

## Chapter 4

# Nuclear Medicine Investigations

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### Introduction

Nuclear medicine techniques are integral to modern urological practice and can be used to investigate almost any organ in the body. Urological usage is primarily confined to—

- Assessment of renal imaging, function, and drainage
- Management of metastatic prostate cancer

Isotopes of an element share the same atomic number (and therefore the same biochemical characteristics) but differ in their mass number (as well as their energy states). An example is the isotopes of iodine ( $^{123}\text{I}$ ,  $^{131}\text{I}$ ,  $^{125}\text{I}$ ). When an isotope has radioactive properties, it is called a radioisotope or radionuclide. Radionuclides undergo spontaneous disintegration, while emitting high—penetrating, electromagnetic gamma rays (measured in electron volts [eV]). Radionuclides are used to label a compound, with a specific interaction with the target organ (e.g., kidney, bone) and the resulting ionizing radiation is detected and quantified by a gamma camera. A nuclear medicine image, therefore, is a map of where the tracer has accumulated, and is dependent on blood flow to the target organ as well as tracer metabolism by the organ (an indicator of function).

The characteristics of the three main radionuclides used in urological practice are summarized in Table 4.1.

The half-life of a radiopharmaceutical (radionuclide + labeled compound) is determined by its natural rate of nuclide decay and metabolism/handling by the body. Decay is measured in Becquerals (Bq) and 1 Bq equals 1 disintegration per second. Typically, diagnostic procedures result in a dose delivery of  $10^6$  Bq (1 MBq) and therapeutic interventions in  $10^9$  Bq (1 GBq). The ideal radiopharmaceutical should have the following characteristics:

TABLE 4.1. Radionuclides

| Radionuclide   | Isotopes                                                  | Half-Life                   | Energy of<br>Gamma Rays<br>(keV) | Labeled<br>Compounds |
|----------------|-----------------------------------------------------------|-----------------------------|----------------------------------|----------------------|
| Technetium-99m | $^{99m}\text{Tc}$                                         | 6.02 h                      | 140                              | DTPA<br>DMSA<br>MAG3 |
| Iodine         | $^{123}\text{I}$ , $^{131}\text{I}$ ,<br>$^{125}\text{I}$ | 13.2 h ( $^{123}\text{I}$ ) | 159                              | Hippuran             |
| Chromium       | $^{51}\text{Cr}$                                          | 27.7 days                   | 320                              | EDTA                 |

1. Easily and cheaply generated
2. Radiochemically pure
3. Non-toxic
4. Should emit only gamma rays (100–200 keV energy)
5. Half-life long enough to complete investigation
6. Half-life short enough to minimize patient radiation risk

Table 4.2 describes the characteristics of the commonly used radiopharmaceutical.

Therefore, nuclear medicine techniques in renography can evaluate—

- Renal blood flow
- Renal cortical imaging
- Renal glomerular filtration
- Renal handling
- Renal excretion

The agent of choice will primarily depend on the precise function being evaluated.

Positron emission tomography (PET) is an emerging radionuclide technique which has recently enjoyed a migration from the research setting into clinical practice. The most commonly used radionuclide in PET scanning is fluorine-18 which binds to a D-glucose analog. The basic principles of PET and possible application in urology are discussed in Chapter 4e.

In general, radiopharmaceuticals—

- Are safe in the short term
- Rarely cause allergic reactions

TABLE 4.2. Commonly used radiopharmaceuticals in urology practice

| Radionuclide          | Radiopharmaceutical                                           | Half-life | Injected adults dose (MBq)                              | Effective dose (mSv) | Characteristics                                                                                                                                                                                                                                                                    | Applications                                                       |
|-----------------------|---------------------------------------------------------------|-----------|---------------------------------------------------------|----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|
| <b>Technetium-99m</b> | Dimercaptosuccinic acid ( <sup>99m</sup> Tc-DMSA)             | 6.02 h    | 1/kg body weight (max dose 80)                          | 1                    | All activity in plasma with strong binding to plasma proteins; not filtered by glomerulus; slow extraction of DMSA from blood into proximal tubule cells; bound to cytoplasmic proteins and mitochondria within cells; tracer accumulation within both proximal and distal tubules | Renal imaging<br>Most accurate measurement of split renal function |
|                       | Diethylenetriamine pentaacetic acid ( <sup>99m</sup> Tc-DTPA) | 6.02 h    | 10–300<br>10 for GFR estimation<br>50–75 for renography | 1                    | Slowly cleared by glomerular filtration; cheap and easy to produce; poor target-to-background ratio in poor renal function                                                                                                                                                         | GFR estimation<br>Renography                                       |

|                 |                                                                 |              |                                             |       |                                                                                                                                                                         |                                                                                                          |
|-----------------|-----------------------------------------------------------------|--------------|---------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|
|                 | Mercaptoacetyltriglycine<br>( <sup>99m</sup> Tm-MAG3)           | 6.02h        | 50–100<br>50–100 for<br>renography<br>800   | 3     | Cleared by tubular<br>secretion and<br>glomerular<br>filtration                                                                                                         | Renography<br>Estimation<br>of ERPF                                                                      |
|                 | Methylene<br>diphosphonate<br>( <sup>99m</sup> Tm-medronate)    | 6.02h        | 800                                         | 8     | High uptake of<br>immature bone<br>results in<br>increased tracer<br>uptake in areas of<br>rapid bone<br>turnover                                                       | Bone<br>imaging                                                                                          |
|                 | Orthoiodohippurate<br>( <sup>123</sup> I-Hippuran)              | 13.2h        | 20–75<br>20 for<br>renography<br>2 for ERPF | 0.3   | Hippuran has best<br>clearance of all<br>tracers; fast<br>renal handling;<br>eliminated mainly<br>by tubular<br>secretion and<br>glomerular<br>filtration;<br>expensive | <sup>123</sup> I—ideal<br>for<br>renography<br><sup>125</sup> I and<br><sup>131</sup> I best<br>for ERPF |
| <b>Iodine</b>   |                                                                 |              |                                             |       |                                                                                                                                                                         |                                                                                                          |
| <b>Chromium</b> | Ethylenediamine<br>tetraacetic acid<br>( <sup>51</sup> Cr-EDTA) | 27.7<br>days | 3                                           | 0.007 | Stable compound<br>which is cleared<br>by glomerular<br>filtration; not<br>widely available                                                                             | GFR<br>estimation                                                                                        |
|                 |                                                                 |              |                                             |       |                                                                                                                                                                         |                                                                                                          |

- Have long-term risks common to all forms of radiation, including development of malignancies and genetic injury which may be inheritable. A safe level of radiation does not exist and all exposure must be kept as low as reasonably achievable (ALARA principle)
- Ought to be avoided in pregnant and lactating women unless in exceptional circumstances. Since most radiopharmaceuticals are excreted in breast milk, lactating mothers are advised to stop nursing for 2–3 days
- Are excreted primarily in urine and patients must be advised to urinate frequently post-examination to minimize radiation risk
- When given to pediatric patients must be dose adjusted for body weight of patient

