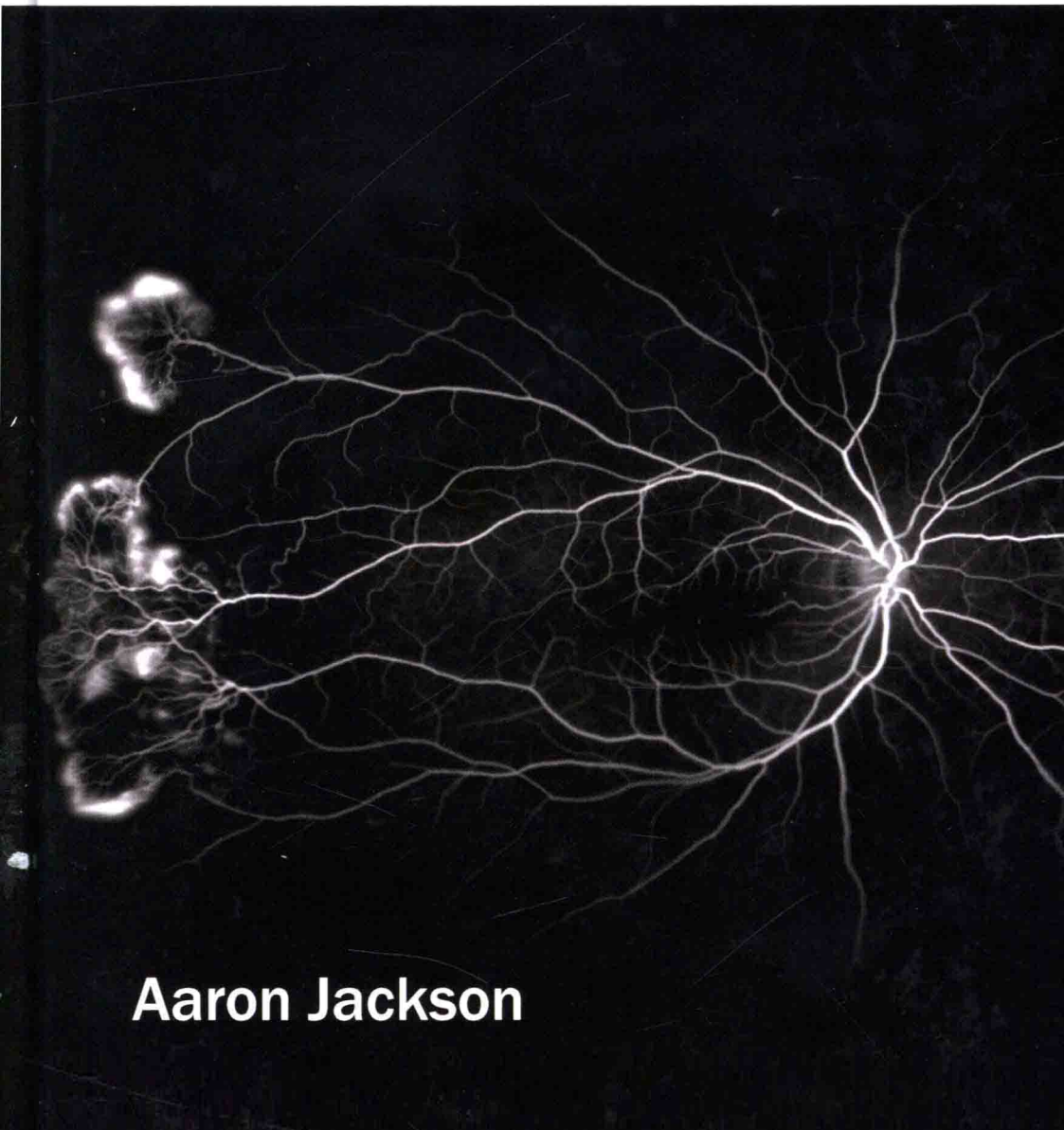
Magnetic Resonance Angiography

Essentials and Applications



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Magnetic Resonance Angiography: Essentials and Applications

Edited by **Aaron Jackson**

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Preface

The world is advancing at a fast pace like never before. Therefore, the need is to keep up with the latest developments. This book was an idea that came to fruition when the specialists in the area realized the need to coordinate together and document essential themes in the subject. That's when I was requested to be the editor. Editing this book has been an honour as it brings together diverse authors researching on different streams of the field. The book collates essential materials contributed by veterans in the area which can be utilized by students and researchers alike.

