Résumé

Angiographie par résonance magnétique avec injection de produit de contraste : évolution vers le corps entier et le temps réel

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L’ARM désigne l’ensemble des techniques qui permettent la visualisation des vaisseaux par imagerie par résonance magnétique. L’injection de gadolinium couplée aux séquences en écho de gradient avec injection est la technique de choix pour l’imagerie vasculaire. Les développements technologiques successifs autour de cette technique permettent d’effectuer des acquisitions de plus en plus rapides.

L’objectif de cet article est de présenter deux principales évolutions de l’ARM, respectivement l’ARM corps entier et l’ARM 3D dynamique. Les principes techniques, les méthodes d’acquisition, les avantages et limites à partir d’une expérience réalisée sur un appareil 1,5T seront détaillés afin de permettre leur utilisation en routine clinique pour le radiologue.


Abstract

MRA includes all techniques used to depict vessels with MR. Gadolinium contrast injection combined with gradient echo sequences is the technique of choice for vascular imaging. Technical advances now allow faster acquisitions. The purpose of this article is to present two main advances with MRA: whole-body MRA and dynamic 3D MRA. Technical considerations, acquisition techniques, advantages and pitfalls based on our experience with a 1.5T MR unit will be discussed in order to promote their use in routine clinical practice.

Key words: MRA. Gadolinium. Technique.


MRA is a magnetic resonance imaging technique suitable for vascular imaging that can be performed with or without contrast enhancement. The two main MRA techniques without contrast injection are time-of-flight MR imaging (TOF) (1-4) and phase-contrast MR imaging (5-8). The signal obtained for these two imaging techniques is based on blood flow, i.e. blood circulating through the vessels is the basis of the non-contrast-enhanced MRA signal. This image acquisition method has some drawbacks such as long acquisition times, small imaging fields and even artefacts related to different flow phenomena. Image acquisition techniques have changed with the advent of gadolinium contrast agents. The signal no longer originates from the circulating blood but rather from gadolinium present in the blood vessels. Gadolinium substantially reduces the T1 of blood, thus enabling a much greater intravascular signal intensity (9). In MRA, images are usually acquired via T1-weighted 3D volume sequences synchronised with contrast enhancement to generate a vascular hypersignal. The acquisition time is considerably reduced by using these sequences, and obtaining a 3D volume of a given region is consistent with breath-hold MRA (10-12). This quick acquisition time is especially interesting as it avoids the problem of kinetic breathing artefacts in chest and abdominal MRA.

Review of the contrast-enhanced MRA technique

Gadolinium accelerates the proton phase-shift velocity, thus reducing T1 and T2. The T1 of blood usually ranges from 800 to 1200 ms. T1 can be reduced to as low as 50 ms after gadolinium enhancement, depending on the injection volume. The T1 of fat at 1.5 T is 270 ms, so the vascular T1 must be below this value to ensure contrast with the surrounding fatty tissue (13). The extracellular distribution and pharmacokinetics of gadolinium are comparable to those of water-soluble ioinated contrast media. In addition, it has lower nephrotoxicity at the dosages and concentrations at which it is administered in MRA. Vials contain 0.5 mmol/ml of gadolinium chelates, with the standard dose generally being 0.1 mmol/kg, or 0.2 ml/kg. Gadolinium administration is immediately followed up with an injection of physiological saline at the same rate of injection. This latter injection flushes the vessels, the peripheral vein, while forcing the gadolinium bolus into the bloodstream. Rapid gradient echo sequences are used in 3D MRA (13). Gadolinium-enhanced MRA sequences are designed to acquire images with high vascular contrast and as short as possible acquisition times. Low spin angles (25°) and short TR are therefore used for the acquisition sequences. These two features reduce the signal from the surrounding

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Contrast-enhanced MR angiography (MRA) is a diagnostic imaging technique that uses a contrast agent to enhance the visibility of blood vessels in the body. The contrast agent, typically gadolinium, helps to highlight the vascular structures by increasing the signal from regions with a short T1 (vessels containing gadolinium). Moreover, the contribution of the residual transverse magnetization signal is minimized by “spoiling” the acquisition sequence, thus increasing the T1 contrast. A spoiled RF wave is applied during acquisition to destroy a signal (magnetization) so as to improve contrast between tissues.