### **Clinical applications**

A discussion of all radionuclide clinical applications and their techniques is beyond the scope and purpose of this book and the authors will limit the discussion to the following categories:

- (a) MAG3 renography
- (b) DMSA scan
- (c) Obtaining a GFR
- (d) Bone scan
- (e) PET scan
- (f) Detection of prostate cancer metastases

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### **(a) MAG3 RENOGRAPHY**

#### **Overview**

$^{99m}\text{Tc}$ -MAG3 has become the agent of choice for dynamic radionuclide imaging of the renal tract in most centers. It was first developed as an alternative to hippuran, but has a plasma clearance 50–65% slower than that of hippuran. Nevertheless, it gives images comparable to  $^{123}\text{I}$ -hippuran. Following intravenous injection, it remains loosely bound to serum proteins, and only a small proportion undergoes glomerular filtration. Clearance is predominantly by tubular secretion. The 30-minute excretion of  $^{99m}\text{Tc}$ -MAG3 is approximately 70%, and by 3 hours 90% of the tracer is cleared by the kidneys. Renography can be combined with administration of a diuretic (usually frusemide) to produce a high urine flow diuresis renogram. The  $^{99m}\text{Tc}$ -MAG3 is an adequate tool for the assessment of urinary uptake, transit, excretion, and split renal function. In addition, simple conversion

methods will allow reproducible estimations of ERPF from the  $^{99m}\text{Tc}$ -MAG3 activity curve.

### **Indications**

- Assessment of whole or relative kidney function
  - Before and after surgical intervention (e.g., pyeloplasty, partial/total nephrectomy)
  - Investigation of acute or chronic renal failure
  - Assessment of the transplanted kidney
  - Assessment of renal function following trauma
- Assessment of kidney drainage in obstructive uropathy (e.g., uretero-pelvic junction obstruction, renal stones)
- Assessment of congenital renal abnormalities (e.g., duplex, horseshoe, absent, ectopic, or cystic kidneys)
- Identification of vesico-ureteric reflux

### **Technique and radiation**

The Consensus Committee of the Society of Radionuclides in Nephrourology (1994) have published guidelines aimed at standardizing the renography protocol in order to enhance uniformity and reproducibility. These are summarized below.

### ***Patient preparation***

- Adequate hydration (500 mL of oral fluid 15–30 min before examination) is vital to ensure good diuresis (urine flow of 1–3 mL/min). Avoid study if patient appears clinically dehydrated
- The patient may be placed supine or erect, reclining against the camera
- Assess need for catheterization. If not, patient must void before study
- Position patient in either supine or sitting up position. The posture of the patient may have an effect on the renography curve (discussed later)
- A typical adult dose of 50–120 MBq is carefully injected intravenously to avoid local extravasation
- An image is taken every 10–20 seconds for up to 40 minutes following administration of radiopharmaceutical
- Analog images are taken every 5 minutes and the hard copy must include several serial analog images as well as the renogram curve
- The first 12 and last 12 frames may be summed to exhibit the kidneys more clearly
- If the kidney fails to empty by 20 minutes, frusemide may be administered (F+20). Data is collected for 30–45 minutes (or 20 min following diuretic injection)

- The patient is asked to void at the end of the procedure (minimizes radiation to the bladder as well as allowing assessment of urine production rate)
- The renogram curve demonstrates change in kidney activity over time

The radiation activity detected by the gamma camera is first stored as a computer image. Regions of interest (ROI) are mapped out for the kidneys and bladder, in addition to a background region to enable precise measurement of activity count for each time frame. The background region is usually chosen just lateral to the kidneys, but care must be taken to avoid the liver, due to its high tracer uptake. Additional ROIs (different moieties of a duplex kidney) may also be delineated. The renogram curve can be obtained following subtraction of the background count from the kidney and bladder ROI count and is displayed as a percentage of the injected dose (y-axis) against time (x-axis). The relative function of each kidney is calculated by comparing the percentage dose at 2 and 3 minutes' uptake.

Following the procedure, the patient is informed about the possibility of a prolonged diuresis. Frequent voids will help reduce bladder irradiation.

### ***Diuresis***

If diuresis renography is indicated, an intravenous bolus of frusemide (dose 1 mg/kg in infants, 0.5 mg/kg in children aged 1–16 years, and 40 mg in adults) is commonly used. Ensure there are no contraindications to diuretic therapy. Frusemide will produce a maximal diuretic response within 5–10 minutes and rationale is to 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. The timing of diuretic administration is a matter of local policy but the various techniques have distinct advantages. The traditional technique (F+20) involves frusemide administration 20 minutes after injection of the radiopharmaceutical. The study must continue for at least 20 minutes following frusemide injection. This enables study of initial unmodified renal handling, followed by the response to increased urine flow rate.

The F-15 technique (frusemide given 15 min before radiopharmaceutical) ensures maximal diuresis at commencement of data acquisition, thereby revealing minor levels of obstruction. Administration of the tracer simultaneously with frusemide (F+0 technique) has been practised in pediatric units and has the

advantage of significantly reducing examination times. The F+0 technique is not recommended in patients with significant renal failure (GFR < 15 mL/min per kidney) and renal units with significant hydronephrosis.

The timing of diuretic does not significantly alter split renal function result, but centers should standardize practice to enable meaningful comparisons (e.g., before and after surgical intervention). The F-15 technique will separate the majority of equivocal curves on F+20 renography in to either unobstructed or obstructed, and therefore is preferred in patients with equivocal results or with gross hydronephrosis.

### ***Factors influencing MAG3 renography***

1. Renal function: a GFR of <15 mL/min per single kidney will result in urine flow rates of <10 mL/min, with poor subsequent tracer washout. This may result in an “obstructed” (false-positive) curve. Frusemide is usually insufficient to increase diuresis significantly and perfusion pressure-flow studies (Whitaker test) ought to be considered. Renal disease affecting the parenchyma (e.g., acute tubular necrosis) may diminish the response to diuretics.

2. Hydration: minor levels of obstruction may be masked in dehydrated individuals. In addition, diuretic administration may be perilous if the patient is already dehydrated. Oral hydration (500 mL of water 30 min before study) will usually suffice although on occasions intravenous fluids may be required.

3. Collecting system capacity: in the massively dilated system, urine flow may be inadequate to prevent tracer accumulation in the renal pelvis. In such cases, a false-positive “obstructed” curve may be the end result. The F-15 technique will help minimize the effects of a capacious system.

4. Collecting system compliance: increased diuresis, within a normo-compliant system, should result in distension of the renal pelvis with no significant increase in pressure. However, poor compliance may cause rapid elevations within a non-dilated system, such that any obstruction is overcome and there is reasonable tracer flow distal to the obstruction (false negative). Conversely, a hyper-compliant upper tract will result in renal pelvic tracer accumulation, in spite of the absence of obstruction, resulting in a false-positive curve.

