

## Physical Principles of Magnetic Resonance Angiography

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Magnetic resonance angiography (MRA) methods assess the body's arteries and veins for indications of disease. MRA is most typically associated with imaging the lumen of arteries. In most anatomic regions, X-ray angiography (DSA) is the clinical gold standard due to its high temporal and spatial resolution. However, MR angiography has several advantages. MRA methods typically are either non-invasive or require a venous injection of contrast agents without the use of invasive catheters. DSA typically utilizes an arterial injection that is accompanied by a higher level of risk. MRA methods also normally acquire volumetric data that allows retrospective selection of the optimal viewing angle. DSA typically acquires projections at a few angles and is inherently a 2D method. Finally, MR angiograms are naturally spatially registered to the other MR acquisitions completed in the same exam that can provide further anatomic information and clinical insight.

MR angiography methods can be divided into three main categories: time-of-flight (including 2D TOF, 3D TOF, and MOTSA), phase contrast, and contrast-enhanced methods.

### **Time of Flight**

Time-of-flight (TOF) methods rely on effects related to the longitudinal magnetization of spins and capitalize on the fact that flowing spins and stationary spins experience a different RF excitation history. For example, if spins in a vessel are flowing through a slice, fresh spins (that were not excited by the previous RF pulse) may replace some or all of the excited spins before the next excitation. Stationary spins that are excited by every RF pulse are in "steady-state" and produce less signal than flowing spins that see only one or several RF excitations. This is the "in-flow" effect that TOF methods utilize to generate angiographic contrast.

To maximize the contrast generated by in-flow, TOF methods typically utilize a gradient-echo acquisition with a TR that is much shorter than the  $T_1$  of blood and other surrounding tissues. The optimal flip angle depends on the degree of spin replacement each TR. A higher percentage of spins are replaced with higher velocity and/or thinner excited volume. Flow direction also influences the percentage of spin replacement, with through-slice vessels having more spin replacement than vessels that flow within the plane of the slice. A higher flip angle can be used when there is a higher percentage of spin replacement.

TOF methods normally acquire volumetric data, either through the acquisition of a stack of two-dimensional slices (2D TOF), by acquiring a 3D volume (3D TOF), or by using MOTSA (multiple overlapping thin slab acquisition).

In 2D TOF, a stack of slices is prescribed perpendicular to the main flow direction. For example, a stack of axial slices can be used to image the carotid arteries. The use of thin slices maximizes the in-flow enhancement effect. The minimum slice thickness used in 2D TOF is limited by RF pulse design constraints, the desired TE, and SNR (since SNR scales proportionally to slice thickness).

3D TOF acquires a single 3D volume. As a result, thinner “slices”, shorter TE, and smaller in-plane voxels are possible compared to 2D TOF. In addition, the SNR of the angiogram is directly proportional to the square root of the total scan time. The tradeoffs of 3D TOF compared to 2D TOF include increased saturation of blood on the more distal edge of the slab. This can result in more distal vessels being less well visualized.

In MOTSA (multiple overlapping thin-slab acquisition), thin 3D slabs are prescribed perpendicular to the main flow direction. Within each slab, it is possible to prescribe thin “slices”. MOTSA is an attractive compromise between 2D TOF and 3D TOF in terms of SNR and saturation effects. The one additional complication with MOTSA is the “Venetian blind” or slab boundary artifacts that can result from vessel signal being brighter at the proximal edge of each slab relative to the distal side where blood spins have experienced more RF excitations. Ramped excitations or TONE (tilted optimized non-saturating excitation) pulses can be used to lessen this effect. The excitation profile of these pulses is generated so that the flip angle is reduced at the in-flow edge of the volume and is progressively increased in the through-slab direction to compensate for signal losses due to saturation.

Time-of-flight methods can selectively image arteries or veins by using spatial saturation pulses that excite either superior to or inferior to the imaged volume. These spatially-selective pulses “saturate” the flowing spins before they enter the imaging volume and drastically reduce the in-flow enhancement for vessels where spins “up-stream” are affected by the saturation pulses. These saturation pulses are most effective with 2D TOF and least effective with 3D TOF, with MOTSA falling between these two extremes.

In certain applications of TOF techniques, for example in imaging the intracranial arteries with 3D TOF, magnetization transfer (MT) can be used to improve suppression of background tissue and hence improve visualization of small distal vessels. Magnetization transfer methods utilize extra RF pulses to provide additional suppression of certain tissues. For example, white matter and muscle are both sensitive to MT effects.

