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S5: State-of-Science Review: Non-invasive Scanning and Screening

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1 Introduction

This review is concerned with imaging techniques. Currently, these are predominantly used in medical, that is, in human disease diagnosis and screening. In this context, screening is generally limited to the detection of early disease in individuals in whom a condition has not yet resulted in noticeable symptoms. Moreover, screening is usually restricted to those diseases that are more likely to be cured when detected early and that otherwise have substantial adverse effects. These are also diseases for which treatment is cost-effective and for which the screening method is safe, acceptable to the patient and financially affordable by society.

The primary motivation for screening is to confer potential benefits to the individual patient, perhaps the most obvious example being X-ray mammography for early breast cancer. In the case of screening for infectious diseases, however, reducing the risks of spread of infection to other members of the community may be more important than benefiting the individual patient. The use of chest X-rays for the detection of tuberculosis is an example.

The potential exists to screen animals for appropriate infectious diseases in the same way, but the economics are likely to be unfavourable. There is also the possibility of detecting infectious disease remotely in plants.

2 State of the art of the principal current imaging techniques

In this context, the principal current imaging techniques are considered to be those which are most commonly used in medical applications.

Worldwide, traditional X-radiography is still used for the largest proportion of imaging studies. This is followed closely by ultrasound, with radionuclide scanning, X-ray computed tomography and magnetic resonance imaging some distance behind – and in that order. In this review, thermography is included as one of the principal current imaging techniques, not because it is in widespread clinical use, but because it has some potential for detecting infectious diseases.

In Table 1, trends in the development of each technology are identified and their relevance to the detection and identification of infectious diseases is summarised.

2.1 X-radiography

X-rays are a form of electromagnetic radiation. The X-rays used for biomedical imaging usually have energies in the range 30–150keV and are produced at the anode of an X-ray vacuum tube. When X-rays traverse matter, interactions take place between the energy (in quantum steps) and the matter. Some of the energy in the incident beam is removed, partly by absorption and partly by scattering.

If the X-ray energy interacts with a tightly bound electron in one of the inner shells of an atom, the electron may be completely ejected from it as a secondary electron. This, having a low energy, is soon absorbed by excitation or ionisation, giving rise to heat. The vacant place now in the inner shell of the atom is filled by an electron from a shell further out, the energy giving rise to the emission of a quantum of radiation characteristic of the particular element.

In biomedical imaging, the quantum energy of the characteristic radiation is very low because of the generally low atomic numbers of the materials concerned and, therefore, the low binding energy of the electron shells. Hence, this characteristic radiation is very soon absorbed and the whole of the energy of the original interacting quantum is absorbed to appear as heat: the process called ‘photoelectric absorption’. This is inversely proportional to the cube of the X-ray energy. It is also directly proportional to the fourth power of the atomic number of the material.

If the X-ray energy interacts with a less tightly bound electron in an atom, the electron behaves as if it were free and recoils in a direction at an angle to the path of the incident energy, so-called ‘Compton scattering’. The energy of this electron is soon absorbed by ionisation and excitation processes and appears as heat. This heat represents the energy that is truly absorbed. The quantum of X-ray energy, on the other hand, is scattered away in another direction. Although it loses energy in the collision, it may still have sufficient to allow it to escape completely from the material. In effect, energy is removed from the beam although it is not truly absorbed.

Traditional X-radiography (Hay 1982) is the process by which a two-dimensional representation of a three-dimensional object is produced. The relative intensities (or ‘contrast’) in the image depend on the differing attenuations of X-rays as they pass from what is ideally a point source through the object to the two-dimensional detector (often, a photographic film designed to be sensitive to X-rays).

Two characteristics of the X-ray exposure are of fundamental relevance to the appearance of the image. First, the spectrum of the X-ray energy (expressed in keV) determines the contrast in the image. This spectrum is actually made up of two components. The first is a continuous spectrum of X-ray energies (called ‘Bremsstrahlung’), the upper energy limit of which is determined by the peak voltage applied to the X-ray tube (the kVp). The second component consists of energy peaks which are characteristic of the electron energy levels of the target anode material. These peaks appear only when the incident electron energy is sufficient to displace electrons from the inner shells of the target anode material in the X-ray tube (usually tungsten, with an energy of about 70keV).

The second characteristic of an X-ray exposure controlling the appearance of the image is the actual magnitude of the exposure, or the dose of X-rays used to form the image. If the dose is too low, the intensity of the X-rays falling on the detector is too weak for a satisfactory image to be formed. If the dose is too high, the detector becomes saturated, and the risk of adverse bioeffects resulting from exposure to radiation may outweigh the potential benefit arising

from the investigation. With an X-ray tube as the source, this aspect of the exposure is measured in mAs, the product of the current flowing through the tube (mA) and the duration of the exposure (s).

Basically, image contrast depends on the exposure (mAs) and the tube voltage (kVp). The lower energy components of the X-ray spectrum may not contribute usefully to the image contrast. So, in order to minimise their contribution to the potential hazards of the investigation, they are usually filtered out by placing a suitable material such as aluminium or copper between the source and the object. The primary contrast may also be reduced by scattered radiation arising mainly within the object. The deleterious effects of scattering may be reduced by: limiting the physical size of the X-ray field so that it irradiates only those parts of the object to be imaged; maximising the distance from the object to the detector; using the lowest practicable value of kVp; and, perhaps most usefully, by placing a grid consisting of slats of lead, separated by low atomic number material, close to the detector, so that only radiation travelling along the primary ray paths contributes to the formation of the image.

Photographic film was a commonly used X-ray detector. It is simple and cheap to use. For real-time X-ray investigations, the X-ray image intensifier operates with an electronic display and can be interfaced with a computer for image processing and analysis. Other stimulated-emission (Rowlands 2002) and solid-state (Yaffe and Rowlands1997) image detectors are now used for filmless and specialised applications.

Historically, X-ray imaging was the first technique to allow the internal structures of an intact body to be visualised. And, indeed, the great majority of medical imaging investigations today are still made using this technique. On plain radiographs, the overlapping nature of the shadows and the low contrast between different soft tissues make it difficult to determine more than the anatomical positions of different organs and only possible to identify obvious problems, such as bone fractures and solid tissues or fluid collections in the lungs. However, it is often possible to circumvent these limitations by using contrast agents, administered orally or into the vascular system. These agents contain compounds of elements with relatively high atomic numbers, such as barium or iodine. They have high X-ray absorption coefficients, so they produce shadows which can easily be seen on the X-ray image. The administration of contrast agents is inevitably to some extent invasive and this needs to be borne in mind when the use of X-ray or any other kind of contrast agent is being considered in the context of non-invasive scanning and screening.

