Pediatric* MR Urography

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MR urography represents the next stage in the evolution of uroradiology because it fuses superb anatomic and functional imaging in a single test that does not use ionizing radiation. It has the potential to revolutionize the imaging approach to renal disease in children. MR urography has advantages over other modalities in that it generates tissue contrast from a variety of sources. In addition to spin echo T1 and T2-weighted images, dynamic imaging is performed in conjunction with the injection of a Gadolinium based contrast agent (GBCA) in order to assess the concentrating and excretory functions of the kidney. The evaluation of the dynamic contrast-enhanced images is similar to renal scintigraphy but with the important distinction that the signals originating from the renal parenchyma can be separated from those originating from the collecting system. The primary indication for MR urography is in the evaluation of hydronephrosis. Other evolving indications for MR urography include evaluation of renal scarring and dysplasia, identification of ectopic ureters in children with urinary incontinence and characterization of renal masses.

Patient preparation of MR urography is of crucial importance. For a patient where the indications are hydronephrosis, renal scarring and dysplasia the patient preparation consists of hydration, injection of a diuretic agent, bladder catheterization and, in younger children, sedation. When the indication is a renal mass the diuretic and the bladder catheter can be omitted. Because a fluid challenge is integral to a high quality study, and because we want to limit the concentration of the GBCA in the kidney, the patient has to be hydrated prior to the start of the study and the hydration regime needs to be as reproducible as possible. For this reason we use standardized intravenous hydration regime. If children are to be sedated, we correct their nil per os (NPO) deficit using Ringer’s solution according to the following formula:

1. For first 10 kg of patient’s weight:
   - 4 cc/kg/hour
2. For next 10 kg of patient’s weight:
   - 2 cc/kg/hour
3. For each kg above 20 kg patient’s weight:
   - 4 cc/kg/hour

If the child is not going to be sedated we hydrate with Ringer’s solution at a dose of 10 cc/kg and given intravenously over 30–40 minutes. The second element of the fluid challenge is an injection of a loop diuretic (Furosemide). We use a standard dose of 1 mg/kg, up to a maximum dose of 20 mg, injected 15 minutes prior to the injection of the GBCA. In addition to being an integral part of the fluid challenge the early administration of the furosemide distends the urinary tract and minimizes the duration of the study. By administering the GBCA after

1 Two oblique views of a MIP created from the heavily T2-weighted volumetric sequence for a patient with an ectopic insertion of the ureters from the upper pole of a duplex kidney.
2 T2-weighted axial images from 4 patients. Fig. 2A is from a relatively normal subject and shows good cortico-medullary differentiation. Fig. 2B is from a patient with pyelonephritis, poor cortico-medullary differentiation is seen in the left kidney along with a fluid level in the collecting system. Fig. 2C is through the isthmus of a patient with a horseshoe kidney. Fig. 2D is from a patient with severe renal dysplasia and shows cortical scarring and poor cortico-medullary differentiation.

3 Shows images from a child with nephroblastomatosis. Figs. 3A and 3C are the ADC and isotropic diffusion-weighted images respectively. Figs. 3B, 3D and 3E are pre-contrast T2-weighted, post-contrast STIR and post-contrast T1-weighted (delayed volume) images respectively. There are multiple small peripheral masses that are homogeneous in appearance on all imaging sequences as well as demonstrating restricted diffusion when compared with normal kidney.
the fluid challenge and during the time of maximal diuresis, pathophysiological changes in the kidney that occur in response to this stressed state can be visualized. A bladder catheter is placed whenever possible. The main reason for placing a catheter is that children become uncomfortable and tend to wake from sedation if the bladder is full. There are additional imaging benefits from using a bladder catheter in that interpretation of the images is easier as confounding issues such as vesico-ureteric reflux and transmitted bladder pressure are eliminated. If there is a question of a bladder abnormality, the catheter can be clamped and images of the distended urinary bladder obtained. Almost all children under 7 years of age will need to be sedated. Optimal solutions include general anesthesia or dedicated sedation physicians who are able to titrate the depth of sedation for the individual patient. Many of our patients are referred for the evaluation of antenatal hydronephrosis. In this population our sedation physicians usually like to wait until the patient is at least 3 months of age before scheduling the MR urogram. Older children who are not sedated are asked to either breathe quietly or if they are able to co-operate, breathhold imaging is performed for most sequences.

