Nuclear Medicine Portfolio

IPEM Grade A Training Scheme

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Preface

During my six months of training in Nuclear Medicine, I have been involved in all the aspects of three separate departments within the North Glasgow University Hospitals N.H.S. Trust.

The first two and a half months, I was based at the Department of Nuclear Cardiology at the Glasgow Royal Infirmary (GRI), where a fundamental service to cardiology care is provided. This department is run with the support of three medical technical officers (MTOs), two part time secretaries, a part time physicist and a full time physicist, Dr. W Martin, who coordinates, supervises and co-operates in all the work. The department uses a dual headed gamma camera (IGE Optima) and a IGE StartCam 300XC/T to perform around 3000 cardiac studies per year. Radiopharmaceutical activities are obtained during the early morning from the central radiopharmacy at the Western and they are checked with a 271 VINTEN radionuclide calibrator.

The following two months and a half, I trained in the Department of Nuclear Medicine, also at GRI. This department provides various nuclear medicine imaging services and a non-imaging thyroid uptake as well as therapies for thyrotoxic patients. These services are provided by two consultant physicians, one senior registrar, two nurses, four MTOs, two receptionists, a part time physicist and a full time physicist, Dr. R Bessent, who acts as Director of the Medical Physics duties. This department uses three gamma cameras to perform around 6000 scans per year: an IGE StarCam XC/T; an IGE StarCam XR/T; and an IGE MaxiCam 400. The department also has a Lunar DPX bone densitometer, a CAPINTEC radionuclide calibrator, several contamination monitors, an automatic gamma counter and a thyroid uptake counter.
Finally, I spent the last month of my Nuclear Medicine training in the Department of Nuclear Medicine at the Western Infirmary (WIG). Here, 3 full time physicists (one of them is DR T E Hilditch, Director of the Department), 4 MTOs, an auxiliary nurse, a receptionist and a part time secretary, provide a wide range of diagnostic and therapeutic services. To do so, the department consists of a dual headed Picker Prism 2000XP and a single headed Siemens Orbiter ZLC, attending to 4000 patients per year. Similarly to the two departments at the GRI, this department counts on equipment to perform non-imaging investigations, such as a thyroid uptake counter, a Cobra auto-gamma counting system and a sample counter. The physicists also have some involvement with the Nuclear Cardiology Department in the hospital and have responsibility in the West of Scotland Radionuclide Dispensary - the central radiopharmacy for the area.

In each of these departments I have been involved in all the areas of the work of Physicist in the department, allowing me to fulfill all the competencies of the IPEM grade A training scheme. As well as being involved in the provision of the routine clinical service in the departments I have carried out a number of projects. These have included several audits on the activities administered to patients on different types of studies in the two departments at GRI. In particular, in the Nuclear Cardiology Department at the GRI, these activities have to be measured using the gamma camera due to the distance between the Wards and the radionuclide calibrator site. Consequently, I was asked to do a complete investigation on the reliability of this method to measure activities, versus the use of the radionuclide calibrator. This gave me the opportunity to investigate the performance of a gamma camera in many different aspects as well as to perform QC measurements on a 271 VINTEN radionuclide calibrator. Similarly, I extended these measurements to other equipment of routine use in a Nuclear Medicine Department, such as a thyroid uptake counter and an automatic gamma counter. Finally, I monitored and reported the effective dose received by MTOs in the Nuclear Cardiology Department at the GRI.
Chapter 1

Nuclear Medicine Technology and Quality Control

The concept of Quality Control (QC) refers to the assessment, maintenance and optimisation of a particular aspect of the instrumentation. The procedures concerned with the QC of different aspects of the technology involved in Nuclear Medicine are covered in IPEM reports 65 and 66 [1, 2]. These two reports review all the quality control procedures relevant to equipment used in Nuclear Medicine.

Nuclear Medicine Science embodies techniques and technology used for diagnosis and therapy purposes using radionuclides. This includes the measurement of radionuclides and the assessment of their impurities, the visualisation of the distribution of radioactivity once the radionuclide is inside the human body, the use of digital computers to process this information, and the optimisation of images. The next subsections will deal with my personal experience assessing the QC of nuclear medicine equipment.

1.1 The gamma-camera and its performance

The gamma camera is the main instrument used in Nuclear Medicine. It is the only piece of equipment in Nuclear Medicine, which allows qualitative and quantitative information to be simultaneously acquired for both diagnosis and dosimetry purposes.
In this section I will outline the design characteristics and principle of operation of a gamma camera. Then I will focus the rest of the section on my experience assessing the performance of a General Electric Star Cam gamma camera.

1.1.1 Gamma camera detector head

A schematic diagram of a gamma camera detector head is shown below.

![Schematic diagram of a gamma camera detector head](image)

Figure 1.1: Schematic diagram of a gamma camera detector head. (A) Collimator, (B) NaI(Tl) crystal, (C) Light guide, (D) Photomultipliers, (E) Pulse arithmetic circuit, (F) Shielding.

