Changing Trends in a Decade of Vascular Radiology - The Impact of MRI and CT for Non-Invasive Angiography

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Purpose

The imaging modalities of choice in vascular imaging have changed considerably over the last decade, with advances in Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) technology and increasing availability of MRI and multislice CT scanners. This poster aims to illustrate the impact on the respective workloads of conventional angiography, interventional angiography, contrasted enhanced MRI angiography (CE-MRA) and contrast enhanced CT angiography (CE-CTA) of evolving technology, clinical need and changing clinical repercussions in a referral centre, and the impact on clinical practice.
Methods and Materials

This study was conducted in Glasgow Royal Infirmary, a 900 bed teaching hospital providing vascular surgical services as well as a renal medicine unit. The contrast-enhanced MRI angiography (CE-MRA) service was initially introduced in June 1998 after a CE-MRA capable MRI service was implemented - a 1.5T Philips Gyroscan ACS-NT MRI Scanner (Philips Medical Systems, Best, the Netherlands), including a contrast pump injector (Medrad Spectris, Medrad, Indianola, PA). Following an upgrade in 2002, the scanner was enhanced with a software and table upgrade to moving table peripheral angiography plus phased array coils enabling implementation of parallel imaging techniques. A second MRI scanner was added in 2009, a 1.5T Siemens Magnetom Avanto (Siemens Healthcare, Erlangen, Germany), again with a Medrad contrast pump injector and a dedicated peripheral vascular phased array coil. Several CT scanners have been employed in this time, the single detector row scanner initially installed in 1997 that was effectively unable to perform extended CTA studies being supplemented by a 4-detector row Siemens in 2002 upon which lower limb angiographic studies with limited slice resolution could be performed. A 64-detector row Toshiba Aquilion CT scanner (Toshiba Medical Systems, Tochigi-ken, Japan) equipped with a Medrad Stellant contrast pump injector was installed in 2007 replacing the original single detector row machine and allowing thin collimation peripheral run-off studies. A second identical 64-slice Toshiba scanner was installed in 2009 bringing the complement of CT scanners to 3, one 4 detector row and two 64 detector row.

The baseline angiography and interventional vascular caseload was established for the year June 1997 to end May 1998. The subsequent workload to the end of May 2010 was prospectively collated each year and comparison drawn with the CE-MRA caseload each year. Latterly CE-CTA numbers were also collected for additional comparison. The number of investigations, procedures performed and body area examined (grouped into aortic arch and carotid arteries, thoracic aorta, renal vascular studies, abdominal aorta, iliac and lower limb arterial run-off and venographic studies) were recorded. CT pulmonary angiograms and more recently CT coronary angiograms have been excluded, with only CT angiographic vascular studies generated via the vascular service included. Ultrasound is not employed for primary investigation of lower limb peripheral vascular disease (ultrasound is reserved for graft surveillance), and hence has not been studied.

Changes in waiting times over the decade have been compared to baseline, whilst a marginal cost analysis for diagnostic procedures was computed accounting for consumables (contrast media, film, archive media, catheters, guidewires etc.), staffing (radiographers, nursing staff and radiologist time) and hospital bed costs. Marginal cost for CE-CTA and CE-MRA was also calculated taking similar relevant parameters into consideration.
The equivalent dose of CE-CTA performed on our 64 detector row scanner was estimated by calculating the mean of the effective dose of all such studies performed in the final month of data acquisition (22; 23).

The angiographic, CT and MRI workload was evaluated for May 2010 using the Radiology Information System (RIS), and compared with the workload in May 1998 using the vascular theatre logs.
Results

The study period, now numbering 13 years, runs from 1st June 1997 to 31st May 2010, during which time there have been a total of 8769 invasive angiographic procedures of which 5105 were diagnostic procedures and 3664 were interventional. In the same period there have been 6859 CE-MRA procedures, with the overall number of vascular studies numbering 16 872.

