Introduction

• The gold standard for differentiation of obstructive and non-obstructive hydronephrosis and hydroureter is diuretic renography.

• This imaging is accomplished with either 99mTc-diethylenetriaminepentaacetic acid (DTPA) or, more commonly, 99mTc-MAG3.

• A strict protocol should be followed to ensure accurate and reproducible results.

• The clinician should review the actual drainage images, regions of interest used, and curves because any variation in technique can lead to misleading results.
Radiopharmaceutical

- Pharmaceutical
  - DTPA, DMSA, MAG3 (commonly used)
  - EDTA, Hippuran, medronate (less common)

- Radionuclide label
  - Technetium - 99
Role of radionuclide studies in Urology

- Renal perfusion and relative function
- Obstruction (diuretic renal scan)
- Infection (renal morphology scan)
- Pre-surgical quantitation
- Renal transplant
- Congenital anomalies, masses
## Renal Radiotracers

- **Excretion mechanism**

<table>
<thead>
<tr>
<th></th>
<th>Glomerular Filtration</th>
<th>Tubular Secretion</th>
<th>Tubular Filtration</th>
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<tbody>
<tr>
<td>DTPA</td>
<td>&gt;95%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAG3</td>
<td>&lt;5%</td>
<td>95%</td>
<td></td>
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<tr>
<td>DMSA</td>
<td>SOME</td>
<td></td>
<td>60%</td>
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Choosing Renal Radiotracers

<table>
<thead>
<tr>
<th>Clinical Question</th>
<th>Agent</th>
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<tr>
<td>Perfusion</td>
<td>MAG3, DTPA</td>
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<tr>
<td>Morphology</td>
<td>DMSA</td>
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<tr>
<td>Obstruction</td>
<td>MAG3, DTPA</td>
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<tr>
<td>Relative function</td>
<td>All</td>
</tr>
<tr>
<td>GFR</td>
<td>DTPA</td>
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Renogram - DTPA

- Commonly used
- Cheaper 6x (compared from MAG3)
- Cleared solely by glomerular filtration
- Kidney uptake low, blood background high
- Background subtraction more difficult, especially children or patient’s with poor renal function
Renogram – MAG3

- Clearance is predominantly by tubular secretion
- Small proportion undergoes glomerular filtration
- Greater kidney uptake, less blood background
- 30 minute excretion is 70% and 90% by 3 hours
- Preferred tool for the assessment of urinary uptake, transit, excretion and split renal function.
Indication

• Assessment of whole or relative kidney
• Assessment of kidney drainage in obstructive uropathy
• Assessment of congenital renal abnormalities
• Identification of vesicoureteric reflux
Principles of Performing

• There are three key elements to successful diuretic renography:
  • hydration
  • bladder drainage
  • timing of diuretic administration.
Hydration

• Ideally, an intravenous line is placed for hydration before the study in addition to encouragement of oral hydration before arrival for the study.
• Poor hydration or poor renal function can lead to false-positive results owing to a slow uptake curve and diuretic response.
• For this reason, it is best to wait until the child is at least 1 month old.
Data Acquisition

• Seated comfortably (have to remain so for 40 minutes) with back to gamma camera
• Very small infants can be lain on the camera
• Dynamic series images of 1 frame/20 seconds for 30-40 minutes and at least 15 minutes after giving diuretics in the case of diuretic renograms.
Bladder drainage

• A catheter is helpful in eliminating any concerns of bladder filling affecting upper tract drainage; difficult interpretation secondary to VUR, hydroureter, or voiding dysfunction and increased gonadal radiation exposure secondary to radioactive urine.

• Omit if child able to void on instruction.
Advantages of nuclear renogram

• Provides sensitive indices of tubular function and urinary excretion
• Virtually no contraindications
• Non-nephrotoxic
• No significant allergic reactions
• Serial examination possible and often required
• Minimal side effects (unless frusemide used)
Disadvantages

- Exposes patient to radiation
- Lengthy study (up to 1 hour)
- Prone to artefactual errors
- Limited anatomical information
- Equivocal results require repeat procedures
- Inaccurate outlining of ROIs can affect curve dynamics
Diuresis Renogram

• First described in the 1960’s, then popularized by O’Reilly as a simple method to differentiate patients with equivocal obstruction of the upper urinary tract which pre-empted the Whitaker test.