A gamma camera detector head is composed of:

- Collimator
- Scintillation crystal
- Light guide
- Photomultiplier tubes

Radionuclide disintegration events produce gamma rays. These gamma rays pass along the holes of the collimator and then are absorbed in the crystal at a location corresponding to the original location within the body. Those gamma rays
travelling along paths outside the acceptance angle of the collimator holes will be absorbed in the collimator lead septa. Those gamma rays absorbed by the NaI(Tl) crystal will be converted into light photons, which will be guided by the light guide to the photomultiplier tubes. Here the light is converted into electrical pulses, where the total charge in the pulse from each photomultiplier tube is proportional to the mean number of photons received by the photocathode of that tube. These pulses, containing information on both the position of the scintillation event and the gamma ray energy absorbed within the crystal, are routed to a pulse arithmetic circuit which produces signals suitable for transmission to cathode ray tube display and image processor. The whole assembly is housed in a protective shield made from steel and lead which serves both as a mechanical framework and as an absorber of extraneous radiation. A more detailed analysis of each of these components is given below.

**The Collimator**

The purpose of the collimator in a scintillation camera is to allow $\gamma$-rays originating from a selected area of an organ to reach a selected area of the detector. Thus, a collimator establishes a one-to-one correspondence between different locations on the detector and those within the organ.

Collimators are classified according to their spatial resolution and sensitivity. Collimator sensitivity can be defined as the ratio of the number of gamma rays detected to the total number emitted by the sources. The spatial resolution of a collimator can be defined as its ability to transfer detailed information on the distribution of the radioactive material from the object to the image. This spatial resolution is measured from a profile through the image of a very thin line source and it is usually expressed in terms of the full width half maximum (FWHM) height of the line spread function (LSF) corresponding to this line source (see section 2.1.2).

The relationship between spatial resolution and sensitivity will depend on the type of collimator used. The most common type of collimator is the parallel-hole collimator. In this case the spatial resolution depends on various collimator parameters, such as collimator length ($L$), diameter of the holes ($d$), thickness of the crystal ($c$), and the distance $F$ of the source from the collimator face, as follows
1.1 The gamma-camera and its performance

\[ \text{Resolution} \approx \frac{d(L + F + c)}{L} \]  

(1.1)

where the following diagram explain the arrangement of each of this elements.

Figure 1.2: Collimator parameters in relation to spatial resolution.

Thus, when a source is at a distance \( F \) from the collimator, to improve the resolution we have to either reduce \( d \) or \( c \), or increase \( L \).

The sensitivity however depends on \( d \), \( L \), \( D \) (crystal diameter) and \( s \) (septa thickness), as follows:

\[ \text{Sensitivity} \propto \left( \frac{d^4}{L^2} \right) \cdot \left( \frac{D}{d + s} \right) \]  

(1.2)

From this last equation, it can be seen that sensitivity can be increased by either increasing \( d \) or decreasing \( L \), which is the opposite of that required to improve the spatial resolution.

There is, therefore, always a trade-off between spatial resolution and sensitivity in collimator design. The choice of collimator will depend on the radionuclide to be used and the nature of the clinical investigation being performed. In static imaging, for example, the collimator should be designed so that it offers a high resolution as increasing the acquiring time can compensate to some extent for its poor sensitivity. For a dynamic study, however, it is normally necessary to choose a collimator with higher sensitivity due to the short-exposure images.

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Collimators are also be classified according to the energies of $\gamma$-rays for which they have been optimised, such as low-energy (0 – 200 keV), medium energy (200–400 keV) and high-energy (400 – 600 keV) collimators. The main difference between collimators designed for different energies is the septal thickness of the collimator which increases with energy. Four main types of collimators can be used with scintillation cameras:

1. **Parallel hole.** It is the collimator used in the great majority of studies. Its main characteristic is that the holes are parallel along the vertical axis of the collimator, which provides a fixed relationship between the object size and the image size. I used the next three different types of parallel-hole collimators to perform Quality Control measurements and imaging studies:

   (a) Low energy general purpose (LEGP)

   (b) Low energy high resolution (LEHR)

   (c) Low energy high sensitivity (LEHS)

The next table summarises some of the common features of these collimators:

<table>
<thead>
<tr>
<th>Collimator</th>
<th>Field of view (mm)</th>
<th>No. of holes</th>
<th>Hole Length (mm)</th>
<th>Septal thick. (mm)</th>
<th>Hole diam. (mm)</th>
<th>Relative sensitivity (cpm/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEGP</td>
<td>400</td>
<td>18 000</td>
<td>41</td>
<td>0.3</td>
<td>2.5</td>
<td>90.4</td>
</tr>
<tr>
<td>LEHR</td>
<td>400</td>
<td>32 000</td>
<td>40</td>
<td>0.3</td>
<td>1.8</td>
<td>52.6</td>
</tr>
<tr>
<td>LEHS</td>
<td>400</td>
<td>9 100</td>
<td>36</td>
<td>0.5</td>
<td>3.4</td>
<td>189</td>
</tr>
</tbody>
</table>

Relative sensitivity is quoted for $^{99m}$Tc with a 20% window.

Table 1.1: *Characteristics of some of the collimators suitable for a IGE StarCam 300XC/T$\gamma$-camera.*
2. **Pinhole.** It consists of a single hole, about 5 mm in diameter, at the top of a hollow lead cone. It is used to magnify small organs, where the magnification factor is \( m(z) = \frac{z + d}{z} \). Here, \( z \) is the distance from the aperture of the collimator to the organ and \( d \) is the distance from the aperture to the crystal. Some of the disadvantages of this collimator is its low sensitivity due to the small size of the aperture and the distortion of the images near the edges of the field of view (FoV).

