

ISMRM SYLLABUS: MRI of Kidney Function and Disease

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Overview of this presentation and the learning objectives

1. Define renal “function”
 - a. Major functions of the kidney include salt and acid-base balance in the blood and tissues of the body, resulting in control of body water and blood pressure. However, a useful determinant of normal versus diseased kidney that has been of value for clinical applications is the measure of glomerular filtration rate (the amount of blood or plasma that is filtered by the filtration unit of the kidney per unit time). Renal blood flow may be another useful physiological measurement, although this has not been generally available as a measured entity.
 - b. The functional structure of the kidney will be reviewed
2. Review methods of GFR measurement used for research and clinical applications
 - a. The methods used mostly are biochemical and include more complicated methods using an agent that is injected or infused into the blood and then repeated blood and urine samples taken in order to determine the rate at which the kidneys clear the agent. The “gold-standard” measure of GFR is based on this approach using Inulin; a non-reactive chemical that, when injected into the blood, is cleared only by kidney filtration. This test is cumbersome and takes upwards of 4 hours with two intravenous lines running, while the patient has to provide timed urine samples. Inulin is now rarely available and considerably more expensive, even compared to an MRI scan.
 - b. Other simpler tests are widely used, but generally considered to be inaccurate and to have poor reproducibility (when monitoring patients’ renal function, it is reproducibility that is the most important attribute of a test method). Such tests include the 24 hour creatinine clearance and the serum creatinine MDRD calculated GFR methods.
3. Review imaging based methods
 - a. Generally, imaging methods have the potential advantage over biochemical methods in that the structural information can provide additional insights into pathology, and may be more sensitive to disease affecting only one kidney, or one part of a kidney, that would be missed using biochemical methods.
 - b. Nuclear Medicine: the limitation of nuclear techniques has been inadequate spatial resolution and soft tissue information. A radioactive tracer produces the anatomic and the distribution-function information, hence limiting the amount of soft tissue information that can be derived from this approach alone.
 - c. CT: the use of 4D (soft tissue spatial data [3D] + time data [4th D]) is a potential strength. Limitations are related to radiation dose being unacceptably high, and iodinated contrast used in CT is intrinsically nephrotoxic to malfunctioning kidneys.

- d. MRI: provide superior soft tissue contrast, good time resolution, and best safety profile compared to radiation + iodinated contrast. (Our current understanding of the relative safety of gadolinium in renal failure patients will be briefly summarized)
4. Describe the components that comprise a contrast enhanced MRI approach to kidney function measurement
- a. There are 3 major elements, regardless of the details on how these are achieved, that must be accounted for in MR nephrourography (MRU):
 - i. Image acquisition
 - ii. Image post-processing and data extraction (currently performed off-line)
 - iii. Kinetic modeling and data fitting
 - b. In any method there must also be
 - i. Validation A.- statistical measures of the quality of the data fit for each analysis
 - ii. Validation B.- comparison against a standard of reference and a measure of reproducibility

Numerous kinetic models have been proposed that account for 2-compartment, 3-compartment, and higher number of compartments (1-8). The basic compartments in which the injected gadolinium contrast distributes, and which must be accounted for include the blood space, and the filtered space within the renal tubules. Contrast entering the filtered space cannot return into the blood. Gadolinium contrast agents may also cross from the blood into the interstitial spaces; the volume of the kidney comprised of the spaces between the cells within the tissue. The molecules of contrast agent that moves from the blood into the interstitial space may also migrate back into the blood, and it is presumed that this occurs down concentration gradients, without any active transport mechanism. Initially the blood concentration is higher than in the interstitial space and the contrast agent will migrate out of the blood. As the kidney clears the contrast, the blood levels will fall and the concentration will fall below the level of the interstitial spaces, resulting in a reversal and net movement of contrast back into the blood.