When X-ray images are available in digital format, whether they have been acquired by an image intensifier, by ‘computed radiography’ using a detector with stimulated emission, or by a two-dimensional digital detector, they can be enhanced by digital image processing. Examples include grey-scale manipulation and the subtraction of images obtained before and after the administration of contrast agent.

Essentially, X-radiography is an anatomical, or structural, imaging modality. It does not usually provide information on physiological or metabolic function.

2.2 Ultrasonic scanning

Ultrasound is a mechanical wave motion with a frequency that lies above the range of human hearing. The speed of ultrasound in biological soft tissues is about 1,500m/s; at a frequency of 3MHz, the wavelength is about 0.5mm. Because of this short wavelength, directional beams of ultrasound can be produced by electrically driven vibrating sources called ‘probes’ (and containing transducers) with dimensions typically of around 5–15mm. Thus, short-duration pulses of ultrasound can be transmitted into tissue where they travel along a narrow beam at a speed of about 1.5mm/μs.

As each pulse travels through the tissue, it encounters changes in the characteristic impedance (the product of the density and the propagation speed) of the material, for example, at the interfaces between different organs, within parenchymatous tissue, at the surfaces of lesions and within lesions themselves. Where there is a change in impedance, a fraction of the incident ultrasonic pulse is reflected or scattered. Some of this energy may be directed back along the beam towards the probe, where it can be detected and transduced into an electrical signal. The time delay between the original transmission of an ultrasonic pulse and the reception of its echo is proportional to the depth along the beam of the reflecting or scattering structure. There is actually a delay of 1.3μs for every additional 1mm of penetration into the tissue.

In two-dimensional ultrasonic scanning (Wells 1999), ultrasonic pulses are transmitted from a hand-held probe in rapid succession (typically at a rate of 5000/s) along an ultrasonic beam which is swept repetitively through a sector to receive echoes from within the scanned tissue plane. These echoes are amplified electronically and registered on a two-dimensional display according to the corresponding directions of the ultrasonic beam and the delays in the echo returns. The whole process is repeated rapidly, at a frame rate typically of 25/s, so that the display appears in real time. This is fast enough, for example, to follow the motion of the structures of the beating heart.

In ultrasonic scanning, it is the wavelength of the ultrasound that fundamentally limits the achievable spatial resolution. Thus, in order to obtain better resolution, it is necessary to use a higher ultrasonic frequency. The attenuation of ultrasound as it travels through tissue increases with frequency, so, for a given depth of penetration, there is an upper limit to the frequency (and hence, to the resolution) because, as the frequency is increased, the echoes eventually become too weak to be detected. In practice, in abdominal scanning, a penetration of 150mm is typically needed and the maximum usable frequency is around 3.5MHz. The corresponding spatial resolution is around 0.5mm.

Because the ultrasonic scanner has a real-time display, a skilled operator can use its probe to explore the internal structures of a body and thereby obtain an understanding of its three-dimensional anatomy. True three-dimensional

scanning is also possible using, for example, a probe in which the two-dimensional scan plane is altered either mechanically, electronically or freehand (Gee et al. 2004) to acquire a set of contiguous scans of the volume of interest. Typically, three-dimensional imaging is possible at a rate of around 4/s.

In addition to the time delay associated with the depth of the scattering target within the tissue, information about the motion of the target can be obtained from the Doppler shift in the frequency of the detected echo signal. It is serendipitous that, at the ultrasonic frequencies generally used in biomedical scanning and with typical blood flow and structure motion velocities, Doppler shift frequencies usually lie in the audible frequency range. Clinically useful information about, for example, foetal heart rate and the presence or absence of blood flow can be obtained simply by listening to the Doppler signals.

These signals can be analysed electronically to provide quantitative data. Doppler or related signals can also be used to superimpose, on the grey-scale anatomical image, a map colour-coded according to some aspect (such as the blood-flow velocity) of the corresponding physiological motion.

The most commonly used ultrasonic scanning procedure employs a hand-held probe in contact with the patient's skin. In some situations, however, intravascular and intracavitary probes may be used. These devices have the advantage of bringing the probe into close proximity with the tissue to be imaged. This means that, when scanning the uterus, for example, with a transvaginal probe, a frequency of 7.5MHz can be used, with a resolution of around 0.2mm.

Improved spatial resolution, accompanied by a reduction in image artefacts, can be obtained by ultrasonic harmonic imaging (Tranquart et al. 1999). This technique depends on the non-linear propagation characteristics of biological tissues. Following its transmission into tissue, some of the energy in an ultrasonic pulse is transferred into higher harmonic frequencies and, particularly, into the second harmonic frequency. Thus, by receiving echoes at twice the frequency of the transmitted pulse, some of the advantages of using a higher frequency can be obtained without incurring all the disadvantages, such as the increased attenuation.

Ultrasonic contrast agents (Albrecht et al. 2004), consisting of a suspension of gas-filled microbubbles with dimensions comparable to those of red blood cells, can be administered via an intravascular route to enhance the echogenicity of blood. Methods for the selective targeting of contrast agents and their use in drug delivery are being investigated.

The use of ultrasound to estimate the elasticity of internal tissue structures from the displacement due to applied static or dynamic mechanical pressure or to ultrasonic radiation force is beginning to show some real diagnostic promise for the detection of pathological processes associated with hardening or softening of tissue (Hall et al. 2003).

Essentially, ultrasonic scanning is an anatomical, or structural, imaging modality. The application of the Doppler effect and the use of contrast agents enable it also to provide some functional information.

2.3 Radionuclide scanning

In radionuclide scanning, a small dose of a radioactive isotope – a radionuclide – is administered as a 'tracer' which, in biomedical applications, is distributed in the body according to physiological, metabolic and pathological functions. Usually, the radionuclide is tagged onto a pharmaceutical agent chosen specifically to target the site relevant to the function under investigation. The distribution of this radiopharmaceutical within the body is then imaged by a scanner.

The gamma camera (Weber et al. 1982) (so called because it images the gamma rays emitted as a result of the decay of the radionuclide) produces a two-dimensional image of the three-dimensional distribution of the radiopharmaceutical. Other types of scanner (see SPECT, single photon computed emission tomography, below) show two-dimensional cross-sections through the body, which may be displayed as such or which may be assembled into images resembling those produced by a gamma camera.

