## Contrast by Body Part: Angiography: How and Why?

**Specialty Area:**

Multi-Disciplinary, Vascularized Tissue

**Speaker Name:**

Kevin M. Johnson, PhD
University of Wisconsin – Madison
kmjohnson3@wisc.edu

**Highlights:**

- Virtually all of imaging is impacted by vascular system, sometimes in non-obvious ways
- Subtle changes to pulse sequence can drastically change sensitivity to flow allowing tailoring to maximize or minimize the signal and artifacts from vascular structures
- Acceleration is an enabling technology for angiography; however, physician-scientist dialogue is required to understand artifacts

**Target Audience:** Students, scientists, physicists, engineers, and clinicians interested understanding how the vascular system influences imaging and state of the art methods to enhance and diminish blood signal.

**Objectives**: This talk aims to provide insights in to how the vasculature system is imaged and what challenges exist in imaging moving blood. At the end of this talk, participants should:

- Be able to identify basic mechanisms of angiographic imaging but also recognize the angiographic sensitivity of sequences targeted at tissue.
- Contemplate potential impact of blood flow/vessels on current practice/research and potential solutions to mitigate or enhance effects
- Learn from the story of acceleration in MR angiography and contemplate how this story may translate to the clinical adoption of new reconstruction techniques

**Purpose**: The human body contains a dense and multi-scale vascular network that is intertwined with almost every organ. This all but assures that some fraction of the MR signal will arise from or be related to the vascular space. For better or worse, the vascular signal exhibits key features that distinguishes its MR signal behavior and properties from static tissue. This has allowed imaging sequences to be tailored to image the vascular system for angiography and impacts sequences which image vascularized tissue. The purpose of this talk to develop an understanding and intuition for the flow sensitivity of sequences and how to maximize contrast and minimize artifacts for angiographic imaging.

**What? : Blood Flow and Vessels**: Approximately 8% of the human body is composed of blood. Blood flow is of course, pulsatile with high level of synchronous arterial pulsatility at the heart, which is dampened in the distal vasculature. At its peak, blood velocity is ~150cm/s which is quite fast considering it to be 5.4 km/hr or about walking speed. You can imagine what images would look like if patients tried to move as if they were walking in the scanner. The pulsation of blood leads to additional pulsation of the other structures (e.g cerebral spinal fluid flow is driven by blood flow). Upon crossing the capillary bed, pulsation is much reduced due to viscous forces with dampen the flow and velocity of blood. It is important to note that a high level of pulsation also creates significant deviation from the typical parabolic flow expected by constant flow in rigid pipes. The amount of flow in a given pipe is a driven by the driving pressure of the heart and the cross sectional area and length of the vessels. As is

well known from fMRI, the healthy arterial vascular system has smooth muscle cell that contract to reduce blood flow. Lesser discussed is the "pulsatility" of the venous system. In contrast to the arterial system, the healthy venous system is a depressurized and flow is driven by muscle forces, including respiration. For example, the diameter of the inferior vena cava (blood returning from the heart) changes with breathing. Observation of venous system, especially near the heart, need careful control for respiration [1], as well as gravitation, and subject hydration.

**Why ? : Common Vascular Diseases:** Disease in the vascular system presents from both native and secondary pathologies. Native vascular diseases include such diseases as atherosclerosis, arterial venous malformations, and aneurysms. In general, these diseases can be considered abnormal remodeling of the vascular wall and the general risk is for hemorrhage or impaired blood deliver. Since geometry is highly coupled to the remodeling itself and resulting blood flow [2], most diagnostic imaging has focused on measuring the lumen of the lesions. The size and shape of the lesions is often sufficient to guide treatments which are often conservative (e.g. a large aneurysm would indicate treatment). The vascular system is also indicated in a vast array of diseases including neurodegenerative, cancer, and fibrotic disease and responsible for treatment efficacy. It is therefore often important gauge the effects disease on the vascular system. This includes but is not limited to the pre-surgical mapping to avoid collateral vessel damage and the indication of vascular involvement.