Glomeruli filter the blood of water and electrolytes, the rate of which is referred to as the glomerular filtration rate (GFR). While blood flow to both kidneys is normally around 500ml/min, the GFR is around 120 ml/min, each kidney contributing around 50% of this total function. The filtered fluid will eventually become urine, but before that undergoes considerable alteration by the kidney. From the glomerulus the filtered fluid and electrolytes pass down the proximal collecting tubules where 90% of the sodium and water is reabsorbed. The filtered gadolinium chelate will stay in the collecting tubules without any reabsorption. By the time the filtered urine travels to the end of the distal collecting tubules approximately 99% of the filtered water is absorbed, and urine is spilled from the kidney into the ureter and bladder at a rate of around 1 ml/min.

Each of the major pathways that the contrast may traverse should be modeled mathematically in order to calculate the variables and solve for GFR. Two-compartment models ignore the interstitial

spaces. More complex models that consider the events related to the different parts of the kidney become rapidly more demanding of the image acquisition and analysis side and may introduce more variables that depend on solution in order to solve for GFR.

Implementation of highly accelerated post-contrast 3D GRE has also been shown useful for the quantitative evaluation of renal function(5-8). Advances in imaging technology have reduced imaging times such that a coronal volume of images through the kidney can now be acquired in approximately 1 second, while maintaining isotropic resolution of 3mm. Such rapid acquisition allows contrast perfusion-filtration imaging of the kidney that can be performed in a freely breathing patient. Repeated 3D GRE images are acquired through the kidney every second during the administration of intravenous gadolinium-chelate (Gd). Perfusion data from the graft is then post-processed on an independent workstation to segment out the kidney. A methodology has been developed to simplify the analysis using mathematical modeling that accounts for the compartmentalization of the Gd within the kidney. This simplified approach facilitates image processing by requiring only that the entire amount of Gd signal within the kidney be measured at every time point. The iliac artery at the level of the transplant renal artery is also segmented and serves as an input function. A fundamental assumption is that the signal measured from each image voxel within the kidney, or artery, is proportional to the molar amount of Gd. Since the relationship between Gd and the signal generated becomes non-linear on T1W images at higher Gd concentrations, this method benefits from use of the lowest possible concentration of Gd administration. The precontrast images taken prior to arrival of the intravenously administered Gd are used to calculate the background signal of the tissue or blood, and the ratio of the difference is used to calculate the Gd signal.

Glomerular filtration rate has been computed from this post-processed data using the Rutland-Patlak plot, which assumes a two-compartment model of the vascular and nephron spaces . There are significant theoretical limitations of the 2-compartment model, which considers only the intravascular compartment and the filtered contrast within the renal tubules, but does not account for interstitial distribution. More thorough evaluation using mathematical multi-compartment modeling with three) or more compartments have been described and considered potentially more accurate. However, detailed comparisons between these techniques have not yet been fully evaluated.