A basic gamma camera typically has a 500mm diameter field of view. Radiation from the object to be imaged arrives at a disk-shaped, lead collimator about 20mm thick and penetrated by very many parallel holes separated by thin septa. The purpose of the collimator is to collect radiation travelling from the object in the direction perpendicular to the collimator's flat surface. On the other side of the collimator is a disk of thallium-activated sodium iodide, about 2mm thick and separated from the collimator by a light-tight membrane.

Gamma rays which have passed through the collimator arrive in the sodium iodide crystal where they interact to produce brief flashes of light or scintillations. These are detected by an array of photomultiplier tubes arranged in a regular pattern so that they cover the entire surface of the crystal. The positions of the scintillations within the crystal are determined by analysis of the relative amplitudes of the corresponding outputs from the photomultipliers. The absolute brightness of the scintillation depends on the energy of the gamma rays. The output signals from the photomultipliers are processed to produce the two-dimensional image.

The time needed to acquire a sufficient number of counts to form a satisfactory image depends on the dose of radioactive material administered (usually by intravenous injection). Typically, the dose is chosen to allow an image to be acquired in about five minutes.

The necessary characteristics of a radionuclide for it to be a satisfactory tracer for imaging are: that it should emit gamma rays of an appropriate energy (typically 100–200keV) for efficient detection; that its half-life should be long enough for practical use but not so long that repeat investigations have inconveniently to be delayed and that the radiation exposure becomes

worrisome; and that it can be conveniently tagged to appropriate pharmaceuticals. In clinical medicine, the radionuclide ^{99m}Tc (technetium-99m) is very commonly used. This emits 140.5keV gamma ray photons, has a half-life of 6.03h and its radiochemistry is convenient. Moreover, it can be produced on site by elution from a radioactive molybdenum generator which itself has a half-life of about 66h.

Cross-sectional radionuclide images can be acquired by single photon emission computed tomography (SPECT) (Tsui 1996) and positron emission tomography (PET) (Maisey 2002). A typical SPECT scanner consists of a gamma camera (or multiple gamma cameras) arranged to rotate around the object to be imaged. The gamma camera (or cameras) acquires a set of line projections of the radiation emitted from the cross-section through the object. These projections are then reconstructed by computer processing to form an image of the cross-section. In this way, depth information, which is absent from an ordinary gamma camera image, is acquired. Moreover, the sensitivity to different levels of radioactivity is greater in a set of contiguous SPECT images than in the gamma camera image, allowing a more useful two-dimensional image of the entire three-dimensional object to be generated.

PET is based on the use of a radionuclide which decays with the emission of positrons. These positrons (positively charged electrons) travel only a very short distance, a matter of millimetres, before they are annihilated by interaction with an electron. As a result of this annihilation, two gamma ray photons, each with an energy of 511keV, are produced, travelling in almost exactly opposite directions.

Important advantages of PET are that suitable positron-emitting radionuclides are isotopes such as ^{15}O (half-life 2 min), ^{11}C (half-life 20 min) and ^{18}F (half-life 110 min), which, in the case of ^{15}O and ^{11}C, can be integrated directly into biologically active molecules, rather than being tagged onto them. Also, their half-lives are so short that rapidly repeated tests are possible at acceptable dose levels. In the case of ^{18}F, the half-life is sufficiently long for the isotope to be produced by a cyclotron located remotely from the site of clinical use.

Although PET is possible with rotating gamma cameras, the results are not very satisfactory, partly because of the relatively high gamma ray energy. Dedicated PET cameras typically consist of a ring of detectors, with the object to be imaged positioned within the central aperture. As the annihilation of a positron results in the simultaneous production of two oppositely-travelling gamma ray photons, the coincident detection of the event by a pair of detectors in the ring allows the line passing through the site of the event to be determined. This forms the basis of cross-sectional image reconstruction.

Essentially, radionuclide scanning is a functional imaging modality. It is not characterised by high spatial or temporal resolution.

2.4 X-ray computed tomography

In its original and simplest practical realisation, X-ray computed tomography (CT) (Davidson 1982) produces cross-sectional images of the distribution of

X-ray attenuation coefficients within an object by a two-stage process. First, a complete set of transmission profiles is acquired, by translating a narrow beam of X-rays across the object from side to side, with a detector positioned to receive the transmitted beam, and by rotating the scanning assembly around the body by a small angular increment between the acquisition of each attenuation profile. Then, these data are back-projected to reconstruct the image by computer processing.

The great advantage of the method, in comparison with traditional X-radiography, lies in its very much higher sensitivity (typically by a factor of 1,000) to small differences in the attenuation of the various structures within the scanned plane.

Modern X-ray CT scanners employ several stationary annuli containing very many detectors (Flohr et al. 2005). The X-ray tube rotates around the object so that a complete set of X-ray attenuation projections is acquired by each ring of detectors for every revolution of the source. The acquisition time for a single image can be as short as 0.5s. With helical (or spiral) CT, the object is moved continuously through the fan beam to acquire a full three-dimensional data set in 20–30s. This is short enough for the patient to hold their breath, thus minimising motion artefacts, apart from those due to the beating of the heart. For cardiac imaging, the CT acquisition needs to be gated by the electrocardiogram.

The basic physics of X-ray CT is the same as that of traditional X-radiography as far as the characteristics that govern absorption and scattering are concerned. The computer calculates the CT number for each pixel of the image matrix in a scale of 2,000 Hounsfield units. The CT numbers range in value to up to about +80 in soft tissues and to over +1,000 in bone. A band of CT numbers can be selected for display by choosing a particular window level and width. The CT numbers within the band can be displayed as a full range of grey tones.

The high sensitivity of CT to slight differences in X-ray attenuation results in clinically useful images for many pathological conditions. The contrast can often be further enhanced, however, by administering contrast agents, usually intravenously. This is a particularly sensitive technique for visualising neovascularisation associated with the development of malignant tumours.

Essentially, CT scanning is an anatomical, or structural, imaging technique, although functional data can be derived by analysing enhancement characteristics following administration of contrast agents.

2.5 Magnetic resonance imaging

Nuclei which contain an odd number of protons, or an odd number of neutrons, or both, have a spin and a magnetic moment. They may, therefore, be thought of as behaving like small, spinning magnets. Examples of such nuclei are ^{1}H, ^{19}F and ^{31}P. The magnetic properties of atomic nuclei are very weak, which is why they are not apparent in everyday life.