5. Bladder effects: a full bladder may inhibit drainage from the ureters and cause artifacts. The patient must be asked to void prior to commencement and again before completion of data acquisition. Alternatively, in patients with chronic retention or a neurogenic bladder, catheterization should abolish any effects of a full bladder.

6. Ureteric dilatation or obstruction: in cases of gross ureteric dilatation, an ROI drawn around the kidney and renal pelvis may miss the distal obstruction, resulting in a false-negative study. Care must be taken to study the analog images and ROI must include the ureter proximal to the obstruction. Furthermore, multiple simultaneous levels of obstruction will not be apparent by MAG3 renography.

The maximal recommended activity per test is 100 MBq for MAG3 renography, which corresponds to an effective radiation dose of 1 mSv (equivalent to 6 months of background radiation).

### **Interpretation**

#### ***Normal renogram curve***

The shape of the renogram curve (following subtraction of background activity) is dependent on—

1. MAG3 uptake from blood into kidney
2. MAG3 elimination from kidney into bladder

Classically, the normal MAG3 renogram curve has three phases (see figure 4.1):

- The first phase: steep upward rise following intravenous contrast injection; this is indicative of the speed of tracer injection and its delivery to the kidneys (i.e., renal vascular supply)
- The second phase: a more gradual slope which represents renal handling of MAG3 (renal uptake by tubular secretion and glomerular filtration) and peaks between 2 and 5 minutes. Time taken for the curve to peak following tracer injection is referred to as T<sub>max</sub>. This may be delayed in patients with renovascular insufficiency, renal failure, and obstruction
- The third phase: commences after the peak. Associated with the emergence of tracer in the bladder. Represents elimination (but also delivery) of tracer from the kidney. After 3 minutes

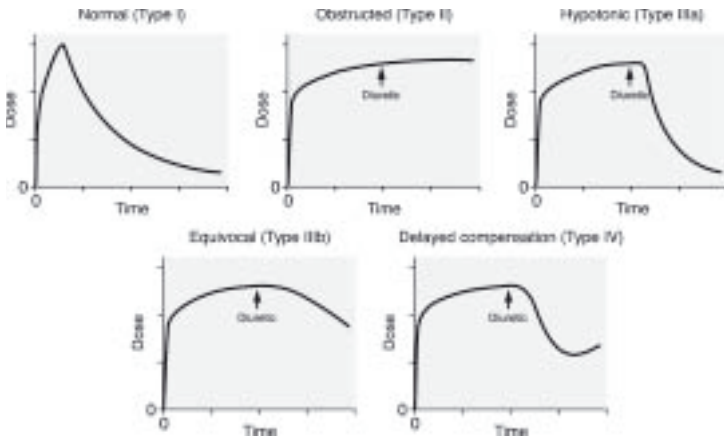


FIGURE 4.1. MAG3—Renography curve patterns in F + 20 diuresis renography (with permission from *Comprehensive Urology*, Weiss, Mosby, 2001, 141)

both elimination and uptake are in competition, but the former subsequently dominates. It is this elimination curve that is dependent on the upper tract urodynamics. The elimination curve may have a smooth or stepwise (variant of normal) pattern and when normal, excludes the presence of obstruction. A delayed upward deflection may indicate intermittent obstruction or vesico-ureteric reflux

### Split renal function

This is expressed as the ratio of the area under the renogram curves of the two kidneys obtained during the period 40 seconds to 2 minutes 40 seconds after tracer injection. The shortest transit time for filtrate in the Bowman's capsule to the renal pelvis is 2.5 minutes, and therefore it can be safely assumed that the MAG3 will not be found in the collecting system within 2.5 minutes of injection. The initial 40 seconds are excluded to prevent artifactual errors. The relative function in a pair of normally working kidneys may vary between 40% and 60%. Similarly, relative functions in different moieties of a duplex kidney can also be calculated.

### Scarring

Since 80% of MAG3 is metabolized by tubular secretion, the analog images can be analyzed for the presence of parenchymal scarring. Although DMSA renography remains the gold standard

for the investigation of scarring, MAG3 studies show good correlation between the two techniques.

### ***Renogram curve patterns***

When interpreting MAG3 renography, five distinct patterns (based on the F+20 technique) are recognized. It is important not merely to assess the shape of the curve, but also to examine the sequential analog images to determine the level of obstruction, as the calyces, pelvis, and ureter may all be easily visible (Fig. 4.1).

#### *Type I—normal response*

This is characterized by a rapid uptake curve leading up to a peak within 2–5 minutes, followed by gradual (but sometimes step-wise) elimination of tracer. Administration of frusemide results in no appreciable difference in speed of elimination. A normal curve virtually excludes obstruction, although it may be argued that increasing urine flow rate (i.e., using the F-15 technique) may expose lesser degrees of impedance.

#### *Type II—obstructive response (high-pressure system)*

In the absence of any other factors affecting drainage (e.g., dehydration, renal impairment, etc.), an obstructive pattern is denoted by a rising curve. In addition, the lack of an exponential tracer elimination curve is also suggestive of a degree of obstruction. Typically, there is little or no response to frusemide. On the analog images, the affected kidney will often display good parenchymal uptake and accumulation of tracer above the level of obstruction (e.g., in the renal pelvis in patients with UPJO). The diagnosis of obstruction cannot be satisfactorily made (even in the presence of a rising curve) if the affected kidney has a GFR of <15 mL/min, since the rate of urine production may be insufficient to produce tracer washout (usually 1–3 mL/min urine production is required).

#### *Type IIIa—dilated but not obstructed (low pressure/hypotonic system)*

There is an initial accumulation of tracer in the kidney, resulting in a rising curve similar to an obstructive response, but there is prompt elimination following frusemide injection. The analog images usually demonstrate tracer accrual in a dilated system secondary to stasis rather than obstruction. The increased urine flow produced by the diuretic is adequate to effect free drainage.

*Type IIIb—equivocal response*

Following an initial “obstructed” rising curve, a frusemide injection produces a somewhat languid response. The curve demonstrates some tendency to washout, albeit incompletely. Examination of the analog images may help clarify whether this represents partial obstruction or inadequate tracer elimination (e.g., due to a dilated renal pelvis). In this situation, an F-15 study will help categorize the majority of equivocal curves into either obstructed or non-obstructed.

*Type IV—delayed compensation (Homsy’s sign)*

Described by Yves Homsy in 1988, the characteristic shape is a “double peak” response to diuretic. This pattern is seen in patients with subclinical intermittent obstruction. A repeat F-15 diuresis renography will often reveal an obstructed pattern. The first “peak” is due to an initial rising curve, which then exhibits a good response to frusemide. However, as the diuretic effect increases, the threshold is reached and tracer accumulation causes the curve to either flatten or rise.