There was a dramatic year on year rise in the number of CE-MRA studies performed each year from 1997/98 (13 studies) to 2002/03 (760 studies, with a reciprocal 50.4% drop in conventional diagnostic angiography during the same period (Figure 1 on page 7). Intervventional angiographic procedures have remained largely constant. A drop in the number of CE-MRA studies occurred after 2003/04, with no discernible change in angiography patterns. This drop is in part accounted for by a decrease in the number of CE- MRA renal studies performed (Figure 2 on page 7), the other factor accounting for this change was that until 2003 this was effectively the only centre in the region equipped to perform such investigations, and hence attracted outside referrals for CE-MRA. Subsequent to this other centres started their own CE-MRA practice and the MRA activity has been largely driven by referrals from within the institution alone with much fewer referrals from other regional hospitals. The more recent increase in CE-CTA (excluding CT Pulmonary Angiography) is again a technology driven phenomena subsequent to the acquisition of multidetector row CT scanners.

The renovascular imaging strand within the overall story of the development of the non-invasive vascular imaging service is of particular interest. The number of renal investigations performed is detailed in figure 3 on page 7, demonstrating a very rapid initial growth in renal CE-MRA and subsequent decline on a background of relatively constant low numbers of renal angiograms, angioplasties and stents procedures performed. In 2009/10, 50 of the 84 CE-MRA (59.5%) performed were for investigation of hypertension(red arrow in figure 3 on page 7), whilst in 2002/03, the majority of studies were performed for investigation of renovascular disease (black arrow in figure 3 on page 7)

e number of CE-MRA studies performed in various body regions in demonstrated in figure 4 on page 8, with the largest increase in studies of the abdominal aorta, iliac vessels and lower limb run-off, with a reciprocal drop in the conventional invasive angiograms performed for this purpose.
Until 2003, the numbers of total radiological vascular investigations and procedures showed a steady rise between 1997 and 2002, and have remained roughly constant to present day (Figure 5 on page 9).

Waiting times have varied considerably over this period, with the wait in 1997 for a non-urgent conventional invasive angiogram for investigation of claudication peaking at seven months. This had reduced to three weeks by 2003, and stands at a maximum of four weeks currently. The waiting period for CE-MRA has varied with popularity and availability of the technique, rising to around four months in 2003 following the service's inception. This is also currently reduced to less than a four week wait, with CE-CTA requiring a similar waiting period for non-urgent studies.

Marginal cost analysis was performed in 2001 and 2009, with costs for CE-MRA actually reducing from £149 per study to around £100 currently. Conventional diagnostic angiography, including the cost of a day or overnight bed, cost £515 in 2001, and in 2009 is a similar cost. CE-CTA marginal cost is estimated at £68 per study in 2009. The overall cost of the diagnostic angiography service is demonstrated in figure 5, with the individual costs of conventional diagnostic angiography, CE-MRA and CE-CTA included.

Comparison of a month in angiographic diagnosis and intervention demonstrates significant changes in working practices. Comparison of monthly workloads at the start and end of data acquisition demonstrated a change in practice. In May 1998, 52 conventional diagnostic angiograms were performed, along with 22 invasive interventional procedures. In May 2010, 3 conventional diagnostic angiograms were performed, along with 23 invasive interventional procedures. Moreover, 40 CE-MRA studies and 23 CE-CTA studies were undertaken in this period.
Images for this section:

**Fig. 0:** CE-MRA, Conventional Diagnostic and Interventional Angiography

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**Fig. 0:** CE-MRA Renal Studies

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Fig. 0: Total Numbers of Renal Investigations

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**Fig. 0:** CE-MRA by Body Site

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**Fig. 0:** Cost of the Diagnostic Angiography Service Compared to Total Number of Studies

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Conclusion

The advent of non-invasive vascular imaging using CE-MRA and CE-CTA has resulted in non-invasive alternatives to invasive diagnostic angiography providing excellent quality images whilst avoiding the potential complications associated with invasive procedures. The overall impact of CE-MRA and CE-CTA in our institution has been a marked overall reduction in the conventional diagnostic angiography workload, with extensive use of CE-MRA and more recently CE-CTA in a wide range of clinical scenarios, with tailoring of modality to individual cases. The volume and modality of examinations performed has been widely influenced by modality availability, clinical trends and developments, and consequential theoretical and real adverse effects.