Consider a magnetic nucleus, for example, a proton (^{1}H, the nucleus of a hydrogen atom), placed in a magnetic field. The magnetic moment of the nucleus experiences a couple, which tends to turn it to the direction of the field. Since it is spinning, the nucleus responds to this couple in the manner of a gyroscope with its axis precessing around the direction of the field. The angular frequency of this precession is proportional to the strength of the magnetic field; in the case of a proton in a magnetic field with a strength of 1T, this frequency is 42.6MHz. The corresponding frequency for ^{19}F is 40.1MHz and, for ^{31}P, it is 17.2MHz.

Now consider a small volume (perhaps 1ml) of water placed in a magnetic field with a strength of 1T. This volume contains approximately 10^{23} protons. In a state of equilibrium, more protons will be aligned with the field than against it, and this will generate nuclear magnetisation in the direction of the field.

By applying a weak radio-frequency rotating magnetic field in a direction perpendicular to the static field, its interaction with this nuclear magnetisation will cause the latter to tilt away from the direction of the static field. If the frequency of the rotating magnetic field is equal to the frequency of precession of the magnetic nucleus, nuclear magnetic resonance (NMR) occurs. Moreover, if the radio-frequency field is applied as a short pulse of appropriate duration, the nuclear magnetisation tilts through 90^{o}; the nuclear induction signal following the pulse does not last indefinitely, but dies away. This is a ‘free induction decay’ (FID), and its time constant is called the ‘transverse relaxation time’ (T2).

If a radio-frequency pulse with twice the duration needed to tilt the nuclear magnetisation through 90^{o} is applied, the tilt becomes equal to 180^{o}. When the pulse cuts off, the nuclear magnetisation decreases to zero and then grows along the direction of the static magnetic field to its full equilibrium length. This return to equilibrium has a time constant equal to the ‘longitudinal relaxation time’ – more commonly called the ‘spin-lattice relaxation time’ (T1).

Using classical physics to explain NMR in this way is helpful in conceptualising the process. Strictly speaking, however, it is more rigorous to look at NMR from the viewpoint of quantum theory.

Magnetic resonance imaging (MRI) (Andrew 1982), as now commonly used in biomedical applications, displays characteristics of the protons located in two-dimensional slices or three-dimensional volumes. This is achieved by applying relatively weak magnetic field gradients in addition to the relatively strong static magnetic field, so that the actual value of the magnetic field depends on the position in the volume of tissue examined. This enables the position of the protons giving rise to detected signals to be localised in space according to their precession frequencies and phases. Modern MRI scanners use refinements of this basic principle of localisation for the reconstruction of their images.

MRI scanners are substantial pieces of equipment. Typically, the static magnetic field is 1.5T, which is about 30,000 times greater than the Earth’s

magnetic field. The field needs to be highly uniform in the scanned volume. It may be provided, for example, by a superconducting solenoid magnet with a length of 1.5m and a bore of 500mm, or between the poles of an 'open' permanent magnet. The object to be imaged is positioned within the uniform magnetic field, surrounded by the coils which generate the magnetic field gradients necessary for spatial localisation. In addition, another coil has to be close to the structures to be imaged, in order to receive the NMR signals.

Typically, a single MR imaging examination occupies around 30 minutes. During this time, images are likely to be acquired with a variety of pulse sequences, chosen optimally to visualise the anatomical and pathological features that might reasonably be anticipated. For at least some of the images, contrast agents (usually based on gadolinium (Saini and Nelson 1995)) are likely to be administered to patients to enhance the diagnostic process.

Essentially, MRI and spectroscopy are capable of providing both anatomical or structural, and functional information. The technique is advancing rapidly and it may become possible to detect molecular species that might be useful in defining the presence and even the extent of disease.

2.6 Thermography

Many animals, notably mammals and, especially, humans, maintain their body temperatures within very close limits around what is called the normal body temperature. In humans, normal body core temperature ranges between about 36.1^{o}C to 37.2^{o}C, with a mean value of 37.0^{o}C. Also of relevance is the fact that some plants are thermogenic (Chaerle et al. 1999).

The body core temperature is one of the factors controlling skin surface temperature. Other important factors are the blood flow in the skin and in structures close to the skin, and the temperature of the external environment. If the core temperature is elevated above the normal value as the result, for example, of a fever, skin temperature is also likely to be elevated. Also, if a localised region of the skin has a relatively elevated temperature, this may be due to vascularisation, such as may occur in certain types of skin and superficial cancers.

Just like all other objects, human and animal skin and plant epidermal tissue emits infrared radiation as a function of its absolute temperature. Absolute zero temperature is –273.15^{o}C. Hairless skin emits radiation in direct proportion to the fourth power of its absolute temperature; the presence of hair reduces the rate of infrared radiation. Physiologically, infrared radiation from the skin is one of the mechanisms by which a body loses the heat resulting from metabolism and by which animals control their body temperatures.

Skin at a temperature of 30^{o}C emits infrared radiation maximally at a wavelength of 9.5μm and, significantly, over a range of 4–40μm. Infrared imaging maps the spatial distribution of the surface radiation intensity, which can be directly related to surface temperature.

Infrared thermography seems, at least at first sight, to be a promising method for disease detection and diagnosis. In principle, there are two approaches to infrared thermography (Jones 1982; Jones 1998). In one, a small-area temperature sensor is remotely scanned point-by-point over the surface of the object and the individual surface temperature measurements are displayed as a two-dimensional image. The scanning system may, typically, consist of a mechanically actuated mirror arranged to raster-scan the scene and to direct the radiation point-by-point onto a detector. In the second approach, a two-dimensional infrared imaging sensor array may be used in a camera-like system to acquire a thermal image effectively in real time.

Infrared thermography is a passive technique in which the naturally occurring radiation from the object (human, animal or plant) is imaged. Consequently, it involves no biological hazard. It needs to be borne in mind, however, that the ability to obtain consistent information depends on aspects of the local environment, including other heat sources, humidity and air speed, and so the scanning process needs to be controlled. Variations in emissivity can also cause challenges in interpreting differences in detected radiation as being due to underlying temperature differences.

Significant work has been done on plant thermal imaging, mostly in natural or semi-natural environments. For example, it has been shown to be possible to visualise plant–virus interactions by thermography (Chaerle et al. 2004).

3 Emerging imaging techniques

In this section, we look at imaging technologies which are currently the subject of research and which, apart from in a few specialised applications, have not yet been introduced into regular use.

In Table 2, current research activities in each technology (with the exception of microscanning) are identified and the potential relevance to the detection and identification of infectious diseases is summarised.