***Modifications of the MAG3 renography****Deconvolution analysis*

This is a mathematical manipulation of the renogram to produce a theoretical curve that would be derived if the tracer had been injected in the renal artery (rather than a peripheral vein). This allows calculation of a range of transit times through the renal tubules, including mean parenchymal transit time as well as whole kidney transit time. Transit times are increased in obstruction and renal failure. Attention to technical detail is paramount, and as yet deconvolution techniques have not gained widespread acceptance.

*Captopril-enhanced renography*

This modification is indicated for the investigation of renal artery stenosis. Patients should be instructed to stop any angiotensin-converting enzyme (ACE) inhibitor or diuretics for at least 3 days prior to examination. Ensure patient is well hydrated. A baseline study is performed first. Following this, a further study is repeated (on the same day or consecutive days) with 25 mg of Captopril (ACE inhibitor) given orally 1 hour before tracer injection. Renin converts angiotensinogen to angiotensin I, which in turn is converted (by an ACE) into angiotensin II. Angiotensin II effects efferent arteriole vasoconstriction and thereby maintains GFR.

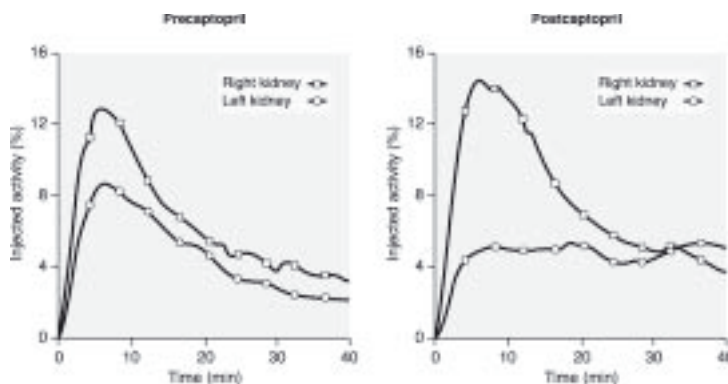


FIGURE 4.2. Captopril renography demonstrating a left renal artery stenosis (with permission from *Comprehensive Urology*, Weiss, Mosby, 2001, 145)

Patients with reno-vascular (e.g., renal artery) stenosis have higher levels of angiotensin II. The captopril-enhanced renogram therefore will display reduced function (reduced gradient in the uptake part of the curve) and delayed transit, with a delay in  $T_{\max}$  (time taken for renogram curve to peak) (see fig 4.2). The overall sensitivity of this technique is 80–90% for the detection of reno-vascular hypertension, and patients with positive results can often be successfully treated.

### Renal transplant evaluation

MAG3 renography is non-nephrotoxic and a vital tool in the assessment of renal transplant patients. Clinical applications include—

- Pre-transplant evaluation of renal function and drainage in the potential living related donor
- In the immediate post-transplant period, serial MAG3 studies can help distinguish between a variety of potential pathologies:
  - Within the first 4 weeks, renography demonstrating no tracer uptake is usually indicative of a renal perfusion disorder (renal artery stenosis or renal vein thrombosis) or acute rejection
  - Diminished uptake of tracer with delayed and sluggish drainage is typical of acute tubular nephrosis or urinary tract obstruction (renal perfusion is usually maintained)

- With serial renography, a deterioration of function over time is indicative of rejection
- Renal outflow obstruction (e.g., at the ureterovesical junction) can be diagnosed easily
- Locations of urinary leakage and urinoma formation are readily identified

### **Indirect micturating cystography**

Practice of this technique, which negates the use of a catheter, has many advantages in the pediatric population:

- Will primarily demonstrate reflux
- Enables estimation of split renal function
- Demonstrates cortical scarring
- Measures drainage
- Allows valuable assessment of bladder function

The well-hydrated patient is injected with an MAG3 tracer. If renography is required, data collection can commence immediately. The patient is then asked to void 30–60 minutes following tracer injection as data acquisition continues. An upward deflection in one or both of the kidney curves is suggestive of VUR. The main disadvantages are the prerequisite for children to be potty trained and the lack of anatomical detail. Unfortunately, this technique is associated with a high false-negative rate, especially for milder grades of reflux.

### **Advantages of MAG3 renography**

- Provides sensitive indices of tubular function and urinary excretion
- Virtually no contraindications
- Non-nephrotoxic
- No significant risk of allergic reactions
- Serial examinations possible (often required)
- Side effects are rare (unless frusemide or captopril is used)

### **Drawbacks of MAG3 renography**

- Exposes patient to radiation
- Length of study (can take up to 1 hour)
- Prone to artifactual errors (e.g., due to renal impairment, posture, bladder effect, etc.)
- Limited anatomical information
- Equivocal results require a repeat procedure (usually F-15 study)
- Inaccurate outlining of ROIs can affect curve dynamics

## (b) DMSA RENOGRAPHY

### Overview

- $^{99m}\text{Tc}$ -DMSA has a high affinity for the renal cortex
- $^{99m}\text{Tc}$ -DMSA is the preferred radiopharmaceutical for static parenchymal imaging
- Provides the most accurate assessment of relative renal function compared to other tracers

Following tracer injection,  $^{99m}\text{Tc}$ -DMSA is mostly plasma protein bound, and therefore clearance by GFR is minimal. In the kidney, the cells of the proximal convoluted tubules (and the distal tubules to a lesser extent) extract the  $^{99m}\text{Tc}$ -DMSA by tubular secretion allowing slow concentration of radioactivity in the renal cortex. After 3 hours, about 50% of the injected tracer is concentrated in the kidneys, remaining there for up to 24 hours. The majority of the other 50% is excreted unchanged in urine. Increased hepatic accumulation, and subsequent biliary excretion is noted in patients in renal failure. Owing to the slow renal extraction of  $^{99m}\text{Tc}$ -DMSA, the optimal time for imaging is between 2 and 4 hours after tracer injection.

$^{99m}\text{Tc}$ -DMSA scanning represents functioning tubular mass, yields excellent cortical images, and is an invaluable tool in the assessment of both adults and children.

### Indications

- Assessment of relative renal function
- Detection of renal scarring with a sensitivity of 96% and specificity of 98% (due to urinary tract infections or reflux nephropathy in children)
- Investigation of renal anomalies (e.g., horseshoe, solitary, or ectopic kidneys)
- Examination of space occupying renal lesions

### Technique and radiation

The optimal time for DMSA scanning remains an unresolved issue. Many units perform the study in the acute phase (i.e., during or soon after a UTI) in order to determine the extent of parenchymal involvement. Critics of such practice point out that an acute abnormality does not necessarily represent a permanent scar and a repeat scan is often required after 3–6 months to determine longstanding injury. Deferring the DMSA scan for such a period of time may avoid the initial examination.

