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Rapid magnetic resonance venography in a pediatric population using a blood pool contrast agent and multi-station fat-water separated volumetric imaging

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Abstract

A rapid, reliable radiation-free method of pediatric body venography may complement ultrasound by evaluating veins in the abdomen and pelvis, as well as providing a global depiction of venous anatomy. We describe a MR venography technique utilizing gadofosveset, a blood pool contrast agent, in pediatric patients. The technique allows high-spatial-resolution imaging of the veins from the diaphragm to the knees in less than 15 minutes of total exam time.

Keywords

venography; MRI; gadofosveset; blood pool contrast agent

Introduction

Venography may be performed by ultrasound, CT, conventional catheter-based contrast venography, and MR [1]. Ultrasound is operator- and patient-dependent, and has suboptimal sensitivity when evaluating the pelvic veins [2]. Both CT venography and catheter-based contrast venography rely on ionizing radiation, use iodinated contrast with its risk of contrast nephropathy, and are limited by rapid clearance of contrast from the blood pool [1]. MR venography using 2D time of flight suffers from long acquisition times, as well as sensitivity to patient motion, pulsatility artifact, and confounding signal voids from flow turbulence [3], while MR venography with standard extracellular gadolinium agents is hampered by rapid distribution of these contrast agents into the surrounding tissues, restricting image acquisition time and hence image resolution or anatomic coverage. In addition, variability in the rate of venous return can result in heterogeneous opacification of the iliac veins and inferior vena cava [4].

We describe a technique using gadofosveset, a blood pool gadolinium contrast agent, that allows rapid, reliable, venographic, high-spatial-resolution MR venographic imaging. Reversible binding of gadofosveset to plasma albumin prolongs the residence time of the contrast agent in the blood pool, resulting in a relatively constant steady-state plasma concentration, thus permitting a higher spatial resolution acquisition and greater anatomic

coverage. This binding also increases the magnetic relaxivity of gadofosveset, producing robust vascular enhancement [4–7]. Acquisition of MR images during the steady state after injection of blood pool contrast agents has been used in the setting of traumatic hemorrhage, arterial stenosis, coronary artery disease and deep venous thrombosis in adults [6,7].

Technique

Imaging was performed on a 3T GE MR 750 scanner (GE Healthcare, Waukesha, WI). A 32 channel phased array coil was placed on the abdomen and pelvis. To avoid prolonging the exam time for coil repositioning, the body coil was used for the extremities. Patients were scanned in the supine position. A single dose (0.12 mL/kg body weight, i.e. 0.03 mmol/kg) of gadofosveset trisodium (Ablavar, Lantheus Medical Imaging, Billerica, MA) was diluted in saline to a volume of at least ten milliliters and administered intravenously at a rate of 0.5 mL per sec using a power injector (MEDRAD, Inc., Warrendale, PA) via peripheral venous access (22 gauge angiocatheter in an antecubital vein), followed by a 20 mL normal saline solution flush.

After a two minute delay, post-contrast axial images were obtained in multiple stations, from superior to inferior, with a dual-echo RF-spoiled gradient-recalled echo T1-weighted sequence with Dixon-based fat-water separation (LAVA-Flex). Parameters were: a ~4.5 msec repetition time, a ~2 msec echo time, a 12° flip angle, a field of view between 28–38 cm, and an 166 kHz bandwidth. For the abdomen and/or pelvis, images were obtained with 320 × 256 matrix, 3 mm slice thickness, 1.5 mm slice spacing, 72 – 244 per station, and acceleration factor of 2–3; the sequence was either performed as a single breath-hold of approximately 25 seconds, or modified to enable navigation for respiratory motion correction. In the lower extremities, images were obtained with 320 × 384 matrix; 1.6–3 mm slice thickness; 0.8–1.5 mm slice spacing; 152–504 slices per station, two signal averages, and 1–5 minutes per station. The total acquisition time for the entire exam averaged 11 ± 3.5 minutes (range 7 – 15 min). By comparison, based on a repetition time of 20 ms and a phase matrix of 200, 75 cm of coverage obtained at 3 mm slice thickness would conservatively require approximately 40 minutes for a time-of-flight MR venogram.

