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Pitfalls and Limitations of Radionuclide Renal Imaging in Adults

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To understand pitfalls and limitations in adult renography, it is necessary to understand firstly the physiology of the kidney, especially the magnitude and control of renal blood flow, glomerular filtration rate and tubular fluid flow rate, and secondly the pharmacokinetics and renal handling of the three most often used tracers, Tc-99m-mercaptoacetyltriglycine (MAG3), Tc-99m-diethylene triamine pentaacetic acid (DTPA) and Tc-99m-dimercaptosuccinic acid (DMSA). The kidneys may be imaged dynamically with Tc-99m-MAG3 or Tc-99m-DTPA, with or without diuretic challenge, or by static imaging with Tc-99m-DMSA. Protocols are different according to whether the kidney is native or transplanted. Quantitative analysis of dynamic data includes measurement of renal vascularity (important for the transplanted kidney), absolute tracer clearance rates, differential renal function (DRF) and response to diuretic challenge. Static image reveals functional renal parenchymal damage, both focal and global, is useful in the clinical management of obstructive uropathy, renal stone disease and hypertension (under angiotensin converting enzyme inhibition), and is the preferred technique for determining DRF. Diagnosis based on morphological appearances is important in transplant management. Even though nuclear medicine is now in the era of hybrid imaging, renal imaging remains an important subspecialty in nuclear medicine and requires a sound basing in applied physiology, the classical supporting discipline of nuclear medicine.
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Applied Physiology of the Kidney

To understand the pitfalls and limitations of renal imaging with radionuclides, it is essential to understand the relevant physiology of the kidney.

For a standard-sized adult, renal blood flow is approximately 500 mL/min per kidney, which is approximately 20% of cardiac output. Renal perfusion is 300-350 mL/min/100 g. The blood volume of a single kidney is approximately 50 ml. Renal plasma flow (RPF) is 250-300 mL/min per kidney. Glomerular filtration rate (GFR) is 50-60 mL/min per kidney, so filtration fraction (GFR/RPF) is 0.2. Ageing results in loss of renal function at a rate of approximately 1 mL/min per year from age 40 years onward. This is faster in women than in men.[1]

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Most of the incoming renal blood flow enters the glomeruli, which are located in the cortex of the kidney. Blood that does not perfuse glomeruli directly enters the peri-tubular capillary network where it is joined by blood leaving the glomeruli. Renal blood flow is high, with each kidney receiving more than twice that, say, of the spleen. A single kidney has about the same volume as the spleen so renal perfusion is at least twice that of the spleen.

Approximately 20% of RPF (the filtration fraction) is filtered into Bowman's capsule as the glomerular filtrate from where it starts its journey through the renal tubule. Glomerular capillaries offer relatively little resistance to blood flow; if they did, postglomerular blood pressure would be insufficient to perfuse the peri-tubular capillary network. Nevertheless, as water filtration progresses, glomerular hematocrit and plasma oncotic pressure increase towards the efferent end of the glomerular vessels. This raises viscosity and tends to raise pressure. As fluid reabsorption takes place from the renal tubules, blood viscosity in the renal vessels is gradually returned to baseline levels.

In a normally hydrated individual, only approximately 1% of the glomerular filtrate reaches the collecting system, the

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remaining 99% being reabsorbed by the tubule and returned to the blood. The minimum time it takes for a molecule, such as the classical indicator, inulin, that is filtered at the glomerulus and not reabsorbed by the tubule to travel from the glomerulus to the collecting system (the minimum parenchymal transit time) is approximately 2 minutes. Most of the water reabsorption takes place in the proximal tubule, more or less irrespective of the state of hydration, with only a relatively small flow made available to that part of the nephron that is regulated by antidiuretic hormone to vary urine output. This means that the minimum and mean parenchymal transit times are not significantly elevated in moderately dehydrated individuals. Nevertheless, a fivefold increase in urine flow rate (which would be associated with a reduction in total glomerular water absorption from approximately 99%-95%) would have a profound effect on the time a molecule of inulin would spend in the collecting system waiting for entry into the proximal ureter. In other words dehydration prolongs whole kidney transit time but has little effect on parenchymal transit time.

