ORIGINAL PAPER

FUNCTIONAL MR UROGRAPHY - PRINCIPLES AND APPLICATIONS IN CONGENITAL OBSTRUCTIVE UROPATHIES

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ABSTRACT

Congenital obstructive Uropathies are a leading cause of Chronic Kidney Disease in children. The gold-standard for renal functional imaging is Diuretic Renal Scintigraphy. Different alternatives to Renal Scintigraphy have been suggested, many of them based on Magnetic Resonance Imaging (MRI). The accurate morphologic details of MRI with its more specific application - MR-Urography are well known. The prospect of adding functional information is very attractive, as it will make the MRU a comprehensive "all in one" examination for obstructive uropathies. We chose to investigate DCE MR urography and DTI as tools for the evaluation of congenital obstructive uropathies. Also, we suggest a different technique that describes the urinary flow in the collecting system – phase contrast imaging of the urinary flow in the renal pelvis. Therefore we performed three different studies, all with different sets of patients.

KEYWORDS: *mr urography, congenital obstructive uropathies*

INTRODUCTION

Congenital obstructive Uropathies are a leading cause of Chronic Kidney Disease in children [1]. The hallmark of these diseases is the dilation of the urinary tract – the hydronephrosis. Given recent advances in imaging and an increase of prenatal ultrasound screening, the number of fetuses and children with urinary tract dilation increased tremendously. Some epidemiologic studies report a prevalence of congenital hydronephrosis up to 11.5 cases in 10,000 living newborns [2], while antenatal studies identified antenatal hydronephrosis in up to 1% of pregnancies [3]. However, in most cases, the dilatation regresses, or persists but without significant functional renal damage, a meta-analysis study reporting only 36% of cases requiring corrective treatment [3].

Current diagnostic protocols and guidelines are based firstly, on ultrasound [4], as shown in Figure 1. For low degrees of dilation, the risk of renal damage is low, therefore only follow-up is recommended. However, for patients with high grade hydronephrosis, some sort of functional imaging is required to detect those patients with altered renal function that need corrective treatment. The gold-standard for renal functional imaging is Diuretic Renal Scintigraphy. This technique uses a radioactive tracer (99mTc-MAG3 or 99mTc-DTPA) and by measuring its uptake and excretion it can calculate the Split Renal Function for each kidney, a parameter used to guide treatment [5]. However this technique is not readily available,

it involves radiation exposure and for small children, necessitates sedation.
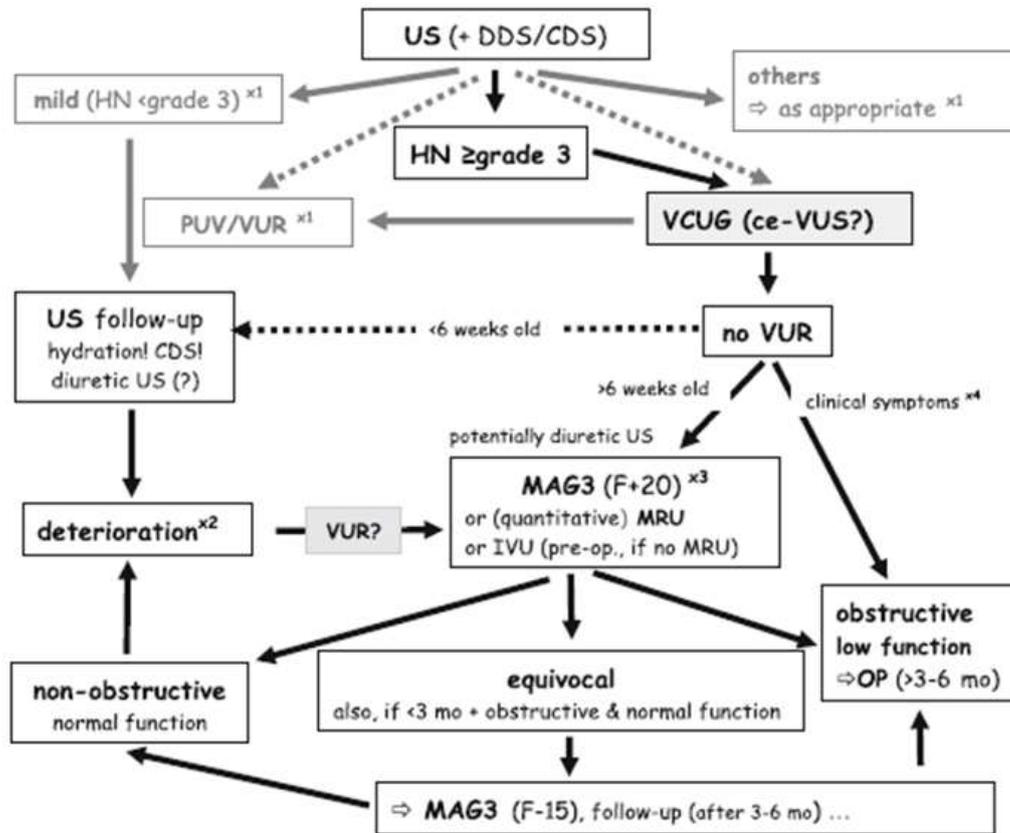
Figure 1 – Imaging protocol for Urinary tract dilation in children. From Riccabona M, Avni FE, Blickman JG, Dacher J-N, Darge K, Lobo ML, et al. Imaging recommendations in pediatric uroradiology. Pediatr Radiol [Internet] 2009;39(8):891–8.

