BOOK CHAPTER

Introduction – The role of imaging in teaching and diagnosis: technical aspects and applications

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& Abrahams' Imaging Atlas of Human Anatomy, x-xv

...le role of imaging in anatomical education

Imaging has become an increasingly important component in the field of medical anatomy instruction since the 1960s, and in most academic curricula today it has been integrated as a part of anatomical education, albeit taught using a very wide variety of strategies with considerable variation in the time allocation, content and delivery. Medical students unanimously agree that early radiology exposure is beneficial not only to their anatomical education but to their careers, with early exposure to multi-modality imaging techniques being particularly beneficial. In particular, clinical imaging tutorials have been shown scientifically to enhance anatomy education, and self-guided radiology tutorials, such as those accompanying this book, are becoming an increasingly promising learning solution in a flexible environment throughout the entirety of medical school, into junior doctor training and beyond, especially given the overall trend of decreasing time in anatomy instruction under the increasing envelope of vertical integration.

Most publications conclude that imaging enhances the quality and efficiency of instruction in human anatomy and that a relative standardisation could be useful in improving the teaching of imaging anatomy and could facilitate its assessment, thus reinforcing its effectiveness. Although more medical schools around the world are using medical imaging to teach anatomy, some regions, such as the US, show a decline in the proportion of imaging taught by radiologists. Radiology as a specialty must overcome several challenges for it to become more involved in anatomy education, including teaching incentives and protected academic time.

Recent technical advances in diagnostic radiology, such as multi-planar imaging, virtual endoscopy and functional, molecular and spectroscopic magnetic resonance imaging (MRI), as described later in this introduction, offer new ways in which to use imaging for teaching. This coupled with the broad dissemination of picture archiving and communications systems is making such revelatory images readily available to medical schools, providing new opportunities for the incorporation of diagnostic imaging into the undergraduate medical curriculum, in which current reforms on a background of the establishment of new medical schools in the UK further underline the prospects for an expanding role for imaging in medical education.

Plain radiography and legal responsibilities of diagnostic radiation exposure

A ‘plain film’ is an X-ray radiograph taken without the use of a barium- or iodine-based contrast agent. In an X-ray tube, thermionic emission from a heated cathode generates electrons which are accelerated through kilovoltage to collide with a rotating tungsten target, creating X-rays that pass through the body, today captured by a digital detector rather than photographic film. Four densities are demonstrated: gas (shown in black), fat (dark grey), soft tissue/fluid (light grey) and bone/enamel/calcification (white).

At diagnostic energies, X-ray photons interact with atomic electrons of tissues either through the photoelectric effect at lower energies with total photonic absorption (with the emergence of a highly energetic electron) or via Compton scatter at higher X-ray energies– the freeing of a lower energy outer electron and a deflected less energetic X-ray photon. These emergent electrons create highly reactive ions that alter chemical bonds in tissue, inducing cancer with a latent period of years or decades after exposure.

X-rays were discovered by the German Wilhelm Roentgen in 1895, gaining him the first Nobel Prize for Physics in 1901. In 1896 Major John Hall-Edwards made the first use of X-rays diagnostically at Birmingham General Hospital when he radiographed a needle stuck in a colleague’s hand. A month later he took the first radiograph to direct a surgical operation. His left arm was amputated in 1908 due to X-ray dermatitis.

Today in the UK the Ionising Radiation (Medical Exposure) Regulations define the legal standards and aims of the justification process for analysis of the risk/benefit ratio to patient radiation exposure, whether X-rays generating plain films, contrast studies or computed tomography (CT) or particulate radiation generating nuclear medicine or antimatter generating positron

emission tomography (PET) images. The criminal law states the referrer is responsible for the provision of sufficient clinical information to enable justification, involving consideration of the appropriateness of each and every request, optimisation of the imaging strategy, analysis of risk versus benefit, understanding of the immediate and cumulative radiation effects, consideration of age-specific issues (e.g. seeking alternative non-ionising radiation procedures in children and younger adults), the urgency of the exposure (e.g. in potential or actual pregnancy), the efficacy of imaging in different clinical situations and appropriate delegation. The referrer has a legal responsibility to ensure the completeness and accuracy of data relating to the patient's condition and to be kept fully informed about patient history, the presenting complaint and relevant physical signs, past history and previous imaging. If an inappropriate exposure occurs, legally termed a 'radiation incident', this must be reported by law to the local Radiation Protection Advisor and then to the Department of Health in London.

The diagnostic value of plain films is greatly enhanced with full, legible and accurate clinical information. It is best practice to record immediate interpretation of plain films in the medical notes, and legally compulsory if there are no arrangements for formal reporting.

Angiography/interventional radiology

Angiographic imaging began in 1927 by Egas Moniz, a physician and neurologist, with the introduction of contrast X-ray cerebral angiography. In 1949 he was awarded the Nobel Prize for his work. The field of angiography however was revolutionised with the advent of the Seldinger technique in 1953, in which no sharp needles remained inside the vascular lumen during imaging.