For instance, spoilers may be emitted to reduce fat signals. In contrast-enhanced MRA, imaging sequences use TR of less than the T2 of the imaged tissue; transverse magnetization (T2 contrast) therefore persists at the end of each acquisition. In such cases, spoiling is used to minimize the impact of this magnetization in order to increase the T1 weighting of the image.

Parallel imaging techniques are generally used to reduce the acquisition time for MRA sequences (14-18). Phased-array coils are required for this technique. These coils include several small diameter elements. Each coil element separately and simultaneously captures the different signals. All parallel imaging techniques implemented to accelerate acquisition are based on this concept. The idea is to reconstruct an image from the different signals received by each coil element.

There are two main techniques. First, a complete k space is reconstructed and a reverse Fourier transform is applied to it to generate a complete image – this technique is used by GRAPPA (GeneRalized Auto-calibrating Partially Parallel Acquisition). Secondly, the final image is reconstructed after the reverse Fourier transform has been applied to each signal – this technique is used by SENSE (SENSitivity Encoding), PILS (Partially Parallel Imaging with Localized Sensitivity) and ASSET (Array Spatial Sensitivity Encoding Technique). The SENSE technique is described here.

The SENSE principle (19-23) involves reducing the number of lines scanned in the coding phase to lower the acquisition time. The k-space scanned is reduced via the so-called “reduction factor”. Down-sampling the k-space reduces the field of view and generates folds. These have to be unfolded to be able to process the image. The initial image is obtained from the different coil elements.

The aim is to reconstruct a complete image from these different intermediate images. Each coil element receives a specific signal according to its position, and the goal is to determine the contribution of each coil element in generating the image so as to correct the folding. The contribution of each coil element is established during a sequence obtained at the beginning of the examination – the final image can be reconstructed on the basis of this information (fig. 1). The amount of time saved depends on the selected SENSE factor value. The maximum value of the factor depends on the number of coil elements.

For instance, if there are two coil elements, the maximum acceleration factor is two, which means that every other line in the coding phase in the k-space is scanned. Consequently, the acquisition time is twofold lower.

Contrast-enhanced MRA acquisitions are based on a k-space filling strategy called CENTRA (24, 25) (Contrast-Enhanced Timing Robust Angiography).

The MR image is not acquired pixel by pixel. The information required to obtain the image is captured in a frequency space called the k-space or Fourier space. The so-called Fourier transform is then applied to obtain the image. The k-space thus contains all information required for reconstructing the image.

![Fig. 1: The SENSE principle.](image)

obtained after applying the mathematical algorithm, i.e. Fourier transform. The centre of the k-space contains information encoding the image contrast (main features of the image), while information encoding small image structures and details is located at the periphery. The CENTRA technique involves filling the k-space starting at the centre when the contrast reaches the target vessel and then encoding the periphery of the Fourier space (fig. 2). A high quality vascular hypersignal is thus obtained. The arterial peak is perfectly synchronised with the acquisition at the centre of the k-space, inducing a maximum arterial signal and a minimal venous signal.

MRA can detect stenoses in a given region, therefore facilitating high quality accurate diagnoses in carotid, renal, abdominal, pelvic and peripheral arteries. MRA has become the gold standard for screening these indications. However, whole-body MRA has greater screening potential for diseases that affect several different parts of the body.

Whole-body MRA

MRA was previously used only to image areas containing a single 40-48 cm field of view because of problems of rapid tissue enhancement and contrast dosage limitations. The “bolus-chase” technique can now be used after a single contrast injection to successively cover regions including the pelvis, femur, popliteal and calf arteries. Thanks to recent software improvements, bolus-chase MRA can be used to image the entire body. In whole-body MRA, arterial areas extending from the carotids to lower limb vessels are covered by four fields of view. The acquisition time does not exceed 90 s with a single contrast injection. The whole-body acquisition principles are described on the basis of an example from an Achieva 1.5 T MRI (Philips. Medical System, Suresne, France). A scanner table extension is required before the examination in order to increase the spatial coverage by around 1 m, so that patients as tall as 2 m can be imaged. The patient is positioned back down with feet at the tunnel entrance. The scanner coil emits and receives signals. SENSE cannot be used with this type of coil.