Pre-contrast imaging

One of the strengths of MR urography is the ability to combine both contrast-enhanced imaging with T2-weighted images so that both static and dynamic evaluation of the urinary tract is obtained. This is particularly helpful in cases of marked hydronephrosis or poorly functioning systems. We obtain a 3D heavily T2w urogram which is used to generate maximum intensity projections (MIPs) and volume rendered images of the pelvicalyceal system and ureters (Fig. 1). Volume rendered images are very helpful in analyzing duplex systems or complicated anatomical variants. We also perform an axial T2w TSE through the bladder to identify abnormalities of the bladder base including ureteroceles and ectopic ureteric insertion. Additionally we have come to rely on axial high resolution T2-weighted images in the assessment of the renal parenchyma (Fig. 2). These are typically performed immediately after the HASTE scouts and are obtained prior to the Furosemide injection so that we have a baseline evaluation of the degree of hydronephrosis to which we can compare the delayed images. In the case of a renal mass we have found diffusion-weighted imaging to be helpful in the characterization of

![Image](4A)

![Image](4B)

![Image](4C)

![Image](4D)

Shown images from a 3-year-old girl with Wilms tumors. Figs. 4A and 4C are the ADC and isotropic diffusion-weighted images respectively. Figs. 4B and 4D are pre-contrast T2-weighted and post-contrast STIR respectively. Wilms tumors are large and heterogeneous in signal characteristics containing both solid and cystic areas. There is restricted diffusion within the mass, but it is not as homogeneous as in areas of nephroblastomatosis.
the mass and we acquire high resolution diffusion images using either RESOLVE** (readout-segmented EPI) or zoomed-EPI**. The former splits the EPI readout into segments thus reducing the length of the individual EPI echo trains resulting in reducing distortion and allowing higher resolution images with little distortion to be obtained. The latter uses a two dimensional RF pulse to limit the field-of-view in the phase direction in order to achieve the same goals. Because of the limited amount of respiratory related motion in younger patients high quality diffusion images can be obtained using these techniques, leading to reduced partial volume effects and higher image quality (Figs. 3 and 4).

**Contrast-enhanced imaging**

The change in T1 induced by a GBCA is directly related to the concentration and relaxivity of the GBCA. Thus if the T1 relaxation time can be measured, and we assume the relaxivity is the same as that measured ex-vivo, we can calculate the contrast agent concentration. However, a dynamic measurement of T1 is not straightforward, so in clinical practice one tends to use the change in signal, with respect to the pre-contrast images, in order to estimate the concentration of the GBCA. At low concentrations T1 effects predominate and the relationship between signal change and GBCA concentration is relatively linear, however, as the concentration increases T2* effects become increasingly important, leading to signal dephasing and an increasingly non-linear relationship between the change in signal and the concentration of the GBCA. If the signal change is to be used to estimate the concentration of the GBCA then it is important to keep the concentration of the GBCA low enough to ensure it is within the linear range. We use a standard dose (0.1 mmol/kg) of a GBCA (Magnevist) and have found that the standard dose provides excellent enhancement of the kidneys and allows evaluation of the MR nephrogram by differentiating the enhancing parenchyma from the background. Others have used smaller doses of contrast but we have found that using a lower dose is particularly challenging when trying to segment poorly functioning kidneys. Because of the risks associated with using a GBCA on patients in renal failure a serum creatinine test is used to estimate the glomerular filtration rate (GFR) on all patients. If the total estimated GFR, as measured with serum creatinine, is below 60 ml/min we change the GBCA to an agent with a cyclic structure and no net charge (Gadoteridol). Children with estimated GFR below 30 ml/min are not typically referred for an MR urogram. For the dynamic, contrast-enhanced, sequences some groups have used one, or a limited number of slices in conjunction with higher temporal resolution. We have preferred to use a 3D acquisition covering the entirety of both kidneys with a more modest temporal resolution. The 3D approach has several advantages, it ensures that small areas of interest, such as renal scarring are included in the acquired volume, it means an ideal rectangular slice profile can be assumed (in 2D approaches imperfections in the slice profile must be corrected for) and it allows measures which are representative of the whole kidney to be derived. Because of the lower temporal resolution (typically 8 seconds on a scanner with a standard gradient system) and the desire to keep the arterial concentration of the GBCA in the linear range we typically use a power injector to deliver a slow infusion of the GBCA at a rate between 0.1 and 0.25 ml/sec, depending on the patients weight, resulting in an injection duration of between 20 and 60 seconds. The dynamic sequence is started prior to the commencement of the injection and due to the slow rate of infusion we have at least 5 pre-contrast dynamics which can be used to obtain a robust estimate of the pre-contrast signal. The dynamic sequence is a 3 dimensional, T1-weighted, fat saturated, gradient echo sequence acquired in an oblique coronal plane. The flip angle is set at 30° in order to improve the linearity of the signal intensity and a high bandwidth is used to minimize the echo time. The slice thickness is typically 2 mm. In most cases 50 volume acquisitions are acquired in the first 10 minutes after contrast injection. Volumetric data is acquired continuously for the first five minutes of scanning and then delays of increasing duration are inserted between the subsequent dynamic acquisitions since high temporal resolution is not required for the washout phase. A MIP image of each dynamic series is automatically generated which facilitates rapid review of the data sets (Fig. 5). This MIP image of each volumetric data set is termed a concatenated MIP. Following the dynamic sequence high resolution STIR and a high resolution 3D, T1-weighted volumetric data set are acquired. The post-contrast STIR sequence provides an excellent depiction of the renal morphology and in particular renal scarring (Fig. 6). In younger children the volumetric 3D, T1-weighted sequence is acquired with isotropic resolution and requires around 2 minutes of imaging. The resulting images, and associated MIPs, provide a good overview of the functioning renal tissue and the excreted contrast (Fig. 7). In older children three orientations are acquired with thicker slices, with each orientation being acquired in a breathhold. We typically acquire our MR urograms on 1.5T scanners, using a 3T scanner improves the T2 volumetric and other non-contrast images but the SAR limits typically require that the dynamic sequence is run either without fat saturation or with a lower flip angle. The former complicates the visual inspection of the images and in particular the concatenated MIPs, while the latter reduces the linear range for the relationship between the change in signal and the contrast agent concentration.