• Principles; if a system is genuinely obstructed, flow is impaired at high and low urinary flow rates.

• In contrast, slow elimination caused by urinary stasis alone responds to an increase in the flow rate with a rapid washout of tracer, produced by giving frusemide.
<table>
<thead>
<tr>
<th>True</th>
<th>Misleading</th>
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<tbody>
<tr>
<td>Pelviureteric junction obstruction</td>
<td>Dehydration, low flow</td>
</tr>
<tr>
<td></td>
<td>Large collecting-system volume</td>
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<td>Back pressure from bladder</td>
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**Causes of an 'obstructive' standard renogram curve**
Figure 10.18 Principle of diuresis renography. (Top) Increased urine production leads to an accumulation of tracer. (Bottom) Increased urine production leads to a corresponding increased washout.
Diuresis Renogram

- Maximal diuretic response within 5-10 minutes
- Rationale: increase the sensitivity of the dynamic renal study by increasing urine flow rates to stress the system such that minor degrees of obstruction are unmarked
- Make sure no contraindications
- Various protocols; F+20, F-15, F+0
Timing of diuretic administration

• Intravenous furosemide (1 mg/kg) is ideally given when the dilated collecting system is determined to be maximally filled;
• however, timing of diuretic administration is largely institution specific.
• Other common protocols give the diuretic 20 minutes after injection of the tracer (F+20), right after the tracer (F+0), or 15 minutes before the tracer (F−15).
The maximal effect of furosemide occurs 18 minutes after injection. As such, an F+20 renogram demonstrates obstruction late in the investigation and may give equivocal results in 15% of cases. This enables the urodynamics through the upper tracts to be studied without modification or manipulation.
F-15

• If maximal flow rate is required from the outset, the diuretic is injected 15 minutes before the radiopharmaceutical, so that the start of the test coincides with the maximum effect of the diuretic.

• This results in maximal stress on the PUJ (in terms of urine flow) earlier in the study and reduces equivocal rates to around 7%.
F+0

• First suggested by Sfakianakis et al.
• Said to reduce interruptions due to the discomfort of the injections and reduced interruptions due to voiding compared from the F-15 protocols.
• Liu *et al.* have reported that a shorter period between diuretic administration and completion of study probably reduces the bladder distension and voiding disruptions in the F + 0 group
Studies F-15, F+0, F+20

• Ramesh Babu, Dhandapani Venkatsubramaniam, and Eswaramoorthy Venkatachalapathy
• F+0 diuretic protocol is superior to F-15 and F+20 for nuclear renogram in children
• PMC4495501
• Between August 2011 and July 2013, 148 diuretic renograms were performed to evaluate unilateral grade 3–4 hydronephrosis (reflux, posterior urethral valves, post-pyeloplasty status excluded).
• Patients were allotted into three groups based on the timing of diuretic administration: Diuretic given 15 min before (F-15), at the same time as (F + 0) and 20 min after (F + 20) radionuclide administration.
• Dynamic images and renogram curves were inspected to identify in each group (1) number of equivocal curves and (2) number of interrupted studies due to patient movement/discomfort/voiding.
• Statistical significance was determined by the Fisher exact test.
The $F+0$ and $F-15$ protocols are superior to the $F+20$ protocol in reducing the number of equivocal curves, while the $F+0$ protocol is superior to the other two in reducing interruptions due to patient movement or voiding. $F+0$ is the diuretic protocol of choice for renogram in children.
• It is important to know which protocol is being used to interpret the test accurately and/or compare with previous studies.

• During the diuretic phase, the region of interest should be drawn around the collecting system, including the ureter only in cases of hydroureter.
• After completion of the diuretic phase recording, the child should be held upright for 5 minutes and allowed to void if no catheter was used. ? Still practiced

• A repeat image is captured to assess residual activity after gravity-assisted drainage.