3. **Converging.** In this collimator, the holes converge towards a point in front of the gamma camera. This arrangement provides enlarge images of relatively small organs. This arrangement improves resolution and sensitivity, although they introduce distortion in the image.

4. **Diverging.** Opposite to the converging, the holes are arranged divergently, which allows an object larger than the gamma camera field of view to be imaged. This collimator is rarely used.

**The Crystal**

All commercial gamma cameras use NaI(Tl) (sodium iodide activated with a trace of thallium) as the scintillation crystal. This has a high attenuation coefficient due to its high atomic number (Z=53) and density, giving a theoretical intrinsic efficiency (photon stopping power) of 90% at 140 keV for a 13 mm thick crystal. Another characteristic is its high conversion efficiency of gamma photons to visible light. Gamma cameras presently available use up to 13 mm thick crystals. However, cameras with thinner (9 mm) crystals are available. This does not affect the count rate capability or field uniformity but does improve intrinsic resolution. The sensitivity of a 9 mm thick crystal is significantly lower than the 13 mm crystal at 141 keV and the loss becomes even more significant when imaging radionuclides such as \(^{111}\text{In} \) or \(^{131}\text{I} \) (245 keV and 364 keV, respectively).

Some of the disadvantages of a NaI(Tl) crystal is that it is hygroscopic (tending to absorb moisture from air) so the crystal is hermetically encapsulated in an aluminium cylinder with one flat Pyrex face. The crystal also has a high thermal expansion coefficient, so a maximum rate of temperature change of 1°C per hour.
at the crystal is recommended. This is controlled maintaining the room temperature stable with a maximum temperature change of 3°C to 5°C per hour. Small mechanical shocks can also dramatically damage the crystal.

**Light Guide**

The light guide acts as an optical coupler between the exit window of the crystal and the photomultipliers (PMTs). It is made from a transparent plastic such as quartz impregnated plexiglass with an optimum thickness of 0.7 times the PMT radius.

The crystal exit window is coupled to the lightguide, and the latter to the PMTs, by an optical coupling material, usually silicone grease or oil. Care must be taken that no air bubbles become trapped in the grease, otherwise total internal reflections will reduce light transmission. The whole system is assembled in such a way that no change of refractive index occurs in between the different surfaces of crystal, light guide and photomultiplier. Refractive effects will introduce distortion and noise in the images.

**Photomultiplier Tubes**

The light output from the scintillation crystal/lightguide is measured by an array of PMTs. The object is to gather as much light as possible and, as most PMTs are hexagonal, this leads to the adoption of a close-packed array. Current cameras employ between 61 and 91 PMTs.

Each PMT is constituted of a photocathode facing the window through which light enters, a series of metallic electrodes known as *dynodes* arranged in a special geometric pattern, and an anode - all enclosed in vacuum in a glass tube. When a light photon hits the photocathode, it produces an electron of low energy (0.1–1 eV) through photoelectric interaction. This photoelectron is then accelerated toward a dynode by the application of a voltage (between 50 and 100 V) to that dynode. As a result of this acceleration, the electron acquires sufficient kinetic energy (50 – 100 eV) to produce a number of secondary electrons when it collides with the dynode. The number of secondary electrons produced varies between 1 and 10, depending on the kinetic energy of the first electron. These electrons are then accelerated toward a second dynode (at two times the voltage applied on the first dynode) where a
similar multiplication in the number of electrons occurs. Eventually, at the last dynode (generally the tenth), there are between $10^5$ and $10^8$ electrons for each of the photoelectrons produced. These electrons generate a current pulse of a few microamperes in amplitude and less than a microsecond in duration at the anode. Thus the initial flash of light produces a pulse of charge or voltage large enough to be measured electronically. The amplification factor is very sensitive to changes in the overall voltage, which has to be highly stabilized.

**Pulse Arithmetic (position logic)**

The next figure explains how the light pulse illuminates differentially the array of photomultiplier tubes.

![Diagram](image)

Figure 1.3: *The amplitude of the electrical pulse produced by the photomultipliers around the scintillation event is bigger than the pulse produced by the rest.*

This light pulse will produce the largest electrical pulse in the photomultiplier nearest to the collimator hole through which the gamma ray passed - and smaller pulses in adjacent photomultipliers. A microprocessor chip, the ‘pulse arithmetic circuit’, combines the pulses from all the photomultipliers according to certain equations. This yields three voltage pulses (X, Y, Z) which are proportional to:

- The horizontal or X and vertical or Y coordinates of the light flash in the crystals, the hole through which the gamma ray has passed, and so the position of the body of the radioactive atom that has emitted it (X,Y).
1.1 The gamma-camera and its performance

- The photon energy of the gamma ray (Z). For this purpose the pulses from all the photomultipliers are simply summed, as if there were one large photomultiplier, measuring all the light produced by the gamma ray in the phosphor crystal. The size or ‘height’ of the Z-pulse (so many volts) is proportional to the gamma ray energy (in kiloelectronvolts) absorbed. For convenience the pulse height is generally stated in the corresponding kiloelectronvolts (keV).

**Pulse Height Spectrum**

So far, two facts have been ignored:

1. Gamma rays are scattered in the patient, so those gamma rays which have originated outside the line of sight of the collimator can enter a collimator hole, and as they have been scattered, do so with reduced energy.