3.1 Imaging with light

Optical methods of scanning are of interest because they exploit the optical properties of tissues and their constituents. Of particular importance, in clinical applications, is the fact that oxygenated and deoxygenated haemoglobin have different absorption spectra in the visible (300–800nm) and near-infrared (800–1,500nm) wavelengths.

3.1.1 Optical tomography

Optical tomography (Gibson et al. 2005) is similar in principle to X-ray CT, except that visible or near-infrared light is used in place of X-rays. The corresponding wavelengths are in the range 300–1,500μm. This radiation is non-ionising and so there is no risk of it causing cancer. In X-ray CT scanning, the detected X-rays can be assumed to have travelled in a straight line from the source, through the object, to the detector. The transport of light through

tissue, however, is characterised by a high degree of scattering, so that the majority of the photons travel along irregular and lengthy paths. Consequently, a very short pulse of light transmitted into the object is detected as a first-arriving ballistic (but very weak) component, followed by photons arriving after further delays, depending on their actual path lengths.

In order to reconstruct an image from the light transmission profiles obtained in optical tomography, the models of light transport demand substantial computation for their solution. This is an active area of research, particularly into techniques involving the measurement of the times-of-flight of photons in order to determine their path lengths.

3.1.2 Optical coherence tomography

Optical coherence tomography (Fercher et al. 2003) resembles two-dimensional pulse-echo ultrasonic imaging, but uses pulses of light instead of ultrasound. Since the speed of light is relatively very high (about 200,000 times faster than that of ultrasonic waves), the time delays between the transmission of a pulse of light and the reception of light backscattered by the internal structures of an object are proportionally shorter. Moreover, light is strongly scattered by tissues. So the useful depth of penetration is limited to a few millimetres at most.

In order to form an image, the time delays are not measured directly, but are determined from measurements of the phase changes between the transmitted and received signals. The wavelength of ultrasound used for millimetre-depth imaging is usually around 50μm (at a frequency of 30MHz), whereas the wavelength of visible light is around 0.5μm. Thus, the spatial resolution of OCT could be 100 times better than that of ultrasonic imaging, over the very limited depth of penetration which can be achieved.

3.2 Microwave imaging

Microwave imaging seems to be an attractive possibility, because the permittivities of different biological tissues cover a very wide range. Microwaves are electromagnetic radiation with frequencies in the range 500MHz–50GHz. The corresponding wavelength range (in free space) is 0.6m–6mm. The absorption of microwaves in biological tissues increases with frequency, so consideration of penetration means that imaging with microwaves needs to be at the lower end of the frequency range. Typically, the wavelength (in free space) cannot be less than about 25mm. Thus, even though the wavelength in tissue is shorter than that in free space, microwave imaging is unlikely to have a good spatial resolution.

Two approaches to imaging are being explored (Giocan et al. 2004; Poplack et al. 2004), depending on whether the absorption or the reflexion of microwaves is measured. In either case, the image can be formed by a point-by-point mapping process using a probe which acts as transmitter and receiver of backscattered signals, or by two probes to measure attenuation resulting from transmission through the object, or by CT, either in the reflexion or in the transmission mode.

3.3 Terahertz imaging

Terahertz imaging (Fitzgerald et al. 2002) employs electromagnetic radiation with frequencies in the range 0.1–30THz (1THz = 10^{12}Hz). The corresponding wavelength range (in free space) is 3mm–1μm. Thus, terahertz radiation straddles that part of the electromagnetic radiation spectrum occupied by higher-frequency microwaves and longer-wavelength infrared. Ultrafast semiconductor lasers are used both to generate and to detect radiation in this frequency range (Borak 2005).

Terahertz radiation is strongly absorbed by water, although its penetration through biological tissue is somewhat greater. Because of its longer wavelength, scattering is less of a problem with terahertz radiation than it is with infrared light. Consequently, terahertz imaging has proved to be most promising in dermatology and, to some extent, in dentistry. It is worth noting that hair and fur should not be substantial obstacles to imaging skin and subcutaneous structures.

Terahertz imaging is inherently a slow process, since the data have to be acquired by point-by-point scanning. Although two-dimensional solid-state image converters do exist, these devices currently have relatively poor sensitivity, so imaging is restricted to superficial tissues of the body.

It is worth noting that, in addition to its potential for biomedical imaging, terahertz radiation may have applications in biomedical spectroscopy.

3.4 Thermoacoustic imaging

Thermally induced ultrasound can be produced within an object by absorption of a pulse of electromagnetic radiation (Kruger et al. 1999; Xu et al. 2003). This induced ultrasound may be detected either by point-by-point scanning or by a two- or three-dimensional array of transducers. It can then be used to produce an image of the spatial distribution of the absorption coefficients within the object (Yin et al. 2004). The technique has been demonstrated both with light (where depth of penetration is a limitation) and with microwave radiation (where the low frequency of the induced ultrasound limits spatial resolution). It is possible that the problem of limited light penetration might be ameliorated, albeit invasively, by using a fibre optic for deep delivery.

3.5 Electrical impedance tomography

In electrical impedance tomography (Holder 2004), an array of electrodes is, typically, attached to the surface of the object in the plane which is to be imaged. Constant current kHz-frequency sources are multiplexed to the electrodes, resulting in electrical potentials which are measured between the other electrodes. An image of the distribution of the electrical conductivity within the object can be reconstructed from these data. This involves the solution of the inverse problem, which is subject to ambiguity.

Currently, images are characterised by poor spatial resolution and the presence of artefacts. Some additional information may be obtained by

processing images obtained over a range of frequencies. Whether or not measurable changes occur in the impedances of tissues as a result of disease processes remains to be established. The advantages of the method are that it is fast, free from any apparent hazard and, in principle, relatively inexpensive.

3.6 Magnetic field imaging

Muscle activity and nerve function are both associated with electrical changes. For example, the action of the myocardium gives rise to voltages which can be detected by surface electrodes and displayed as the electrocardiogram. In the same way, electrodes placed on the head are used for electroencephalography. Some idea of the distribution of electrical activity in the brain can be obtained by studying the potentials detected by arrays of electrodes attached to the head. The problem, however, is that images formed in this way are distorted by the varying conductivities of the different tissues which lie between the locations of electrical activity and the surface electrodes.

Electrical activity in muscle or nerve tissue results in the flow of electrical current within the relevant tissue, which gives rise to magnetic fields, albeit very weak ones. A characteristic of magnetic fields is that they are not distorted by the presence of biological tissues, so the magnetic sources can be localised by arrays of detectors placed outside the body.