• Differential renal function, washout curves, and washout half-times can be computer-generated for proper interpretation of the test.
• Management decisions are based on renal function, radiotracer washout half-time, shape of the washout curve, and gravity-assisted drainage.
• In contrast to adults, in children there are no established washout half-times that define an obstructed or unobstructed state.
• The washout curve is typically more revealing than the absolute half-time values, especially in young children or children after pyeloplasty in whom a dilated system may be slow to drain but not obstructed.
Factors Influencing MAG3 Renogram

• Renal function
• Hydration
• Collecting system capacity
• Collecting system compliance
• Bladder effects
• Ureteric dilatation or obstruction
Interpretation

• Depends on uptake from blood into kidney and elimination from kidney into bladder
• 3 phases
• Renogram curve patterns; to assess the shape of the curve and examine the sequential analog images
Renogram phases

1. **Vascular phase**
   - first few seconds after injection
   - rapid rise reflecting the speed of injection and the blood supply to the kidneys
2. Uptake/parenchymal/concentration phase
- slightly more gradual slope
- represents renal handling of the radiopharmaceutical and transfer across tubular cell or glomerular membrane into the lumen of the nephrons.
- As such, it is liable to be affected by poor uptake and impaired renal handling.
- This part of the curve continues to rise as long as more radiopharmaceutical is being extracted from the plasma than leaves the region of interest in the urine.
- In the normal kidney, this curve peaks between 2 to 5 minutes.
• 3. Elimination/excretory phase
• After the peak of the uptake phase, coincides with the time that activity starts to become distinguishable in the bladder.
• During this phase, although tracer continues to arrive in the kidney, the characteristics of this part of the curve reflect mainly the efficiency of excretion of tracer in the urine.
• A normal pattern virtually excludes any degree of obstruction. (20-40 minutes depending on drainage)
The graph illustrates the phases of a process over time, with activity on the y-axis and minutes on the x-axis.

- **Vascular Concentration**
  - The graph shows a rapid increase in activity within the first 5 minutes, indicating a peak in vascular concentration.

- **Excretion**
  - After the peak, there is a gradual decline in activity, representing the excretion phase, which lasts from 5 to 20 minutes.

- **T 1/2 (8-12 min)**
  - The half-life (T 1/2) of the process is marked at 8-12 minutes, indicating the time it takes for the activity to reduce by half during the excretion phase.
O’Reilly Curves

• Type I – Normal response
• Type II – obstructive response (high-pressure system)
  • -rising curves continue to rise despite diuretic
  • -no response to frusemide
  • -inconclusive if GFR <15mL/min, because increase in flow in an F-15 study is likely to be minimal compared from a F+20 study
Classical responses of F+20 diuresis renography

Normal (Type I)

Obstructed (Type II)

Hypotonic (Type IIIa)

Dose

Time

Diuretic

Dose

Time

Diuretic

Dose

Time

Diuretic

Equivocal (Type IIIb)

Delayed compensation (Type IV)

Dose

Time

Diuretic

Dose

Time

Diuretic
• Type IIIa – dilated but not obstructed (low pressure/hypotonic system)
• -initially obstructive curve falls on injection of the diuretic
• -Dilatation is the result of stasis rather than obstruction
• -prompt elimination following frusemide injection
Type II F+20 diuresis renogram curve

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>64</td>
<td>36</td>
</tr>
<tr>
<td>2</td>
<td>12.9</td>
<td>6.7</td>
</tr>
<tr>
<td>3</td>
<td>14.2</td>
<td>9.2</td>
</tr>
</tbody>
</table>

Relative function (%) at 60–160s
Uptake (% injection) at 2 minutes
Uptake (% injection) at 3 minutes
Time to peak (minutes)