2. Gamma rays may lose energy through Compton interactions in the crystal before being absorbed photoelectrically, and so produce only pulses of reduced height.

When a large number of gamma rays are emitted in succession within a patient, the Z-pulses therefore vary in height. If the frequency of pulses having various heights or energies is plotted for a given period of time, the result is what we can see in the following pictures. These figures correspond to the pulse height spectrum I measured from two different patients.
Figure 1.4: Pulse height spectrum measured from two different patients with different radionuclides injected: upper a $^{99m}$Tc spectrum; and lower a $^{131}$I spectrum. It is possible to observe the relative frequency of pulses of various heights.

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These two spectrums are made up of:

- A photopeak, in yellow, comprising pulses produced by the complete photo-electric absorption in the crystal of those gamma ray photons which have come from within the patient without suffering Compton scattering.

The spread of energies in the photopeak, evident in these two figures, is due to statistical fluctuations in both (a) the number of light photons produced in the crystal by each gamma ray photon; and (b), the number of electrons produced in the photomultiplier by each light photon.

- A Compton tail, in white, containing pulses of lower energy, mostly produced by those gamma rays, which have suffered Compton interactions in either the patient or the crystal.

The same spectrums taken from sources of radioactivity not subjected to any attenuation (i.e., measured out of patients) should not show these Compton tails, as it is shown in the following two pictures corresponding to the spectrums I measured using the same sources than previously but out of the patient.
1.1 The gamma-camera and its performance

Figure 1.5: Pulse height spectrum measured from two different radioactive sources ($^{99m}$Tc on the upper image, and $^{131}$I on the lower) out-of-patient, showing the relative frequency of pulses of various heights.

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1.1 The gamma-camera and its performance

Only pulses in the photopeak are of use in locating the source of the radioactivity in the patient, and a pulse height analyzer is used to reject those in the Compton tail.

**Pulse Height Analyser**

The pulse height analyser (PHA) processes the Z-voltage pulses produced by the pulse arithmetic circuit before these arrive to the analog-to-digital converter (ADC) for further processing. This PHA is set by the operator to reject pulses, which are either (a) lower than a pre-set value or (b) higher than another pre-set value. It lets through only those pulses which lie within a window of 10% of the photopeak energy, as is the case of the spectrums shown in the previous figures.

1.1.2 Gamma Camera Performance

In order to ensure a reliable clinical performance of the gamma camera, quantitative and qualitative performance data must be collected and recorded on a regular basis. These data should refer to the main parameters characterizing the performance of the gamma camera: spatial resolution, non-uniformity, sensitivity, count-rate characteristics, and energy resolution. The guidance to test these parameters is well documented, and in my particular case I have been following similar procedures as those described in [2].

In the following lines I will describe how I carried out these performance tests on a GE StarCam 300 XC gamma camera and present the results obtained.

**Spatial Resolution**

The first parameter I tested was the system resolution of the camera, and the purpose of the experiment was to measure the camera resolution.

The material used to perform the measurement was a perspex phantom of 440 × 300 × 25 mm dimension with two parallel lines of narrow-bore tubing, 0.5 mm diameter. These lines were 200 mm apart being equidistant from the middle axis of the phantom (See following diagram).
1.1 The gamma-camera and its performance

Figure 1.6: Geometry and dimensions of the phantom used to measure the resolution of the gamma camera.

This phantom was placed on the top of a parallel-hole LEGP collimator (the distance between the plane containing both lines and the surface of the collimator was 12.5mm), aligning its central axis with the X-axis of the gamma camera. Then 2.6 MBq of $^{201}$Tl was injected into the parallel lines and an image acquired by counting for 2000 seconds.

Figure 1.7: Image of a two-line source phantom. This image was acquired with a resolution of $512 \times 512$ pixels. The two line sources were positioned parallel to the X-axis of the gamma camera, and then in order to obtain the LSF, the image was scanned perpendicular to the direction of these lines (i.e. parallel to the Y-axis).
Once the image of the phantom was acquired, the image was analysed in order to obtain the line spread function (LSF) of the resultant activity distribution profile along the Y-axis of the camera. The next figure shows the LSF obtained from the image.

From this profile, I calculated the number of mm represented by a pixel of the image. To do so, I compared the distance between the centres of the two parallel lines with the number of pixels between the peaks of the LSF associated to these lines. The resultant relationship between pixels and mm was 128 pixels to 200 mm distance between peaks, giving as a result 1.56 mm/pixel.
Once the relationship between pixels and mm was established, I measured the FWHM (in pixels) corresponding to the LSF of a point source placed at different distances from the collimator.

Figure 1.9: Point sources at four different distances from the collimator. This image was acquired with a resolution of 512 × 512 pixels.

Then, using the relationship above, I expressed the FWHM at each distance in mm. In this way, the resolution of the gamma camera can be studied by plotting the FWHM versus distance between point source and collimator (see Figure 2.13).

The same measurement was done using a parallel-hole LEHS collimator in order to study the influence of the collimator resolution on the system resolution. These two resolutions are related by the equation:

\[ SR^2 = IR^2 + CR^2 \] (1.3)

Where IR represents the intrinsic resolution of the system, CR is the collimator resolution and SR is the system resolution.