Acquisition technique

A patient’s entire body cannot be imaged in a single field of view, so the scan is divided into several parts, or acquisition stations. Four acquisition stations are required to cover the patient’s entire body. The first encompasses the carotids and chest, the second the abdomen and pelvis, the third the thighs and the fourth the calves and feet (fig. 3).

Images are acquired at the four acquisition stations in the three main planes (coronal, axial and sagittal) at the beginning of the examination to position the fields of view in order to be able to accurately focus on the patient’s main arteries. Once the four fields of view are positioned, two acquisitions are performed, the first without contrast injection and the second with injection. This is followed by a post-treatment step whereby the contrast-enhanced image is subtracted from the non-enhanced image in order to highlight the vascular information. The examination begins with an acquisition without injection, with the patient placed back down and feet at the tunnel entrance. The feet are scanned first (station 4, described in figure 3). The images are obtained in the coronal plane with a rapid gradient echo sequence (TR/TE: 3.1/1.2 ms, 30° flip angle, 320 x 320 scan matrix, 512 x 512 reconstruction matrix). The table is quickly moved between each angiographic acquisition to obtain four 3D volumes in less than 90 s with a reconstructed voxel size of 0.95/0.95/2 mm.

The acquisition without contrast is followed by an acquisition with gadolinium enhancement. At this examination step, the patient’s chest is located at the centre of the tunnel. The acquisition with contrast enhancement thus begins with the carotid and chest field of view (station 1, described in figure 3). 0.2 ml/kg of gadolinium is administered at 0.8 ml/s followed by a flush of 30 ml of saline at 0.4 ml/s. The contrast flow is

Fig. 2: The CENTRA principle. The centre of the k-space encoding the image contrast (low frequency) is filled during the arterial phase, whereas the periphery of the k-space is encoded during the venous phase. The venous return signal is thus reduced.
monitored by bolus tracking. Bolustrak is a fast 2D imaging sequence that detects the contrast as it enters the target region with image renewal every second. Acquisition is triggered when the contrast enters the examined region. Acquisition in the first field of view is triggered when the contrast enters the carotid regions, and the table then moves sequentially to enable acquisition in the three other fields of view. The parameters of this sequence are identical to those used with the non-enhanced sequence (fig. 3). Note that during the acquisitions with and without enhancement, patients are asked to hold their breath to avoid artefacts at stations 1 and 2.

The main problem encountered with this type of acquisition is synchronising the contrast medium with the acquisition parameters. Too rapid blood flow (acquisition starts too late) induces lower limb venous signal spoilage, whereas no signal will be received from this region when the acquisition is triggered too early. Some authors recommend using bi-phase contrast medium injection to avoid image spoilage due to venous return. Acquisitions at stations 1 and 4 are obtained after the first injection and acquisitions at stations 2 and 3 are obtained after the second injection (26).

For each station, PPM reconstructions are performed from the contrast-enhanced/non-enhanced subtraction images. These PPM can be adjacent and a whole-body PPM can be obtained by using special software. Finally, MPR reconstruction can also be obtained for target regions (fig. 4 and 5).

**Limitations**

The first shortcoming of this technique concerns the difference between the progress of the gadolinium bolus and the acquisition. The resulting image is thus spoiled due to venous return if the acquisition is triggered too late. This issue can be overcome through better synchronisation of the acquisition at the last station with the arrival of the contrast agent. In practice, this is hard to do because bloodflow differs between patients. An acquisition procedure would have to be developed to assess the bloodflow rate of each patient. A small quantity of medium (2 ml) could first be injected to determine the contrast transit time between the carotid arteries and the lower limbs. Then the acquisition could be adjusted to the patient's bloodflow rate. Theoretically this strategy would reduce artefacts due to venous return.

A whole-body MRA intravascular signal is weaker than that of a targeted MRA. This signal deficiency is associated with the use of body coils, not surface coils. Siemens has developed a whole body surface coil which, according to two authors, generates an optimal signal because of the higher sensitivity of each coil element (27, 28). However, the spatial resolution is a limiting factor for accurate stenosis quantification and small vessel imaging, regardless of the technique used.

