Table 7 Presence of artefacts

Artefacts	N	No discrepancy	Artefacts less serious according to SS by 1 level	Artefacts more serious according to SS by 1 level	Artefacts more serious according to SS by 2 levels
SVC	29	23 (79%)	4	2	0
RB	29	17 (59%)	7	5	0
RS	29	21 (72%)	6	2	0
RA	29	17 (59%)	8	4	0
RI	29	24 (83%)	3	2	0
LB	29	12 (41%)	10	7	0
LS	29	17 (59%)	8	3	1
LA	29	17 (59%)	5	6	1
LI	29	19 (66%)	5	5	0
Total	261	167 (64%)	56	36	2

See table 1 for abbreviation

Table 8 shows the SS artefact scores against the FP artefact scores. The kappa coefficient was only 0.29; indicating only fair agreement between SS and FP. Agreement was not very high between the two imaging techniques in terms of artefact assessment. A McNemar's test was performed on the reduced table of counts with the "Mild" and "Major" categories combined to form a single category. The p-value was calculated to be 0.04, so there was a significant difference in artefact assessment between the two techniques. Images were significantly more likely to be assessed as "mild" or "major" by FP compared to SS. However, in 2 venous segments the SS imaging concluded major artefact while the FP imaging concluded no artefacts.

Table 8 Artefact scores between first pass (FP) and steady-state (SS) imaging techniques

Artefacts		SS			Total
		None	Mild	Major	
FP	None	97	33	2	132
	Mild	55	70	3	128
	Major	0	1	0	1
Total		152	104	5	261

Discussion:

Imaging of the central veins usually requires a combination of techniques that may include colour Doppler ultrasonography (CDUS), computed tomography (CT), intravenous digital substraction angiography (IV-DSA) and magnetic resonance venography (MRV). Each modality has advantages and disadvantages depending on the location and nature of the venous disease.

CDUS is widely available and is usually the first investigation of choice. It is non-invasive and particularly useful in assessing upper extremity and neck venous system. However, it is relatively operator dependent and full evaluation including compression of more centrally located veins (superior vena cava and brachiocephalic veins) is not possible due to overlying bones and lungs. Haire et al. has reported that CDUS cannot demonstrate 45% of short segment occlusions at the medial aspect of subclavian vein and 43% of non-occlusive subclavian venous thrombosis [1]. The gold standard, IV-DSA, has some limitations including neprotoxicity risk due to iodine contrast agents, allergic reactions, ionized radiation exposure, requirement of bilateral injections and lack of opacification in jugular veins. Misregistration artefacts along SVC due to motion are also recognised. CT venography is particularly susceptible to contrast agent artefacts which may persist despite bilateral injections. Moreover, bilateral venous cannulation in patients with limited venous access can be highly challenging.

MR imaging of the vascular system has been increasingly utilised due to increased MR availability and the advantages of avoiding risks associated with iodine contrast media and ionising radiation. Initial MR venography techniques were based on

unenhanced MR sequences, most commonly two-dimensional (2D), time-of-flight (TOF) techniques. These have been used in imaging of deep vein thrombosis of the lower limbs and assessment of central veins [2]. However, the clinical use of TOF techniques has been limited by long examination times and misleading artefacts. Overall, interpretation of two-dimensional TOF images is difficult, as indicated by the high degree of inter-observer disagreement seen particularly in the study of Rose et al [3]. Balanced steady-state free precession MR venography has been reported to be highly accurate in the diagnosis of lower extremity deep venous thrombosis but it is prone to magnetic susceptibility artifact [4]. The accuracy of true fast imaging with steady state precession (FISP) imaging for the detection of thrombus in the central veins are too limited for this sequence to serve as the sole means for diagnosis [5].