CE-MRA has emerged as a realistic alternative to traditional diagnostic angiography, with gadolinium-based contrast material enjoying a minimal side effect profile(1; 2), with three quarters of those patients suffering any reaction suffering only mild side effects such as nausea, vomiting or urticaria(3). Surgical or angiographic correlation reveals CE-MRA to have 88% sensitivity and 97% specificity for detection of peripheral occlusions or stenoses, and 100% sensitivity and specificity for detection of aortic or iliac aneurysms(4). Whole-body CE-MRA has been accepted as a rapid examination of the lower peripheral arterial system, with high accuracy (5). However, drawbacks are encountered in a number of patients which may preclude the use of MRI, including cardiac pacemakers and resynchronisation devices, ferromagnetic intracranial aneurysm clips, shrapnel injuries, claustrophobia and intravascular stents made of steel. The transfer of primary investigation to CE-MRA is observed in the increase in patients undergoing studies of the aorta, iliac vessels and lower limb run-off.

MRI angiography employs a range of techniques and sequences to maximise the differences in signal intensity between the flowing intravascular blood and the surrounding tissue. Initial angiography using non-contrast techniques such as Time-of-Flight or phase contrast MRA was hampered by long acquisition times, artefacts and poorer imaging of deeper vessels. Initial breakthrough in angiographic imaging was via the use of Fast Low Angle Shot (FLASH) sequence, which resulted in improvement in image acquisition time. A gradient echo sequence, FLASH uses a low-flip angle as well as quick repetition time, much less than that of the usual T1 relaxation time. The resulting 100% sensitivity for stenoses of greater than 50% of the abdominal aorta, iliac and common femoral arteries led to the advancement of MRI as a useful and practical non-invasive imaging method(6; 7). Although gadolinium based contrast agents (GBCA) had been used as early as 1983, CE-MRA as a practical imaging tool emerged in the early 1990s, with the intravascular agent causing shortening of the blood T1 relaxation time. As a result, artefact production is much less than in Time of Flight imaging with initial investigation demonstrating 88% sensitivity and 97% specificity for detection of occlusion or stenosis, and even higher for aortoiliac aneurysms(4). Later in
the decade, the technique was gradually refined with improvement of bolus timing to gain peak enhancement(8). Fluoroscopic triggering resulted in more reliable arterial phase imaging and resulting greater image quality(9). The use of a breath hold gradient echo sequence during administration of gadolinium chelate was advocated for renal, celiac and superior mesenteric vessels in comparison with free breathing, with a statistically significant improvement in the signal to noise ratio(24). The development of centric ordering, where the middle line of K-space is acquired first to improve signal-to-noise or to reduce artefact, provides greater venous suppression, with longer acquisition times and excellent spatial resolution(10; 11; 25). Sensitivity encoding followed, offering marked reduction in scan time with preservation of spatial resolution, reducing conventional Fourier encoding by utilisation of the spatial information related to the coils of a receiver array(26). Extension of these techniques was made possible by progressing from the earlier single view studies to employ a moving table, allowing the acquisition of several pre- and post-contrast runs and evaluation of the aorta and peripheral vessels in a single study with digital subtraction(12). In order to maximise the arterial information from these studies, bolus chase 3D CE-MRA was preceded by 2D acquisition, with the bolus chase resulting in tight arrival of the contrast. Venous signal, due to fast-arterial-venous transit, is limited by this method, with clinical conditions such as cellulitis (which increases contamination) and previous myocardial infarction (decreasing contamination) worthy of pre-study consideration(13; 14). The use of phased array coils allows a decreasing of the number of signal averages, resulting in a shortening of the scan time due to the higher signal-to-noise ratio and resolution. Image acquisition is further accelerated by highly sensitive radiofrequency surface coils along with improved processing algorithms which increase spatial resolution, resulting in better imaging of the crural vessels. Parallel imaging is also employed to reduce the image acquisition time, with signal received simultaneously by several receiver coils with differing spatial sensitivity and resulting increased signal to noise ratio, spatial resolution and reduction of artefact. Compression techniques involving inflation of blood pressure cuffs has also been mooted to increase image resolution to the increase in contrast bolus transit time and the greater time allowed for image acquisition(15).