**How? : Contrast Mechanisms for Imaging Blood:**

***Inflow*:** The very purpose of the vascular system is to transport nutrients and waste into and away from cells. It is no coincidence that the transport of blood also lead to the transport of MR signal into and out of the volume of interest. For example, fresh blood entering the imaging volume often will have a dramatically higher signal than the signal from water that has been in the imaging volume for an extended period of time. This basic principle led to the development of time-of-flight (TOF) angiography, which aims to maximize the signal from blood while minimizing the signal from static tissue. The TOF effect can be observed by imaging a single 2D spoiled gradient echo slice collected with a high flip angle and relatively long TR. The 3D manifestation of this technique has become a staple for imaging the cranial vasculature in which multi thin 3D slabs are imaged [3]. With the development of multi-slab excitation [3], use of magnetization transfer background suppression [4, 5], and use of 3T scanners TOF has improved dramatically over the years. However, TOF is quite insensitive to slow flowing blood. To examine this, please define the time-of-arrival (TOA) as the time required for blood to enter the slab and reach a given location. The inflow sensitivity of any sequence can be determined by calculating the time-of-arrival response function. Given the strong background signal from grey and white matter, a TOF sequence is only sensitive to vessels with TOA less than ~500ms. Perhaps due to this stagnation, TOF has been relegated to use in to head but rarely used in the body.

Over the last decade there has been a resurgence of inflow base angiography imaging by means of arterial spin labeling (ASL)[6]. In this imaging paradigm, blood is specifically tagged during a preparation module and subsequently imaged. This decoupling of imaging and preparation allows background free intracranial MRA via subtraction of images collected with and without the preparation module. Furthermore, rapid high SNR sequences such as balanced steady state free precession (bSSFP) can be used in body applications to increase SNR. ASL imaging techniques relatively easy produce images of vascular structure with TOA less than 3s. With this substantial reduction in flow sensitivity, single slab intracranial inflow MRA images are feasible [7, 8] with better depiction of anatomy with complex or tortuous flow. Furthermore, small modifications to the pulse sequence allow vessel selective tagging [9], bringing complete feature set of DSA to MRA. Despite these promises, the ASL angiography landscape is far from unified. There is currently great variety of ASL tagging schemes in question (i.e.

PCASL, FAIR, STAR, etc) and the readout options (i.e. gradient echo vs. bSSFP/TrueFISP, Cartesian vs. Non-Cartesian). Further studies are required to determine true clinical efficacy.

***Blood Motion/Negative Contrast MRA*:** As previously mentioned, blood flow is relatively fast which has enabled blood vessel imaging by exploiting the speed of spins compared to the surrounding tissues. Slightly different, than inflow based sequences, these sequence depend on the motion (velocity and acceleration) to impart phase to moving spins. For these reasons, the flow sensitivity is directly linked to the gradient played out while the spins are in the transverse plane. As an example, for a sequence with a long echo time, e.g. multiple spin echo (CUBE/RARE/FSE/HASTE/etc), spins experience a large number of gradient pulses before being imaged, thus this sequence is relatively flow sensitive. One of the earliest inceptions of motion based MRA is the use of 3D phase contrast, which aims to directly detect the phase imparted to moving spins [10]. This is generally done utilizing a bipolar gradient inserted after RF excitation and before the readout of a spoiled gradient echo sequence. It was recognized early on, that 3D phase contrast sequences [11] may be more sensitive to artifact due to slow flow. However, these sequences are insensitive to inflow time and background signal making them more practical for venography and applications with significant background signal. Of course the rich velocity information within the phase contrast data may be great value, aside from its angiographic properties. A greater interest in alternative motion sensitive sequences, so called black blood sequences [12], has recently been rekindled. Instead of directly detecting the imparted phase, these sequences utilize the phase to cause magnitude loss similar to crushing gradients used in spin and gradient echo sequences. Or perhaps a more direct comparison would be to diffusion sequences, since they are often functionally identical. These sequences avoid imaging blood, the structure of which is of little interest directly, and image the vessel wall, the origin of vascular disease. When coupled with a bright blood imaging these also can provide images of the lumen of the vessel. In such settings, very high levels of motion sensitivity can be impacted, leading to greatly improved sensitivity to slow flow compared to the direct detection of phase.

***Exogenous Contrast Agents:*** Contrast enhanced MRA shares the most similarity to CTA and DSA. Contrast enhanced MRA pairs a simple but rapid T1 weighted gradient echo sequence with an intravenous injection of a Gd based contrast agent. When Contrast Enhanced MRA (CE-MRA) was introduced; it made incredible inroads to almost every vascular territory cue to its high SNR and speed advantages. Currently, CE-MRA is by far the most dominant method for MR angiography outside the head. CE-MRA is almost entirely limited by the speed of the sequence and the timing of the injection, and often demands for both high temporal and spatial resolution. For example, a temporal resolution of 1s with 0.5mm spatial would be sufficient to detect most abnormal intracranial filling patterns and prevent most significant errors from venous and perfusion overlap. However, this leads to an estimated required acceleration >100x. This is far greater than what is achievable with common acceleration techniques such as parallel imaging. Thus for the past decade, CE-MRA techniques have either ignored dynamic information entirely or relied on clever schemes to accelerate image acquisition (i.e. TRICKS [13],CAPR [14], TWIST, etc). Subsequent CE-MRA images often have substantial artifacts, most often at vessel edges, which must be carefully interpreted to prevent misdiagnosis. With recent developments in reconstruction algorithms, an incredible opportunity exists to more explicitly harness assumption regarding CE-MRA. These techniques, which will often be labeled “compressed sensing” and “low rank approximation”, provide opportunities to provide substantially higher accelerations and/or reduced imaging artifacts[15, 16]. All of these techniques exploit known assumption about the underlying structure (i.e. few vessels, similar temporal dynamics). With these techniques, required acceleration factors of 100x may be possible in the near future. However, similar to the adoption of viewsharing schemes, the impact of new artifacts on clinical interpretation must be considered.