Contrast-enhanced MR venography was first used in 1997 for lower extremity deep venous system evaluation [6]. Results of MR venography of upper extremity deep venous system were consistent with conventional venography [7]. The initial experience of this technique in imaging of central veins was described in 1999 [8].
The technique is an indirect method requiring subtraction of selective arterial phase from late arterio-venous phase. Subsequently static high-spatial-resolution contrast-enhanced MR venography has been shown to be equally sensitive and specific for revealing stenoses and occlusions as conventional venography of the central veins of the chest [2,7,8,9,10,11,12]. However, a gadolinium-based contrast medium is required, and the majority of contrast media are extracellular agents that rapidly leave the vascular pool. The dose administered commonly exceeds the standard single dose used for most contrast-enhanced MR studies. This is less than ideal given the concerns regarding nephrogenic systemic fibrosis after high-dose contrast enhanced -

MR examinations in patients with impaired renal function, which is relatively common in the group of patients that require central venous assessment [13].

Further improvement of MR techniques using time-resolved serial acquisition methods has improved this situation. By rapid acquisition of sequential images combined with "K" space manipulation, time-resolved MRV can show the temporal dynamics of blood flow as in conventional venography. Visualisation of collateral vessels can help to assess the haemodynamic significance and chronicity of the diseased vessel. As a stand-alone sequence, time-resolved MRV has high sensitivity that is equal to that of high-spatial-resolution MRV for the detection of central venous stenoses and occlusions, but with only a moderate specificity. These findings imply that if the central veins are patent without stenosis, the sensitivity and specificity will be excellent; however, when stenosis or occlusion is present, it might be difficult to determine which veins are abnormal and to what extent, likely because of extremely slow contrast material flow into severely diseased vein segments. However, it has been shown to be a useful adjunct to the conventionally acquired static high-spatial-resolution MR data set by improving specificity for detecting occlusions and enhancing reviewer confidence without increasing the overall study interpretation time [14]. Additional advantages of this approach include a lower contrast material dose requirement (10 mL vs 30 mL) and a shorter acquisition time (2 minutes vs approximately 5 minutes) [15,16]. The side of contrast material injection can also be detected on time-resolved images. This is of clinical importance, as non-diluted contrast material occasionally becomes trapped in the venous valves within the subclavian veins, causing potential image degradation in adjacent vessels because of T2*-related susceptibility artifacts [17,18]

Although adequate to characterize the general morphology and degree of stenosis, the spatial resolution, and hence image quality of time-resolved images may not be optimum. High resolution steady state imaging may improve this but the temporal window steady-state imaging is very limited using extravascular contrast agents.

Macromolecular blood pool agents such as Vasovist® owe their intravascular retention to a strong but reversible affinity to albumin, which extends the vascular lifetime of the contrast medium. As a result, lower doses are required and this agent can still be used for the multiphase first pass imaging of blood vessels as it has similar relaxivity properties to conventional gadolinium media. A higher vascular signal-to-noise ratio can be obtained during equilibrium phase or steady-state imaging but they also allow more prolonged imaging less dependent on bolus dynamics, permitting increased signal averaging and repeated additional high-resolution images in the steady-state. A longer acquisition time permits increased matrix size with preserved or higher signal-to-noise ratio, thus improving the spatial resolution. Steady-state imaging offers the possibility of depicting the entire vascular system without relevant extravasation of the contrast medium from the intravascular space, thus imaging of a larger anatomical area can also be achieved. In addition, vessels with different flow velocities can be properly depicted.

Hartmann et al [19] estimated that T1 of blood in the equilibrium phase, 3–5 minutes after injection of 0.03 mmol/kg gadofosveset, is about 130 ms, increasing to about 150 ms after 10–15 minutes. This prolonged T1 reduction offers the opportunity to obtain images of the vascular tree up to about 45–60 minutes after injection. In clinical practice this means that scan duration is no longer determined by the transient

T1 shortening, but by the capacity of the patient to sustain a breath-hold or to remain motionless.