As MRI has proved its function in diagnostic angiography, MRA has the ability to give more physiological and pathophysiological data about the illness along with anatomical information. This book discusses the fundamentals of MRI angiography, starting with contrast agents that are majorly used in MR angiography with a comprehensive discussion of benefits and conditions of various types of contrast. The book also presents the technical considerations that add to better 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 distinct body systems and MR venography. It also includes the reviews of the clinical applications of MRI, primarily in the head, neck and brain ischemia imaging. Topics like high resolution intracranial plaque imaging of the branch athermanous illness, the hemodynamic of intracranial atherosclerotic stroke and quantitative MRA imaging in neurovascular imaging are also discussed in this book. It also includes future potential and new frontiers of MRI angiography, in addition to emphasizing on cardiac MRA and MRA of aortic disease in children.

Each chapter is a sole-standing publication that reflects each author's interpretation. Thus, the book displays a multi-facetted picture of our current understanding of application, resources and aspects of the field. I would like to thank the contributors of this book and my family for their endless support.

Editor

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Part 1

Basics and Applications of MR Angiography

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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 armoury. 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
Gadoterdol	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 ($l \cdot mmol^{-1} \cdot s^{-1}$)	r2 ($l \cdot mmol^{-1} \cdot s^{-1}$)	r1 ($l \cdot mmol^{-1} \cdot s^{-1}$)	r2 ($l \cdot mmol^{-1} \cdot s^{-1}$)
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.

Bueltmann 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 ($p\leq0.026$) 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 ($p\leq0.021$)

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 benefiticial in brain perfusion imaging than gadopentetate dimeglumine (Figure 1 courtesy) [23].

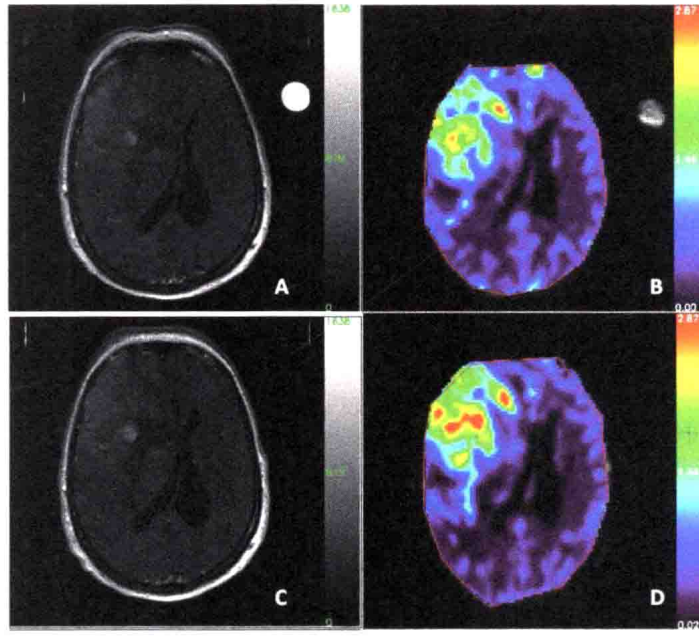

Fig. 1. Intraaxial tumor: T1-weighted image (A) with Gd-DTPA showing a brain tumor in the frontal lobe of the right hemisphere; maximum concentration color map for perfusion-weighted image with Gd-DTPA (B). T1-weighted image with gadobutrol (C); maximum concentration color map for perfusion-weighted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