The ability of MRI to non-invasively visualise blood flow and create angiographic images was first reported in the mid to late 1980s when Laub introduced the background concepts behind time-of-flight (TOF) angiography and Dumoulin first described the method of phase contrast (PC) angiography.

The PC technique relies on creating angiographic images based upon the relative phase shift induced in the MRI signal as blood moves along the direction of a magnetic field gradient compared to stationary background tissue, whereas the TOF techniques rely on the relative contrast developed between the high signal of blood flowing into an imaging slice and the reduced signal from the stationary background tissue.

Images are acquired either as multiple 2D slices or as 3D volume acquisitions, with 3D angiographic images produced by stacking the slices and performing a maximum intensity projection (MIP) algorithm in which parallel rays are cast through the 3D volume and a 2D projection image is created using the maximum pixel intensity traversed by the ray. Over the subsequent years these techniques were refined but essentially remained unchanged.

Since a typical magnetic resonance angiography (MRA) acquisition could take several minutes to acquire they found their primary application in the cranial and extracranial carotid circulation. While a number of groups attempted thoracic, abdominal and peripheral MRA, image quality was not sufficiently robust for routine clinical use, primarily due to artefact caused by cardiac and/or respiratory motion or pulsatile flow. It was not until Prince introduced the concept of (exogenous) contrast enhanced MRA (CE-MRA) in 1994 that it became possible to robustly image the systemic vasculature. CE-MRA involves rapidly imaging the desired vascular territory during the first pass of a gadolinium-based MR contrast agent, which has the effect of transiently (for a few tens of seconds) increasing the signal intensity from blood. This transient increase in signal is achieved by administering the contrast agent as a compact bolus using a power injector. Careful determination of the circulation time from the point of injection to the time the contrast agent arrives at the anatomy of interest is crucial to obtaining high quality images.

Subsequent improvements in MR gradient performance as well as receiver coil technology, eg multi-element coil arrays, have significantly reduced CE-MRA acquisition times, to the point of allowing time-resolved 3D angiograms to be acquired with high temporal and spatial resolution, obviating the need for the operator to determine the circulation time. The development of moving table technology allows extended field-of-view coverage by moving the patient out of the scanner during the acquisition. Such multi-station images allow the operator to chase the contrast agent bolus down the legs, producing high quality peripheral angiograms.

CE-MRA has now become the standard method for thoracic, abdominal and peripheral angiography, as well as carotid MRA in some centres. However, in 2008 concerns started to arise about a possible link between gadolinium-based contrast agents and nephrogenic systemic fibrosis (NSF), particularly in patients with impaired renal function. This caused a renewed interest in the development of so-called non-contrast enhanced MRA (NCE-MRA) techniques. NCE-MRA has developed into a catch-all term that covers all non-exogenous contrast MRA techniques. While both PC and TOF are now retrospectively catalogued as NCE-MRA techniques, the term has primarily been used to characterise a new class of methods that attempt to leverage more recent developments in MR pulse sequences in order to address the deficiencies of TOF and PC in imaging the systemic vasculature.

Fresh blood imaging techniques

A number of groups, mostly notably the Toshiba research group led by Miyazaki, have attempted to develop NCE-MRA methods for whole-body applications. The most successful technique, to date, being that of ECG, or peripheral pulse, triggered 3D fast spin echo (FSE), originally referred to as fresh-blood imaging (FBI) by Toshiba. Similar implementations by other vendors include non-contrast MR of arteries and veins (NATIVE) by Siemens, triggered angiography non-contrast enhanced (TRANCE) by Philips and Inhance 3D Deltatflow by GE.

In these methods, two ECG-triggered 3D FSE acquisitions are performed; the first is gated to systole and the second to diastole. In the systolic images fast arterial flow results in the dephasing of the MRI signal and hence the blood appears dark. In the diastolic image the arterial flow is comparatively slower hence the blood is not substantially dephased and therefore appears as a high signal. Venous flow is relatively slow and constant throughout the cardiac cycle and therefore appears bright in both acquisitions. Similarly the signal from stationary background tissue is the same in both acquisitions.

