The recent recognition of Nephrogenic Systemic Fibrosis, an important, sometimes lethal disease associated with gadolinium exposure in patients with severe renal disease has led to a rethinking of our approach to MRA. The many benefits of evaluating patients with vascular disease using MRA still exist, including the lack of ionizing radiation, lack of a nephrotoxic contrast agent and soft tissue contrast that allows anatomic and functional evaluation of vascular disease and its effect on the end organ. Nevertheless, with the advent of Nephrogenic Systemic Fibrosis (NSF) there is worldwide caution regarding the use of gadolinium based contrast agents in patients with renal insufficiency. Therefore, the emergence of NSF as a disease has been the driving force behind a host of new non-contrast MRA techniques, or at least MRA methods that use a low dose of gadolinium contrast agents. The objective of this discussion is to review the factors leading to the development of new, state-of-the-art MRA methods that do not use contrast media, or significantly lower the required does of Gadolinium.

**Nephrogenic Systemic Fibrosis**

Our understanding of NSF is evolving rapidly. The measures put into place throughout the world have resulted in a dramatic reduction in the number of reported cases worldwide. Specifically, the institution of screening programs to identify and avoid using Gadolinium in patients at risk, transition to agents that have lower risk profiles, and move to non-enhanced techniques have significantly reduced the number of reported cases of NSF. Specific measures in our program at the University of Wisconsin will be discussed, which have resulted in no additional documented cases of NSF at our institution.

**Time of Flight Techniques**

Time of Flight (TOF) MRA has long been used a method to evaluate the vessels in regions of relatively high flow, for example at the circle of Willis. The advent of gadolinium-enhanced techniques largely supplanted the time of flight methods for evaluating the aorta and its major branches, due to a host of artifacts and the length of the acquisition for time of flight MRA. However, recent developments in MRA using the time of flight method have led to improved techniques, with more rapid acquisitions and improved fat suppression, which allow better visualization of the contrast between the lumen of the vessel and the surrounding soft tissues. These new fat suppression techniques result in a method that is insensitive to local magnetic field variations, which significantly improves overall image quality and contrast between the vessel and surrounding background tissue.

Likewise, with the advent of more routine dissemination of 3 Tesla scanners, time of flight imaging overall has improved in image quality. The higher field strength associated with 3 Tesla allows a stronger signal to be acquired from the inflow enhancement while simultaneously allows improved background suppression due to the prolonged T1 values at 3 Tesla. These two factors, when combined, allow for high resolution time of flight MRA to be performed. In addition, image acceleration techniques using parallel imaging allow for more rapid time of flight acquisitions, although these can be limited by signal to noise ratio. Therefore, 3 Tesla imaging also is beneficial to facilitate increase signal associated with the parallel imaging methods in time of flight MRA.
Phase-contrast MRA
Phase-contrast MRA has also been used for a long time, however, the general application has been limited by a host of factors including 1) prolonged acquisition time, 2) artifacts associated with the flow disturbances in the presence of phase-contrast flow encoding gradients, 3) motion artifacts, 4) pulsatile flow artifacts. Many of these limitations have been recently addressed with the advent of several technology improvements, including image acceleration using parallel imaging, stronger gradients therefore allowing for fewer flow and motion artifacts, higher field strength associated with improved signal intensity and more advanced processing algorithms to glean physiologic data from phase-contrast MRA. In concert, these recent technical developments have led to a dramatic improvement in the spatial resolution and quantitative flow information available from phase-contrast MRA. In this lecture, the new phase-contrast MRA acquisition techniques will be discussed and clinical applications showing the use of these methods will be presented.

Flow-Independent MRA
A number of recent technical developments have led to the emergence of several flow-independent MRA techniques as viable clinical alternatives to contrast-enhanced MRA. These include the use of steady state free procession (SSFP) as well as other flow-independent techniques based on fast spin-echo readout. In many patients, especially those with relatively high flow, these techniques have resulted in dramatic MRA images without the need for instituting an intravenous contrast agent.

The methods that use SSFP imaging rely on improved techniques for background suppression, which allow better visualization of the arterial lumen. These methods include the application of selective inversion pulses, a delay time, followed by the SSFP readout when the stationary tissues are reaching a null point in their signal recovery curve. These methods have worked extraordinarily well when focused on a specific area of the body, for example, the renal and mesenteric arteries.

Likewise, investigators have used fast spin-echo techniques to recover intravascular signal using cardiac-gated flow-compensated MRA. These methods have been effectively used for visualization of the peripheral vessels in patients with lower extremity inclusive disease. One limitation of the techniques, however, is in patients with severe disease the protocols must be timed very critically to each patient. Nevertheless, the methods have shown significant promise in several trials.

Low Dose Contrast MRA
With the advent of improved relaxivity contrast agents, it is possible to significantly reduce the dose of gadolinium injected, therefore lowering the overall risk of NSF. In addition the application of gadolinium MRA at high field allows investigators to use a lower dose, due to the stronger differential contrast between the arterial enhancement and background stationary tissues. The high relaxivity contrast agents have been disseminated more rapidly in the European market where several new MRA-specific contrast agent applications have been approved.

In summary, the recognition of and new screening programs for NSF have led to the development of a number of creative solutions for acquiring excellent quality MRA images without contrast or at the very least with a very low dose of contrast. In combination, these methods can be used to significantly reduce the risk of Nephrogenic Systemic Fibrosis, as evidenced by the lack of cases emerging in the world today.