Figure 10.20 Type II F+20 diuresis renogram curve.
Figure 10.21  Type IIIa nonobstructive F+20 diuresis renogram curve.
• Type IIIb – equivocal response
• - initial obstructive rising curve on injection of diuretic neither washes out briskly nor it continues to rise.
• - weak response to diuretic
• - need to be established whether the result reflects a good diuretic response and a partially obstructed outlet, or a suboptimal response and normal unobstructed outlet.
• May also represent a massively dilated system that an optimal diuretic response still cannot wash out.
• -repeat study with F-15
Figure 10.22 Typé IIIb F+20 equivocal diuresis renogram curve.
• Type IV- delayed compensation (Homsy’s sign)
• Delayed double peak pattern
• The initial washout in response to diuretic is good, but then the curve flattens or even starts to rise.
• The explanation- the steady increase in diuretic induced urinary flow rate that does not peak until 15 minutes after injection. During the resting and early diuretic phase, the resulting flow can be transported by the PUJ.
• Eventually, the flow rate reaches a level at which the system under stress can no longer transmit the urine load.
• It decompensates and further dilatation occurs. In fact, outflow obstruction may even increase.
• The balance is tipped and the amount of tracer that enters the ROI drawn around the kidney exceeds the amount eliminated. The curve starts to rise again.
Figure 10.23 Type IV F+20 delayed decompensation diuresis renogram curve.
Type IIIb (equivocal) and Type IV (delayed compensation) curves can be resolved by F-15 diuresis renography.
Diuretic response (washout T1/2)

- Time required for 50% of tracer to leave the dilated kidney
  - Normal < 10 mins
  - Obstructed > 20 mins
  - Indeterminate 10-20 mins
Factors influencing

• Hydration
• Volume of dilated pelvis
• Bladder catheterization
• Dose of lasix
• Renal function
Pitfalls

- False positives for obstruction
  - Distended bladder, gross hydronephrosis, poor function, dehydration
- False negative
  - Low grade obstruction
- Poor function
DMSA (Dimercaptosuccinic Acid)

- High affinity for the renal cortex
- Preferred pharmaceutical for static parenchymal imaging
- Provides the most accurate assessment of relative renal function
- Minimal GFR clearance
- Extracted by the cells of the proximal convoluted tubules allowing slow concentration of radioactivity in the renal cortex
- After 3 hours, about 50% of the injected tracer is concentrated in the kidneys, remaining for about 24 hours
Indications

- Assessment of relative renal function
- Detection of renal scarring with a sensitivity of 96% and specificity of 98%
- Investigations of renal anomalies
Interpretation

• Normal kidney – homogenous parenchymal distribution

Acute pyelonephritis
• -single or multiple ‘cold’ defects
• -renal contour not distorted
• -diffuse decreased uptake
• -diffuse enlarged kidney or focal bulging

Chronic pyelonephritis
• -volume loss, cortical thinning
• -defects with sharp edges
Advantages

• Provides excellent cortical images
• Accurate split renal function estimation
• Non-nephrotoxic
• No significant complications
• Allergic reactions extremely rare
Disadvantages

• Involves radiation
• Does not allow dynamic assessment of renal excretion
Radioisotope GFR study

- DTPA (diethylene-triamine-pentaacetic acid)

- Advantages
  - Accurate
  - No need 24 hour urine collections
  - Mandatory in clinical trials investigating progressive renal failure

- Drawbacks
  - Invasive- repeated blood samples
  - Involves small amount of radiation
  - Lengthy procedure
  - Artifacts can be caused by inaccurate recording of times, tracer extravasation at injection site, significant oedema or ascites
Role in Paediatrics

- Nuclear studies require a happy, relaxed cooperative child.
- Staff needs to be sensitive to a child's needs and moods.
- Toddlers may require sedation.
- May need a catheter
- Small children can be placed supine on the gamma camera.
- A vacuum extractor mattress helps maintain position.
• Children are more susceptible to the stochastic effects of radiation, so doses should be scaled down on the basis of bodyweight, to ensure the minimum effective dose is used.
When can be performed?