**Applications**

Whole-body MRA is a simple, rapid noninvasive technique to obtain clear accurate information on the vascular status of a patient. This technique just requires a scanner table extension and no surface coils are used. Such coils can nevertheless be used to improve the signal ratio as a better signal is received, but the scanning
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period is increased due to the time required to install the different coils. In our case, it just takes 15 min or less to perform all acquisitions for the examination. Stenoses or additional aneurysms present in the different peripheral segments can be detected by using this technique in conjunction with other preimaging diagnostic examinations. This technique can be used to clearly highlight the extent and impact of a dissection or aortic aneurysm throughout the patient’s body. For instance, patients with coronary heart diseases generally develop atherosclerosis in other vascular regions. One study showed that, in 160 patients, 16 (10%) had infarct signs, 77 (48.1%) had stenoses of over 50% in peripheral arteries (other than coronary), 17.5% of which were in renal arteries, 12.5% in carotid arteries (29).

Some teams have recommended a complete vascular system examination for patients presenting with peripheral arterial occlusive diseases (PAOD). A whole-body 3D MRA with several acquisition stations is carried out to screen the entire vascular system. TOF MRA is used to image cerebral arteries whereas sequences focused specifically on the heart are obtained to collect functional information and for late myocardial enhancement. This technique is implemented to screen for concomitant cardiovascular diseases in PAOD patients or those with suspected atherosclerosis (30). According to the concept described above, specific examinations are conducted to screen cerebral, cardiac and vascular regions, especially for cardiovascular disease detection and prevention. This technique would enable earlier detection of these diseases and thus earlier treatment (31).

Fig. 4: Whole-body imaging of a 59 year-old patient.

a Left primitive iliac stenosis and post-stenotic ectasia.
b Thrombosis of the left subclavicular artery.
c Direct emergence of the left vertebral artery aorta.
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Dynamic 3D MRA

4D TRAK (Time Resolved Angiography used Keyhole) is the dynamic 3D imaging technique developed by Philips, whereas it is called TREAT (Time Resolved Echo-shared Angiography Technique) by Siemens and TRICKS (Time Resolved Imaging of Contrast Kinetics) by General Electric. These three techniques are used to obtain several 3D volumes over a time course and at regular intervals, thus offering the possibility of temporal analysis of MRA examination data. The dynamic 3D MRA sequences described above include two phases. One is obtained without contrast enhancement and a post-processing mask is acquired during this phase. The second phase is performed with enhancement, and the different dynamic data are acquired during this phase.

The main difference between these three techniques is the method used to improve the temporal image acquisition resolution. The TREAT and TRICKS techniques are quite similar with respect to processing k-space data. With these two techniques, the k-space is divided into three concentric parts of the same area going from the centre to the periphery. Only one of these three parts is acquired during dynamic data acquisition. At the end of acquisition, the different acquired k-space fractions are combined to reconstruct several complete k-spaces. Then a Fourier transform is applied to obtain different 3D volumes. Contrary to TRICKS and TREAT, 4D TRAK scans only the central part of the k-space during dynamic data acquisition. Then, in the data processing phase, the mask frequency information is combined with that of the different dynamic features in order to generate a complete k-space.

TRICKS has been described to boost the temporal and spatial resolution when screening pulmonary embolisms with these different techniques. With the sequence proposed by the authors, a 3D chest volume can be obtained with a spatial resolution of 0.7 x 0.7 x 1.5 mm every 3.3 s (32). 3D thoracic volumes are obtained every 3 s using the 4D TRAK method, with a spatial resolution of 0.9 x 0.9 x 1.3 mm. The high temporal resolution of these sequences improves arteriovenous differentiation. This time-resolved MRA technique is described for screening pulmonary vessels (33) and vascular shunts such as arteriovenous fistula (34). Conventional contrast-enhanced MRA and MRA using the CENTRA keyhole technique were compared for screening pulmonary veins (35). Pulmonary vein diameters were measured. More accurate measurements were thus obtained in images acquired with the conventional technique (less measurement variability), but dynamic 3D MRA performed better in separating the arteriovenous phase.