Different alternatives to Renal Scintigraphy have been suggested, many of them based on Magnetic Resonance Imaging (MRI). The accurate morphologic details of MRI with its more specific application - MR-Urography are well known. The prospect of adding functional information is very attractive, as it will make the MRU a comprehensive "all in one" examination for obstructive uropathies.

Different techniques of functional MRU (fMRU) have been developed, which investigate different aspects of the renal function: Dynamic Contrast Enhanced MR Urography [6–12], Diffusion Tensor Imaging [13–19], Arterial Spin Labeling non-contrast perfusion imaging [20,21] or BOLD imaging [22,23]. We chose to investigate DCE MR urography and DTI as tools for the evaluation of congenital obstructive uropathies. Also, we suggest a different technique that describes the urinary flow in the collecting system – phase contrast imaging of the urinary flow in the renal pelvis. Therefore we performed three different studies, all with different sets of patients.

MATERIALS AND METHODS

DCE MR Urography

This technique involves imaging the kidneys dynamically during contrast medium administration for about 10-15 minutes. The signal characteristics over time are used to create a plot – the signal intensity-time curve. By analyzing the shape and amplitude of the curve, information about the renal function is extracted, most importantly, the split renal function (SRF).

Patient preparation is important. Good hydration is mandatory. Furthermore, diuretic load by Furosemide IV administration is helpful reducing artifacts and to make the method more sensitive.

We imaged one patient with obstructed pyelo-ureteral junction on a 1.5Tesla machine (Magnetom Aera, Siemens©, Erlangen, Germany). A 3D T1 MR Angiography sequence was used to acquire the images. The sequence should be very fast, with temporal resolution of less than 10 seconds. Specifically, we used a TWIST sequence (Time-resolved angiography With Interleaved Stochastic Trajectories) which allows scanning times as fast as 2.5 seconds. The field of view is set in coronal plane and must include the kidneys, bladder and aorta. The scanning is started after injection of the contrast medium and is repeated continuously for 10-15 minutes (Figure 2).

Figure 2 – Snapshot of excretion phase in the dynamic scan of the kidneys by DCE Note the severely dilated, hypo functioning left kidney (Personal collection).
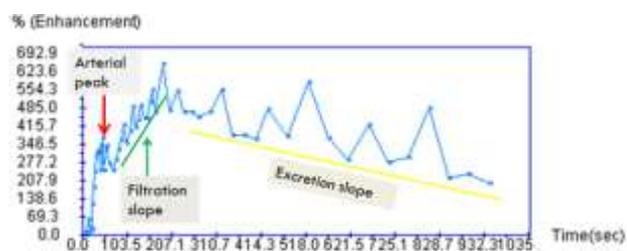
Figure 3 – Signal intensity – time curve with its components.