More recently, CE-CTA has been employed as a useful alternative for those patients unsuitable for gadolinium based contrast, or who are not MR compatible. Despite the preclusion of those with renal impairment, the adverse event rate experienced with low-osmolar iodinated contrast media has been demonstrated as just 0.153%, with nearly 82% of these cases experiencing only mild side effects(3). 64-slice CE-CTA has been shown to be superior to 4- or 16-slice studies, with comparison with digital subtraction angiography demonstrating 97.2% sensitivity and 97% specificity(16). Several techniques of contrast delivery exist to maximise required vessel enhancement, including high injection rates (up to 5 ml/sec)(17) and highly concentrated iodinated contrast. A post injection saline flush delivers a tighter contrast bolus and minimises residual pre-cardiac contrast medium not contributing to vessel enhancement, and decreases the volume of contrast required by up to 29%, reducing the risk of contrast induced nephropathy(18-20). Biphasic injections also improve peak aortic enhancement.
and can be used in conjunction with a flush(21). Unfortunately the patient's cardiac output, the third variable of contrast dynamics as well as injection duration and iodine concentration, is impossible to manipulate, and can vary widely in efficiency in the group of patients undergoing angiographic assessment given their inherent co-morbidities.

A steady increase in diagnostic vascular imaging activity is demonstrated until 2002/03, with an additional 382 patients (an additional 32.4%) examined in the year 2001/02 as opposed to 1997/98. This is in part due to a proliferation in renovascular imaging in this period, with just 22 conventional renal angiograms performed prior to the advent of CE-MRA in 1997/98 for investigation of suspected renal artery stenosis. In the year 2002/03 a total of 377 renovascular studies were undertaken, the large majority undergoing CE-MRA for investigation of possible atherosclerotic renovascular disease, as a cause of renal impairment with or without hypertension. This was due to its non-invasive nature, good sensitivity and specificity relative to digital subtraction angiography, and vast superiority over Doppler ultrasound(27). A reduction in the total number of renal diagnostic procedures in 2002/03 is accounted partly by a move in services to another city site capable of a CE-MRA service, whilst a large backlog of chronic kidney disease patients attending clinics had by then been investigated for renovascular disease, with largely only new presentations of hypertension being referred for CE-MRA. Despite this huge increase in investigation of suspected renal artery disease, the number of renal revascularisations undertaken remained consistently low, a situation likely to continue given the now proven efficacy of medical management and slower rate of renal function decline than previously believed. Renal vascular intervention in our institution is now largely reserved for patients with recurrent flash pulmonary oedema, rapid renal function deterioration or uncontrolled hypertension despite maximal medical therapy(28; 29). Development of other sites in the region capable of CE-MRA also impacted on the drop in the total number of studies in 2002/03 (demonstrated by the red arrow in figure 2).

A drop in the number of CE-MRA studies by 11.5% (66 studies) and in CE-MRA renal studies by 41.2% (98 studies) in 2007/08 is attributable to the reporting in May 2006 (the black arrow in figure 3) of GBCA as a contributory factor in the development of Nephrogenic Systemic Fibrosis (NSF) by the FDA, a serious disorder characterised by hardening and thickening of the skin and body tissues, leading to fixed flexion deformities and resultant limitation of movement, presenting in a similar fashion clinically to scleroderma. This condition was first described by Dr Shawn Cowper & Prof Philippe LeBoit in a paper published in 2000 in The Lancet as a disease with 'scleromyxoedema-like skin thickening' affecting the limbs and trunk but typically sparing the face, the first case having been observed in 1997(30). This new dermatological disease was seen in patients on dialysis and hence the term nephrogenic fibrosing dermopathy (NFD) was coined to reflect this (31). Causes were intensively sought, but no definitive trigger found. Once it was determined that the fibrosing condition also affected internal organs such as muscles, the heart, liver, pleura etc. the condition was renamed nephrogenic systemic fibrosis (NSF). Some patients only manifested localized non-progressive skin thickening/
induration though this could be problematic if it interfered with dialysis shunt access. In other patients a progressive disease could be fatal, with contractures due to skin thickening adjacent to joints and terminal illness through the development of a hypostatic pneumonia, particularly where there was diaphragmatic involvement. As yet there are no clearly effective treatments though in some cases regression has followed improvement in renal function, particularly after transplantation while more recently therapy with the tyrosine kinase inhibitor Imatinib mesylate has shown promise in individual cases. A review by Cowper in 2003 provided more information on the reported cases of NFD/NSF up to that date, but failed to confirm the cause(32) other than the universal setting of renal failure (33; 34). However, due to the sudden appearance of cases in 1997, it was postulated the condition must be due to exposure to a new toxin, medication or medical technique in these severely renal impaired patients.