Regarding the fistula study (34), dynamic 3D MRA was used to image 12 patients presenting with a fistula in the lower or upper limbs. Two MRA sequences were used for screening the lower limbs and then the upper limbs. The temporal and spatial resolutions of each sequence were 2.2 s for a voxel size of 1.14 x 1.14 x 3 mm, and 3.2 s for a voxel size of 1.64 x 1.64 x 3 mm, respectively. The diagnostic quality was assessed for the 12 patients during the study. Two stenoses were detected in the arterial branch, two stenoses within the arteriovenous fistula, 13 along the venous segment, and three aneurysms. For comparison, the authors reported the findings of two studies. In one of these studies, a sequence with a temporal resolution of 10 s and a voxel size of 1.5 mm was used, with a stenosis detection specificity of only 10% (35). The resolutions in the second study were 32 s for a voxel size of 0.84 x 0.84 x 3 mm, with a stenosis detection specificity of as high as 99% (36). However, the authors argued from experience that the 10 s and 32 s resolutions were not sufficient to separate the arteriovenous phase and accurately analyse the shunt anatomy.

Fig. 5: Whole-body 3D MRA imaging of a 68 year-old man.

- **a** Composite bypass (prosthesis – vein) of the left femoral popliteal vein.
- **b** Diffuse lesions, especially left outer iliac stenosis above the bypass.
- **c** Left distal lesions, right superficial femoral thrombosis.
The authors of both studies concluded that this imaging technique is fast enough for separation of the arteriovenous phase and anatomical shunt analysis (32-34).

Dynamic 3D MRA principle

Dynamic 3D MRA involves acquisition of several so-called “dynamic” 3D features at regular time intervals. Information on each dynamic feature is obtained from just a fraction of the central Fourier space. With 4D-TRAK, the keyhole provides an opportunity to regulate the quantity of information used to construct the (dynamic) image. Before the start of acquisition, the operator selects a value within the 1-70% range. This value represents the percentage of space used for constructing each dynamic image. The keyhole function reduces the acquisition time by encoding only a portion (percentage value) of the k-space. The size of the k-space is thus reduced, the image acquisition is faster and the temporal resolution of the sequence is boosted. A dynamic reference information is acquired at the beginning or end of the acquisition time, depending on the operator’s preference, and its time is greater because the k-space is filled completely. This reference thus contains all the structural (image details) and contrast (outlines of large structures) information. During the reconstruction phase, each dynamic volume overlaps the reference image, thus creating a 3D image containing the reference information (structural) and the dynamic information (contrast changes over time).

The PPM reconstructed images are then acquired for the different dynamic features (fig. 6).

Time-resolved dynamic 3D MRA

The main feature of this sequence is its temporal resolution (time to acquire a dynamic image). The high temporal resolution of this sequence is achieved to the detriment of the signal-to-noise ratio and the spatial resolution. The acquisition time for a dynamic image thus depends on the extent of k-space filling, i.e. the acquisition time increases and the temporal resolution is weaker as the extent of k-space filling increases. The temporal resolution depends on three main factors: the CENTRA keyhole, slice number and matrix size. The acquisition time increases as the values of these parameters increase. By tailoring these parameters and using manufacturers’ different k-space data acquisition and interpolation strategies, sequences with a temporal resolution of 3 s and a spatial resolution of 0.9 x 0.9 x 1.3 mm can be obtained for large regions like the chest and abdomen. Moreover, like conventional contrast-enhanced MRA, breath-hold acquisitions can be obtained for chest and abdominal regions to avoid the problem of respiratory artefacts.

Acquisition parameters

Rapid gradient echo sequences are used for acquisition (TR/TE: 4.2/1.2 ms, 25° flip angle), usually in the strict coronal plane, and the incidence can be adjusted according to the clinical indications. The dynamic 3D MRA sequence consists of a dynamic series of a few seconds and a specific dynamic feature called the “reference”, which has a longer time interval. Breath-hold acquisitions are used when scanning the heart and large vessels. The patient must hold his/her breath for 20 s when the reference is acquired at the beginning of the examination. Once the reference is acquired, the patient can breathe again for a few seconds (8-10 s), and then he/she is asked to hold his/her breath until the end of the acquisition interval (fig. 7). With this procedure, 10-15 dynamic acquisitions of 3 s are generally enough to screen the arterial and venous phases of the heart.

Contrast injection parameters

The injection time is reduced to 5 s (10-2 cc/s) so as to be able to better monitor the bolus transit progress and differentiate the venous and arterial phases. The bolus

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**Fig. 6:**  Thoracic PPM MRA images showing enhancement of large heart vessels every 3 s.
track is not used. The time between the beginning of acquisition and the injection is determined according to the structure explored. When exploring pulmonary arteries, for instance, the injection is triggered 25 s after the beginning of the acquisition (20 s for the reference and 5 s for contrast transit) in order to enhance the pulmonary arteries during the first dynamic sequences. However, when studying the aorta, the injection is triggered 15 s after the beginning of acquisition so that the gadolinium will have enough time to reach the aorta. It is also essential to avoid enhancing the target structure when the patient is breathing freely, otherwise the dynamics of interest will generate artefacts.