The resultant profiles of the point source at different distances using two different collimators is shown in the next two figures.
1.1 The gamma-camera and its performance

Figure 1.10: LSF of point source at different distances from a LEHS collimator.

Figure 1.11: LSF of point source at different distances from a LEGP collimator.
1.1 The gamma-camera and its performance

The reason the height of the LSF of a source decreases with distance can be explained as follow. As the sensitivity of a parallel-hole collimator is independent of source-to-collimator distance (see Study of the change of sensitivity with distance in section 2.1.3), the total counts enclosed by each of these curves should be the same. However, as we can see in the next figure, the resolution is distance dependent as the FWHM of the source profile increases with source-to-collimator distance.

![Diagram of Line Spread Function (LSF) of a parallel-hole collimator as a function of source-to-collimator distance.](image)

Figure 1.12: Line Spread function (LSF) of a parallel-hole collimator as a function of source-to-collimator distance. The FWHM of the LSF increases linearly with distance from the source to the collimator (see Figure 2.13); however, the total area under the LSF (photon fluence through the collimator) decreases very little with source to collimator distance.

Therefore, if the area under the curves represents the total counts and the curves get wider as the source-to-collimator distance increases, the height of the curves should decrease to keep the area (i.e. total counts) constant.

In the next figure, the FWHMs obtained from the LSFs of Figures 2.10 and 2.11 were plotted versus source-to-collimator distance. From here, I calculated that the FWHM at 0 mm from the surface of the collimator to the surface of the phantom was $5.47 \pm 0.78$ mm in the case of the LEGP collimator, and $6.35 \pm 0.78$ mm in the

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case of the LEHS collimator. Then, as the distance increases the FWHM increases, i.e. the resolution decreases (see Figure 2.13).

It is possible to observe how the system resolution is much poorer when using a high sensitivity collimator than with a high resolution collimator. The FWHM measured with the former gets wider much faster as source-to-collimator distance increase.

**Count Rate Characteristic**

A gamma camera has a pulse processing time associated with each scintillation event and so, as the count rate increases, a region is reached in which the response of the gamma camera (observed count-rate) is no longer linear with increasing source radioactivity (true count-rate).

The next curves show the count rate response in the linear and non-linear ranges...
1.1 The gamma-camera and its performance

of the gamma camera I used in Nuclear Cardiology (StarCam camera). The experiment was carried out with a 2 GBq source of $^{201}$Tl and counting at different stages of decay of the source. The window width used was ±10% centred at the maximum of the photopeak.

To obtain the incident (input) count rate for those activities at which the camera behave non-linearly, I obtained a relationship between count rate and activity from the linear region and then applied it to the activities of the non-linear region to find out their correspondent count rate. The activities, at which the gamma camera was supposed to behave linearly, were measured using a VINTEN radionuclide calibrator immediately before counting for 100 seconds on the gamma camera. The activities of $^{201}$Tl selected for this purpose were chosen based on the range of activities used for the imaging procedures (up to 150 MBq) in Nuclear Medicine. Selecting activities within this range, it was guaranteed the linear response of the camera. The next plot shows the expected linear relationship.

![Figure 1.14: Linear range of the count rate response of the gamma camera.](image)

From where a conversion factor between radionuclide activity and count rate can
be given:

\[
\text{Count Rate (kcps)} = 0.285 \times \text{Activity (MBq)} \tag{1.4}
\]

This measurement was performed using a LEGP collimator.

After having obtained this conversion factor between activity and count rate, the 2 GBq source of $^{201}$Tl was used to obtain the following curve.

![Image](image.png)

Figure 1.15: Curve illustrating the count-rate response of the gamma camera.

The IPEM Report 66 establishes that the count rate performance of a gamma camera should be expressed quantitatively by quoting the input count rate at the point where the input and the output values differ by a certain percentage, usually 10% or 20%. In this particular case, these two percentages were 31,000 and 39,000 incident counts per second, respectively.

**Uniformity**

Uniformity can be defined as the ability of a gamma camera to reproduce a uniform radioactive distribution produced by a flood source. This can be assessed either
by visual examination of a flood image or by quantitative measurement. Visual examination provides a quick assessment of the uniformity but may fail to reveal subtle changes caused by the deterioration of the gamma camera over a long period. For this reason quantitative methods are used ([6]).

Quantitative measures can be divided into two types: those which measure global changes in uniformity and those for detecting local effects. The first type gives the Integral Uniformity of the gamma camera while the second gives its Differential Uniformity. There are different methods to calculate these two quantities, but the way it was calculated for both useful field of view (UFOV) and central field of view (CFOV) was based on the following formulas:

- Integral uniformity is a measure of the difference between the maximum \( C_{\text{max}} \) and minimum \( C_{\text{min}} \) counts per pixel in the image:

  \[
  \text{Integral Uniformity} = \frac{C_{\text{max}} - C_{\text{min}}}{C_{\text{max}} + C_{\text{min}}} \times 100\% \tag{1.5}
  \]

- The measurement of differential uniformity is carried out on sets of 5 pixels. In this case only the maximum difference found between the counts in two pixels in these sets is used. If the higher of these two pixels has \( H \) counts and the lower \( L \), then:

  \[
  \text{Differential Uniformity} = \frac{H - L}{H + L} \times 100\% \tag{1.6}
  \]

These two quantities are calculated automatically by the computer.