Although the field of angiography began with X-ray and fluoroscopic imaging of blood vessels and organs of the body by injecting radio-opaque contrast agents into the blood, it has evolved to so much more. Many of the procedures performed by angiography can be diagnostic; as newer techniques arose, it has allowed for the advent of minimally invasive procedures performed with image guidance and thus the name change of the discipline to 'interventional radiology' (or vascular and interventional radiology).

Angiograms are typically performed by gaining access to the blood vessels; whether this is through the femoral artery, femoral vein or jugular vein depends on the area of interest to be imaged. Angiograms can be obtained of the brain as cerebral angiograms, of the heart as coronary angiograms, of the lungs as pulmonary angiograms and so on. Imaging of the arterial and venous circulation of the arms and legs can demonstrate peripheral vascular disease. Once vascular access is made, then catheters are directed to the specific location to be imaged in the body by the use of guide wires. Contrast agents are injected through these catheters to visualise the vessels or the organ with X-ray imaging.

In addition to diagnostic imaging, treatment and/or interventions can often be performed through similar catheter-based examinations. Such procedures might involve angioplasties where a balloon mechanism is placed across an area of narrowing, or stenosis, in a vessel or lumen.

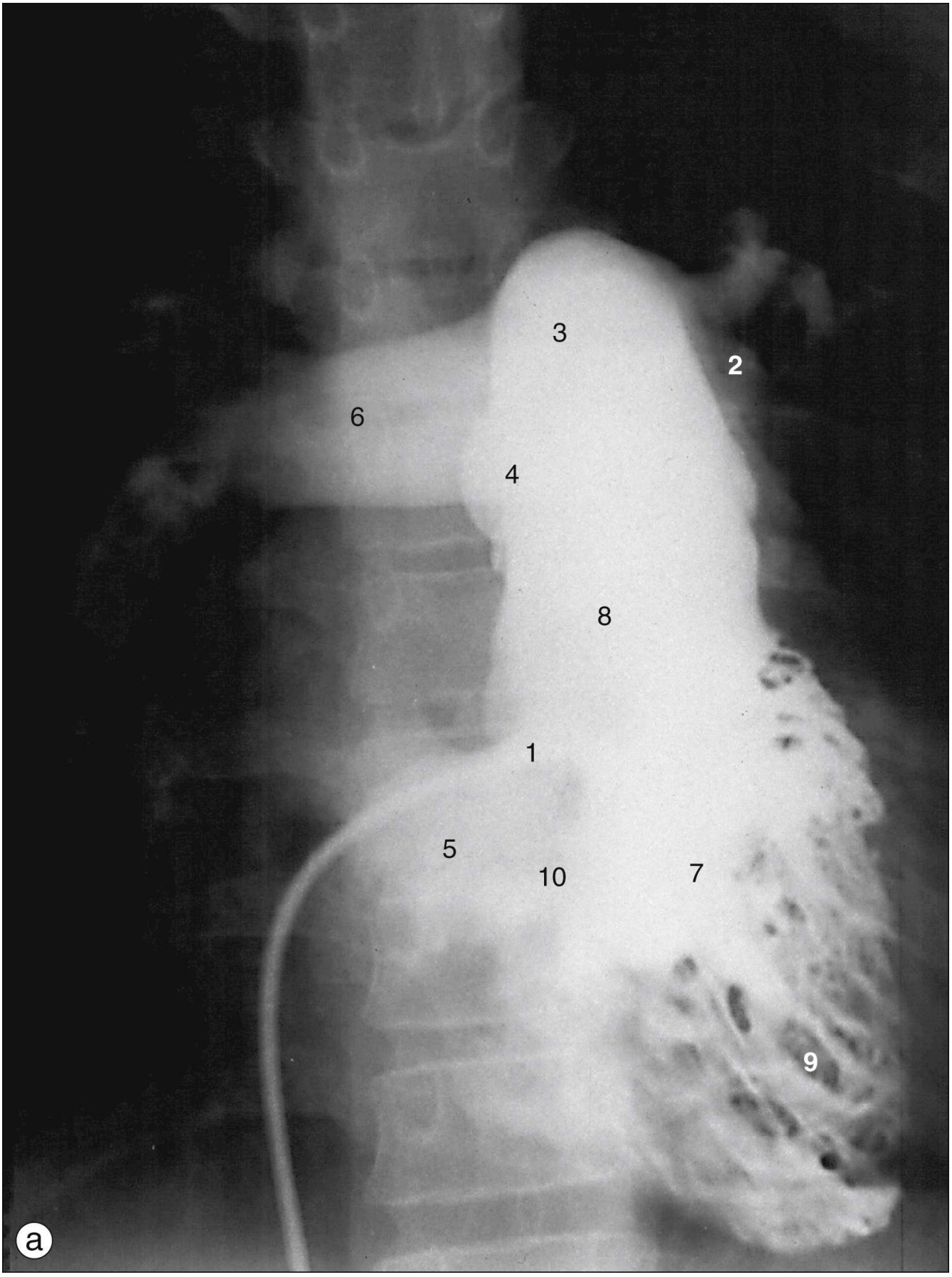
With controlled inflation of the balloon, the area of narrowing can be widened. Often to keep these areas from narrowing again, stents can be placed within the lumen of the vessel or even in the trachea or oesophagus.

