Investigative

Intravenous urography
Confirm indication
Exclude contraindications

Absolute	Pregnancy
	Contrast anaphylaxis
	UnRx hyperthyroidism
Relative	Previous contrast allergy
	Renal impairment
	Lactation and seafood allergy not a problem

Preliminary (control) film	(35 x 43cm) supine KUB	Opacities, soft tissue outlines etc.
Immediate*	(24 x 30cm)	Nephrograms
5 minute	(24 x 30cm +/- compression)	Pelvicalyceal systems: symmetry, filling
15 minute	35 x 43cm release if compression has been applied)	pelvicalyceal systems and ureters
25 minute	(24 x 30cm) 15° caudal angulation centred 5 cm above upper border of symphysis pubis	Distended bladder
Post-micturition	(24 x 30cm) 15° caudal angulation centred 5 cm above upper border of symphysis pubis	Distal ureteric drainage, bladder emptying

Bolus dose	eg. 50ml Omnipaque (350mg/ml)
Additional films	inspiratory/expiratory, tomography, prone, delayed Tomography at 9cm means F2 located 9cm from loin skin - therefore 9cm = upper pole, 11cm lower pole Prone films – contrast heavy, therefore tends to pool in kidney when supine; prone more readily identifies level of obstruction

Contrast media and reactions
All contrast agents have a 2,4,6-tri-iodinated benzene ring.
Relatively constant half-life ~1 hour
Maximum dose 1ml/kg standard strength iodine solution
Type of molecule at position 1 important: carboxyl group = ionic dissociation (high osmolar contrast media); hydroxyl group = water soluble (low osmolar contast media)
Allergy, anaphylaxis, renal failure and lactic acidosis important side effects of contrast administration
Side effects 5 x higher with high osmolar (ionic) contrast media

Increased risk of severe reaction in patients with history od severe allergy, asthma (6x)

	Ionic high osmolar (1200 mosm/l)	Non-ionic low osmolar (600 mosm/l)
Allergy	1:50	1:250
Non-fatal anaphylactoid	1:500	1:2500
Fatal anaphylactoid	1:100,000	1:100,000

Ultrasonography

Piezoelectric effect

Electrically induced oscillation of crystal - sound waves (frequency > 20,000 cycles per second or 20 KHz) - interact with tissues causing reflection, refraction and absorption.

Water = good transmission, low reflection BLACK
Fat = poor transmission, high refelction WHITE

Increased frequency – improved resolution but decreased penetration

Standard probe frequency

Renal 3.5 MHz
Rectal 7 MHz
Testis 7-10 MHz
Penis 7-10MHz

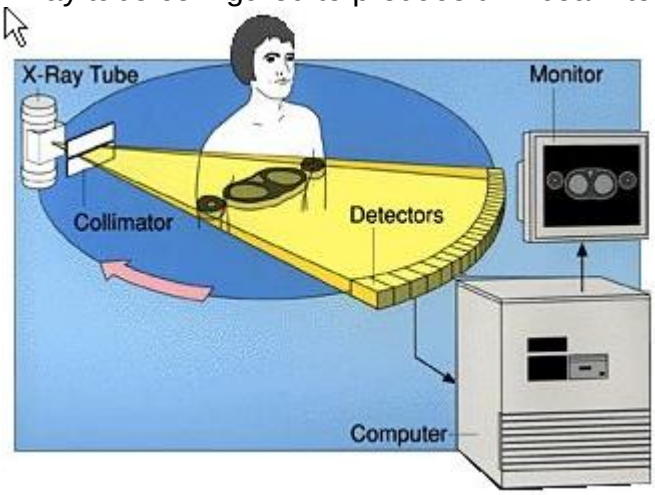
Doppler effect – denotes frequency shift in wave intereacting with a moving object. Degree of change in frequency proportional to velocity

Doppler effect can be enhanced by injection of stable microbubbles – not commonly performed however

Computed tomography

Fixed X-ray tube with arc of detectors arrayed opposite

X-ray tube configured to produce thin beam towards detectors



X-ray tube and detector array housed within gantry which can rotate 360 degrees around patient.

Individual ‘snap shots’ taken at defined intervals during rotation – typically 1000 per revolution.