Subtraction of the matching systolic images from the diastolic images results in suppression of the background and venous signals, leaving only the arterial signal (Figure 1). The use of an additional short TI inversion recovery (STIR) preparation helps to reduce the background signal from fat. Limitations of the technique include spatial misregistration, as only part of the 3D acquisition can be performed in each heartbeat, and image blurring caused by the FSE readout occurring while the MRI signal decays due to T2 relaxation. The use of parallel imaging techniques, such as SPEEDER (Toshiba), SENSE (Philips), GRAPPA (Siemens) or ASSET (GE) to reduce the length of the echo train can be used to help reduce this effect. Identification of the optimal systolic and diastolic trigger delays for each body area is also required, necessitating the use of a separate ECG-prep scan beforehand in order to identify the appropriate trigger delays. For example, a single slice, multiphase, single-shot fast spin echo acquisition with progressive ECG trigger delays can be used with visual inspection to identify the optimal systolic (darker intravascular signal) and diastolic (brightest intravascular signal) trigger delays.

The scan time for these methods is approximately four minutes for a single 3D location. Multiple vascular territories can be covered by moving the patient and repeating the acquisition. Given the differences in flow profiles, it is often necessary to repeat the ECG-prep scan in order to optimise the timings for each location. Since this technique primarily relies on having a good differential flow between systole and diastole, its primary application is in peripheral angiogra-
phy. Limitations of the technique include difficulties in the presence of turbulent blood flow secondary to severe stenosis, when the signals in both systole and diastole can be similar resulting in loss of signal in the subtracted angiogram. It is therefore important, like all MR angiography techniques, to review the individual source images before MIP. A MIP of a clinical case using Inhance 3D Deltaflow is shown in figure 2.

**Balanced steady-state free precession techniques**

Balanced steady-state free precession (bSSFP) is a particular type of gradient echo sequence that has also been used as the basis of NCE-MRA techniques due to its inherently high signal from blood that is relatively independent of flow. ECG and/or respiratory-triggered volumetric (3D) bSSFP techniques have been used in a number of body areas including the coronaries and thoracic aorta. However, a disadvantage of standard 3D bSSFP sequences is that both arteries and veins appear bright as well as background tissues. This led to the development of inversion pulses being applied prior to the bSSFP readout. Commercial implementations of these sequences are known variously as NATIVE slab-selective inversion: Initial results. Kidney Int 2004;65:602-608.

Figure 1 shows the principles of fresh blood imaging: (A) the acquisition is usually triggered by the patient’s peripheral pulse waveform. A portion of the MRI acquisition in the systolic phase is acquired after the systolic trigger delay (T3). Following a typically 2xRR interval repetition time, the diastolic phase data is acquired after the diastolic trigger delay (T0). The whole acquisition is completed over a number of heart beats; (B) shows a single slice from a coronal 3D acquisition acquired at T0, note the signal loss in the popliteal artery (arrowed); (C) shows the subtraction of (B) and (D) demonstrating only the arterial vessels; (E) is a coronal MIP of the full subtracted 3D data demonstrating excellent depiction of the vessels over a 40cm field of view in a total acquisition time of three minutes.

### References

FIGURE 2
MIP of an Inhance 3D Deltaflow acquisition in a patient where the superficial femoral arteries are occluded from the origin down to the adductor hiatus on the left side and down to the popliteal artery on the right side. Image courtesy of Professor W Gedroyc, St Mary’s Hospital, London.

FIGURE 3
Principles of balanced steady-state free precession: (A) the acquisition is usually triggered by the patient's respiratory motion. Following the application of a selective inversion pulse the magnetisation in the green region is inverted. The static tissue and venous blood then recovers via T1 relaxation (green curve), while inflowing blood from the heart has a high signal (red line). After a suitable TI, approximately 1200ms in this case, the static tissue and venous blood magnetisation approaches zero. At this point a fat suppression pulse is applied and then part of the axial 3D bSSFP acquisition is performed in the red region, which is smaller than the inversion region. The whole acquisition is repeated over a number of respiratory cycles; (B) shows the inversion region (green) and the imaging region (red); (C): shows a single slice from the acquisition with a high signal in the abdominal aorta and segments of the renal arteries; (D) shows an axial MIP; and (E) a coronal MIP through the full 3D data demonstrating excellent visualisation of the renal arteries over a 28cm field-of-view in a total acquisition time of four minutes.

FIGURE 4
Comparison of (A) IFIR and (B) CE-MRA MIPs in a patient with three normal right renal arteries and two normal left renal arteries.