Imaging in diagnostic or interventional procedures can be still images or motion (cine) images. The technique often used is called 'digital subtraction angiography'. In this type of imaging, images are taken at 2–30 frames per second to allow imaging of the flow of blood through vessels. A preliminary image of the area is taken before the contrast is injected. This 'mask' image is then electronically subtracted from all the images, leaving behind only the vessels filled with contrast. This technique requires the patient to remain motionless for optimal subtraction.

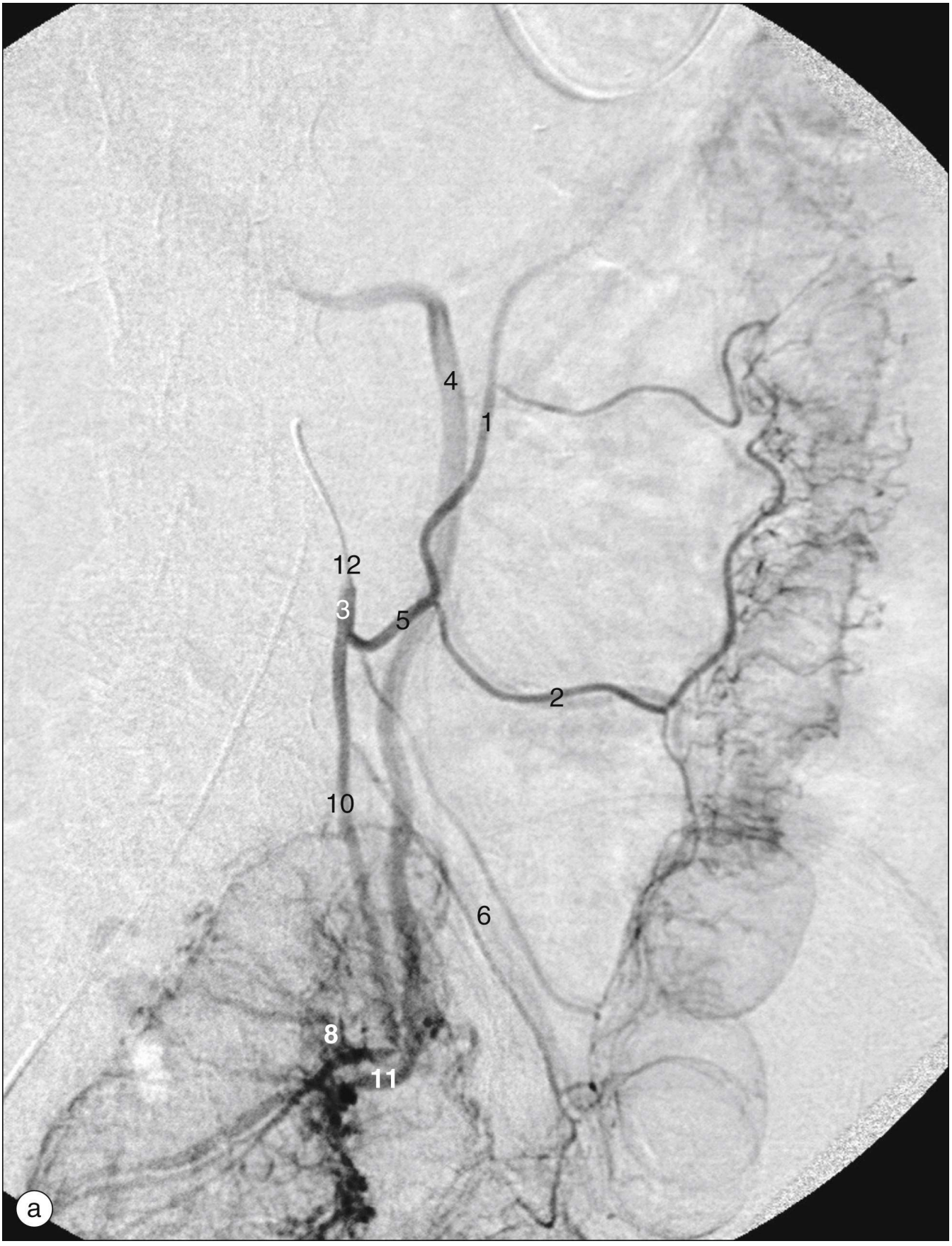
Angiograms can be performed of the heart to visualise the size and contractility of the chambers and anatomy of the coronary vessels. The thorax can also be studied to evaluate the pulmonary arteries and veins for vascular malformations, blood clots and possible origins of haemoptysis. The neck is often imaged to visualise the vessels that supply the brain as they arise from the aortic arch to the cerebral vessels, in the investigation of atherosclerotic disease, vascular malformations and tumoural blood supplies. Renal artery imaging can elucidate the cause of hypertension in selected patients, as can imaging of the mesenteric vessels discover the origin of gastrointestinal bleeding or mesenteric angina.