After a rapid MR venography technique was established, exams were performed for clinical purposes. However, given the new imaging approach and our intention to evaluate it, the study was approved by our Institutional Review Board, and informed consent/assent was obtained prior to inclusion in the study. Nine consecutive patients referred for clinically indicated studies were recruited for our study from October, 2009, to April, 2011. Patients ranged from 1 – 16 years of age (average 12.4 ± 5.2 years). Depending on the clinical indication, patients were imaged in different stations from the diaphragm to the knees. Representative images from venograms are displayed (Figures 1 – 8). Examples of the various pathologies identified in these patients using this method are also included (Figures 9 – 12).

The veins were assessed segmentally to demonstrate that this imaging technique results in adequate and homogeneous conspicuity of the veins relative to the surrounding anatomy. Noise in the setting of parallel imaging is spatially varying, so a simple region of interest in the air surrounding the patient is not a valid measurement of noise [8]; therefore, in the abdomen and pelvis where parallel imaging was used, a contrast to background ratio (CBR) was calculated. A region of interest was placed in the venous segment, and the signal intensity of the vessel segment was divided by the similarly derived signal intensity of adjacent muscle that demonstrated homogeneous signal intensity. In the lower extremities, where parallel imaging was not utilized, the contrast to noise ratio (CNR) was also determined by measuring the signal intensity in the vein, subtracting the signal intensity in

the adjacent muscle, and dividing the result by the standard deviation of the signal in the air [8]. Calculations for the bilateral common and external iliac veins were averaged together, as were results for the bilateral common femoral and proximal, mid and distal superficial femoral veins, and also the bilateral popliteal veins, respectively. The CBR for the inferior venae cavae was 3.6 ± 0.6 ; for the iliac veins, 3.2 ± 1.0 ; for the femoral veins, 2.9 ± 0.6 ; and for the popliteal veins, 3.0 ± 0.7 (numbers represent the mean $\pm$ SD from between 3 – 9 different patients). The CNR was 27.4 ± 6.8 for the femoral veins and 26.5 ± 7.2 for the popliteal veins (mean $\pm$ SD, 3 – 9 different patients). These numbers suggest the method will consistently yield good contrast between veins and adjacent tissues.

Discussion

A rapid, reliable method is needed for venography, especially in the abdomen and pelvis, in the pediatric population without the use of radiation. While ultrasound is commonly used to evaluate the extremities, it is of limited sensitivity in the assessment of pelvic veins [1, 2]. Methods utilizing iodinated contrast for venography are not optimal in the pediatric population because of the exposure to ionizing radiation. MR time-of-flight venography requires prolonged acquisition times, thereby introducing patient motion artifacts, and suffers in the setting of slow or in-plane flow, as well as turbulent flow. Post-contrast MR imaging using conventional extracellular gadolinium contrast agents largely overcomes these limitations, but introduces a requirement for accurate bolus timing to overcome the inconsistent venous opacification that can result from variations in venous flow rates [5].

Binding of gadofosveset to plasma albumin increases the magnetic relaxivity of gadofosveset, resulting in pronounced vascular enhancement, with shortened blood T1 values still present up to 4 hours after intravenous injection [6]. Binding also prolongs the residence time of the contrast agent in the blood pool [5]; the half-life of the distribution phase of gadofosveset is approximately 30 minutes, while the half-life of the elimination phase is approximately 16 hours, with primarily renal elimination. The relatively constant steady state plasma concentration allows for imaging up to 30 – 60 minutes after contrast administration [6].

Our application of gadofosveset is “off-label”, as the FDA-approved indication is aortoiliac atherosclerotic disease in adults, with no specific information currently available on its use in children [8]. As with all gadolinium based contrast media, gadofosveset is contraindicated if there is: a history of prior allergic reaction to gadolinium-based contrast agents; acute kidney injury, which may be worsened by gadolinium administration; or chronic severe renal disease (defined as a glomerular filtration rate less than 30 mL per min per 1.73 m² body surface area), which may increase the risk of developing nephrogenic systemic fibrosis. Of note, the package insert recommends caution when QTc may be prolonged, as there may be a risk of torsades de pointes.