There are two main problems with this. First, the magnetic fields are very weak, which means that measurements have to be performed in a magnetically shielded enclosure to avoid interference by naturally occurring and man-made environmental fields. Typically, such enclosures are massive steel structures. Secondly, very sensitive detectors have to be used. Currently, the most satisfactory detector is the superconducting quantum interference device – SQUID – which has to operate at liquid helium temperatures. Based on this principle, magnetocardiographs and magnetoencephalographs have been constructed to image the magnetic activities of the heart and the brain (Schneider et al. 1990), respectively. Whether or not measurable changes occur as a result of infectious disease processes remains to be determined.

3.7 Microscanning

Contemporary scanning techniques, certainly those used in medical diagnosis, generally have spatial resolutions which seldom are better than around 100μm. This is satisfactory because that is about the size of the smallest structure that can be seen by the unaided eye. Often, the resolution is considerably worse, being of the order of tens of millimetres, for example, in radionuclide scanning.

Microscopy is not within the scope of this review. Typically, that technology is concerned with the visualisation of structures with sizes of less than around 10μm. Thus, there is a range of structures, 10–100μm, that lies between the

interests of, for example, histopathologists and clinical radiologists. Devices that image structures in this size range are called ‘microscanners’.

A particularly important field of microscanning is small-animal research in genomics and drug development. But this is not the only potential application for the technology.

Microscanners have been developed that are miniaturised variants of the X-ray, radionuclide, CT, MRI and ultrasonic systems used in clinical radiology. Microfocal radiography involves the use of an X-ray tube with a very small spot size. Micro-CT (Psarros et al. 2005) also uses an X-ray tube with a small spot size, together with a ring of very small detectors. Micro-MRI uses a small high-field-strength magnet and miniature gradient and radio-frequency coils. Ultrasonic microscanners (Wells 2000) operate at frequencies in the 30–100MHz range. High-resolution radionuclide scanning does not achieve a high enough spatial resolution strictly to satisfy the formal definition of a microscanner, but small-animal single-photon-emission CT and PET can be used to visualise structures of down to around a millimetre in size. Many of these devices have the potential to be used for ‘molecular imaging’. Intuitively, it seems reasonable to anticipate that the ability to distinguish specific molecules could represent a critical breakthrough in disease detection, but this has apparently not yet been clarified.

4 Detection and identification of disease by scanning techniques

Images are representations of a corresponding reality. What is seen by direct vision is actually an image of the spatial distribution of the brightness, contrast and colour of the scene.

Images produced by different scanning techniques are characterised by differing contrast mechanisms. The contrast in X-ray images, whether plain radiographs or CT scans, is determined by spatial differences in X-ray attenuation, which itself is dependent on the atomic number of the material in question. Radionuclide images display the spatial distributions of the concentration of radioactive tracer. The contrast in ultrasonic images derives primarily from spatial variations in reflectivities or backscattering strengths, which depend on the densities and elasticities of the tissues. Magnetic resonance images demonstrate the spatial distribution of proton densities and their relaxation times. In all these cases, the image contrasts may be modified and enhanced by various kinds of contrast agents. In the case of thermography, placing the subject in a cold environment may enhance the visibility of abnormality.

In addition to the primary contrast in the image, supplementary information may be overlaid on it. For example, in two-dimensional ultrasonic images of anatomical structures, information about blood flow may be superimposed as a colour-coded map.

In medical screening and diagnosis, interpreting an image depends essentially on detecting some deviation from normality and identifying its likely causes. This means that the observer needs to be trained to interpret the relevant images. In any kind of test, including tests based on image interpretation, it is necessary to compromise between sensitivity and specificity. If the sensitivity of the test to the presence of an abnormality is increased (by lowering the threshold for a positive result), the specificity of the test to any particular abnormality is necessarily reduced, and vice versa. Thus, any test can give results which are true positive or false positive, and true negative and false negative.

The best tests have both high sensitivity and high specificity, so they result in high levels of true positives and true negatives and low levels of false positives and false negatives.

In the case of human image observers, it is their perception of the visual information (Hendee and Wells 1997) that determines how effectively a test detects and identifies disease. In some cases, the information in the image is obvious even to an observer with a minimal level of training. Usually, however, a high degree of skill is needed, both to perceive any abnormality and to recognise and compensate for any artefacts. In order to assist human observers in the task of image interpretation, automated radiological advisory systems are beginning to show some promise. Two approaches are being tried (Doi 2005). In the first, the observer can call up a display of numerous images of confirmed lesions of the type which he or she suspects may be visible in the image. This allows the observer to form a judgement about the likelihood of the lesion actually being present. In the second approach, the image is automatically scanned and any textures or patterns which are then identified by the machine as possibly corresponding to the lesion in question are highlighted on the display. This serves to draw the attention of the human observer to the suspect regions in the image so that he or she may judge whether or not pathology really is likely to be present.

Attempts have been made to fully automate the process of image interpretation, so that the need for a skilled observer would be eliminated. At this stage, work is confined to images of well-defined structures and screening for a limited number of possible pathologies. One example is in X-ray mammographic screening for breast cancer. Currently, the performance of automated systems compares rather unfavourably with that of skilled observers, so they are unacceptable when screening depends on high levels of both sensitivity and specificity. It is appropriate to point out that the whole question of automation or partial automation is likely to be critical to any expanded screening concept. Intelligent systems for filtering information, directing enhanced scanning to key regions of the object and prioritising follow-up would be essential capabilities for success.

Traditionally, medical image interpretation has been regarded as the unique preserve of medically qualified observers. However, as medical manpower becomes scarcer and as the numbers of images requiring interpretation escalates, so it becomes pragmatically necessary for this attitude to be relaxed. The current situation is that skilled non-medical personnel are

sometimes permitted, in well-defined circumstances and under medically qualified supervision, to examine images and to identify those that can confidently be judged to be normal.

Recognising that image interpretation requires training and skill, technologies have been developed to transmit images from the point of their acquisition to a distant location where the necessary expertise for their interpretation may exist. Examples of where these 'teleradiology' technologies may be useful include situations in which antisocial hours might otherwise exist, and in remote (e.g. sparsely populated) and dangerous (e.g. battlefield) environments.

Until now in this review, we have only considered the use in isolation of single types of imaging modality. In practice, this is seldom the reality. For example, in medical diagnosis, the person whose task it is to interpret images usually has access to the patient's notes and, often, may be able to conduct a clinical examination of the patient while the images are being acquired. There is also information from laboratory and other relevant tests to be taken into account.