In addition to angiograms and venograms, the field of interventional radiology also performs such procedures as coil-embolisation of aneurysms and vascular malformations, balloon angioplasty and stent placement, chemoembolisation directly into tumours, drainage catheter insertions, embolisations (e.g. uterine artery for treatment of fibroids), thrombolysis to dissolve blood clots, tissue biopsy (percutaneous or transvascular), radiofrequency (RF) ablation and cryoablation of tumours, line insertions for specialised vascular access, inferior vena cava filter placements, vertebroplasty, nephrostomy placement, gastrostomy tube placement for feeding, dialysis access, transjugular intrahepatic porto-systemic shunt (TIPS) placement, biliary interventions and, most recently, endovenous laser ablation of varicose veins.

Right ventricular angiogram (p. 127).



Inferior mesenteric arteriogram (p. 192).



Computed tomography

The limitation of all plain radiographic techniques is the two-dimensional representation of three-dimensional structures: the linear attenuation coefficient of all the tissues in the path of the X-ray beam form the image.

CT obtains a series of different angular X-ray projections that are processed by a computer to give a section of specified thickness. The CT image comprises a regular matrix of volumetric elements (voxels). All of the tissues contained within the voxel attenuate the X-ray projections and result in a mean attenuation value for the voxel. This value is compared with the

attenuation value of water and is displayed on the Hounsfield scale. Water by definition has an attenuation of 0 Hounsfield units (HU); air typically has an HU number of–1000; fat is approximately–100 HU; soft tissues are in the range +20 to +70 HU; and bone >+400 HU.

Modern multi-slice helical CT scanners can obtain images of the whole body in as little as a few seconds, allowing dynamic imaging of arteries and veins at different times after the injection of intravenous contrast agents. The continuous acquisition of data from a helical CT scanning allows reconstruction of an image in any plane (multi-planar reconstruction [MPR]), commonly sagittal and coronal and axial. This orthogonal imaging greatly improves the understanding of the three-dimensional aspects of pathological radiological anatomy.

No specific preparation is required for most CT examinations of the brain, spine or musculoskeletal system. Studies of the chest, abdomen and pelvis usually and those of the brain with complex histories require intravenous contrast medium that contains iodine, defining vascular relationships and discerning normal and pathological soft tissues to a greater extent. Opacification of the bowel in CT studies of the abdomen and pelvis can be accomplished by oral ingestion of a water-soluble contrast medium from 24 hours prior to the examination to show the colon, combined with further oral intake 0–60 minutes prior to the scan, for outlining the stomach and small bowel. This is much less frequently performed with the latest generation of scanners that exquisitely differentiate different enhancing layers within the bowel wall. CT colonography, in which the colon is pre-prepared with ingested contrast medium and insufflated with gas immediately prior to the scan, is also known as virtual colonscopy and has become an increasingly popular alternative procedure for bowel cancer screening in select patients.

Generally all studies are performed with the patient supine, and images are obtained in the transverse or axial plain. Modern CT scanners allow up to 25 degrees of gantry angulation, which is particularly valuable in spinal imaging. Occasionally, direct coronal images are obtained in the investigation of cranial and maxillofacial abnormalities; in these cases the patient lies prone with the neck extended and the gantry appropriately angled, but this technique has largely been superseded by the orthogonal imaging described above. CT for the investigation of urinary tract calculi can be obtained in the prone position to show that a calculus is not lodged at the vesico-ureteric junction, while CT colonography involves scanning in several different positions, e.g. supine and in the lateral positions.

Magnetic resonance imaging

MRI produces images by first magnetising the patient in the bore of a powerful magnet and then broadcasting short pulses of RF energy at 46.3 MHz, the resonance frequency of mobile protons (hydrogen nuclei) found in the fat, protein and water of body soft tissues and bone marrow. Resonance of magnetically aligned spinning hydrogen nuclei protons occurs due to their behaviour akin to tiny bar magnets, aligning either with or against the magnetic field, producing a small net magnetic vector. This temporary energy store within altered resonated nuclear states is rapidly given up as radio waves, ‘RF echoes’, which enable the density and location of these single-proton hydrogen nuclei to be exactly correlated using complex mathematical algorithms (Fourier transformation) into an image matrix.

RF energy from various types of coil, some built into the scanner and some attachable to specific body parts, generates a second magnetic field, perpendicular to the static magnetic field, which rotates or ‘flips’ the protons away from the static magnetic field. Once the RF pulse is switched off, the protons flip back (relax) to their original position of equilibrium, emitting the RF energy they had acquired into the antenna around the patient, which is then amplified, digitised and, finally, spatially encoded by the array processor.

MRI systems are graded according to the strength of the magnetic field they produce. Routine high-field systems are those capable of producing a magnetic field strength of 3–8 T (Tesla) using a superconducting electromagnet immersed in liquid helium. Open magnets for claustrophobic patients and limb scanners use permanent magnets between 0.2 and 0.75 T. For comparison, the earth’s magnetic field varies from 30 to 60 uT. MRI does not present any recognised biological hazard. Patients who have any form of pacemaker or implanted electro-inductive device, ferromagnetic intracranial aneurysm slips, certain types of cardiac valve replacement and intra-ocular metallic foreign bodies must never be examined due to high risk of death or blindness. Many extra-cranial vascular clips and orthopaedic prostheses are now ‘MRI friendly’, but these may cause local artefacts, although newer sequences exist to reduce artefact. Loose metal items, ‘MR unfriendly’ anaesthetic equipment and credit cards must be excluded from the examination room. Pillows containing metallic coiled springs have been known to near suffocate patients, and heavy floor buffing equipment has been found wedged in the magnet bore due to suboptimally informed domestic staff!