**Post-Processing**

The basic steps in the post-processing of the dynamic series are the segmentation of the kidneys, the derivation of arterial and parenchymal curves and the fitting of these to an appropriate model in order to derive indices of renal function. The segmentation provides both an estimate of the renal volume which is required when calculating the GFR for the whole kidney and provides a mask.
5 Shows images from a single slice (top row) and the corresponding MIPs (lower row) through the entire volume for three different time points corresponding to the vascular (5A, 5D), parenchymal (5B, 5E) and excretory (5C, 5F) phases. In the individual slices in the vascular phase the renal cortex is well seen due to its high vascularity while the MIP of this phase provides a good overview of the vasculature and allows features such as crossing vessels to be detected. In the parenchymal phase the cortex and medulla are iso-intense, while in the excretory phase high signal intensity is seen in the collecting system, ureters and bladder. The dark area in the bladder is the balloon for the bladder catheter.
Post-contrast STIR image from a patient with a small, poorly functioning, left kidney and bilateral scarring.

Post-contrast STIR (7A) and delayed, high resolution, T1-weighted (7B) images from the patient with horseshoe kidney shown in figure 2. While the right kidney has contrast in the collecting system and ureter and has drained contrast into the bladder the left kidney shows minimal contrast in the collecting system indicating very delayed filtration/concentration of the GBCA.

which determines the pixels that contribute to the average time course for the kidney. We currently use either in-house software or a beta version of a processing tool that has been developed by Siemens to perform the segmentation. In both cases the user performs an initial segmentation which is then reviewed and refined as necessary until an acceptable segmentation is obtained.

**Arterial input function (AIF)**

In order to model renal function an estimate of the time course of the vascular concentration of the GBCA is required and this is generally referred to as the arterial input function (AIF). The AIF is required since the vascular concentration affects the rate of filtration of the GBCA by the kidneys and even with a standardized dose and injection protocol there will be idiosyncratic variations in the AIF caused by physiological differences. For pediatric renal studies the arterial signal is usually measured in a region-of-interest (ROI) in the descending aorta, the renal arteries being typically too small for reliable measurements in children. The aorta is viewed in both coronal and sagittal planes in order to minimize partial volume effects by excluding, if possible, regions where the aorta cuts through the imaging plane. The ROI consists of an arbitrary number of points – the points typically being positioned at or below the level of the renal arteries in order to minimize in-flow effects. Even with careful selection of the location of the ROI pulsatility effects can still be present and it is not always possible to eliminate partial volume and inflow effects. In order to reduce the noise in the AIF we routinely fit the measured AIF signal to a model, however, even after fitting the imprecision in the AIF still limits the accuracy of GFR quantification with MR urography. For methods based on the differential function then the imperfections in the AIF are common to both kidneys and hence cancel out.