The process of image fusion is another important clinical tool. For example, the low-spatial-resolution functional-image information obtained using radionuclide scanning can be fused with the high-spatial-resolution anatomical-image information obtained with X-ray CT scanning. Indeed, machines are now available which quasi-simultaneously acquire, for example, X-ray CT and cross-sectional radionuclide images and display them either separately or superimposed (Czermin 2004; Townsend and Beyer 2002).

5 Current applications of scanning techniques in the detection and diagnosis of infectious diseases

5.1 In humans

Table 3 lists the principal applications of current imaging techniques in the detection and identification of infectious diseases in humans.

5.2 In animals

Although infectious diseases in animals are often somewhat similar to those in humans, scanning individual animals is unlikely to be economically viable.

5.3 In plants

The temperature of thermogenic plants may be slightly increased by the presence of infectious disease and this may be detectable remotely by thermography. Perhaps more importantly, leaf or root disease or damage can reduce transpiration and this may result in temperatures that are higher than in freely transpiring plant material. Apart from this, however, current scanning techniques do not appear to have any applications in the detection and identification of infectious diseases in plants.

6 Visions of the future

6.1 Prospects for the development of novel scanning techniques

With the development of terahertz imaging, there is no part of the electromagnetic frequency spectrum from 10^3 to 10^{20} Hz, which is not now exploited for biomedical imaging. The corresponding frequency band for mechanical waves extends from 10 to 10^{10} Hz.

On the one hand, such comprehensive use of radiation might seem to suggest that opportunities developing novel scanning techniques may be limited. But on the other hand, the existence of techniques for generating and detecting radiation over such wide ranges of frequencies means that there are no fundamental obstacles to extending existing methodologies and inventing new ones. Judging from the lessons of history, the prospects for both must be good.

6.2 Safety considerations and acceptable levels of radiation exposure

All today's principal imaging techniques involve the exposure of the object (human, animal or plant) to some form of probing radiation, or depend on the detection of radiation emitted by the object. All exposure to radiation can, potentially, have biological effects, some of which could be hazardous.

The energy of the electromagnetic radiation used in X-radiography, radionuclide scanning and X-ray CT is well above the threshold for ionisation to occur. Consequently, it may cause untoward effects. For example, an exposure of 0.01Gy (equivalent to the dose received from 10 CT scans) will result in a very slight decrease in circulating white cells and platelets in an exposed individual. However, exposing each of 100,000 people to 0.01Gy will also result in about 800 additional cancers above the normally occurring number in that population. To put this into perspective, the lifetime normally occurring number of cancers per 100,000 people is around 40,000.

In the case of MRI, the frequencies involved are typically in the range 10–100MHz. The energies of electromagnetic waves at these frequencies are well below the threshold for ionisation to occur and so there is no risk of inducing cancer. There are, however, several potential bioeffects associated with MRI: heating of tissue; interference with nerve function resulting from magnetic fields; and injury caused by ferromagnetic objects which can become projectiles if carelessly introduced into the vicinity of the magnet.

Ultrasound is a mechanical wave motion. It is absorbed as it travels through tissue, the temperature of which may consequently be significantly increased. Also, ultrasound may have a direct mechanical effect that can be enhanced by the presence of gas bubbles, whether naturally occurring or artificially introduced as a contrast agent. At the exposures used in contemporary medical scanning, however, ultrasound does not appear to produce untoward effects.

In all scanning involving exposure to radiation, whether electromagnetic or mechanical, and whether or not plausible mechanisms for adverse bioeffects have been identified, it is necessary to apply two principles. Firstly, there must be a reasonable expectation that the benefit derived from the information likely to be obtained by scanning will be greater than the cost of any real or hypothetical damage that could result from the procedure. Secondly, it is prudent to apply the so-called ALARA ('as low as reasonably achievable') principle. This means that the radiation exposure should be the minimum necessary to obtain the required information.

6.3 Systems for unobtrusive screening

In this context, 'unobtrusive screening' means that the individual being scanned may be unaware of the process. This is, of course, quite distinct from non-invasive screening, since the exposure of subjects to radiation of any form is to some extent invasive, even though the subjects may be unaware of the process. The system needs to acquire the relevant data from the individual during the course of his or her normal activity, such as walking or sitting. The technologies which, potentially, can be used for this are X-radiography, X-ray CT, MRI, thermography, microwave imaging and terahertz imaging.

Ethical considerations relating to the dose of ionising radiation place constraints on the use of X-ray techniques. X-ray CT and MRI are both very expensive, particularly when configured to operate at very high speed. Moreover, it does not seem to be very realistic to attempt to detect, for example, tuberculosis from X-ray images of passengers walking through airports. This leaves thermography, microwave imaging and terahertz imaging as potential candidates for unobtrusive screening for infectious diseases.

Thermography has been used for screening passengers at airports to try to detect individuals with fever during episodes such as outbreaks of severe acute respiratory syndrome (SARS) (Ng 2005) or of avian influenza. The problem with this is that, ideally, the false-negative rate for fever detection needs to be zero and, even then, people affected by diseases may not necessarily have abnormally high skin temperature. Remote thermography may also be able to detect the temperature elevation caused by infectious diseases in plants (Chaerle et al. 2004; Schmitz et al. 2004).

In the context of the detection and identification of infectious diseases, the status of both microwave and terahertz imaging is unknown. The lack of a relevant contrast mechanism and the poor spatial resolution of microwave imaging make this an unlikely candidate. Terahertz imaging has very limited penetration through biological tissues, so any suggestion that it might have a role in detecting and identifying infectious diseases seems misplaced.

6.4 Automation and de-skilling of scanning and image interpretation

In general, scanning may either be carried out by a standardised process in which the settings of the machine are determined in advance and the object (human, animal or plant) to be scanned is placed in a particular configuration,

or it may depend on the skill of the operator and the collaboration (or restraint) of the object. In the former case, it may be possible to automate the scanning process. But, in the latter, automation is unlikely to be a realistic option without considerable loss of specificity. As has already been mentioned, however, automation will likely be key to the success of practicable screening.

Once images have been acquired, the next problem is to interpret the information they contain. Sometimes, this is self-evident even to relatively untrained observers. Much work needs still to be done, however, before it becomes possible to enable unskilled personnel to interpret data in more complicated situations, let alone to replace human observers by fully automated image analysis systems.

6.5 Integration with complementary detection and identification technologies

It is a well-recognised problem in science that specialisation may inhibit cross-disciplinary interactions. Yet it is essential to integrate technologies for non-invasive scanning and screening for infectious diseases with other technologies such as sensor networks, data mining and data fusion, genomics and bioinformatics, biosensors and biomarkers, epidemiological modelling, Earth observation, genetics and immunology. Although scanning may occasionally be definitive on its own, it will usually provide only a fraction of the information needed to detect and identify infectious diseases.