$^{99m}\text{Tc}$ -DMSA has no specific contraindication and no specific patient preparation is required, since uptake is independent of the hydration state

- A typical adult dose of 80–100 MBq (1 MBq/kg body weight) is injected into a peripheral vein
- Images are acquired after 2–6 hours (usually after 3 h). Imaging must be avoided within the first hour due to the presence of free  $^{99m}\text{Tc}$  in urine
- Regions of interest are created around both kidneys as well as a background area between the kidneys. Subtraction of the background area count from the overall kidney count will result in the correct kidney count

To maximize the detection of scarring, various projections should be utilized to image the kidney. Posterior, right, and left posterior views are standard, but anterior views must be included if a pelvic or horseshoe kidney is suspected. Furthermore, in asymmetric kidneys (e.g., ectopic kidneys, scoliosis), anterior views must be obtained and split function expressed as a geometric mean of radioactivity in both posterior and anterior images.

Reports in literature have suggested that the use of single photon emission computed tomography (SPECT) resolution in the DMSA scan improves sensitivity in the detection of renal scarring, compared to planar imaging. While no guidelines exist at present, SPECT usage is primarily dependent on locally available technology.

A typical dose of 80 MBq for DMSA renography corresponds to an effective radiation dose of 1 mSv (equivalent to 6 months of background radiation).

### **Interpretation**

Normal kidneys should have a homogenous parenchymal distribution with visible demarcation between the cortex and medulla. Preservation of cortical thickness is indicative of acute changes, while cortical thinning is in keeping with chronic damage. The size, shape, and location (normal or ectopic) of the kidneys is readily demonstrated. Scars or other deformities are seen as areas of decreased or absent activity within the parenchyma. Artifacts may arise in kidneys with congenital fetal lobulations or due to splenic overlapping of the left kidney.

### ***Urinary tract infection***

In the acute setting, DMSA may demonstrate a single wedge-shaped area or multiple areas of decreased or absent tracer

activity. Some UTI may resolve without scar formation while scarring (single or multiple) may be the long-term sequelae in others. Scar formation is also associated with decreasing relative function in the ipsilateral side. In patients with complete duplex upper tract, it is the lower moiety that is prone to reflux, and therefore more likely to demonstrate reflux-related scarring.

### ***Renal anomalies***

Functioning ectopic kidneys, usually found in the midline pelvic position, are easily visible due to increased tracer activity. A DMSA will also reveal horseshoe kidneys and confirm the presence of a functioning isthmus.

### ***Renal masses***

Renal masses (e.g., tumors or cysts) appear as either well-circumscribed or ill-defined areas of non-functioning kidney. Although DMSA scanning is not routinely utilized for the investigation of such lesions, it is useful in planning nephron-sparing renal surgery for patients with tumor in a single kidney or those with bilateral tumors.

### **Advantages**

- Provides excellent cortical images
- Accurate split renal function estimation
- Non-nephrotoxic
- No significant complications
- Allergic reactions are exceptionally rare

### **Drawbacks**

- Involves radiation
- Does not allow dynamic assessment of renal excretion

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## **(c) OBTAINING A GLOMERULAR FILTRATION RATE (GFR)**

### **Overview**

- GFR estimation is invaluable in the management of patients with or at risk of renal impairment
- GFR is defined as the volume of blood from which a solute is cleared by glomerular filtration through the Bowman's capsule per unit time (mL/min)
- GFR is regarded as a measure of global function
- Various techniques of GFR calculation have been described
- The more accurate techniques (e.g., inulin clearance) are impractical for routine medical use, but the more workable

methods (e.g., serum creatinine, 24-urine for creatinine clearance) are prone to inaccuracies

- Radionuclide techniques for GFR estimation can be utilized

The ideal radioactive tracer for this purpose would have the following properties:

- Be cleared solely, completely, and unmodified by glomerular filtration
- Should not undergo tubular secretion or resorption. Any tubular secretion will increase the resultant GFR value
- Be non-toxic, stable, and not bound to serum proteins
- Be readily measured in blood or urine
- Should have a constant clearance irrespective of plasma concentration

While inulin fulfils all criteria, it is impractical for clinical use. The chelating agents  $^{99m}\text{Tc}$  DTPA and  $^{51}\text{Cr}$  EDTA, which have a similar clearance to inulin, are therefore utilized. This method assumes that following injection, the tracer is equally distributed between the intravascular and extracellular fluid compartment after 2 hours, and the removal of a small but constant proportion by the kidneys will result in a proportional drop in tracer concentration in the blood. Decreasing tracer concentration can be estimated by taking serial venous blood samples at clearly defined intervals post tracer injection. Plotting the log of plasma tracer concentration over time will enable GFR estimation.

### Indications

This technique can be used if employment of other techniques are impractical (e.g., if 24-hour urine collection is difficult, or if a high muscle mass might distort creatinine-based tests). General indications for GFR estimation include—

- Any clinical situation requiring an accurate measurement of absolute renal function
- Follow-up in patients with chronic renal disease
- Prior to administration of nephrotoxic therapy (e.g., chemotherapy)

### Technique and radiation

No specific patient preparation is required, but ensure that the patient is well hydrated and empties the bladder prior to injection. For GFR studies:

- Doses used are 10 MBq for  $^{99m}\text{Tc}$  DTPA and 3 MBq for  $^{51}\text{Cr}$  EDTA
- A pre-tracer injection venous blood sample is taken for background activity
- The tracer is injected and the exact time noted
- A heparinized blood sample is taken at 90, 150, 210, 270 minutes following injection and corrected (minus background activity) plasma tracer concentration can be plotted against time. Studies have shown that a minimum of four blood samples are required for accurate results
- Plotting the log of tracer concentration will result in a linear curve. Extrapolation of this line back to time zero will indicate the effective volume of distribution. The GFR is then calculated as the product of the distribution volume and the slope of the linear log curve, using the formula

$$\text{GFR} = V \lambda$$

where  $\lambda$  is the slope and  $V$  is injected tracer dose/distribution dose (see fig 4.3).

The *Gates* technique for GFR estimation, though not in common use, involves analysis of tracer activity in the kidneys between the 2- and 3-minute intervals following tracer injection. While the obvious advantage of this technique is the speed of the test and the absence of blood tests, its accuracy has been doubted. This technique has therefore fallen out of favor and most centers use a serial venous sampling method.

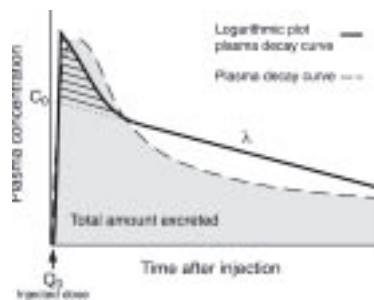


FIGURE 4.3. Logarithmic plot of plasma decay curve in single injection clearance techniques (with permission from *Comprehensive Urology*, Weiss, Mosby, 2001, 137)

An alternative to blood sampling is using three urine samples over 3 hours to measure urinary tracer concentration, but difficulties and inaccuracies in specimen collection make this method unattractive.