It is self evident that as the volume of fluid flowing down the tubule decreases in the face of water absorption, its speed of movement progressively declines. Indicators like the hippurates and mercaptoacetyltriglycine (MAG3), therefore, which are secreted into the proximal tubule, have kidney transit times that are not significantly shorter than freely filtered indicators like inulin, even though they start their journey through the tubule downstream from the glomerulus. Prolonged parenchymal transit time is therefore abnormal and is seen not only in outflow tract obstruction, when it is almost always unilateral, or at least asymmetrical in severity, but also bilaterally and symmetrically in parenchymal renal disease as a result of loss of tubular integrity, increased water transfer from tubular lumen to blood and consequent failure to deliver fluid to the distal end of the tubule. Prolonged whole kidney transit time, with normal parenchymal transit time, is seen in dehydration and when the collecting system is dilated but not obstructed.

Pharmacokinetics of Radiopharmaceuticals for Imaging the Kidneys

For dynamic imaging:

Tc-99m-diethylene triamine pentaacetic acid (DTPA) (*Pentatate;* 492 Da)
Tc-99m-MAG3 (*Mertiatide;* 350 Da)

For static imaging:

Tc-99m-dimercaptosuccinic acid (DMSA) (*Succimer;* 281 Da)

Tc-99m-DTPA, like inulin, circulates in blood with negligible binding to plasma proteins and does not penetrate red cells. It is freely filtered at the glomerulus. As a small hydrophilic molecule, Tc-99m-DTPA crosses capillary endothelium throughout the body by passive diffusion between the interendothelial junction gaps. It therefore distributes throughout the extracellular fluid volume (13 L).

Tc-99m-MAG3 circulates both as free tracer (~20%) and bound to plasma protein (~80%). Like the hippurates that it has superseded for renography, Tc-99m-MAG3 undergoes proximal tubular secretion. Its renal extraction fraction is approximately 50%, giving it a renal plasma clearance of approximately 300 mL/min—not as high as that of the hippurates, but much higher than Tc-99m-DTPA. Its protein binding tends to retain it in the vascular compartment which, in combination with its higher renal clearance, results in a much higher kidney-to-background ratio than is the case with Tc-99m-DTPA, making it the preferred agent for renography. Tc-99m-MAG3 clearance from glomerular filtration is 0.2 (the fraction of free tracer in blood) multiplied by GFR, that is, ~20 mL/min, small compared with clearance by secretion. In other words, of the 50% extracted by the kidney, 96% undergoes tubular secretion where as only 4% is filtered.

Of the renal tracers, Tc-99m-DMSA binds most highly to proteins at approximately 90%. Rich in sulphydryl groups, it is irreversibly bound to proximal tubular cellular proteins via disulfide bonding where, on static imaging, it portrays functioning renal cortical mass. Its renal plasma clearance is quite low; approximately 35 mL/min. Whole body plasma clearance is about twice this because only approximately 50% is cleared by the kidneys, the other 50% entering liver, spleen, and bone marrow. Imaging is therefore routinely performed no less than 2 hour after injection, preferably 3 hour. Tc-99m-DMSA is cleared by filtration at approximately 12 mL/min. This is significant compared with the overall renal clearance. If filtered Tc-99m-DMSA undergoes tubular reabsorption, then glomerular filtration plays a role in determining renal Tc-99m-DMSA accumulation.

Performing a Renal Imaging Study

Dynamic Renal Imaging

Native Kidneys

The patient should be well hydrated and have recently voided. The supine position, with the gamma camera under the imaging couch, is the most comfortable for the patient. Some departments image patients in a semi-recumbent or even sitting position to promote drainage from the renal collecting systems but this is an awkward position for the patient to maintain and is therefore prone to movement artefact. In any event, it should be routine practice to take the patient from the imaging couch at the end of the dynamic study and obtain further images following voiding. Modern dual-head gamma cameras allow simultaneous acquisition of anterior and posterior views that can be very useful in horseshoe and pelvic kidneys. In the case of the latter, the normal and malpositioned kidney can both be optimally assessed.