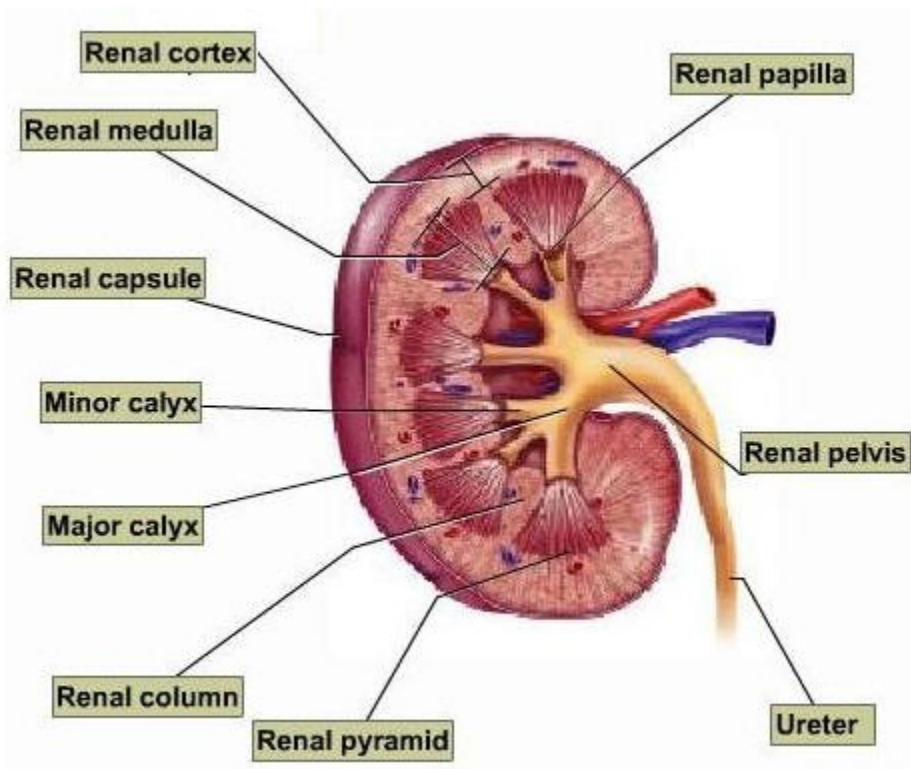
RBF also has been extracted from the perfusion data. We have shown that the 3D GRE images acquired during the first several seconds after arrival of contrast within the kidney can be used to derive the RBF, and that the results are not significantly different from conventional phase contrast flow measurements. There are advantages of the Gd perfusion technique over phase contrast MRI, or ultrasound color Doppler techniques. Limitation of phase contrast and Doppler include the requirement that the measurements are obtained perpendicular to the blood flow. Irregular curvilinear anatomy of transplanted renal arteries can make this technically challenging. The Gd perfusion technique is insensitive to unusual vascular anatomy. In addition, the MRNU acquisition is obtained as part of a comprehensive functional evaluation that also measures GFR and renal functional volume. The ability to measure the anatomic volume of the transplant kidney and the perfused volume represent additional physiological determinants of renal function. The RBF, and the GFR, may then be calculated as a ratio to

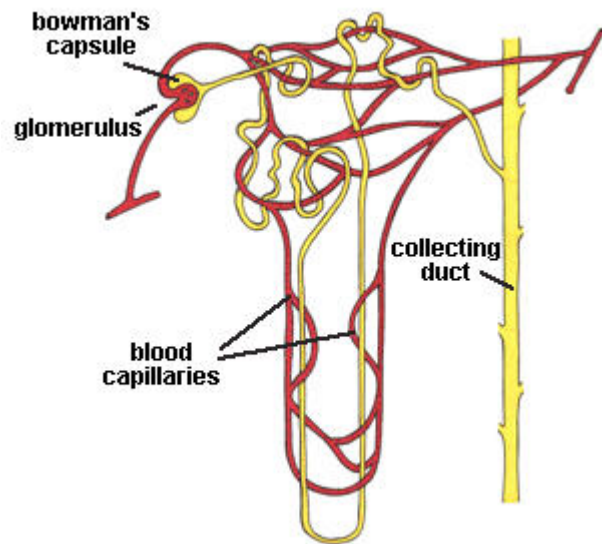
the perfused renal volume. Knowing the hematocrit allows calculation of the renal plasma flow, and this parameter may be also expressed as a quotient dividing by the perfused renal volume.

5. Continued or “Unmet” Engineering Needs

- a. Improvements in image acquisition are feasible by implementing changes in the following
 - i. Surface receiver coil design
 - ii. 3D gradient echo changes in pulse programming and k-space filling
 - iii. Parallel processing algorithms
 - iv. Improved and faster reconstruction in-line
- b. Image extraction tools with greater automation with improved reproducibility between studies and between centers
 - i. Motion correction
 - ii. Automated segmentation
- c. Automated data fitting with statistical modeling of individual results
 - i. Validation of model
 - ii. Most simple model that produces best practical solution to GFR and blood flow measures
 1. Method should have no additional requirements for image processing beyond bulk renal signal from total renal volume

Figures:





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