A typical dose of 10 MBq for  $^{99m}\text{Tc}$  DTPA and 3 MBq for  $^{51}\text{Cr}$  for EDTA for GFR studies corresponds to reasonably small effective radiation doses of 0.1 mSv and 0.007 mSv, respectively. It is therefore feasible to perform serial studies safely if clinically indicated.

### Interpretation

Although cumbersome, these single injection filtration markers techniques provide a more accurate GFR reading than that obtained with traditional creatinine based methods. The GFR value obtained may be used uncorrected to evaluate changes in renal function for an individual patient. However, since GFR varies with age, gender, and body mass, it is recommended that a normalized GFR based on the standard body surface area of  $1.73\text{ m}^2$  be used for comparisons.

- Normal values are  $130\text{ mL/min}/1.73\text{ m}^2$  (men) and  $120\text{ mL/min}/1.73\text{ m}^2$  (women) with a variation coefficient of 14–18%
- Normalized GFR for the newborn is almost half that of the adult, with a gradual increase to adult values by the age 2
- GFR declines by roughly 1% per year after age 40
- Other factors affecting the GFR are time of day (10% higher in the afternoon than at midnight); pregnancy (up to 50% higher in the first trimester); high protein meal (gradual rise in GFR within an hour), and exercise (a transient reduction occurs)

### Advantages

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

### Drawbacks

- Invasive—repeated blood samples
- Involves a small amount of radiation
- Lengthy procedure
- Artifacts can be caused by inaccurate recording of times, tracer extravasation at injection site, significant edema, or ascites (due to altered body compartment distribution)

#### **(d) BONE SCAN**

##### **Overview**

- Bone scintigraphy is the most commonly performed nuclear medicine study
- Diagnostic accuracy of about 95% for skeletal metastatic disease
- Invaluable tool in the staging of urological cancers
- Primary urological malignancies (prostate and kidney) are a common cause of skeletal secondaries

The information provided by the bone scan reflects metabolic activity within the bones. The most commonly used disphosphonate tracer, <sup>99m</sup>Tc-methylenediphosphonate (medronate), is adsorbed onto the surface of bone crystals. The exact mechanism of this high phosphate uptake is unclear, but it reflects osteoblastic activity and skeletal vascularity at sites of active bone formation. Given its ability to detect the functional and metabolic response of bone to disease, the bone scan will often be positive even before plain X-ray changes are apparent. Bone scan findings are often non-specific and clues can be derived from the spatial distribution of activity throughout the skeleton and correlation with plain radiographic images. Serum markers of bone metabolic activity can prove useful and in rare instances a bone biopsy may be required to clarify the nature of a bone scan abnormality.

##### **Indications**

Although a number of other non-urological indications exist, the principal reasons for its use in the urological patient include—

- Staging of cancer (mainly prostate and kidney)
- Assessment of response to therapy in patients with cancer (e.g., prostate)
- Investigation of bone pain in urological patients
- Investigation of hypercalcemia

##### **Technique and radiation**

Medronate is a stable phosphate analog, with more than 50% of the administered activity concentrating in the bone and the rest rapidly cleared by the kidneys (by glomerular filtration). This allows good contrast between bone and soft tissue. The regional skeletal calcium content does not influence tracer uptake in bone. In addition, patients on oral bisphosphonate therapy do

not need to stop their medication as typical doses used in oral therapy do not affect medronate metabolism. However, intravenous treatment using large doses (e.g., for hypercalcemia) may temporarily reduce tracer uptake by normal bone and in such cases although bony metastases may still be visualized, it is recommended that bone scan be deferred for 4 weeks after completion of intravenous bisphosphonate therapy. No specific contraindications exist.

- The typical dose of 500 MBq may have to be increased for SPECT or pinhole (for small bones) imaging, and in patients unable to remain still for long enough. SPECT improves lesion detection rate and provides improved resolution images
- Patients are required to be well hydrated (500 mL of clear fluid between injection and imaging)
- Patients must also be instructed to void several times to decrease bladder radiation and residual urine volume which may obscure the sacral bone
- Although a three-phase study (arterial, blood pool, delayed static imaging) is performed for the detection of inflammatory conditions, this is rarely required in urological patients
- Maximal bone uptake occurs after 2 hours, so delayed static whole body imaging is typically performed after 3–4 hours. Longer intervals (6 h) are used for older and obese patients and those in renal failure
- Whole body images can be taken from a variety of angles and spot images of a specific area of interest are also useful. Image density can be affected by distance from the camera and malpositioning of the patient must be avoided

A typical dose of 500 MBq for bone scan corresponds to an effective radiation dose of 4.5 mSv (equivalent to 27 months of background radiation).

### **Interpretation**

#### ***Factors affecting bone scan***

A number of benign and malignant bone disorders may result in positive findings on the bone scan. Fractures, infections, necrosis, Paget's disease, degenerative changes and primary bone tumors are common causes. Other flaws may arise as a result of—

- Pronounced lumbar lordosis or scoliosis and may result in seemingly asymmetrical uptake

- Residual tracer in the urinary tract which may obscure skeletal areas of interest (consider catheterising the patient)
- Excessive patient movement during imaging
- Extravasation or spillage of tracer which may confuse analysis (remove/change clothing if required)

### ***The normal bone scan***

Assessment of the bone scan requires careful examination not only of the skeleton, but also the soft tissue and renal tract as a number of other incidental non-skeletal abnormalities may be found. In the normal adult—

- There is symmetrical uptake about the spine, with a virtual mirror image between the left and right hemi-skeleton
- There should be uniform uptake throughout the skeleton, although there is greater activity in sites of high metabolic activity, such as joint margins, weight-bearing areas, and points of muscle insertion

In children and adolescents, there is increased uptake at the epiphyseal growth areas.

Soft tissue like the urinary tract is virtually always visualised under normal circumstances. The absence of renal visualisation may suggest a “superscan”. The breast also often shows up in normal studies. Other organs may demonstrate increased uptake, often suggesting local pathological process (e.g., hydronephrosis).

### ***The bone scan in skeletal metastatic disease***

The majority of focal abnormalities, including bony metastases, appear as areas of increased tracer uptake (hotspots) (see Fig 4.4), but may in some instances be tracer poor. In general, a metastatic osteoblastic response is required for a positive hotspot on bone scan. For practical purposes, a negative result rules out the presence of metastatic disease, since false-negative results are rare. Although virtually any malignancy can spread to the bones, primary tumors in the prostate, breast, and lung are the common sources. Metastatic lesions are usually confined to the axial skeleton, but can sometimes affect the non-marrow-containing skeleton.