The images are post-processed with dedicated software – the fMRU plugin [12] for ImageJ [24]. By setting a region of interest (ROI) in the renal parenchyma, the signal is measured over time, creating the signal intensity-time curve (Figure 3). The results were then compared with the information from the diuretic renal scintigraphy.

Diffusion Tensor Imaging

This technique gives a measure of the anisotropy of diffusion of water molecules. That is the property of the water molecules in a specific structure to diffuse preferentially along predetermined pathways. The architecture of the kidney is particular: in the cortex the glomeruli and tubules are chaotically arranged, therefore water molecules are moving in every direction; in the medulla the tubules are organized in a radial distribution, so the water molecules are moving only in certain directions – it is anisotropic. The anisotropy degree can be quantified and is expressed as the fractional anisotropy (FA) coefficient [25]. The diffusion directions can be visualized by tractography which renders the diffusion vectors (Figure 4). The sequence we used is a modified DTI sequenced used to study the brain. For the kidney we applied the diffusion gradient in six directions [13,26] and used the maximum b value of 400 [27].

Figure 4 – Tractography in normal kidney. Diffusion directions are color coded: red – left to right; green – head to feet; blue – anterior to posterior (Personal collection).

The scanning is performed in free breathing and takes 60 seconds, but for optimum quality it may be performed with respiratory triggering. The trace, ADC and FA maps are automated generated (Figure 5). We

imaged 10 patients with no history of renal disease, with the objective of detecting differences in the FA coefficient of medulla and cortex. We then examined 5 patients with obstructed urinary tract to explore if the cortical/medullary FA difference is noted.
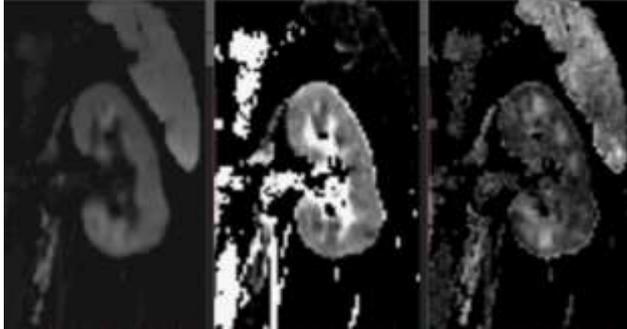
Figure 5 – Trace (left), ADC (middle) and FA map (right) images from DTI. Note the cortico-medullary differentiation in the FA map image (Personal collection).

Urodynamic assessment by phase contrast imaging (PC)

This method is based on the MRI's high sensitivity to motion. This technique encodes the velocity of moving protons by phase shifts. By measuring those phase shifts, the velocity of those protons can be found. The technique has been developed mainly for cardiovascular studies. We adapted such technique, by altering its parameters making it sensitive to the slow flow of the urine in the collecting system. First, we tested the sequence on 10 normal subjects with no renal disease, and then compared them to one obstructive patient. We performed the measurement of a single slice planned strictly perpendicular to the renal pelvis, collecting data about the flow that goes through the plane. Each measurement takes 2 seconds, so we performed several continuous measurements for 60 seconds. After the acquisition of images, regions of interest were drawn around the contour of the renal pelvis and in a control stationary area and flow parameters were measured – peak velocity, average velocity and flow.

RESULTS

DCE MR Urography

The most important part of the curve is the filtration slope. This represents the actual uptake of the Gadolinium by the renal parenchyma. Based on the assumption of bicompartimental distribution of the contrast medium and using linear regression, Rutland-Patlak plots are created considering aortic signal as reference (Figure 6). The slope values of the Rutland-Patlak plots for each kidney are compared and thus, the Split Renal Function is determined. To gain more accuracy, these values are combined with the volumetric assessment of each kidney (Figure 7).
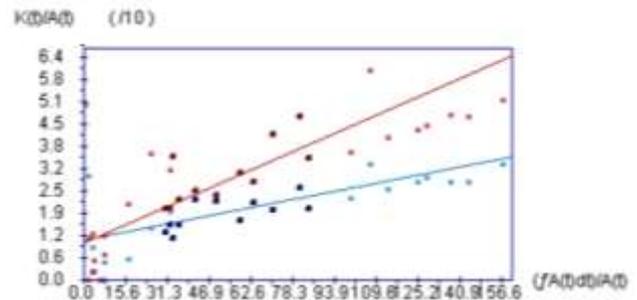
Figure 6 – Rutland-Patlak plots – red: normal kidney; blue: hypofunctional kidney.