Non-uniformity effects occur due to a change in the count rate in the individual pixels in the image. This results in the appearance of increased count rate (‘hot’) or decreased count rate (‘cold’) areas across the image. Different factors can produce this effect, such as: variations in the thickness of the scintillation crystal, non-uniform radioactive flood source and bad transmission of the \( \gamma \)-rays by the collimators.

However, the most predominant cause of nonuniform response is electronic in nature. It is related to differences in response of photomultipliers (PM) tubes and to the difference in transmission light produced at different places in the crystal. This problem can be solved in two different ways. One is by tuning the electronics
of the camera to tune all the PM to have the same sensitivity; and, the other software correction techniques. My experience in uniformity correction is based on the second method, as the first one is done at each service visit. I will discuss two different uniformity images I obtained when performing uniformity tests at the WIG. This images are routinely obtained using a fluid filled perspex phantom of dimension 540mm $\times$ 440mm $\times$ 15mm which covers the entire field of view of the gamma camera. The fluid inside the phantom consists of water mixed thoroughly with 400 MBq of $^{99m}$Tc. $100 \times 10^6$ counts are acquired in each image.

The first image shows the effect on the integral and differential uniformity when the flood source has not been correctly mixed. This flood source would never produce a homogenous distribution of radiation.

![Figure 1.16: Non-uniform flood image. The total counts acquired were $100 \times 10^6$.](image)

In this case, the uniformity values were:

<table>
<thead>
<tr>
<th></th>
<th>UFOV</th>
<th>CFOV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Integral</strong></td>
<td>3.81%</td>
<td>3.18%</td>
</tr>
<tr>
<td><strong>Differential</strong></td>
<td>1.73%</td>
<td>1.73%</td>
</tr>
</tbody>
</table>
The second flood image shows what it should be expected on a camera with a good performance when a uniform flood source is used.

![Uniform flood image. (Total Counts = 100 × 10^6)](image)

In this case, uniformity parameters were:

<table>
<thead>
<tr>
<th></th>
<th>UFOV</th>
<th>CFOV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Integral</strong></td>
<td>1.20%</td>
<td>0.94%</td>
</tr>
<tr>
<td><strong>Differential</strong></td>
<td>0.93%</td>
<td>0.76%</td>
</tr>
</tbody>
</table>
1.1 The gamma-camera and its performance

1.1.3 Study of the influence of other factors related to the performance of the gamma camera

So far, all the performance parameters described above are related to physical (or construction) characteristics of the gamma camera. However, there are other parameters, which can also affect the performance of the gamma camera. Examples of these parameters are the effect of source-detector distance on the count rate; the change of source volume on the count rate; and, the offset of the electronic window on the count rate. I tested these parameters in order to obtain possible errors introduced in the measurement of the activity of a source using a gamma camera. Due to the distance between the radionuclide calibrator and the imaging rooms in Nuclear Cardiology at the GRI (one of the wards is more than one kilometre apart from the radionuclide calibrator), the gamma camera has to be used to monitor the activities administered to the patients. This method of activity measurement is accurate as long as the gamma cameras are calibrated against the radionuclide calibrator, and the activities imparted to patients remain within the region of linear behaviour of the cameras. In this region, as we saw in Figure 14, the relationship between count rate and activity of $^{201}$Tl at 0 cm from a LEGP collimator was given by Equation (2.4):

$$ kcps = 0.285 \times \text{Activity(MBq)} $$

where 0.285 kcps/MBq is the calibration factor used in Nuclear Cardiology. In the next paragraphs, I will describe the experiments I carried out to assess the effect of these factors on the measurement of activities using a gamma camera.

Study of the change of sensitivity with distance

I investigated the effect that distance between source and detector has on the count rate. This was assessed using a 2.5 ml syringe containing 40MBq of $^{201}$Tl in 0.1 ml (this small volume was used to simulate a point source). The syringe was positioned vertically and held steady in a retort stand at different distances from a LEGP parallel-hole collimator. The next plot shows how the total counts obtained from the gamma camera change as the source is separated from the collimator.
This result might be surprising thinking of the ‘inverse square law’. This law establishes that the intensity of radiation from a point source varies as the square of the distance between the source and the detector. It is obvious that this does not explain what happens in the figure above. There must be therefore a competing effect that cancels out the effects of the inverse square law.

It was seen in section 2.1.2 that, with a parallel-hole collimator and when using a radionuclide which emits $\gamma$-rays at such energies that no septal penetration occurs, the effective area of the detector will increase with the source-to-collimator distance (see Figure 2.12). This was the conclusion inferred from the increase of the FWHM of a point source profile when the source-to-collimator distance increases (Figures 2.10 and 2.11).

As more area of the crystal is exposed, more scintillation events will occur producing therefore more detectable light. But at the same time, this increase of scintillation events is balanced by the decrease of the intensity of the $\gamma$-rays reaching the crystal due to the inverse square law. As the result of these two competing effects, the total counts measured with a gamma camera (sensitivity) is
1.1 The gamma-camera and its performance

independent of the source-to-collimator distance.