### ***The bone scan in metastatic prostate cancer***

- Roughly a third of patients with prostate cancer (CAP) will present with skeletal metastases

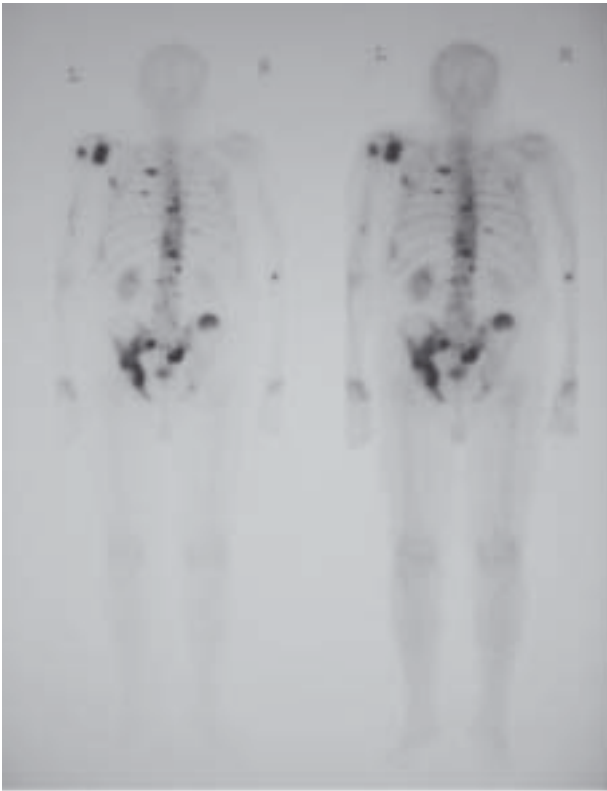


FIGURE 4.4. Bone scan showing widespread metastatic hotspots

- Typically, multiple sclerotic deposits are located in the pelvis and lumbar spine, although any part of the skeleton may be involved
- Skeletal spread is uncommon (<2%) in CAP patients with a PSA of <2 ng/mL and present in >90% of cases with a PSA >50 ng/mL
- Bone scans may also have a prognostic role in that mortality at 2 years in patients with and without a positive scan at presentation is 45% and 20%, respectively
- Endocrine treatment does influence bone scan results, with patients on hormonal manipulation for a period either demonstrating a negative bone scan (after being positive initially) or showing progression with appearance of new lesions

Though the precise role of bone scintigraphy in the management of CAP remains a subject of debate, the general indications specific to this disease include—

1. Staging patients with known CAP
2. Before embarking on radical treatment (even if PSA low)
3. In patients with a high PSA without histological confirmation of CAP
4. Increase in PSA in follow-up patients with CAP
5. New onset bone pain in CAP patients
6. To monitor treatment response

Patients with disseminated CAP may demonstrate a “superscan”, which is characterized by—

- A symmetrical increased uptake throughout the skeleton
- Minimal soft tissue activity
- Absent or dim renal outlining

Due to the increased skeletal uptake by the extensive metastatic disease, very little of the tracer is distributed to the soft tissue or excreted by the kidneys. In patients with suspected metastatic CAP, findings of absent renal tract opacification along with a generally widespread increase in skeletal uptake is suggestive of a “superscan”.

### ***The bone scan in renal cell cancer***

Bone scan is not indicated in the routine assessment of patients with kidney cancer since metastatic spread is uncommon in organ confined tumors. There is little evidence to advocate its routine use prior to radical surgery. In patients with skeletal involvement, the lesions often appear as large areas with a tracer-poor center surrounded by a rim of tracer activity. In some instances, these deposits may be completely photon deficient and another radiological technique (e.g., MR scanning) should be performed if clinical suspicion persists.

### ***Bone scan following therapy for tumors***

Bone scans are often performed in order to assess response to treatment. A favorable response following chemotherapy, hormonal manipulation, or radiotherapy will slow tumor progression and may also permit repair of bone affected by metastatic disease. In such cases, bone scan performed in patients with known bony metastases within 3–6 months of treatment will

usually be positive but may revert to being normal once osteoblastic bone repair is complete. It is worth noting that this may not necessarily indicate a favorable response to treatment, as the bone scan does not represent the primary tumor or any other coexisting non-skeletal metastatic spread.

### ***Bone scan versus other imaging techniques***

Although plain X-ray correlation is often suggested in indeterminate bone scan findings, it must be remembered that both imaging techniques assess different parameters. A plain radiograph is primarily dependent on the amount of calcification present in a lesion, while bone scintigraphy is a measure of local bone vascularity. Sclerotic activity may be readily demonstrated by plain X-ray, but in osteolytic lesion up to half of trabecular bone may have to be lost before becoming obvious on plain imaging. In addition, lesions smaller than 1 cm in diameter may be missed on plain X-ray, but are readily visible on bone scan.

MR scanning has a diagnostic accuracy approaching that of bone scintigraphy in the detection of skeletal metastases. Its other advantages are the lack of radiation and its ability to help discriminate between malignant and benign collapse of vertebral bodies and also reveal coexisting spinal cord compression. Bone scan, however, is more readily available and allows rapid assessment of the whole skeleton.

### **Advantages**

- Accurate method of bone metastases detection
- Whole skeleton imaged at once

### **Drawbacks**

- Requires radiation
- Lengthy procedure
- Low specificity for skeletal metastases
- Prone to artifacts

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## **(e) POSITRON EMISSION TOMOGRAPHY (PET) SCAN**

### **Overview**

In nuclear medicine studies, the planar imaging commonly utilized provides a tracer distribution image in two dimensions. The basic aim of PET scanning is to create an image representing three-dimensional (3D) distribution of tracer, by combining the use of positron-emitting radionuclides and emission CT. Initially,

a research tool for a number of years, PET scanning is now emerging as a useful clinical tool in the management of patients with a variety of pathological conditions, although its efficacy for the urological patient is still undetermined.

Certain radioisotopes decay by releasing positrons, which are positively charged electrons. These positrons travel short distances (less than 2.5 mm) and collide with other electrons, which results in the release of two high-energy (511 keV) photons emitted at 180° to each other. The PET scanner comprises several rings of multiple crystal detectors which detect the emitted photon, thereby reconstructing a 3D image of tracer distribution within the body.

One of the advantages of PET scanning is that it utilizes isotopes of elements ubiquitous in the human body and therefore is able to image physiologically important chemicals throughout the body, providing useful functional and metabolic information. Nevertheless, the majority of these have a very short half-life and are impractical for routine clinical use and mainly confined to the research laboratory. Half-lives of  $^{15}\text{O}$ ,  $^{13}\text{N}$ , and  $^{11}\text{C}$  are 2, 10, and 20 minutes, respectively.

The mainstay of clinical PET scanning is  $^{18}\text{F}$ fluorine (half-life 2 h) which is used to produce  $^{18}\text{F}$ fluorine-2-D-deoxyglucose ( $^{18}\text{F}$ FDG), an analog of glucose. FDG, like glucose, is preferentially transported in tumor cells via specific glucose transporters, due to their inherently increased rate of metabolism and glycolysis. Once within the cell, FDG undergoes phosphorylation by hexokinase to form FDG-6-phosphate, following which it becomes inert and takes no further part in glycolytic pathway. It remains trapped in the tumor cell, and subsequent accumulation will eventually increase tracer activity to levels detectable by the PET scanner. The tracer is excreted through the kidneys. Because small amounts of tracer can be visualized, early tumor detection is possible even before other cross-sectional imaging (like CT or MRI) can detect structural changes. Other tracers, apart from FDG, continue to be developed and tested but remain some way off from entering the clinical setting.