Figure 7 – Calculation output describing the split renal function.

The results observed were similar to the information revealed by renal scintigraphy (Figure 8).

Furthermore, by analyzing the late part of the curve, the excretion curve, a pattern of obstruction is observed in the obstructed kidney (Figure 9).
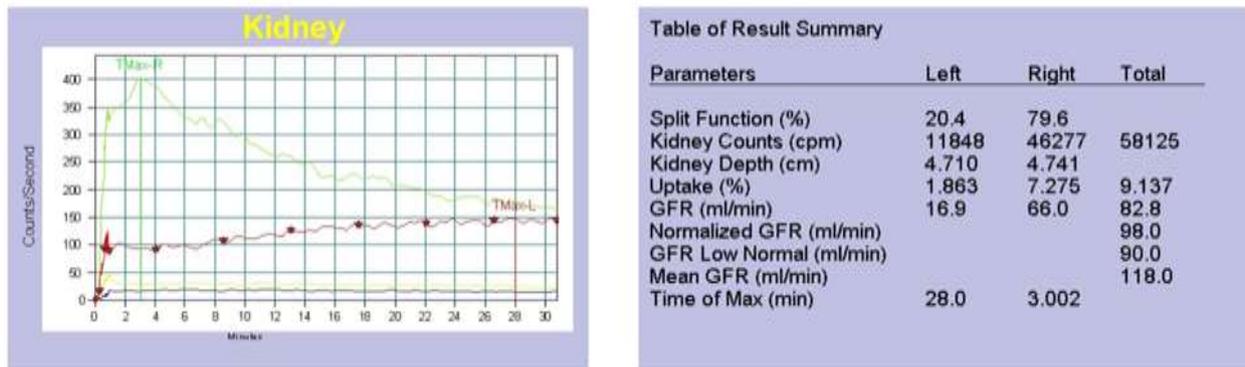
Figure 8 – Renal scintigraphy results. Notice similar split renal function.
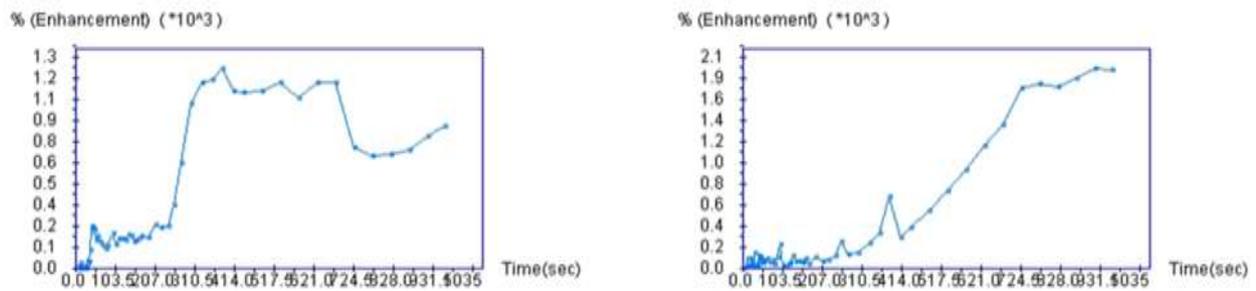
Figure 9 – Excretion curves: left – normal; right – obstruction.

Diffusion Tensor Imaging

In normal kidneys, FA map images reveal a very good cortico-medullary differentiation – the cortex has homogenous low signal, whereas the pyramids are hyperintense (Figure 10).

When measured, the FA values in cortex were significantly lower than in the medulla – 0.19 vs. 0.5 [28].