The comparison of SS imaging with FP imaging using Vasovist® for assessment of the central veins in our study showed favourable results for both techniques but overall better imaging quality and lower artefacts with SS imaging. Our results indicated that in 43% of venous segments where discrepancies on image quality occurred, SS imaging showed better image quality in 5% by 2 or 3 points point and 26% by 1 point scale so overall the image quality was usually better for SS imaging compared to FP. The right sided venous segments showed better image quality using the SS technique by more than 2 or 3 points scale. The SS technique also showed better image quality (9 of the 11 segments where discrepancies occurred) in the left brachiocephalic vein which is most susceptible to transient compression and motion artefacts due to its position between the aortic arch and the sternum. In terms of comparison of the overall image quality scores between the two imaging techniques on the entire central venous system, we found that SS imaging produced images of a significantly higher quality than the first pass imaging.

There was good agreement between SS and FP in grading the level of stenosis. Our findings of 88% of venous segments showing concurrence between the two imaging techniques in identifying and grading stenoses indicated that both techniques wereeffective in providing clinically useful information on assessment of central venous patency. We subsequently reviewed the remaining 12 % where discrepancies occurred and concluded that these are due to overcall from the FP imaging. As with stenotic scores, there was also good agreement between SS and FP in thrombosis assessment.

Our study found that discrepancies in the presence of artefacts occurred in 36% of venous segments where the SS technique usually concluded a lower level of artefact. Discrepancies were particularly prominent along the left brachiocephalic vein (in 59% of all 29 subjects). The use of cardiac triggering (not used in our study) may reduce pulsation artefacts and thus improve the homogeneity of the signal within vessels. We also found that images were significantly more likely to be assessed as having "mild" or "major" artefacts by FP compared to SS.

The use of gadofosveset trisodium in our study has demonstrated improved image quality and the extended window for imaging allows further refinememnt of the imaging techniques. Indeed the feasibility of a combined protocol for the MRI diagnosis of deep vein thrombosis and pulmonary embolism using gadofosveset trisodium has also been reported [20]. Its use for MRV of the leg veins and inferior vena cava using fat-suppressed 3D gradient echo Volume Interpolated Breath-hold Examination showed high diagnostic image quality with no cases of moderate, poor or nondiagnostic image quality. Additionally, an excellent inter-rater reliability was observed [21].

Although the SS-MRA offers all the advantages of a near isotropic 3D sequence, no information on flow dynamics can be obtained from the SS-MRA. Its use as a stand alone technique is clinically adequate to assess central veins but a combination of FP and SS techniques would complement each other and in our experience avoiding the need for a conventional venography. The two different imaging sets allow for more detailed assessment on any ambiguous venous segments. A similar finding was reported in the assessment of carotid artery stenosis using gadofosveset-enhanced MR angiography where steady-state image reading is superior to first-pass image reading,

but the combined reading protocol is more accurate [22]. The use of gadofosveset trisodium with SS imaging has also been found favourable in the assessment of other thoracic vasculature. In an analysis of 25 patients, ECG-gated, motion-compensated high-resolution SS-MRA of the thoracic vasculature (left superior pulmonary vein, left pulmonary artery and aortic arch) with gadofosveset trisodium offered significantly higher image quality and vessel sharpness compared to standard FP-MRA. The authors found that although SS-MRA delivered no dynamic information it may prove specifically helpful as an add-on to FP-MRA for imaging of small vascular structures. SS-MRA revealed lower intra- and interobserver variability for vessel diameters compared with the FP-MRA. The FP-MRA showed higher contrast ratio compared to the SS-MRA [23].

Despite the lack of cardiac and respiratory gated technique, the outcome of our study is strongly favourable for the addition of SS-imaging to our conventional FP technique. The technique could be enhanced and the outcome may be significantly favourable should the motion effects be addressed. Naehle CP et al demonstrated that the high-resolution cardiac- and respiratory-gated SS-MRA showed less overall image artefacts and a higher diagnostic confidence than FP-MRA. They found that vessel sharpness itself was not only improved due to the higher spatial resolution, but also due to motion compensation through navigator-respiratory compensation in comparison to the breath-hold, nongated FP-MRA, and through ECG-gating [24].

