MR Evaluation of Deep Venous Thrombosis (DVT) of the Lower Extremities using Ferumoxytol,

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INTRODUCTION

Magnetic resonance venography has been previously reported using two-dimensiona1 (2D) time of flight (TOF) and gadolinium-enhanced MRA. The former is inefficient and suffers from sensitivity to flow patterns, whereas the latter suffers from rapid leakage of contrast agent into the extravascular space. Compared with extracellular agents, ferumoxytol (Advanced Magnetics, Cambridge, MA), a novel iron oxide blood pool agent, has a very long intravascular half-life (14 hrs). It can provide a much longer time window for data acquisition than gadolinium chelates to permit high resolution, multi-station imaging. Moreover, ferumoxytol provides a novel dual contrast mechanism for evaluation of the deep venous system. T1 shortening results in enhancement of venous signal intensity on 3D gradient-echo images, whereas T2 shortening eliminates all vascular signal on T2-weighted fast spin-echo images without altering the signal intensity of thrombus. Using the T1 effect of an iron oxide blood pool agent for detection of deep vein thrombosis (DVT) has been reported (1), but use of a dual contrast mechanism has not. The purpose of this study was to evaluate the feasibility and potential benefits of using the dual contrast mechanism of ferumoxytol to detect DVT.

MATERIALS AND METHODS

Nine patients (8 men and 1 women; age range, 42-86 years; average age, 60.2 years) with known DVT of lower extremities were evaluated with MR imaging using ferumoxytol. The DVT was detected by duplex sonography (DUS) 1-19 days (average, 5.6 days) before MR exams. Three patients had bilateral DUS, and 6 patients had unilateral DUS. Totally 10 thrombi were reported in 12 DUS studies of the 9 patients.

MR exams were performed on a 1.5 T Signa Lx 11.0 TwinSpeed MR scanner equipped with EXCITE technology (GE Healthcare, Waukesha WI, USA). An 8-channel torso phased array was used. Four imaging techniques, including **1)** pre-contrast axial two-dimensiona1 2D TOF venography, **2)** three-dimensiona1 (3D) first-pass time resolved imaging (TRICKS) with ferumoxytol, **3)** 3D spoiled gradient echo (SPGR) bright blood equilibrium angiography with sub-millimeter spatial resolution, and **4)** two-dimensiona1 (2D) T2 weighted fast spin echo (T2 FSE) dark blood imaging with and without fat suppression (FS) were performed. Bright blood and dark blood images could be acquired over extended periods because of the long vascular half-life of the contrast agent. Typical parameters for these sequences are summarized in Table 1. In addition, selective venography for better venous depiction was obtained with subtraction of arterial phase TRICKS images from equilibrium phase images (2). In order to get first-pass T1-weighted bright blood images, the contrast agent was diluted in four-fold (i.e. from 537.2 µmol Fe/ml to 134.3 µmol Fe/ml) to minimize T2*effect (2). The diluted full dose of ferumoxytol (4 mg, 71.6 µmol Fe/kg bw) was administered with a power injector (Medrad Spectris; Medrad, Indianola, PA) at a rate of 2 ml/sec, followed by 15 ml saline at the same injection rate.

Qualitative analysis of image quality of 2D TOF and MR images using ferumoxytol was assessed using a 4-point scale (1 = non-diagnostic, 2 = fair, 3 = good, 4 = excellent). The scores were determined by two radiologists. The averaged scores from the two reviewers were used for the comparison.