**Concentration versus time curves**

Deriving the mean signal from the segmented volumes and converting the signal values to concentrations allows concentration versus time-curves to be derived. Although the contrast dynamics can be assessed visually, the curves can provide extra information that is not always apparent from a visual inspection. Figures 8A and 8B show whole kidney curves for the patients shown in figures 5 and 7 respectively. The curves enable an assessment of perfusion, concentration and excretion for each kidney and are analogous to the time activity curves of renal scintigraphy. These curves reflect only the changes occurring in the renal parenchyma, rather than in the parenchyma and collecting systems as is the case with renal scintigraphy. The initial sharp increase in signal predominantly reflects the perfusion phase, with the renal cortex enhancing more than the medulla due to its higher blood volume. The subsequent slower increase in signal intensity reflects the accumulation of contrast agent in the renal parenchyma as it passes through the nephrons. Peak parenchymal enhancement typically occurs at approximately 150 seconds after the initial perfusion phase. After this peak there is a general decline in signal intensity due to the excretion of contrast into the urine and the on-going decline in the plasma concentration of the GBCA. The late parenchymal curves tend to parallel the aortic signal curve. As the post-processing becomes easier, segmental analysis will become more practical and provide greater insights into the anatomic and pathophysiologic
The curves are shown in terms of relative signal, which is defined as \( \frac{S(t)-S_0}{S_0} \), where \( S_0 \) is the pre-contrast signal and is linearly related to the contrast agent concentration providing the contrast agent concentration is not too elevated. Figure 8A shows the curves from the normal subject shown in figure 5 with relatively symmetrical curves from both kidneys and a peak relative signal approx. 3 minutes post-contrast. Figure 8B are the curves from the subject with the obstructed horseshoe kidney shown in figures 2 and 7. The curve for the right kidney shows a similar pattern to that seen in figure 8A but the curve for the left kidney shows no peak, even though the dynamic imaging covers over 15 minutes after the injection of contrast. Figure 8C shows the fits to the Annet model for the curves shown in figure 8A. The top row shows the overall fit for the model while the lower row shows the vascular and filtered components of the model.
changes occurring in the different compartments with various renal diseases. Similarly, fitting the models on a pixel by pixel basis to produce statistical parametric maps of the model parameters is currently too time consuming for routine clinical use but as increased computational power becomes available these will also become clinically feasible. The dynamic series can also be used to visualize the uptake of contrast in renal masses and hence help characterize the mass.

Modeling renal function

Several models of renal function have been developed. The Rutland-Patlak model, which is widely used in SPECT and CT, has also been applied to DCE-MRI data. This model measures the GFR as the transfer of a GBCA from arterial blood to the renal tubules and the fact that the kidney includes both vascular and tubular components is taken into account. The amount of GBCA in any one kidney at a time point prior to the excretion of the GBCA can be expressed as the sum of the GBCA in the vascular space and nephrons respectively. Assuming that the plasma concentration of the GBCA in the vascular space is proportional to the plasma concentration in the aorta one can then define constants to represent the vascular volume within the kidney and the clearance of the GBCA from the vascular space and write an equation for the GFR in terms of the measured arterial and renal curves. This equation can be rewritten in the form of a linear equation and values for the vascular volume and the clearance of the GBCA can be derived from the plot of this equation. Typically one measures the average concentration of the GBCA within the kidney, thus the equation calculates the clearance per unit volume of tissue, which we refer to as the unit GFR. We believe this quantity is related to the single nephron GFR and have noted that this quantity is reduced in decompensated, as well as dysplastic and uropathic kidneys. An estimate of the single kidney GFR (SK-GFR) can be obtained by multiplying the unit GFR by the renal volume. The Patlak model breaks down after a certain time because it fails to take account of the onward transport of the GBCA (i.e. the drop in signal seen at later time points in the parenchymal curves). Several more advanced models have been developed, the most widely used of these being the model developed by Annet et al. which includes an additional term which accounts for the onward transport of the GBCA and hence allows the whole time course to be modeled. Figure 8C shows the results of fitting the data from the subject shown in figures 5 and 8A to the Annet model. In the case of renal masses other models, such as the Tofts model, can be applied to the dynamic data to extract other parameters such as the tissue permeability or the size of the various tissue compartments.

The results from the renal modeling can then be reported as absolute values or in terms of the differential renal function. The differential renal function (DRF) is widely used in nuclear medicine and simply expresses the results of functional measurements for each kidney as a percentage of the total function (i.e. sum of both kidneys). Despite the obvious shortcomings, which include the assumption of a normal contra-lateral kidney as a reference and hence neglecting the effect of compensatory changes in the contra-lateral kidney, the DRF is very useful clinically since it removes the effect of the main source of error in the functional calculation, the AIF.

References


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*MR scanning has not been established as safe for imaging fetuses and infants under two years of age. The responsible physician must evaluate the benefit of the MRI examination in comparison to other imaging procedures.

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