In summary, we demonstrate a simple protocol in a pediatric population using a blood pool contrast agent for high resolution MR venography, consisting of multiple stations of axial volumetric imaging, obtained in less than 15 minutes of total exam time. As demonstrated, the prolonged steady state high intravascular signal from gadofosveset reliably yields homogeneously high contrast between the veins and the adjacent anatomy. While the Dixon-based fat saturation does prolong both the scan time and the echo time, which may introduce dephasing artifact, Dixon-based fat saturation remains a robust method for uniform fat suppression over a large field of view and also improves the differentiation of contrast-enhanced vessels from adjacent anatomy by increasing the dynamic range of the image. Both arteries and veins are opacified using this method, but the distinction between the vessels is quite simple on the high resolution images, particularly in the axial plane. This

potential shortcoming is offset by the rapid examination time. In addition, if there is motion or other artifact during a sequence acquisition, gadofosveset-enhanced sequences may be repeated without the need for a repeated contrast bolus. 3D MR acquisition of delayed steady-state post-contrast images after gadofosveset administration provides a robust method of venography.

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Figure 1. Representative MR venographic images of the suprarenal inferior vena cava of a 14 year old female patient. White arrows on the a) axial source image and b) coronal oblique maximum intensity projection image indicate the position of the suprarenal inferior vena cava.

Figure 2. Representative MR venographic image of the infrarenal inferior vena cava of the same patient as in Figure 1. White arrows on the a) axial source image and b) coronal oblique maximum intensity projection image indicate the position of the infrarenal inferior vena cava.

Figure 3. Representative MR venographic image of the iliac venous convergence of the same patient as in Figure 1. White arrows on the a) axial source image and b) coronal oblique maximum intensity projection image indicate the position of the iliac venous convergence.

Figure 4. Representative MR venographic image of the common iliac veins of the same patient as in Figure 1. White arrows on the a) axial source image and b) coronal oblique maximum intensity projection image indicate the position of the common iliac veins.

Figure 5. Representative MR venographic image of the external iliac veins of the same patient as in Figure 1. White arrows on the a) axial source image and b) coronal oblique maximum intensity projection image indicate the position of the external iliac veins.

Figure 6. Representative MR venographic image of the common femoral veins of the same patient as in Figure 1. White arrows on the a) axial source image and b) coronal oblique maximum intensity projection image indicate the position of the common femoral veins.

Figure 7.

Representative MR venographic image of the superficial femoral veins, part of the deep venous system of the thigh, of the same patient as in Figure 1. White arrows on the a) axial source image and b) coronal oblique maximum intensity projection image indicate the position of the superficial femoral veins.

Figure 8. Representative MR venographic image of the popliteal veins of the same patient as in Figure 1. White arrows on the a) axial source image and b) coronal oblique maximum intensity projection image indicate the position of the popliteal veins.

Figure 9. Example of a venous malformation. a) Axial source image and b) coronal maximal intensity projection image centered below the knee joint of a 15 year old male demonstrate findings of a venous malformation (white arrows) located in the subcutaneous fat medial to the left knee and upper tibia, and show the communication between the malformation and the engorged deep calf veins.

Figure 10. Example of a deep venous thrombosis. a) Axial source image and b) coronal multiplanar reformatted image of the pelvis of a 16 year old male demonstrate acute thrombosis causing a filling defect (white arrows) within the left common iliac vein.

Figure 11. Example of anatomy compatible with May-Thurner syndrome. a) Axial source image and b) sagittal curved planar reformatted maximum intensity projection image of the pelvis of a 14 year old female demonstrate marked narrowing of the left common iliac vein (white arrows) as it courses between the right common iliac artery and the lumbar vertebral body, anatomy considered to predispose patients to venous thrombosis, although none is demonstrated here.

Figure 12.

Example of mass effect from a tumor narrowing a pelvic vein. a) Axial source image and b) coronal curved planar reformatted maximum intensity projection image of the pelvis demonstrate a large, enhancing mass in the right pelvis, compatible with a desmoid tumor. Mass effect from the tumor markedly narrows the right external iliac vein (white arrows), which remains patent. Incidentally, note intense uptake of contrast by the tumor.