RESULTS

All patients completed their MR study without complication. A total of 11 thrombi were detected by MRI. All thrombi shown on DUS were confirmed by MR except for a small muscular branch thrombus which was not in the field of view of the MR examination. In 2 patients who had unilateral DUS, an additional thrombus was seen on the opposite side. The MR findings included occluded veins (n=7), filling defect (n=3), and mural thrombus (n=1). The average length of detected thrombi was 20.3 (1.0-53.1) cm. Thrombi on TOF images showed low signal (Fig 1, a), but substantial artifacts were seen on MIP images due to slow, phasic venous flow. Bright blood equilibrium imaging after ferumoxytol provided detailed, comprehensive evaluation of the venous system. Thrombi manifested as abrupt vessel cut-off (Fig 3, b, c), or as filling defects partly surrounded by high-intensity blood (Fig 1, b). Dark blood fast spin-echo images showed uniform suppression of blood signal. Thrombus appeared bright and was highly contrasted with the low signal of arterial and venous blood as well as background tissue (Fig 1, c), particularly on images with fat suppression (Fig 1, d; Fig. 2). Even small calf vein thrombi on the order of a few millimeters were readily detected. The ferumoxytol-enhanced first-pass TRICKS MRA showed the anatomy of the arterial system (Fig 3, a). Separation of arteries and veins was feasible by subtraction of arterial phase images from equilibrium images (Fig 3). Qualitative analysis showed that average scores of MRV images using ferumoxytol were significantly higher than 2D TOF images (3.6 vs.1.4, $p<0.0001$).

Table 1: Pulse sequence parameters used for DVT detection

Sequences	TR (ms)	TE (ms)	FA	BW (Hz)	Thk./zip2 (mm)	Spa. (mm)	Matrix	FOV (cm)
2D TOF	25.0	min ful	60º	±31.2	3.0/---	0.5	256X192	34
TRICKS	4.7	min	45º	±31.2	2.0/---	---	256X192	40
3D SPGR	5.6	min	30º	±62.5	3.0/-1.5	---	512X512	40
T2 FSE	3000.0	50.0	--	±62.5	3.0/---	---	256X256	34

FA = flip angle; BW = bandwidth; FOV = field of view. Spa. = Slice spacing

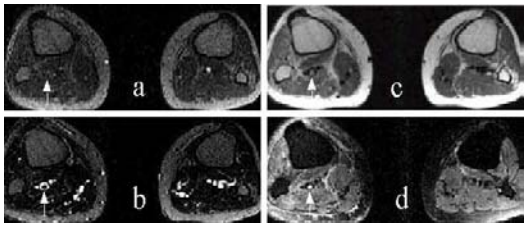

Fig. 1. Small calf vein thrombus (arrows). **a**. pre-ferumoxytol 2D TOF; **b**. post-ferumoxytol 3D equilibrium phase; **c.** post-ferumoxytol FSE; **d**. post-ferumoxytol FSE (with fat suppression).

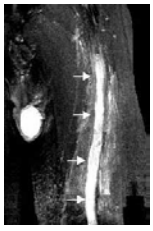

Fig 2. Thrombus on a MIP T2-FSE FS coronal image (arrows).

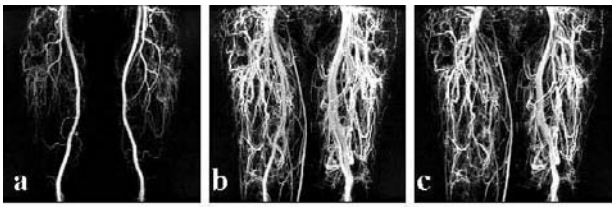

Fig. 3. Right thigh DVT. **a.** arterial phase image; **b.** equilibrium image; **c.** selective venography. Note absence of right SFV in (**c**).

DISCUSSION AND CONCLUSION

Ferumoxytol-enhanced MR imaging provides clear delineation of DVT of the lower extremities. The long intravascular half-life of the contrast agent enables prolonged imaging with large matrix sizes for sub-millimeter spatial resolution. The novel dual contrast mechanism is particularly useful for detection of thrombi in small veins, which were more conspicuous on dark blood than bright blood images. The entire extent of thrombus is visible on dark blood images, which along with the capability of depicting small calf vein thrombi might provide a potential advantage compared with duplex sonography. Moreover, the technique may have potential applications for other thromboembolic disorders such as pulmonary embolism. Further evaluation in a larger patient cohort appears warranted.

REFERENCES

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