**Discussion/Conclusions**: An array of MRI techniques have been developed to image the vascular system with MR. Through the development of these techniques, we have greatly improved our understanding of the impact of blood flow on the MR signal. We have additionally, created An Array of Acronyms (AAA) which describe specific angiographic schemes and acceleration strategies. Certainly, with the correct combination of techniques it is feasible to provide angiographic images in almost every vascular territory. It is always important to note that angiography the MR is challenging, perhaps more so than respective computed tomography techniques which have benefited from the emergence of dual energy techniques and larger detectors. However, new MRA techniques are emerging that may substantially improve imaging performance. More importantly, it is likely that "lumenographic" techniques may become insufficient to grade vascular lesions with advances in pharmaceutical treatment. Here MRI holds potential to become a dominant and comprehensive technique, providing proxy measures of vessel wall health and status of the downstream tissue.

**References**:


1. Hsia, T.Y., et al., *Effects of respiration and gravity on infradiaphragmatic venous flow in normal and Fontan patients.* Circulation, 2000. **102**(19 Suppl 3): p. III148-53.
2. Dzau, V.J. and G.H. Gibbons, *Vascular remodeling: mechanisms and implications.* J Cardiovasc Pharmacol, 1993. **21 Suppl 1**: p. S1-5.
3. Parker, D.L., C. Yuan, and D.D. Blatter, *MR angiography by multiple thin slab 3D acquisition.* Magn Reson Med, 1991. **17**(2): p. 434-51.
4. Pike, G.B., et al., *Magnetization transfer time-of-flight magnetic resonance angiography.* Magn Reson Med, 1992. **25**(2): p. 372-9.
5. Edelman, R.R., et al., *Improved time-of-flight MR angiography of the brain with magnetization transfer contrast.* Radiology, 1992. **184**(2): p. 395-9.
6. Nishimura, D.G., et al., *MR angiography by selective inversion recovery.* Magn Reson Med, 1987. **4**(2): p. 193-202.
7. Wu, H., et al., *Noncontrast dynamic 3D intracranial MR angiography using pseudo-continuous arterial spin labeling (PCASL) and accelerated 3D radial acquisition.* J Magn Reson Imaging, 2013.
8. Robson, P.M., et al., *Time-resolved vessel-selective digital subtraction MR angiography of the cerebral vasculature with arterial spin labeling.* Radiology, 2010. **257**(2): p. 507-15.
9. Okell, T.W., et al., *Vessel-encoded dynamic magnetic resonance angiography using arterial spin labeling.* Magn Reson Med, 2010. **64**(2): p. 430-8.
10. Moran, P., *A flow velocity zeugmatographic interface for NMR imaging in humans.* Magn Reson Imaging, 1982. **1**(4): p. 197-203.
11. Huston, J., et al., *Imtracranial Aneurysms and Vascular Malformations: Comparison of Time-of-Flight and Phase-Contrast Angiography.* Radiology, 1991. **181**(3): p. 721-730.
12. Edelman, R.R., et al., *Extracranial carotid arteries: evaluation with "black blood" MR angiography.* Radiology, 1990. **177**(1): p. 45-50.
13. Korosec, F.R., et al., *Time-resolved contrast-enhanced 3D MR angiography.* Magnetic Resonance in Medicine, 1996. **36**(3): p. 345-51.
14. Haider, C.R., et al., *3D high temporal and spatial resolution contrast-enhanced MR angiography of the whole brain.* Magn Reson Med, 2008. **60**(3): p. 749-60.
15. Trzasko, J.D., et al., *Sparse-CAPR: highly accelerated 4D CE-MRA with parallel imaging and nonconvex compressive sensing.* Magn Reson Med, 2011. **66**(4): p. 1019-32.
16. Lustig, M., D. Donoho, and J.M. Pauly, *Sparse MRI: The application of compressed sensing for rapid MR imaging.* Magn Reson Med, 2007. **58**(6): p. 1182-95.