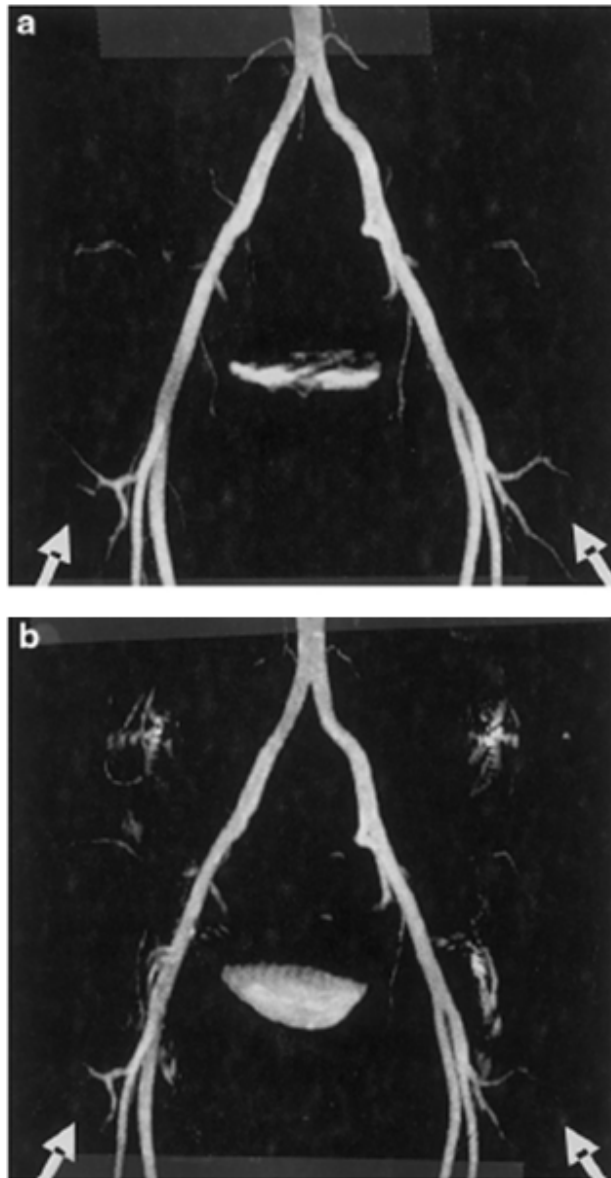


Fig. 4. Targeted maximum intensity projections (MIP) of the pelvic region in the same volunteer after identical dosing (0.1 mmol/kg bodyweight, flow rate of 0.8 mL/second, flush 25 mL saline) of the weakly protein interacting agent, Gd-BOPTA (a) in comparison to Gd-DTPA (b). The intra-individual comparison revealed better conspicuity of smaller vessels (arrows) as well as more homogenous vascular enhancement after Gd-BOPTA.

limiting spatial resolution would be to use contrast agents with preferential vascular contrasting properties. Gadobenate dimeglumine (Gd-BOPTA, MultiHance™; Bracco Imaging SpA, Milan, Italy) is a gadolinium based contrast agent that possesses increased T1 relaxivity *in vivo* compared to other available gadolinium agents ($9.7 \text{ mM}^{-1} \text{ second}^{-1}$ compared to between 4.3 and $5.0 \text{ mM}^{-1} \text{ second}^{-1}$) due to a capacity for weak and transient interaction with serum albumin [59-61]. Preliminary investigations in healthy volunteers revealed that the vascular signal intensity of the abdominal aorta is higher and longer-lasting following administration of Gd-BOPTA than following administration of Gd-DTPA at the same dose and injection rate. More recently, studies in patient volunteers have

demonstrated marked superiority of Gd-BOPTA over Gd-DTPA for time-resolved renal and pelvic CE-MRA [37]. Superiority for multiphasic MRA of the abdomen has also been noted for Gd-BOPTA compared to Gd-DTPA and the more highly concentrated gadolinium agent, Gd-BT-DO3A [56].