T1-weighted images best accentuate fat and other soft tissues, nicknamed the ‘anatomy weighting’ amongst radiologists who publish or teach anatomy. Fluid is low signal. T2-weighted images reveal fluid as high signal as well as fat. Fat suppression sequences using T2 fat saturation (T2FS) or short tau inversion recovery (STIR) are very sensitive in highlighting soft tissue or bone marrow oedema that almost invariably accompanies pathological states such as inflammation or tumour. Contrast-enhanced images with gadolinium, when essentially used with T1 fat saturation (T1FS) sequences, also exquisitely directly highlight hypervascularity, particularly that associated with tumours and inflammation, especially in pathologies causing neuraxial breakdown of the blood–brain barrier. Metallic artefact reduction sequences (MARS) are superior in imaging periprosthetic soft tissues after joint replacement or other orthopaedic metalwork implantation.

High-field-strength magnets of course give significant improvement in spatial resolution and contrast. MR images have been acquired at 8 T of the microvasculature of the live human brain allowing close comparison with histology. This has significant implications in the treatment of reperfusion injury and research into the physiology of solid tumours and angiogenesis. There is every reason to believe that continued efforts to push the envelope of high-field-strength applications will open new vistas in what appears to be a never-ending array of potential clinical applications.

New methods of analysing normal and pathologic brain anatomy are now at the forefront of research, namely MR spectroscopy (MRS), functional MRI (fMRI), diffusion tensor imaging (DTI) and high angular resolution diffusion imaging (HARDI) for MR tractography (MRT; see below) and molecular MRI (mMRI), the latter taking on a new direction since the description of the human genome. MRS assesses function within the living brain.

MRS capitalises on the fact that protons residing in differing chemical environments possess slightly different resonant properties (chemical shift). For a given volume of brain the distribution of these proton resonances can be displayed as a spectrum. Discernible peaks can be seen for certain neurotransmitters: *N*-acetylaspartate varies in multiple sclerosis, stroke and schizophrenia, while choline and lactate levels have been used to evaluate certain brain tumours.

fMRI depends on the fact that haemoglobin is diamagnetic when oxygenated but paramagnetic when deoxygenated. These different signals can be weighted to the smaller vessels, and hence closer to the active neurons, by using larger magnetic fields. mMRI uses biomarkers that interact chemically with their surroundings and alter the image according to molecular changes occurring within the area of interest, potentially enabling early detection and treatment of disease and basic pharmaceutical development; this also allows for quantitative testing.

Magnetic resonance tractography (MRT) is a three-dimensional modelling technique used to visually represent neural tracts using data collected by diffusion tensor imaging and more recently HARDI, with results presented in two- and three-dimensional images.

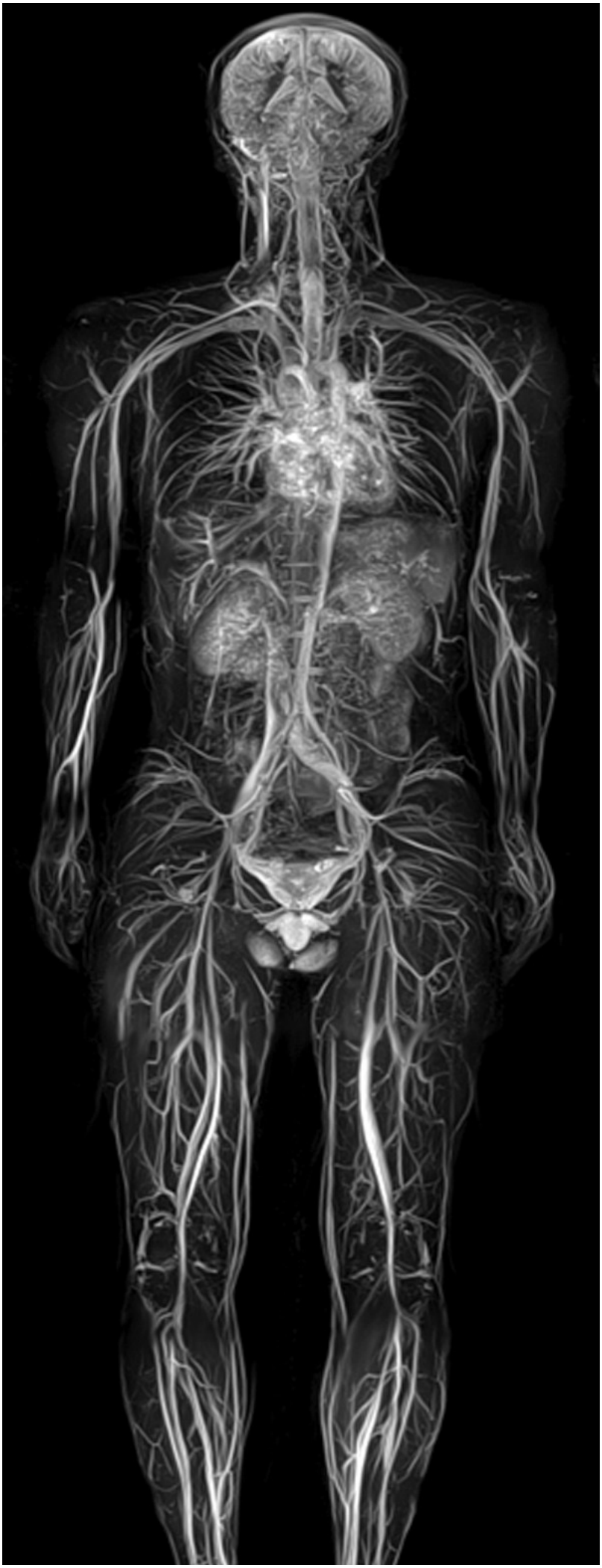
In addition to the long tracts that connect the brain to the rest of the body, there are complicated neural networks formed by short connections among different cortical and subcortical regions, their existence revealed by histochemistry and post-mortem biological techniques. Central nervous system tracts are not identifiable by direct examination, CT or conventional MRI scans, explaining the paucity of their description in neuroanatomy atlases and the poor understanding of their functions.