Internal Absorption Effect

Another important factor that might affect the reading of the source activity when using a gamma camera is the volume of the source. When the volume increases, more internal absorption will occur, as the gamma rays have to travel a larger distance inside the vial before leaving the sample. To prove this, I measured the total counts obtained from different volumes (0.1 to 2.5 mls) of 5.7 MBq $^{201}$Tl within a 2.5 ml syringe placed vertically on the top of the LEGP collimator. At each volume, the total counts were measured five times for 10 seconds each, and then averaged and converted to activity using the Equation (2.4). The next plot shows the change of total counts with volume:

![Study of the Internal Absorption Effect within an Increasing Volume of Thallium](image)

Figure 1.19: *Reduction of the activity of a source due to internal absorption as its volume increase.*

The fall off of the regression line in Figure 2.17 as the volume increase is 10% approximately. Such reduction in the activity can be caused due to either the
change in the volume or the decay of the source activity, or both things at the same time. To discriminate the real reason, I calculated the decay of the source during the period the measurement lasted for. This was 43 minutes (0.72 hours). From the decay law:

\[ I = I_0 \times e^{-\left(\frac{\log 2}{T_{1/2}}\right) \times t} \]

\[ I = 5.68 \times 0.993 = 5.64 \text{ MBq} \quad (1.7) \]

However, the final reading at the end of the experiment was 5.09 MBq. Therefore I concluded that the fall off was produced by the increase of the internal absorption effect as the volume of the source increased.

Most of the \( \gamma \)-rays produced by \textsuperscript{201}Tl have energies around 72 keV, having a theoretical half value thickness in water of 4.0 cm approximately. However, it emits some rays at higher and lower energies (11\% at 16.7 keV and 2.8\% at 135 keV) which will affect the practical half value thickness in water. I performed all my calculations considering the theoretical value of 4.0 cm. Hence, the absorption coefficient in water for \textsuperscript{201}Tl will be

\[ \mu = \frac{0.693}{4.0} = 0.178 \quad (1.8) \]

Hence, if 1 cm of saline is added to the syringe, the source activity will decay to

\[ I = 5.68 \times e^{-0.178 \times 1} = 4.75 \text{ MBq} \quad (1.9) \]

Which represents a 16\% drop from the initial activity. From this result it is more obvious to think that the fall off of the line in Figure 2.17 is due to absorption with a negligible contribution due to decay of the source.

In order to estimate the best set-up of the syringe when a gamma camera is used to assess its activity, the experiment was repeated but with the syringe positioned horizontally on the collimator. In this case, I used a 6 MBq source of Thallium in four different volumes: 0.3 ml, 1 ml, 2 ml and 2.5 ml made up in the same syringe by adding saline to the syringe each time the measurement was performed. The next plot quantifies the difference and describes how different are the readings at different volumes.
1.1 The gamma-camera and its performance

Figure 1.20: Change in activity measured for different volumes at two different geometries. At each volume, the activities were corrected for decay.

From this plot I inferred that the best set-up corresponds to the positioning of the source horizontally, as the activity with this geometry remains practically constant when the volume increases.

**Offset Error**

Another important parameter to be considered when assessing sources activities is the offset value of the camera. As the electronics of the camera drifts, the electronic window can become offset, and this can lead to a wrong estimation of the activity assayed. To estimate the order of the error introduced at different values of window offset, I measured the count rate produced by a 52 MBq of $^{201}$Tl placed on the top of the LEGP collimator when moving the centre of the window (72 keV) from 65 keV ($-10\%$) to 80 keV ($+11\%$). The next figure shows that the count rate is maximal at 70 keV, where this maximum is 15235 cps. If the photopeak is centred in any offset value between 65 keV and 74 keV, the error
introduced in the activity assayed will be less than 10%.

Figure 1.21: Counts measured at different offset of the electronic window. 0% offset represents the centre of the photopeak at 72 keV.
1.2 Radionuclide Calibrator

A radionuclide calibrator is a composite system consisting of an ionisation chamber coupled to appropriate electronic circuitry which allows the conversion of the ionisation current to a measure of radionuclide activity. Although a radionuclide calibrator might be considered as one of the less complicated devices of medical equipment, its response for a particular radionuclide is a function of many variables, each of which may introduce significant errors. I was involved in the assessment of the error introduced in the linearity and precision of a Vinten radionuclide calibrator (type 271) shown in the following picture.

![Vinten radionuclide calibrator](image)

**Figure 1.22: Vinten radionuclide calibrator.**

This type of radionuclide counter uses an ionisation chamber which will measure the ionisation produced in air by the radionuclide. A lead shielding of 3 cm is incorporated around the chamber in order to eliminate the background radiation.

*CHAPTER 1. Nuclear Medicine Technology and Quality Control*
1.2 Radionuclide Calibrator

1.2.1 Linearity

One of the potential sources of error when measuring the activity of a highly active source with a radionuclide calibrator, is the saturation characteristics of the ionisation chamber. The production of ion pairs within the sensitive volume of the ionisation chamber increases with the assayed activity. As a result, a higher probability of ion recombination will occur, which can produce a reduction in the ion current collected per unit of activity. Therefore, this effect can lead to an underestimation of the assayed activity.