6.6 Non-invasive scanning and screening techniques as tools for research into infectious diseases

The need for accurate detection and identification is well established in research into infectious diseases. In humans, non-invasive scanning techniques are (or certainly should be) rationally incorporated into diagnostic protocols. The roles of these techniques in animal research remain fully to be identified. It is clear, however, that devices for scanning small animals, particularly mice, can provide useful information that is becoming more important in genetics research. In this and in traditional areas of non-invasive scanning, it is likely that the development of ‘smart’ contrast agents will be complemented by the development of improved and novel devices.

6.7 An achievable objective

This review has attempted comprehensively to discuss both current and emerging non-invasive scanning techniques in the context of the detection and identification of infectious diseases.

Ultrasound is currently the second most used technology in medical diagnosis. An achievable objective would be the development and production of a hand-held ultrasonic scanner, incorporating the transducer, electronics, display and power supply in a pocket-sized package. Such a device could have a wireless link transmitting video clips to databases and advisory systems. If manufactured in sufficiently large numbers, it could be inexpensive enough – perhaps £500 or less – to be used by medical practitioners and

trained surveillance personnel. It would help to detect and identify some bacterial infections in the thorax, infective and parasitic processes in the abdomen and musculoskeletal infections. It would have very many, widespread applications in almost every area of clinical medicine and in the examination of small animals in veterinary practice.

7 Conclusions

Nearly all serious infective processes in humans currently require non-invasive imaging for diagnosis and/or delineation of extent and/or guiding therapy. (Non-invasive scanning and screening techniques, however, currently have limited applications in the detection and identification of infectious diseases before they become clinically apparent.) They could be used for similar purposes in animals, but existing devices are unlikely to be financially viable. Apart from thermography, there does not appear to be any realistic prospect of their application in plants.

In humans, thermography seems to be the only technology that might be used for unobtrusive infectious disease surveillance. Its reliability in this application, though, is far from satisfactory.

None of the known emerging technologies have obviously useful applications in the detection and identification of infectious diseases.

The development and widespread availability of an inexpensive pocket-sized, simple-to-use ultrasonic scanner would probably be invaluable in the context of the detection and identification of infectious diseases in humans and in small animals. Moreover, it would disrupt and revolutionise the whole practice of medicine by empowering every practitioner, whether medically qualified or not, with a personal and immediate diagnostic imaging capability, backed up by online automated and specialist advisory support. The training implications of this inevitable development are considerable and are already being explored (Royal College of Radiologists 2005).

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Table 1: Features of current imaging techniques

		Modality					
Feature		**X-radiography**	**Ultrasonic scanning**	**Radionuclide scanning**	**X-ray CT**	**MRI**	**Thermography**
Spatial resolution (mm)		0.5	1	10	1	1	1
Contrast mechanism		Atomic number differences	Density and elasticity differences; flow and motion	Radioactive tracer uptake	Atomic number differences	Proton density and relaxation times	Surface temperature
Maximum penetration (cm)		50	20	40	50	50	Surface only
Temporal resolution		1s–50ms	250ms–20ms	5min–30s	5s–0.1s	3min–20s	1s–20ms
Hazardous bioeffects		Low risk of cancer	Probably none	Low risk of cancer	Low risk of cancer	Probably none	None
User acceptability		Good	Excellent	Good	Good	Some claustrophobia	Excellent
Portability		Cart or fixed	Cart or portable	Mobile or fixed	Mobile or fixed	Mobile or fixed	Cart or portable
Capital cost (£'000)		75–750	10–120	150–500	200–500	300–1,000	20–75
Consumables cost (£/scan)	Without contrast	10	5	n/a	10	20	1
	With contrast	50	50	50	50	80	n/a
Running cost (£000/y)	Staff	100	150	150	150	150	100
	Maintenance	20	20	20	30	100	20
Developmental trends		Electronic image sensors	Contrast agents, pocket-size devices, 3D imaging	Novel tracers, PET scanning (with commensurate cost escalation)	Multi-slice systems, better resolution, 3D imaging	Faster devices, open access magnets	Compact image converters

Table 2: Features of emerging imaging techniques

	Modality						
Feature	**Optical tomography**	**Optical coherence tomography**	**Microwave imaging**	**Terahertz imaging**	**Thermoacoustic imaging**	**Electrical impedance imaging**	**Magnetic field imaging**
Spatial resolution (mm)	5	0.05	5	1	0.1–10	5–10	1–5
Contrast mechanism	Optical absorption	Optical reflexion	Microwave absorption or reflexion	Terahertz absorption or reflexion	Optical or microwave absorption	Conductivity differences	Induced currents
Maximum penetration (cm)	10	0.5	20	5	1–10	20	15
Temporal resolution	1min–50ms	50ms	1min–50ms	30s–1s	30s–50ms	1min–50ms	5min
Hazardous bioeffects	None	None	Probably none	Probably none	Probably none	None	None
User acceptability	Excellent	Good	Excellent	Excellent	Good	Excellent	Good
Capital cost (£'000)	50–150	30–100	30–100	30–100	30–100	10–50	1,000–1,500
Developmental trends	Bedside array systems, improved image reconstruction	Disposable catheters, skin scanning	Improved image reconstruction	Better sensitivity, spectroscopy	Better sensitivity, improved image reconstruction	Bedside array systems, improved image reconstruction	Improved detectors
Relevance to DIID	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Research

Table 3: Application of current imaging techniques in DIID in humans

	Modality					
Anatomical focus	**X-radiography**	**Ultrasonic scanning**	**Radionuclide scanning**	**X-ray CT**	**MRI**	**Thermography**
Head and neck					Bacterial infection Viral infection Prion disease	
Thorax	Bacterial infection Parasitic infection Viral infection	Bacterial infection	Bacterial infection	Bacterial infection Parasitic infection Viral infection	Bacterial infection Parasitic infection	
Abdomen		Infective inflammation Parasitic infection			Infective inflammation Parasitic infection	
Musculoskeletal		Joint infection	Joint infection	Joint infection Spinal infection	Joint infection Spinal infection	
Skin						Fever (eg, SARS)

All the reports and papers produced within the Foresight project 'Infectious Diseases: preparing for the future,' may be downloaded from the Foresight website (www.foresight.gov.uk). Requests for hard copies may also be made through this website.

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