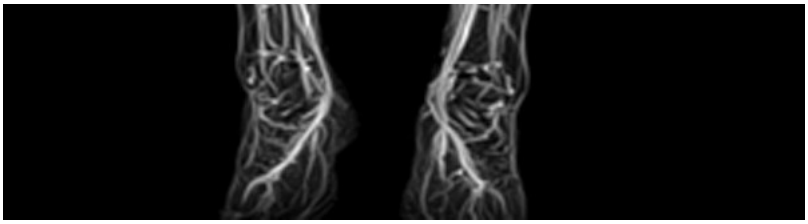
MRI sequences look at the symmetry of brain water diffusion. Bundles of fibre tracts make the water diffuse asymmetrically in a ‘tensor’, the major axis parallel to the direction of the fibres. There is a direct relationship between the number of fibres and the degree of anisotropy. DTI assumes that the direction of least restriction corresponds to the direction of white matter tracts. Diffusion MRI was introduced in 1985, with the more recent evolution of the technique into DTI, where the relative mobility of the water molecules from the origin is modelled as an ellipsoid rather than a sphere, allowing full characterisation of molecular diffusion in the three dimensions of space and formation of tractograms. Barriers cause uneven anisotropic diffusion, and in white matter the principal barrier is the myelin axonal sheath. Bundles of axons provide a barrier to perpendicular diffusion and a path for parallel diffusion along the orientation of the fibres. Anisotropic diffusion is expected to be increased overall in areas of high mature axonal order and conditions where barriers such as the myelin or the structure of the axon itself are disrupted, such as trauma; tumours and inflammation reduce anisotropy and yield DTI data used to seed various tractographic assessments of the brain, including development of arcuate and superior longitudinal fasciculi and corona radiata. Data sets may be rotated continuously into various planes to better appreciate the structure, and colour can be assigned based on the dominant direction of the fibres. A leading clinical application of MRT is in the presurgical mapping of eloquent regions. Intra-operative electrical stimulation (IES) provides a clinical gold standard for the existence of functional motor pathways that can be used to determine the accuracy and sensitivity of fibre tracking algorithms.

DTI will not accurately describe the microstructure in complex white matter voxels that contain more than one fibre population, due to intersecting tracts or to partial volume averaging of adjacent pathways with different fibre orientations, such as in the centrum semiovale, where major white matter tracts such as the pyramidal tract, the superior longitudinal fasciculus and the corpus callosum intersect. This has hindered preoperative mapping of the pyramidal tract in brain tumour patients.