A dedicated full ring PET scanner is the gold standard, but it is expensive. An acceptable alternative is to use a modified multi-head gamma camera. This has the advantage in that it is cheaper and can be used for SPECT imaging. Though costly, a dedicated PET scanner is quicker, more sensitive, has superior resolution

compared to the gamma camera, and does not require a collimator. Combining a CT scanner and PET scanner within a single imaging scaffold will provide excellent anatomical as well as functional information and is likely to become the PET imaging technique of the future.

The majority of data on PET scanning arises from studies in brain metabolism and non-urolological cancers (e.g., lung, colorectal, head and neck, lymphoma). At present clear guidelines for the use of PET in the management of urological patients do not exist and clinical practice is based on local availability and physician preference. Data assessing PET performance in urological malignancies remains sparse and occasionally conflicting, although further evidence may confirm an emerging role.

### **Indications**

The non-urolological indications are not discussed here. Currently, though there are no absolute urological indications, PET may contribute in the following pathological processes:

- Testicular tumors
  - Primary tumor staging
  - Early detection of recurrent disease
  - Assessment of residual tumor burden after therapy
- Renal cell cancer
  - Initial staging of local and distant disease
  - Detection of recurrence
- Bladder cancer
  - Detection of recurrent disease (if other imaging ambivalent)
- Detection of bony metastases (if bone scan equivocal)

### **Technique and radiation**

There are no specific contraindications to PET scanning except for women who are pregnant and breastfeeding.

### ***Patient preparation***

- Patients advised to avoid food for 4–6 hours and oral intake restricted to non-sugary clear fluid
- Blood glucose estimation is performed just prior to the examination to ensure low glucose levels (high levels inhibit FDG uptake by cells)
- In addition, buscopan (20 mg) and/or diazepam may be administered to reduce FDG uptake by the intestines and muscles, respectively

- A preliminary background scan is performed before up to 400 MBq of FDG is injected intravenously
- Imaging is performed between 45 and 90 minutes after tracer injection
- A whole body scan can be performed or imaging restricted to the area of interest, with or without simultaneous CT scanning

A maximal injected dose of 400 MBq corresponds to an effective radiation dose of 10 mSv (equivalent to up to 6 years of background radiation).

### **Interpretation**

Since FDG-PET is a function of glucose metabolism, any organ with a higher metabolic rate will demonstrate greater tracer activity under normal circumstances (e.g., brain, intestines, liver, heart, etc.). Tracer uptake by malignant lesions will also depend on the rate of glycolysis. Although most tumors will demonstrate an inherently higher metabolic rate, some tumors (e.g., prostatic cancers) may have decreased proliferative activity and therefore not be apparent on PET images. The lower limit of the size of lesion detectable by PET scanning is 5 mm in diameter but is likely to improve in the future with improved resolution scanners.

### **Testicular tumors**

Results of PET in the management of testicular tumors show the most promise compared to other renal tract cancers.

- *Primary disease:* PET has a superior performance profile than conventional imaging. CT scan has been reported to have false-negative and false-positive rates of as high as 59% and 25%, respectively, in low-stage disease. By contrast, a number of studies have demonstrated a higher specificity (87–100%), higher sensitivity (70–100%), and better negative predictive value for PET compared to CT scanning. If metastatic disease at presentation is obvious after conventional imaging, then PET has a rather limited role. It may, however, be of value in the assessment of patients with stage II disease and could potentially alter management. Furthermore, emerging evidence may suggest a role for PET in predicting response to chemotherapy, but more data is required
- *Recurrent disease:* patients presenting with raised tumor markers following previous therapy can represent a diagnostic

dilemma, especially if conventional imaging is negative. PET scan performs better than CT in this instance and is more likely to detect recurrent disease earlier than CT or MRI. Some authors have advocated the use of PET as first line investigation in patients with suspected recurrence

- *Residual tumor:* PET can play a significant role in the treatment of patients with residual mass following radiotherapy or chemotherapy for seminoma. CT cannot confidently discriminate between malignant and fibrotic/necrotic tissue in up to 50% of cases. The positive predictive value of PET in such patients is between 80% and 96%. A negative PET scan is indicative of non-cancerous tissue in 88–90% of cases. Thus it is in this category of patients that PET has been found to be most useful

#### ***Renal cell cancer (RCC)***

- *Primary disease:* even though the normal kidney will demonstrate FDG uptake, PET performs as well as CT in the characterization of a renal lesion as benign or malignant. Some renal cell cancers may be PET negative and therefore may be missed. Overall, PET is more likely to detect unsuspected metastatic disease compared to CT and this may hugely influence treatment options. Nevertheless, PET is not routinely indicated prior to radical nephrectomy at present
- *Recurrent disease:* PET can confidently distinguish between malignant and benign disease in patients with a previous history of RCC, presenting with a subsequent indeterminate lesion, in 75–100% of cases. Lymph node involvement and local or distant spread can be effectively identified by PET

#### ***Bladder cancer***

Because of the urinary excretion of FDG, visualization of the bladder is difficult, and PET is not currently indicated in local staging of bladder cancer. Accuracy of lymph node detection is marginally better than with CT or MRI scan and further work is required in this subset of patients.

#### ***Prostate cancer***

Slow glycolytic rates (resulting in poor FDG uptake), low-volume tumors, and suboptimal visualization of the prostate area (due to tracer accumulation in the bladder) have meant that PET has a rather limited role in investigating localized prostate cancer. It may, however, be useful in the detection of metastatic lymph

nodes, recurrent distant disease, and to monitor treatment response (e.g., to androgen deprivation). Emerging new tracers, including  $^{11}\text{C}$ -methionine (amino acid tracer),  $^{11}\text{C}$ -choline, and  $^{11}\text{C}$ -acetate (both lipid based tracers) have shown promising results compared to FDG, but sparse data and their relatively short half-lives have made routine clinical use difficult.

PET is inferior to conventional bone scintigraphy in the detection of skeletal metastases but can be used to provide additional information if the latter is equivocal.

**Advantages**

- Uses biologically important radionuclides to provide pertinent functional and metabolic information
- Proven efficacy in other non-urological cancers
- Generally high specificity for malignant disease
- Whole body can be imaged at once
- Spatial resolution of 5 mm
- Can be combined with simultaneous CT to improve image resolution

**Drawbacks**

- Involves radiation
- Length of procedure
- Expensive (cost of collimator, scanner, and radiochemistry facility is high)
- Radionuclides with a short half-life may need to be produced on site
- Lack of anatomical landmarks (especially in the thorax and abdomen)
- Urinary excretion limits detection of bladder and prostate malignancies

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