There were few limitations in our study. The sample size was not big enough to provide adequate power to detect statistically significant differences. The number of patients needed to provide adequate power would be in the region of 200 patients. Consensus reading did not address variation in subjective assessment but this

approach may enhance accuracy compared to independent single observers, thus leading to a maximum advantage of the techniques studied. Furthermore, use of consensus reading was deemed acceptable since the aim of this study was not to determine the general sensitivity and specificity of MR data sets, as compared with conventional venography data sets, but rather to elucidate the relative degree of diagnostic information obtained and the efficiency in interpretation achieved with FP and SS images. Conventional venography, which has its own limitations, has not been used as the gold standard as the information obtained from MRV provided adequate clinical information that IV-DSA was not required in any of the cases following the MRV examinations. The average interpretation time was not evaluated in our study. However, it has been shown that there was no significant increase in interpretation time when reading both data sets together compared with when the high-spatial-resolution data set was read alone, despite the fact that there were more images to interpret [14].

Conclusion:

In this study MR venography with gadofosveset demonstrated that steady state imaging in the equilibrium phase produced significantly higher quality images with less artefacts than a conventional first pass time resolved technique and was equivalent for the demonstration of venous stenosis and thrombosis.

A larger validation study is required but a combination of FP and SS imaging using gasdofosveset may improve the diagnostic confidence and accuracy of central venous assessment.

REFERENCES

1. Haire WD, Lynch TG, Lund GB, Lieberman RP, Edney JA. Limitations of magnetic imaging and ultrasound-directed (duplex) scanning in the diagnosis of subclavian vein thrombosis. J Vasc Surg 1991; 13. 391-39.

2. Thornton MJ. Ryan R, Varghese JC Farrell MA, Lucey B, Lee MJ. A three-dimensional gadolinium-enhanced MR venography technique for imaging central veins. AJR Am J Roentgenol 1999; 173: 999–1003.

3. Rose SC, Gomes AS, Yoon HC. MR angiography for mapping potential central venous access sites in patients with advanced venous occlusive disease. AJR 1996;166:1181-1187.

4. Lindquist CM, Karlicki F, Lawrence P, Strzelczyk J, Pawlyshyn N, Kirkpatrick ID.. Utility of balanced steady-state free precession MR venography in the diagnosis of lower extremity deep venous thrombosis.. AJR Am J Roentgenol. 2010 May;194(5):1357-64.

5. Pedrosa I, Morrin M, Olcaga L, Baptista J, Rofsky NM. Is true FISP imaging reliable in the evaluation of venous thrombosis? AJR Am J Roentgenol. 2005 Dec;185(6):1632-40.

6. Lebowitz JA, Rofsky NM, Krinsky GA, Weinreb JC. Gadolinium-enhanced body MR venography with subtraction technique. Am J Roentgenol 1997; 169:755-758.

7. Tanju S, Sancak T, Dusunceli E, Yagmurlu B, Erden I, Sanlidilek U. Direct contrast-enhanced 3D MR venography of upper extremity deep venous system. Diagn Interv Radiol 2006; 12: 74–79.

8. Shinde TS, Lee VS, Rofsky NM, Krinsky GA, Weinreb JC. Three-dimensional gadolinium-enhanced MR venographic evaluation of patency of central veins in the thorax: initial experience. Radiology 1999; 213:555-560.

9. Nael K, Laub G, Finn JP. Three-dimensional contrast-enhanced MR angiography of the thoraco-abdominal vessels. Magn Reson Imaging Clin N Am 2005; 13(2): 359–380.

10. Oxtoby JW, Widjaja E, Gibson KM, Uzoka K. 3D gadolinium-enhanced MRI venography: evaluation of central chest veins and impact on patient management. Clin Radiol 2001; 56: 887–894.]