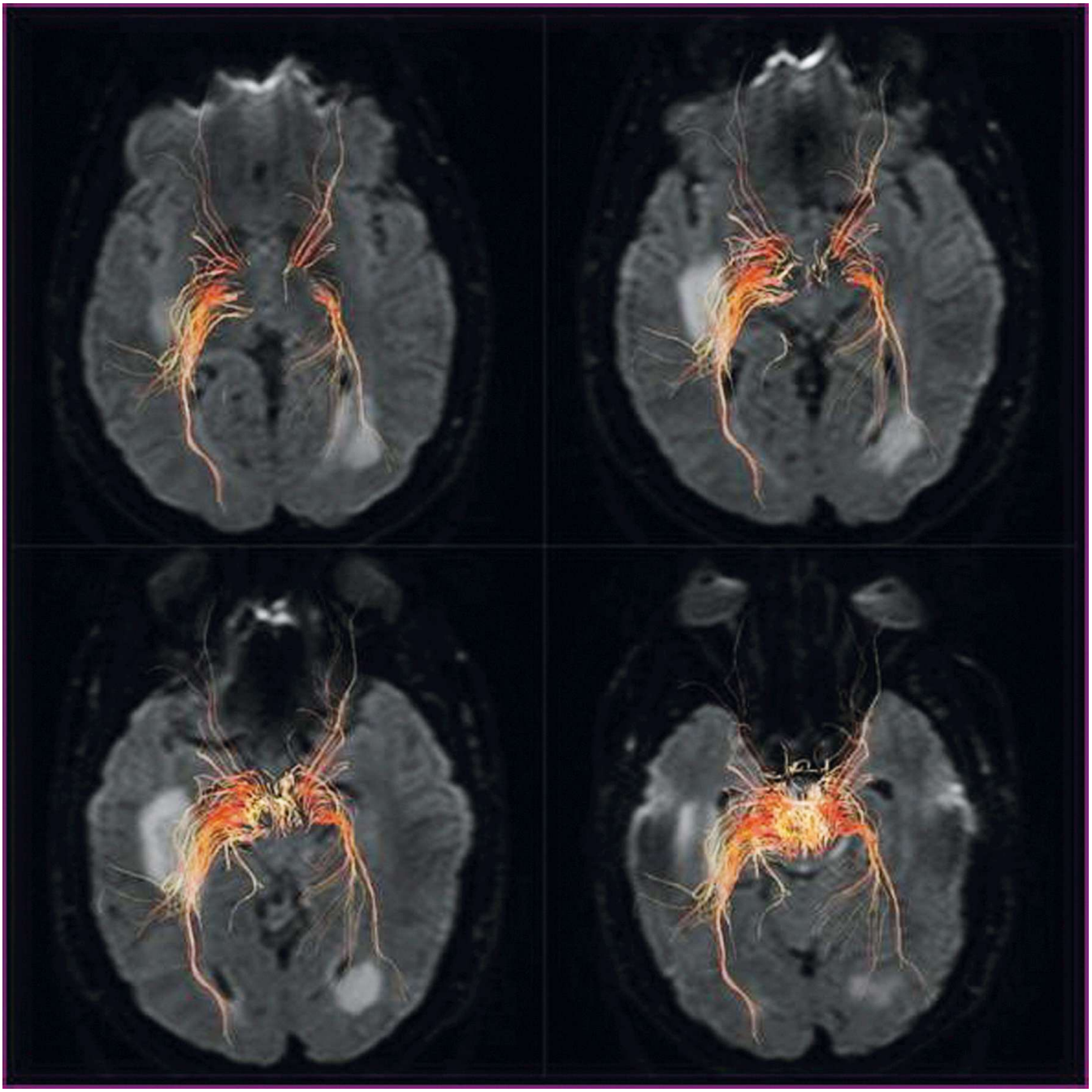
More recently, HARDI has more accurately delineated pathways within complex regions of white matter. The q-ball reconstruction of HARDI data provides an orientation distribution function (ODF) that can be used to determine the orientations of multiple fibre populations contributing to a voxel’s diffusion MR signal, mapping fibre trajectories through regions of complex tissue architecture in a clinically feasible time frame.

Body MRA.





MR tractography.



Ultrasound

Uniquely, ultrasound images do not depend on the use of electromagnetic wave forms. It is the properties of high-frequency sound waves (longitudinal waves) and their interaction with biological tissues that go to form these ‘echograms’.

A sound wave of appropriate frequency (diagnostic range 3.5–20 MHz) is produced by piezo-electric principles, namely that certain crystals can change their shape and produce a voltage potential, and vice versa. As the beam passes through tissues, two important effects determine image production: attenuation and reflection. Attenuation is caused by the loss of energy due to absorption, reflection and refraction in soft tissues with resulting reduction in signal intensity. Reflection of sound waves within the range of the receiver produces the image, the echotexture of which is dependent upon tiny differences in acoustic impedance between different tissues. Blood flow and velocity can be measured (using the Doppler principle) in duplex mode.

Techniques such as harmonic imaging and the use of ultrasound contrast agents (stabilised microbubbles) have enabled non-invasive determination of myocardial perfusion to be recently discovered. These contrast agents clearly improve the detection of metastases in the liver and spleen. Ultrasound is the most common medical imaging technique for producing elastograms, in which stiffness or strain images of soft tissue are used to detect or classify tumours. Cancer is 5–28 times stiffer than the background of normal soft tissue. When a mechanical compression or vibration is applied, the tumour deforms less than the surrounding tissue. Elastography can be used for example to measure the stiffness of the liver in vivo or in the detection of breast or thyroid tumours. A correlation between liver elasticity and the cirrhosis score has been shown.

Real-time nature ultrasound video loops have been included in the eBook in various chapters throughout this 6th edition of *Weir & Abrahams' Imaging Atlas of Human Anatomy* . Interpretation of the anatomy and pathology from static ultrasound images is more difficult than that from other imaging modalities, as the technique is highly operator-dependent and provides unique information on tissue structure and form not obtained from other imaging techniques.

Nuclear medicine

Historically the field of nuclear medicine began in 1946 when radioactive iodine was administered as an 'atomic cocktail' to treat thyroid cancer. Since that time, nuclear medicine has advanced and was recognised in the early 1970s as a diagnostic subspeciality.