Tractography reveals tightly packed diffusion tracts in the pyramids, oriented radially towards the papilla (Figure 11).
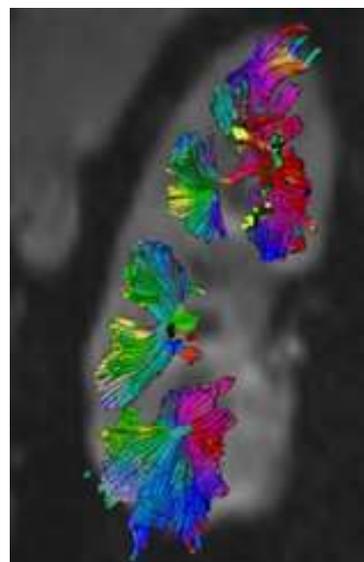
Figure 11 – Tractography image in normal kidney.

In obstructed kidneys with altered renal function, the FA values in medulla decrease considerably, as low as the cortical values (median of 0.15 in cortex and 0.17 in medulla). Tractography reveals changes as well; the medullary tracts in the pyramids are fewer and

Figure 10 – FA map with measuring the FA coefficient in an upper pyramid.

disorganized compared to the normal kidney (Figure 12).
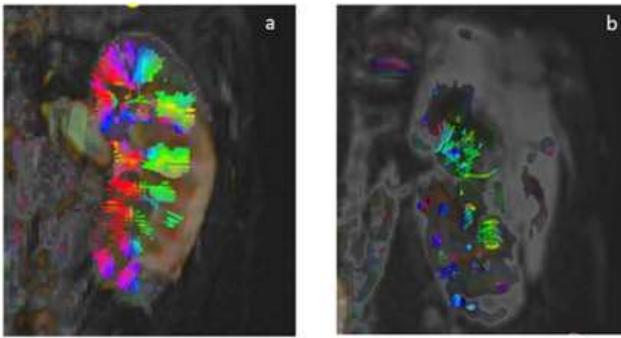
Figure 12 – Tractography images of both kidneys of a patient with Obstruction of the uretero-pelvic junction: a – normal kidney; b – obstructed kidney.

Urodynamic assessment by phase contrast imaging (PC)

In normal kidneys, the urinary flow in the renal pelvis has two components – a baseline low velocity flow over which several peaks of higher velocity are superimposed that correspond to peristaltic waves (Figure 13).

The baseline flow was measured 0.047 ml/sec, whereas the peristaltic waves were an average of 3 per minute, with velocities up to 1,7 cm/s.
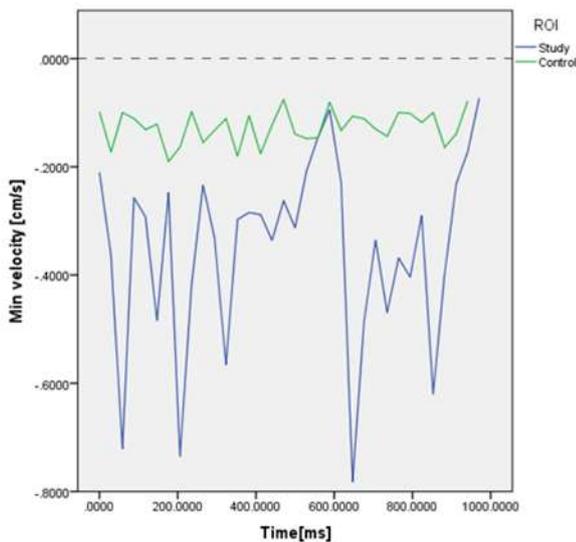
Figure 13 – Peak velocity graph in a normal renal pelvis (blue) compared to control stationary tissue (green).