During the first decade of CE-MRA use no concerns regarding the use of GBCA in haemodialysis patients were raised, studies having shown prompt excretory rates of 78%, 96%, and 99% achieved in the first three haemodialysis sessions following GBCA administration (35). Similarly investigations had shown no acute deleterious reactions in dialysis patients although spurious hypocalcaemia was recognised as a potential problem with gadodiamide administration. Similarly evidence of serious nephrotoxicity at the doses employed for MRI was limited, with initial research demonstrating high-dose gadolinium chelates were significantly less nephrotoxic than iodinated contrast (36). Indeed, this lack of apparent harm from the use of GBCAs at the doses generally employed in MRI led to the widespread use of CE-MRA in particular in patients with renal impairment along with studies showing its diagnostic value in this group. Although some authors had recognised that very high doses of GBCAs were nephrotoxic other authorities advocated GBCA use for radiographic and CT examinations, unfortunately for equivalent radiographic attenuation very high doses of GBCA are required and this was not uncommon practise in some institutions when patients were thought high risk for the use of iodine based contrast media. It was not until 2006 that the gadolinium chelates employed in CE-MRA were first proposed as a potential factor in the development of NSF (37). Subsequent intensive review of NSF cases by several groups suggested its development was strongly associated with gadolinium contrast administration, particularly in high dose on a background of chronic dialysis-dependent renal failure (or less commonly acute renal failure) (38). These suspicions were increased by the discovery of traces of gadolinium in tissue biopsies from affected patients who had been administered GBCAs (39; 40). A warning regarding the use of GBCAs released by the United States Food and Drug Administration in June 2006 added to mounting concerns, recommending physicians carefully assess the need for GBCA in patients with renal failure (41). Subsequently, the linear chelates gadodiamide, gadoversetamide and gadopentetate dimeglumine have been contra-indicated in severe renal impairment. Other GBCAs have not been contra-indicated and it is recognised that in some instances there may be no other alternative to the use of GBCA enhanced MRI and hence an approach balancing risks may on occasion be required proceeding with discussion to inform patients and the use of minimal doses, the cyclic chelates for example not having
undisputed unconfined cases of NSF reported associated with their use. Undoubtedly there is more to the development of NSF than simply the administration of GBCAs to patients with renal failure since in controlled studies such as that from our own institutions some 97% of such patients given relatively high doses (up to 3 times usual) did not develop NSF and further research is needed to try and fully unravel the pathogenesis of this condition.

Avoidance of GBCA in those with a glomerular filtration rate (GFR) of less than 30 ml/minute is recommended and indeed contraindicated for the less stable chelates. This mandates that we know more about our patients prior to deciding upon an imaging strategy, in those patients whose renal function is not known, especially those with diabetes, hypertension or on nephrotoxic medication then estimation of the GFR is important prior to the decision on the imaging mode(42). Recent reviews indicate that the risk of NSF can be eliminated by careful management of risk factors, with up to a 10-fold risk reduction by elimination of just one risk factor (43). One of the major factors is high dose and fortunately modern MRI systems with the use of phased array coils now provide much increased SNR allowing the use of much lower doses for CE-MRA. For example recent work has shown good diagnostic accuracy for single dose aortoiliac and lower limb arterial studies with the use of gadobenate dimeglumine where originally these studies were developed with the use of triple dose. The advent of the blood pool contrast agent gadofosveset trisodium has allowed CE-MRA with even lower doses than the standard extracellular contrast agents, typically just 0.03 mmol/kg is required. Any reduction in the use of MRA will also be countered through the development of newer non-enhanced MRA techniques, such as arterial spin labelling for aortic or renal imaging, as well as ECG-gated 3D partial-Fourier fast spin echo sequences in the evaluation of peripheral arterial disease (44; 45).