By using rotation, individual attenuation values can be generated for a particular area of tissue (known as a voxel)

Sophisticated software reproduces image slices

Hounsfield units

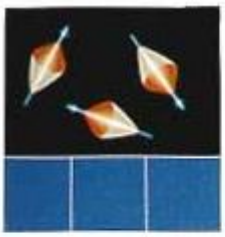
Bone	+1000 HU
Water	0 HU
Fat	-50 to -100 HU
Air	-1000 HU

Contrast enhanced CT (4 phase)

- Unenhanced scan
- IV contrast runs

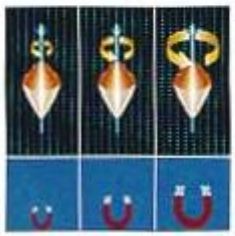
Arterial phase	15-30s
Late arterial (portal venous)	45-60s
Nephrographic phase	75-90s
Excretory phase	180s +

<u>Magnetic resonance imaging</u>

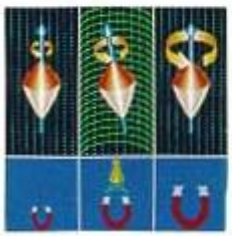


1. Hydrogen protons, positively charged particles in the hydrogen molecule's nucleus, normally spin in random directions

3. A brief radio signal, whose soundwave frequency equals the frequency of wobble of certain protons, knocks those protons out of alignment



2. Protons wobble in alignment with magnetic fields of varying intensity; frequency of wobble is proportionate to strength of individual magnetic field



4. When radio signal ceases, protons snap back into alignment with magnetic field, emitting a radio signal of their own, that announces the presence of a specific tissue

T1-weighted images

- Measures time taken to reach equilibrium in z-axis
- Fat white, water black
- Better for anatomy
- Gadolinium enhances T1-weighted images

T2-weighted images

- Measures time taken to reach equilibrium in xy axis
- Fat white, water white
- Better for pathology

STIR (Short Tau-T1 inversion recovery)

- T2 with fat suppression (fat black)

FLAIR

- T2 with water suppression (water black)

Prostate MRI

- T2 offers excellent visualisation of zonal anatomy
- NVB, DVC and seminal vesicles all bright on T2 images
- Prostate cancer low signal on T2 images

Guidelines for use of gadolinium chelates

Definition	Nephrogenic systemic fibrosis (NSF) is a severe delayed fibrotic reaction of the tissues to some gadolinium-based contrast media (Gd-CM)
1. Clinical features	• NSF may develop from the day of exposure for up to 2–3 months • Starts with red, painful, itchy swellings on the legs and arms • May be localised and non-progressive • May progress to extensive fibrotic lesions of the skin and subcutaneous tissues and sometimes of the internal organs • Fatal in a proportion of cases
2. Patient-related risk factors	• Renal impairment (GFR <60 ml/min/1.73^2), including patients on dialysis • Liver transplant patients who had or are waiting for a transplantation with any degree of renal impairment • Age under one year, because of immature renal function. *Note*: 1. NSF has not been reported in patients with GFR >60 ml/min/1.73m^2 2. The role of other possible co-factors is not proven.
3. Contrast medium-related risk factors	• Less stable Gd-CM (linear agents) • NSF has occurred following the administration of: – Omniscan (gadodiamide, linear chelate) – Magnevist (gadopentetate dimeglumine, linear chelate) – OptiMARK (gadoversetamide, linear chelate).
4. Screening for renal dysfunction before Gd-CM	• Mandatory if considering the use of Gd-CM associated with the development of NSF (Omniscan, Magnevist, OptiMARK)
5. To reduce the risk of NSF in MR examinations in definably at-risk patients *(See 2 for at-risk patients)*	• Use a GD-CM with high stability (Please see Appendix 1) • Give the lowest dose possible to achieve a diagnostic examination • Allow at least one week before giving more Gd-CM • Do not use Omniscan (gadodiamide); Magnevist (gadopentetate dimeglumine) or OptiMARK (gadoversetamide). ***Note: Do not deny at-risk patients clinically important MR examinations.***
6. Radiographic examinations	• Do not use Gd-CM for X-ray examinations[5]
7. Pregnant patients	If the use of a Gd-CM agent is essential, whatever the maternal renal function, choose the most stable Gd-CM in the lowest possible dose to protect the fetus.

High stability gadolinium chelates comprise non-ionic cyclic structure, enclosing gadolinium molecule. Examples include gadovist™ and prohance™

MRI and ferromagnetism

Possible contraindications include intracranial clips, intraocular foreign bodies, pacemakers, defibrillators, neuromodulators and prosthetic heart valves. Surgical clips are invariable surrounded by fibrosis by 6 weeks post-op. Frank Shellock has produced an exhaustive database ('The List') which can be used to determine whether it is safe to proceed, dependent on the type of internal implant (www.mrisafety.com).