Because TOF methods depend on effects related to the longitudinal magnetization, the increased  $T_1$  relaxation times at higher field strengths can offer advantages in SNR and CNR.

There are several potential sources of artifact with TOF imaging including the saturation of in-plane flow, intra-voxel flow dephasing, and motion artifacts related to pulsatility or bulk patient motion.

*In-Plane Flow:* Because TOF methods rely on in-flow enhancement, vessels that flow in-plane in the excited volume can appear artifactually dark relative to blood that flows through-plane and experiences more in-flow enhancement. The saturation of in-plane flow can result in artifactual loss of blood signal that is difficult to distinguish from vessel stenosis or occlusion.

*Intravoxel Flow Dephasing:* In MR imaging, the signal from a given image voxel is the vector sum of all spins within that tissue volume. If there is a range of blood flow velocities within a voxel, the magnetization from different spins in the voxel can acquire very different phase. The signals from these spins can add destructively and result in very low signal or “flow voids”. Again, this artifactual loss of blood signal can be difficult to distinguish from true vessel stenosis or occlusion. Reducing the imaging echo time, or TE, can reduce the opportunity for flow-related signal dephasing.

*Motion Artifacts:* MR imaging is sensitive to motion and TOF imaging is no exception. Both bulk patient motion and pulsatility can cause image artifacts. Cardiac gating can significantly reduce artifacts due to cardiac pulsatility but increases scan time.

### **Phase Contrast**

Whereas time-of-flight methods rely on effects related to the longitudinal magnetization, phase contrast methods utilize effects related to the transverse magnetization of excited spins. Specifically, phase contrast angiography relies on the fact that spins moving through an applied gradient field accrue a different amount of phase than static spins. The phase of spins at echo time (TE) can be written as:

$$\phi(TE) = M_0 + v M_1 + a M_2/2 + \dots$$

where  $M_0$  is the zero<sup>th</sup> moment (area) of the applied gradient waveforms,  $M_1$  is the first moment,  $M_2$  is the second moment,  $v$  is the spin velocity, and  $a$  is the acceleration of the spin. Higher order terms (acceleration and beyond) are typically ignored, leaving the simplified model of:

$$\phi(TE) = M_0 + v M_1$$

The basic idea of phase contrast is to design gradient waveforms to control  $M_1$  without affecting  $M_0$ . The typical approach is to insert a bipolar gradient waveform between the RF excitation and spatial encoding gradients. A bipolar gradient waveform is composed of a positive-amplitude gradient lobe followed immediately by a negative-amplitude gradient lobe of equal area. This waveform has zero net area, so  $M_0$  is unaffected but changing the amplitude and/or duration of the applied gradient lobes can control  $M_1$ . To sensitize the signal to flow in one direction, a typical experiment repeats each phase encode acquisition twice – once with a bipolar gradient with the first lobe having positive amplitude and once with a bipolar gradient with the first lobe having negative amplitude. The phases resulting from these two acquisitions are then subtracted and the result is proportional to the flow velocity and the first moment of the bipolar lobe utilized:  $\Delta\phi = 2\gamma v M_1$ , where  $\gamma$  is the gyromagnetic ratio. The velocity encoding value or

“VENC” is the velocity that produces a phase difference of  $180^\circ$ . It is important to select VENC carefully. Selecting too low of a VENC will result in velocity aliasing (a velocity higher than the selected VENC will appear to be a low velocity; caused by  $180^\circ$  to  $-180^\circ$  “wrapping”). Selecting too high of a VENC results in a reduction of SNR and vessels with slow flow may not be adequately visualized.

Phase contrast methods can also be made sensitive to flow in all three directions. In this case, each phase encode acquisition is repeated four times – once with a bipolar gradient on the x gradient, once with a bipolar gradient on the y gradient, once with a bipolar gradient on the z gradient, and finally a single reference acquisition is acquired. The phase reference image is subtracted from each of the other acquisitions to correct for phase from sources other than flow. A magnitude image depicting flow in any direction can be generated by taking the square root of the sum of the squares of each of the component images or each direction’s image can be examined separately. The signal in the magnitude image is proportional to the magnitude of the velocity but directional information contained in the component images is lost.