The operator thus decides when to begin the injection on the basis of the indications. Then the physician selects the best injection time to meet the screening objectives (pure arterial phase, venous phase, etc.) (fig. 7).

**Limitations**

The main drawback of this technique concerns the image spatial resolution, which is lower than that obtained with conventional MRA. Some authors seem to prefer conventional contrast-enhanced MRA as they consider it provides more accurate vessel measurements (32). The tradeoff in MRI is that the k-space filling has to be limited in order to boost the temporal resolution of the sequence. Low k-space filling leads to loss of information, which has a direct impact on the image quality and spatial resolution. The other shortcoming concerns the post-processing phase, i.e. a high number of native images are generated in a single acquisition. This means that 1600 images would be obtained with a sequence of 15 dynamic acquisitions of 120 slices. Image reconstruction monopolises the console and transferring the images to another console will congest the network. It is thus essential to reduce the number of slices and dynamic acquisitions to the minimum necessary for diagnosis.

**Applications**

Optimisation of this dynamic 3D MRA sequence improves the spatial resolution (millimetre accuracy) while also providing 3 s temporal resolution for 3D volumes, thus adding temporal information to conventional contrast-enhanced MRA. This sequence, as with gadolinium-enhanced conventional MRA, can reveal various pathologies that may be present, such as aneurysms, aortic dissections (fig. 8) or stenoses (fig. 9). However, the main advantage is the excellent temporal resolution, thus enabling separation of the arteriovenous phase. This feature is especially useful for imaging regions in which the blood flow rates are high, including arteries and pulmonary veins (32), carotid arteries, as well as depicting arteriovenous pathologies such as fistulae (33). Temporal information generated by this technique during examinations of the lower or upper limbs makes it possible to select the phase with the lowest venous return. 4D TRAK can then be used to overcome venous return related problems. Moreover, because of its high temporal coverage, this sequence may be useful for screening lower limb arteries especially when the blood flow between the right and left legs varies as a result of stenoses or occlusions. Enhancement of true canals and false canals, i.e. in aortic dissection cases (fig. 8), can provide insight into visceral perfusions and the physiopathology of malperfections. In comparison to conventional contrast-enhanced 3D...
MRA, the signal-to-noise ratio is clearly lower because of the use of various extrapolations used to reduce the size of the k-space in order to increase the temporal resolution of the sequence. This sequence is still advantageous for the temporal information it generates, as well as its capacity to highlight the bolus transit. Images of the target region are thus generated at different injection times to enable the physician to glean key information required for diagnosis.

**Conclusion**

Rather than being limited to a specific region, whole-body MRA provides an opportunity to screen the entire vascular system and assess the impact of various diseases throughout the body. Successive acquisition of several 3D volumes is possible with the dynamic 3D MRA technique, which also enables temporal analysis of vascularisation in a target organ or segment. Dynamic 3D MRA represents a tradeoff between the spatial resolution, temporal resolution and signal-to-noise ratio. Its temporal resolution is excellent to the detriment of the signal-to-noise ratio.

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**Fig. 8:** Aortic dissection. 3D magnetic resonance angiography of an aortic dissection with MPR views (above) and PPM views (below) showing delayed enhancement of a false canal relative to a real canal (3 s acquisitions).

**Fig. 9:** Coronal 3D MRA native kidney slices showing a perfusion lag in the left kidney (3 s image acquisition) resulting from stenosis of the left renal artery.
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ratio. Technological advances have boosted the potential of MRA by increasing the size of the screening areas (all large and medium sized arteries, atheromatous plaque sites) and by enabling temporal analysis (dynamic rather than morphological analysis). Regardless of the screening conditions, vascular imaging techniques should be used for diagnostic purposes, while effectively addressing issues that physicians are seeking to clarify. Once the images are examined and interpreted, the physician should be able to propose a clinical treatment that is tailored specifically to the disease. The potential clinical applications should not be overlooked in the development of new imaging techniques.

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