Nuclear scintigraphy

Typically labelled with 99-metastable technetium: produced from molybdenum 99 generator – half-life 6 hours

DMSA ^{99m}Tc-labelled dimercaptosuccinic acid

DTPA ^{99m}Tc-labelled diethylenetriaminepentamic acid

MAG-3 ^{99m}Tc-labelled dimercaptoacetyltrigycine

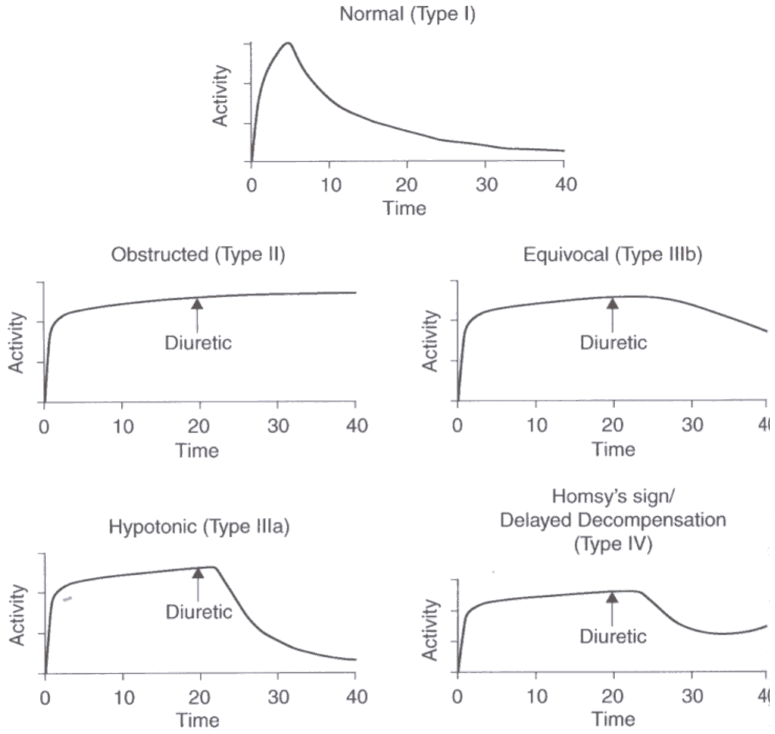
10% filtered, 90% secreted

Static renal scanning (not technically renography as not dynamic)

Usually 2-3 hours between injection and scanning – similar to bone

Dynamic renography:

- Vascular phase 0-10 s
- Uptake phase 10s – 5mins used to calculate split function
- Excretory phase 5 mins onwards
- Diuretic administration
  - Maximum effect of frusemide after 18 mins
  - Therefore maximum effect at 38 mins on standard F+20
  - Equivocal rate of 15% for F+20; most accurate F-15 (reduces equivocal rate to ~7%) but difficult to perform. F+0 compromise.
- Interpretation
  - I Normal
  - II Obstructed
  - IIIa Hypotonic (Baggy)
  - IIIb Equivocal
  - IV Delayed decompensation (Homsey's curve) – obstruction with increased urinary flow
  - NB. F-15 renogram recommended for Type IIIb and IV curves



Bone scintigraphy

Utilises ^{99m}Tc labelled methylene diphosphonate (simple bisphosphonate)

Injection typically followed by scanning after 2-3 hours

Positron emission tomography

Fluorodeoxyglucose (FDG): cancer a/w higher rates of glycolysis. Therefore FDG transported to cells and phosphorylated for breakdown. Increased accumulation of intermediate FDG-6 phosphate in cancer cells cf. normal. FDG-6 releases 18-fluoride labeled positrons. Positrons collide with electrons, destroying them and releasing 2 gamma photons 180 degrees to each other. Multiple emissions effectively pinpoint tumour by intersection of multiple 'lines' of photon pairs. CT scanner in same housing can then be used to locate source of emission.

FDG excreted through kidneys - therefore probs with urology imaging. Newer agents such as carbon-11 labelled acetate targets altered lipid synthesis in tumours and not excreted via kidneys.

Compared with conventional imaging:

- Increased resolution of small lesions
- Better benign vs. malignant primary tumour
- Better for recurrence vs. scarring
- Better for benign vs. malignant lymph nodes

Specific tumour types:

1. CaP
   - Low glucose metabolism and slow turnover limits usefulness of ^{18}F-FDG
   - Overlap BPH vs CaP; low sensitivity for LN and bone mets; unreliable for recurrence vs scar after RRP
   - ^{11}C-acetate better for primary tumour
   - ^{11}C-choline promising for metastases
2. RCC
   - Renal excretion of ^{18}F-FDG hampers use in primary tumour
   - Reasonable for renal bed recurrences and metastases but CT better
3. Bladder cancer
   - Renal excretion and bladder accumulation of tracer makes bladder imaging difficult
   - Better than CT/MRI for lymph node and distant mets
4. Testicular cancer
   - Strongest indication in genitourinary tumours
   - Better than conventional imaging for primary staging and follow-up
   - **Investigation of choice for evaluation residual masses after chemotherapy for seminoma** (SEMPET study – correctly identified 19/19 >3cm and 35/37 < 3cm).
   - Cannot identify mature teratoma – therefore limited effectiveness for residual masses after chemotherapy for NSGCT