Phase contrast data can be acquired for a 2D slice or a 3D volume. In addition, the acquisitions can be cardiac gated to allow for the measurement of velocity throughout the cardiac cycle.

Relative to time-of-flight methods, phase contrast techniques have several advantages and disadvantages. Phase contrast images typically have excellent suppression of static material. In addition, flow of any velocity can be imaged given appropriate VENC selection. Phase contrast methods can yield directional and/or quantitative velocity information. Finally, these methods can be used for large field of view applications where saturation might be an issue for time-of-flight. Unfortunately, the multiple acquisitions required for phase contrast increase the required scan time. Also, the required bipolar gradients increase the minimum TE and can make the method more sensitive to off-resonance and flow-related artifacts.

### **Contrast Enhanced Angiography**

Contrast-enhanced angiography relies on the venous injection of a gadolinium-based contrast agent that shortens the  $T_1$  of blood from its normal value of almost one second to approximately 30ms. This very short  $T_1$  compared to other surrounding tissues (muscle  $T_1 \sim 800$ ms, fat  $T_1 \sim 250$ ms) combined with a short-TR sequence ( $TR \sim 5$ ms) generates high contrast between doped blood and all surrounding tissues. Unlike time-of-flight and phase contrast methods, contrast-enhanced angiography does not rely on blood flow in the volume of interest. The angiographic contrast depends only on the arrival of the contrast agent to the vessels being imaged. However, the timing of the contrast injection relative to imaging is critical.

One of the primary challenges with contrast-enhanced angiographic techniques is how to preferentially image arteries rather than veins. Most methods utilize a rapid 3D acquisition to acquire volumetric data. The 3D acquisition is timed so that the center of k-space is acquired at the peak of the first-pass arterial enhancement, before venous

enhancement. The data at the center of k-space is the primary determinant of image contrast. The edges of k-space contain higher spatial frequency information that depict vessel edges and other structures that change rapidly in space.

Timing errors between injection and acquisition can result in a variety of image artifacts including edge enhancement and insufficient vessel filling. The ideal timing and artifacts resulting from timing errors change with the order k-space is filled. For example, in elliptical centric ordering, k-space is filled from the center moving outward. Hence, an elliptically centric acquisition should be started later than an acquisition that moves from one edge of k-space to the other.

There are a variety of approaches to sequence timing relative to the contrast bolus including using a test bolus, using “fluoro” triggering, or using a dynamic acquisition. The dynamic approach has been gaining popularity in recent years. This method acquires multiple 3D volumes sequentially in time. If these datasets are acquired quickly enough, it is very likely that one or several will have the desired peak arterial contrast.

Compared to time-of-flight and phase contrast methods, contrast-enhanced techniques entail increased cost (for the contrast agent) and invasiveness. In exchange, these techniques generate high SNR angiograms with contrast that depends only on the arrival of the contrast agent. In addition, the short TE used in the short TR acquisitions minimizes any flow-related artifacts.

### **Reconstruction & Visualization**

The three-dimensional angiographic data generated by most MRA methods is typically visualized using a maximum intensity projection (MIP). This non-linear processing technique displays the brightest signal intensity encountered at each pixel when passing a ray through the volume at a given projection angle. MIPs can be calculated at many projection angles to allow more complete visualization of the anatomy.

A technique known as “zero-filling interpolation” is often used in MRA. This method reconstructs data using a larger image matrix than was actually acquired and fills unacquired data-points with zeroes. For example, an image acquired with a matrix of 512x512x32 might be reconstructed using a matrix of 1024x1024x64. As the name suggests, zero-filling interpolation does not change the true resolution of the data but interpolates between known data points and can yield an image with a smoother and more pleasing appearance. Zero-filling is particularly important in the slice encoding direction when reformatting 3D data sets, reducing stair-step artifacts, and creating smooth transitions between slices.

### **Coils and Parallel Imaging**

As in all types of MR imaging, it is important to select appropriate RF coils when acquiring angiographic data. Coils that are local to the anatomy of interest have an inherent SNR advantage over a “body coil” acquisition. In addition, phased-array coils offer potential for increased SNR and also can enable acceleration of acquisitions using parallel imaging approaches (e.g. SENSE, SMASH, GRAPPA, etc).

### **Summary**

There are three major families of MR angiographic methods: time-of-flight, phase-contrast, contrast-enhanced. All three methods are capable of generating high quality angiograms, however, each has advantages and disadvantages. The optimal method depends on the specific application and setting.