11. Kroencke TJ, Taupitz M, Arnold R, Fritsche L, Hamm B. Three-dimensional gadolinium-enhanced magnetic resonance venography in suspected thrombo-occlusive disease of the central chest veins. Chest 2001; 120:1570 -1576

12. Fraser DG, Moody AR, Davidson IR, Martel AL, Morgan PS. Deep venous thrombosis: diagnosis by using venous enhanced subtracted peak arterial MR venography versus conventional venography. Radiology 2003 : 226:812 -820.

13. Public health advisory: update on magnetic resonance imaging (MRI) contrast agents containing gadolinium and nephrogenic fibrosing dermopathy. U.S. Food and Drug Administration Web site. http://www.fda.gov/cder/drug/advisory/gadolinium_agents_20061222.htm. Published December 22, 2006. Accessed May 3, 2007.

14. Kim CY, Mirza RA, Bryant JA, Whiting ED, Delong DM, Spritzer CE, Merkle EM.
Central veins of the chest: evaluation with time-resolved MR angiography. Radiology. 2008 May;247(2):558-66.

15. Korosec FR, Frayne R, Grist TM, Mistretta CA. Time-resolved contrast-enhanced 3D MR angiography. Magn Reson Med 1996; 36(3): 345–351.

16. Du J, Thornton FJ, Mistretta CA, Grist TM. Dynamic MR venography: an intrinsic benefit of time-resolved MR angiography. J Magn Reson Imaging 2006; 24: 922–92.

17. Lee VS, Martin DJ, Krinsky GA, Rofsky NM. Gadolinium-enhanced MR angiography: artifacts and pitfalls. AJR Am J Roentgenol 2000; 175: 197–205.

18. Lee YJ, Chung TS, Joo JY, Chien D, Laub G. Suboptimal contrast-enhanced carotid MR angiography from the left brachiocephalic venous stasis. J Magn Reson Imaging 1999; 10: 503–509.]

19. Hartmann M, Wiethoff AJ, Hentrich HR, Rohrer M. Initial imaging recommendations for Vasovist angiography. Eur Radiol. 2006 Feb;16 Suppl 2:B15-23.

20. Hansch A, Beige S, Pochlmann G, Neumann S, Baltzer P, Pfeil A, Waginger M, Boettcher J, Kaiser WA, Wolf G, Mentzel HJ. Combined magnetic resonance imaging of deep venous thrombosis and pulmonary arteries after a single injection of a blood pool contrast agent. Eur Radiol. 2011 Feb;21(2):318-25.

21. Pfeil A, Beige S, Pochlmann G, Boettcher J, Drescher R, Malich A, Wolf G, Mentzel HJ, Hansch A. Magnetic resonance VIBE venography using the blood pool contrast agent gadofosveset trisodium-An interrater reliability study. Eur J Radiol. 2011 Feb 22. [Epub ahead of print]

22. Anzidei M, Napoli A, Marincola BC, Nofroni I, Geiger D, Zaccagna F, Catalano C, Passariello R. Gadofosveset-enhanced MR angiography of carotid arteries: does steady-state imaging improve

accuracy of first-pass imaging? Comparison with selective digital subtraction angiography. Radiology. 2009 May;251(2):457-66

23. Nachle CP, Müller A, Willinek WA, Meyer C, Hestermann T, Gieseke J, Schild H, Thomas D. First-pass and steady-state magnetic resonance angiography of the thoracic vasculature using gadofosveset trisodium. J Magn Reson Imaging. 2009 Oct;30(4):809-16.

24. Nachle CP, Kaestner M, Müller A, Willinek WW, Gieseke J, Schild HH, Thomas D. First-pass and steady-state MR angiography of thoracic vasculature in children and adolescents. JACC Cardiovasc Imaging. 2010 May;3(5):504-13.

Acknowledgments

This study was supported by a National Institute of Health Research, Biomedical Research Centre grant