Nuclear medicine, unlike diagnostic radiology which creates an image by passing energy through the body from an external source, creates an image by measuring the radiation emitted from tracers taken internally. Overall the radiation dosages are comparable to CT and vary depending on the examination.

Nuclear medicine also differs from most other imaging modalities in that the tests demonstrate the physiological function of a specific area of the body. In some instances this physiological information can be fused with more anatomical imaging of CT or MRI, thus combining the strengths of anatomy and function for diagnosis.

Rather than a contrast medium for imaging, nuclear medicine uses pharmaceuticals that have been labelled with a radionuclide (radiopharmaceuticals), which are administered to patients by intravenous injection, ingestion or inhalation. The method of administration depends on the type of examination and the organ or organ process to be imaged. The emitted radiation is detected and imaged with specialised equipment such as gamma cameras, PET, and single photon emission computed tomography (SPECT). Radiation in certain tests can be measured from parts of the body by the use of probes, or samples can be taken from patients and measured in counters.

The premise of nuclear medicine imaging involves functional biology; thereby not only can studies be done to image a disease process but they can also be used to treat diseases. Radiopharmaceuticals that are used for imaging emit a gamma ray (γ) and those used for treatment emit a beta (β) particle. Gamma rays are of higher energy to pass through the body and be detected by a detection camera, whereas beta particles travel only short distances and emit their radiation dose to the target organ. For example, technetium-99m or iodine-123 may be used to detect thyroid disease, but certain thyroid diseases or thyroid cancer may be treated solely or in part by treatment with iodine-131. The difference in the agent used depends on the type and energy levels of the radiation particle that the radioisotope emits.

Radionuclides, or the radioactive particles, used in nuclear medicine are often chemically bound to a complex called a tracer so that when administered it acts in a characteristic way in the body. The way the body handles this tracer can differ in disease or pathologic processes and thus demonstrate images different from normal in disease states. For example, the tracer used in bone imaging is methylene-diphosphonate (MDP). MDP is bound to technetium-99m for bone imaging. MDP attaches to hydroxyapatite in the bone. If there is a physiological change in the bone from a fracture, metastatic bone disease or arthritic change, there will be an increase in bone activity and thus more accumulation of the tracer in this region compared with the normal bone. This will result in a focal 'hot spot' of the radiopharmaceutical on a bone scan.

Technetium-99m is the major workhorse radioisotope of nuclear medicine. It can be eluted from a molybdenum/technetium generator stored within a nuclear medicine department, allowing for easy access. It has a short half-life (6 hours), which allows for ease of medical imaging and disposal. Its pharmacological properties allow it to be easily bound to various tracers and it emits gamma rays that are of suitable energy for medical imaging.

In addition to technetium-99m, the most common intravenous radionuclides used in nuclear medicine are iodine-123 and-131, thallium-201, gallium-67, 18-fluorodeoxyglucose (FDG) and indium-111 labelled leukocytes. The most common gaseous/aerosol radionuclides used are xenon-133, krypton-81m, technetium-99m (Technegas) and technetium-99m diethylene-triamine-pentaacetate (DTPA).

The images obtained from nuclear medicine imaging can be in the form of one or many images. Image sets can be represented as time-sequence imaging (e.g. cine), such as dynamic imaging or cardiac gated sequences, or by spatial sequence imaging where the gamma camera is moved relative to the patient, such as in SPECT imaging. Spatial sequence imaging allows the images to be presented as a slice-stack of images, much like CT or MRI images are displayed. Spatial sequence imaging can also be fused with concomitant CT or MR imaging to provide combined physiologic and anatomical imaging. Time and spatial sequence imaging offer a unique perspective on and information about physiological processes in the body.

A PET scan is a specialised type of nuclear medicine imaging that measures important body functions, such as blood flow, oxygen use and glucose metabolism, to evaluate how well organs and tissues are functioning. PET imaging involves short-lived radioactive tracer isotopes that emit an 'anti-electron'– actual antimatter! These radioisotopes are chemically incorporated into biologically active molecules, most commonly the sugar FDG. An hour after injection, FDG becomes concentrated into the tissues of interest, and imaging occurs as the isotope undergoes positron emission decay. The positron travels only a few millimetres and annihilates with an electron, producing a pair of gamma photons moving in opposite directions. The PET scan detectors process only those photon pairs that are detected simultaneously (coincident detection). These data are then processed to create an image of tissue activity with respect to that particular isotope. These images can then be fused with CT or even MR images.

A limitation of PET imaging is the short half-life of the isotopes. Thus close access to a cyclotron for generation of the isotopes plays an important role in the feasible location of a PET scanner. Typical isotopes used in medical imaging and their half-lives are: carbon-11 (~20 minutes), nitrogen-13 (~10 minutes), oxygen-13 (~2 minutes) and fluorine-18 (~110 minutes).

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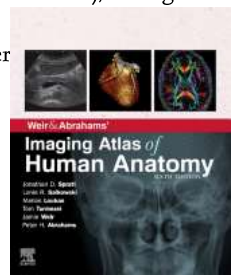

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