Also of note is the increase in the use of CE-CTA, with the number of studies performed increasing over the final five years of the study period. Although in relative infancy with regards to peripheral vascular imaging, its use has been revolutionised by multidetector row scanners. Good accuracy has been demonstrated with 4- and 16-slice scanners, but particularly with the advent of '64-slice' scanners, CE-CTA has become a more mature and robust modality, and in the lower extremities accuracy has been shown to be good for claudicant patients although its role in critical lower limb ischaemia remains relatively unproven (16; 46). CE-CTA can play a useful role in those patients established on renal dialysis with no residual renal function, in whom gadolinium is undesirable due to the risk of NSF since with no residual renal function there is of course no concern regarding potential contrast induced nephropathy although potential adverse effects on the myocardium and volume loading remain. The main problem in this cohort of patients is that the vasculature is heavily calcified and this can significantly obscure the lumen, particularly in small vessels. Though heavy vascular calcification can be problematic, particularly in disease distal to the knee, this calcification is of itself useful information to the surgeon as regards quality of the vessels. CE-CTA also offers improved visualisation
of metallic stents, and in patients in whom CE-MRA is contra-indicated, such as those with pacemakers, other metallic implants or claustrophobia, regarding which CT is generally better tolerated. Despite the requirement for administration of iodine-based contrast media and exposure to ionising radiation (47), patients experience fewer adverse events than from either contrast angiography or CE-MRA (48). Though a lesser radiation burden than digital subtraction angiography (DSA), CE-CTA is a relatively high-dose procedure, on average 13.7mSv per study using a 4-slice scanner (49; 50), although this is higher with more modern 64-slice scanners, and analysis of our own examinations indicates an average dose of 16.6mSv per study. Lack of information on flow dynamics is a major drawback of CT in comparison to both CE-MRA and DSA. In terms of the total number of angiographic studies performed, the reduction in the number of CE-MRA renal studies is likely partly compensated by the use of CE-CTA in those with no residual renal function.

Despite large variations in angiographic modality choice and availability over a decade, the overall number of diagnostic investigations has remained largely constant. The only significant departure from this, 1014 studies in 2004/05, is a result of transfer of a proportion of CE-MRA services to two further city sites within the health board which commenced a CE-MRA service. This suggests that demand for services is much the same, but evolution of technology and its availability has necessitated change.

The significant shift to non-invasive vascular imaging is well demonstrated by comparison of monthly diagnostic workloads at the start and end of data acquisition, with minimal invasive conventional angiography now performed, largely replaced by non-invasive CE-MRA and -CTA. Although the number of interventional cases has remained largely constant over the study period, a marked increase in the complexity of cases, such as EVAR, has occurred with a considerable increase in the time required in the interventional suite to perform such procedures. The advent of sufficient CE-MRA capable systems and the widespread availability of CE-CTA has freed up considerable time in the interventional suite previously reserved for routine diagnostic angiography, allowing the more extensive access required for many interventional procedures.

Vascular imaging has undergone a significant change over the course of a decade, with significant decline in conventional diagnostic angiography and a corresponding increase in CE-MRA and more recently CE-CTA, despite concerns surfacing regarding the incidence of NSF in renal impaired patients exposed to gadolinium based agents and an initial lack of access to MRI scanners. The advent of CE-CTA brings further value to non-invasive vascular imaging in selected patients, and coupled with the now widespread availability of CT and MRI angiography-capable systems, offers a range of cross sectional vascular imaging for many clinical situation, with each modality firmly established for cost effective, time effective and safe diagnostic angiographic use.
References