Effective dosage

1 Gray (Gy) is the absorption of 1 joule of energy

Measured in Sieverts

Formula Sievert = Gray x Q x N Q – type of radiation
N – tissue type, vol and time

CXR	0.02 mSv
KUB	0.5 mSv
Renogram	0.8 mSv

IVU (3-shot)	1.5 mSv
CTKUB	4.7 mSv
CTU	10.0 mSv

Technical

Radiofrequency ablation

First utilised in 1911, when electrical current used to heat probes for treating bladder tumours

First use of RFA to treat renal tumours 1997 (Zlotta 1997)

Mechanism:

- High-frequency electrical current (4-500 kHz)
- Tissue resistance leads to ionic vibration, generating kinetic energy and tissue heating
- Tissue damage = coagulative necrosis (also ischaemic necrosis 2' to vessel thrombosis)
- Extent of tissue damage
  - distance from probe (electrical decay)
  - resistance characteristics of treated tissue (tissue impedance), blood supply (tissue cooling)
- RFA delivered either by temperature control or impedance control – equivalent ablative zones either control
- Animal studies have shown that only relatively small tumours may be treated with RFA.
- Recently it has been shown that eschar increases impedance. Newly-developed wet-RFA uses saline to flush eschar and enhance electricical conductance, leading to larger ablative areas (Tan BJ 2004)
- Multi-tined RFA probes may be able to increase the ablative area.

Cryoablation

First used for palliation of malignancy in 1850 by James Arnott (Lancet 1850)

Dr Irving Cooper neurosurgeon father of modern cryoablation

Beneficial effects of very localised tissue damage with minimal collateral damage now fully appreciated.

Mechanisms:

- Cell death through freeze-thaw cycles
- Pressurise argon forced through a probe resulting in dramatic cooling due to the Joule-Thompson effect. Helium used to re-warm tissue.
- Alternate cycles of cooling/re-warming induce the freeze-thaw effects.

  "In physics, the Joule–Thomson effect effect describes the temperature change of a gas or liquid when it is forced through a valve while kept insulated so that no heat is exchanged with the environment. At room temperature, all gases except hydrogen, helium and neon cool upon expansion by the Joule-Thomson process."

- Intracellular ice crystal formation – intracellular organelle, cytoskeleton and membrane disruption
- Temp required approx. -40 to -50'C to induce complete cell death.
- Typically two cycles necessary

Real-time intra-operative ultrasound performed to monitor size of ice-ball.
Following removal of probe, haemostatic agents and argon beam coagulator used to obtain control of bleeding.

HIFU

High intensity focused ultrasound. Probe focal length varies from 3-4.5 cm in 5 mm graduations. Probe surrounded by water-inflatable sheath, to ensure gas-free contact with rectal wall. Target area imaged, probe fixed in place with multi-articulated arm. Treatment cycle = 4 secs of heat (us intensity of 1.68 kW/cm2), tissue temp of 80-100c. Tissue allowed to cool for 12 secs. Volume treated per cycle = 2x2x10mm vertical cigar-shaped area. Work from BN to veru in one plane then, rotate scope and repeat, working in a circumferential manner. SPC required. Initially used for BPH, current interest in salvage Rx post-DXT. GA/spinal required, takes 1-4 hours. Days to months required for necrosis. Gland volumes < 40cc. Adverse effects associated with salvage HIFU include rectourethral fistula in 6%, severe incontinence in 7%, and bladder neck stenosis in 17%

Uroflowmetry

Paper speed 0.25 cm/s
(i) Weight transducer – weighs voided volume against time
(ii) Rotating disc – spinning disc onto which the urine falls. The disc is kept spinning at the same rate, regardless of the volume of urine hitting the disc. The increase in power required to achieve this is proportional to the flow rate.
(iii) Capacitance flow meter – metal strip capacitor, held vertical in urine collection vessel. The solutes in urine change the capacitance across this strip, and this can be converted to give the flow rate.
NB. Time to maximum flow usually within first third of void.

Levels of Evidence

NICE recommends using SIGN guidelines for levels of evidence:

Level of evidence	Type of evidence
1^{++}	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1^{+}	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*
2^{++}	High-quality systematic reviews of case–control or cohort studies High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2^{+}	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2^{-}	Case–control or cohort studies with a high risk of confounding bias, or chance and a significant risk that the relationship is not causal*
3	Non-analytic studies (for example, case reports, case series)
4	Expert opinion, formal consensus
*Studies with a level of evidence '–' should not be used as a basis for making a recommendation (see section 7.4)	