The trade-off between high spatial resolution and the need for sufficient SNR and CNR for successful diagnosis is particularly pronounced for CE-MRA of the run-off vessels. Currently, CE-MRA is most frequently performed using conventional gadolinium-based contrast agents such as Gd-DTPA whose T1 relaxivities in protein-containing aqueous solution fall in the range between 4.3 and 5.0 mM⁻¹ second⁻¹. These agents possess no capacity for protein interaction and it is frequently necessary to use comparatively high doses or cumulative dosing regimens to obtain sufficient diagnostic quality along the length of the peripheral vasculature. Since the diagnostic quality of CE-MRA is dependent upon the intensity of vascular contrast and thus the extent to which the T1 relaxation time in blood is reduced during image acquisition, contrast agents with higher T1 relaxivity in blood may be expected to provide greater vascular signal intensity enhancement and hence greater diagnostic efficacy. Gd-BOPTA is a gadolinium-based MR contrast agent whose plasma kinetics are indistinguishable from those of Gd-DTPA and other non-specific gadolinium-based contrast agents in demonstrating complete elimination within 3 days of administration. The results of these studies confirm the superiority of Gd-BOPTA over Gd-DTPA for CE-MRA; significantly higher CNR and SNR were noted for Gd-BOPTA for almost all segments from the distal 2 cm of the abdominal aorta to the posterior and anterior tibial arteries [35;62]. The only segment for which statistical superiority have not been demonstrated was the right iliac artery. That superiority was not demonstrated for this vessel can be attributed to the fact that an unusually wide range of values were noted for this segment compared to the other eight segments. It is possible that this was due to this region lying at the edge of the field of view and the coil as mentioned earlier. In terms of the diagnostic quality of images acquired, the results of the studies again indicate superiority for Gd-BOPTA [63]; the overall diagnostic quality score out of a maximum possible score of 18 was 17.4 ± 1.5 for Gd-BOPTA and 13.8 ± 2.4 for Gd-DTPA [64] [63]. Significantly, there were no vascular segments in which diagnostic quality was determined to be poor following Gd-BOPTA administration [63]. On the other hand sometimes diagnostic quality was determined to be poor for the left and right tibio-fibular trunks of four of the fourteen subjects (28.6%) following Gd-DTPA administration in a study. Venous overlay is a potential problem for long time of acquisition. The availability of sequences with shorter TR and TE time which permit more rapid acquisitions may go some way towards overcoming potential problems of venous overlay when using Gd-BOPTA for peripheral MRA [63]. The greatest benefits of Gd-BOPTA are to be found in the most distal, smaller vessels of the lower leg [63]. In terms of its potential usefulness in routine clinical practice, one possibility is that a lower overall dose could be employed to achieve similar increases in SNR and CNR to those increases currently achieved with Gd-DTPA at the same dose. Higher doses of Gd-DTPA and other conventional agents, and a variety of dosing regimens, are currently used to evaluate patients with peripheral vascular disease. Future work might usefully be aimed at evaluating whether better diagnostic performance is achievable with equivalent high doses of Gd-BOPTA or whether lower overall doses can be employed satisfactorily [65]. Similarly, it would be of interest to determine more precisely the influence of injection rate on Gd-BOPTA-enhanced MRA of the peripheral arteries.

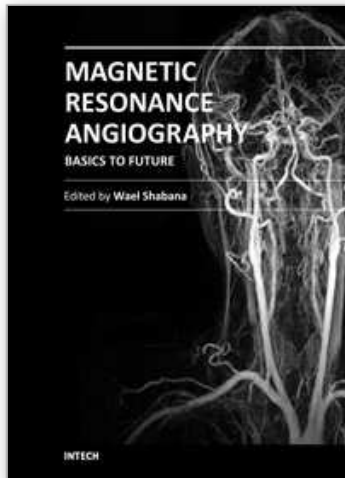
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As MRI has paved its role in diagnostic angiography. MRA has the potential to provide more physiological and pathophysiological data over the disease in addition to the anatomical information. This book is divided into three sections. The first section discusses the basics of MRI angiography. It starts with focus on the contrast agents that are mainly used in MR angiography with detailed discussion of advantage and limitations of different types of contrast. The second chapter is oriented more towards the technical consideration that contribute to good quality examination, both the non contrast and contrast based sequences from black to bright blood imaging , contrast enhanced MRA, review of clinical application of MRA in different body systems and MR venography. The second section reviews the clinical application of MRI mainly in the head and neck and brain ischemia imaging. The new high resolution intracranial plaque imaging of the branch athermanous disease, to the hemodynamic of intracranial atherosclerotic stroke and quantitative MRA imaging in neurovascular imaging, are the topics in this section. Also this section covers the future prospective and the new frontiers MRI angiography is exploring. In the third section, MRA of aortic disease in children with emphasis on cardiac MRA.

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