• Renal immaturity must be taken into account when considering renal scanning.
• **Tubular function** is poor in the early months, but rises to 80-90% of adult levels at 1 year.
• As such, DMSA scans should not be performed before 12 weeks.
• In neonates, **GFR** is low and rise steadily to reach adult levels at 2 years.
• The diuretic response is also unpredictable in the first 4-6 weeks of life and must be considered when performing diuresis renography in the first year of life.
• PUJO is the most common abnormality detected.
• Reno graphic obstruction in the presence of impaired relative function is an indication for surgery.
• Hydronephrosis may occur also as a result of reflux.
Infection

• In acute pyelonephritis, a DMSA scan is the most sensitive investigation for confirming renal parenchymal involvement.

• The majority of defects disappear by a follow up scan at 3-6 months, with remaining defects being investigated accordingly.
Bladder Imaging

- The importance is in the investigation and management of VUR.
- Its advantage over MCUG is its low radiation dose.
Direct Radionuclide Cystography

- Requires instillation of a radiopharmaceutical into the bladder directly via a catheter.
- Indicated in children not yet bladder trained.
- Following catheterization and drainage, Technetium-pertechnetate in saline is instilled in the bladder until full.
- The procedure is conducted on the gamma camera with the bladder and both kidneys in view.
• Its main advantage is the low radiation dose, $1/20^{th}$ of that of an MCUG.
• The disadvantages are the need for a catheter and the lack of imaging of the urethra.
Indirect Radionuclide Cystography

- A more physiologic study, but only possible in toilet trained children.
- About 30-60 minutes after injection of MAG3, the well hydrated child is asked to void in front of the gamma camera.
- A quiet room, with minimal health personnel is vital for a conducive environment.
• The bladder and kidney regions are scanned and 1 second frames are obtained.
• It’s the only study that allows the assessment of both renal reflux and bladder function under physiologic conditions, as well as the effect of micturition on upper tract drainage and the difference between a true post-micturition residue and a false residue caused by secondary filling from dilated upper tracts.
• Utility is in diagnosis and/or follow up of VUR cases which avoids the need for an MCUG, which is more invasive and involves significantly more radiation exposure.
Post Pyeloplasty Renograms

- Renal function before and after pyeloplasty: does it improve?
- McAleer IM1, Kaplan GW.
  - retrospectively reviewed the charts of patients who underwent pyeloplasty between 1990 and 1997 in whom preoperative and postoperative diuretic renography data were available.
  - Complete data were available for review in 79 patients 2 weeks to 18 years old (median age 6 months).
- CONCLUSIONS:
  - Renal function did not improve after pyeloplasty regardless of the initial level of relative function. Renal scan revealed that differential function decreased after pyeloplasty in some patients in whom hydronephrosis was detected prenatally and who were initially followed with observation. In our opinion waiting for renal function to decrease before considering pyeloplasty is not warranted, since function does not improve even when obstruction is corrected and drainage time improves.
The topic of whether improvement can be expected after pyeloplasty in patients with pelvi-ureteric junction obstruction (PUJO) continues to generate debate.

The aim of this study was to analyse the functional outcome of unilateral Anderson-Hynes (A-H) pyeloplasty using differential renal function (DRF) and drainage patterns determined by diuretic radionuclide renography (DRR).

A retrospective study was carried out by evaluation of the records of patients who underwent A-H pyeloplasty for unilateral PUJO and reported for a follow up renal dynamic scan between the years 2000 and 2003.
A total of 126 patients (93 males and 33 females) aged three months to 40 years had undergone pre-operative and post-operative DRR and were followed for at least six months after operation.

Chi square analysis was applied to estimate the proportion of improvement between Groups A and B.

Post-pyeloplasty scans revealed stable renal function in 102 (81%) subjects, while improvement was noticed in 14 (11%) subjects.

The remaining 10 (8%) subjects had deterioration in renal function.

No improvement in renal function was seen in Group C patients. Our results have shown that in the majority of cases studied, after A-H pyeloplasty renal function remains stable.

A-H pyeloplasty applied in patients with preserved DRF and obstruction will result in long term preservation of renal function.
• Thank you!