Next, we assessed the obstructed kidney, and, although we couldn't measure the trans-stenotic velocity and pressure gradient because of poor resolution, we found fewer peaks of lower amplitude, suggesting poor contractility of long-standing obstructed renal pelvises (Figure 14).
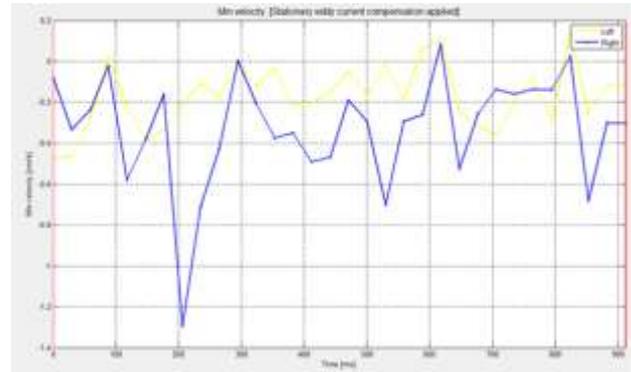
Figure 14 – Peak velocity graph showing a normal pattern of flow in the healthy kidney (blue) and an abnormal flow of the obstructed kidney – few and low amplitude peaks.

DISCUSSIONS

MRI is famous for delivering exquisite anatomical information about the reno-urinary system. Recent research is oriented towards developing MRI methods of functional imaging of the kidney. Several biomarkers have been studied, each exploring a different aspect of the renal function. Describing the uptake and excretion of Gadolinium based contrast media, DCE-MRI gives information about the glomerular filtration [29,30]. The results are compared for both kidneys, and thus the Split Renal Function is determined. For a more thorough evaluation, volumetric data about the parenchyma is added. This method has been proven accurate compared to conventional renal scintigraphy [31] and several applications were studied. In patients with renal artery stenosis with reno-vascular hypertension, by measuring the GFR by DCE before and after administration of Angiotensin converting enzyme inhibitor, a decrease in GFR was noticed compared to controls without stenosis [6]. In renal transplant, DCE-MRI can distinguish between acute tubular necrosis (ATN) and acute reject by perfusion parameters [32].

In obstructive uropathies, the main role for DCE-MRI is to describe to functional impact of the obstruction. The Split renal Function is calculated, which, in turn is used to guide the treatment. Furthermore, the contrast medium

clearance from the excretory system can be analyzed to detect obstruction, a feature useful in operated patients with postoperative dilatation.

There are some limitations, however. This technique is based on several assumptions. Firstly, unlike scintigraphy it doesn't measure directly the concentration of the contrast medium, it measures the signal resulted from the magnetic interaction between the contrast medium and the local environment. Thus, the Gadolinium concentration is an estimate based on the magnetic properties of renal tissue. And studies have shown that in vivo values may be different than in vitro ones [33]. Secondly, in another assumption, the contrast medium is distributed only in the vascular and tubular compartments (bicompartimental pharmacokinetic model), ignoring the possible diffusion outside the tubules [34].

Diffusion Tensor Imaging has the advantage of being an exam without contrast media, thus eliminating concerns about chronic kidney disease patients, or about Gadolinium tissue deposition, especially in children [35]. This technique evaluates damage in the renal tubules. Feasible in a variety of pathologies like chronic kidney disease [36], acute renal injury [37], diabetes [38], polycystic renal disease [18] or renal masses [39], it has been proven useful for congenital urinary obstruction also [40][41]. Jaimes et al [41], for example, detected a significant difference in the FA coefficient in the medulla of obstructed kidneys and medulla of normal kidneys. Thus, kidney DTI provides a quantifiable parameter about the microstructural damage in the renal pyramids. One current limitation is the lack of standardization of the measuring technique between different vendors and different machines.

Urodynamic assessment by phase contrast imaging is a novel technique that we introduced, and although it lacks enough large scales studies, it has potential of delivering of another parameter of a different aspect of renal function. Currently, the gold standard for upper urinary tract urodynamics is the invasive Whitaker test [42]. A tool that would describe the urinary flow non-invasively would be invaluable, especially for dilated systems with non-certain obstruction as is the case for operated patients. The technique we suggest

might be able to fill this gap. However more research is needed.

CONCLUSIONS

In conclusion, renal functional imaging by MRI is an attractive topic as there are several techniques proven to be feasible and other worthy of research. fMRU is also attractive because it studies different aspects of renal function thus helping to better understand different disease processes, non-invasively, without the need for repeating biopsies. However, all these methods have not been standardized for out of the box clinical practice and need to be optimized for each hardware and software setting. Joint effort of medical doctors, medical physicists, engineers and hardware and software vendors is needed to make these techniques reproducible on most machines.

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