During my placement in Nuclear Cardiology at the GRI, I tested the linearity of the radionuclide calibrator used by the department to check the activities of the sources arriving in the morning from the dispensary. The highest activity contained in a single vial used in the Nuclear Cardiology department is 600 MBq of Thallium. I decided to test the saturation characteristics (linearity) of the ionisation chamber of the radionuclide calibrator using a source with an activity of 4 GBq of $^{99m}$Tc. Two reasons made me choose $^{99m}$Tc instead of $^{201}$Tl:

1. $^{99m}$Tc has a greater gamma dose rate constant than $^{201}$Tl (hence greater ionisation current).

2. To obtain an entire decay curve similar to the one obtained for $^{99m}$Tc would take more than three weeks.

To measure the linearity of the calibrator, I contrasted the measured activity with the expected activity, obtaining as a result a quantification of their difference. The next plot shows the theoretical and the actual decay scheme of the $^{99m}$Tc source used.
1.2 Radionuclide Calibrator

Figure 1.23: *Theoretical and actual decay curves of a 4 GBq source of $^{99m}$Tc measured in a VINTEN radionuclide calibrator.*

Each of the red dots was obtained as the average of 10 readings I measured for each activity in the calibrator. The time required to perform these 10 measurements each time was less than 1 minute, and therefore the decay factor was considered negligible. The precision of the measurement was mainly affected by the randomness of the nuclear emissions and the electrical noise of the instrument. The contribution to the imprecision of the measurement due to the electrical noise is measurable as shown in the next section.

From this plot, it is possible to quantify the difference between the two schemes by obtaining their ratio at different activities:
1.2 Radionuclide Calibrator

Figure 1.24: Linearity check of a VINTEN radionuclide calibrator.

In this graph, the mean of the ratio is 1.009, and the maximum and minimum are 1.036 and 0.993 respectively. Hence the response of the radionuclide calibrator is linear at high activities such as 4 GBq (modern calibrators start to saturate at 70 GBq), with a deviation (tolerance) of 3% from the mean. This result is well within the specifications of 5% given in Report 65 of The Institute of Physical Sciences in Medicine ([1]).

1.2.2 Precision

As it has been mentioned above, one of the main factors that affects the repeatability of the measurements performed with a radionuclide calibrator is the electrical stability of the instrument. In order to measure the imprecision introduced in the linearity check due to electronic noise, I measured the activity of a long life source, $^{137}$Cs which has a half-life of 30 years, each time the activity of the $^{201}$Tl source was assayed. The fact that $^{137}$Cs is a long life source and that each measurement was taken with the calibrator set with a long time constant, tell
us that the variability of the figures obtained from the calibrator only depend on the electronic stability of the device. I tested this stability over a period of 24 hours obtaining an average activity of 8 MBq (max = 8.11, min = 7.94). The next figure shows the variability of the figures obtained relative to the mean activity:

Figure 1.25: Precision check of a VINTEN radionuclide calibrator.

From these results I inferred that the electronics of the unit is stable having a variability in its reproducibility of 2.1%. This value is the maximum percentage deviation from the mean of the measurements and, as the maximum deviation recommended by the Institute of Physical Sciences in Medicine is 3%, I concluded the unit complied with the specifications.

1.3 Thyroid Uptake Counter

Two basic components constitute a Thyroid uptake counter:

1. NaI(Tl) Detector
2. Collimator

The next figure shows a representation of the same type of thyroid uptake counter used in Nuclear Medicine at the GRI.

![Diagram of Thyroid Uptake Counter]

Figure 1.26: *Sketch of the organ gamma counter used to assess thyroid uptake.*

The main characteristic of the scintillation crystal of the counter to be considered is its size, which is determined by the energy of the $\gamma$-ray to be detected and the sensitivity requirements of a particular study. In the case of the counter I used in Nuclear Medicine, the crystal size was 5 cm diameter by 5 cm deep. One of the main parameters affected by the crystal size is the efficiency of the counter, which I measured using a $^{99m}\text{Tc}$ source.

The other important component of the counter is the collimator, which is designed to exclude as much of the surrounding neck activity as possible. The collimator used in the GRI has a rectangular field of view with dimension 9 cm $\times$ 7 cm. At the same time, the collimator has an overall sensitivity within the field of view that varies inversely as the square of the distance between the source and the detector. But the uniformity across the organ improves as the distance from the detector is increased. Due to this opposed behaviour of efficiency and uniformity with distance, a collimator length of 30 cm is considered optimum to balance these two effects (see [4], pg. 96). This is the length of the collimator used with the counter. As indicated above, I measured the efficiency of the counter using a 1 MBq point source of $^{99m}\text{Tc}$ placed at 30 cm from the detector. In order to do so, I calculated the number of $\gamma$-rays arriving to the detector and measured the fraction counted by the detector. This fraction expressed as a percentage will represent the efficiency of the counter.
To calculate the number of $\gamma$-rays arriving at the detector, I first calculated the solid angle within which the $\gamma$-rays hit the detector. As the $\gamma$-rays are emitted isotropically, a detector placed at any point of a sphere centred on the source would measure the same number of $\gamma$-rays. This number will be quotient of the area of the detector and the total area of the sphere:

$$A_{\text{detector}} = \frac{\pi r^2}{4\pi R^2} = \frac{(2.5)^2}{4 \cdot (30)^2} = 0.00174$$ \tag{1.10}

Where $r$ represents the radius of the detector and $R$ is the optimum working distance. If the number of disintegrations produced in the source per second is $10^6$, and these disintegrations correspond to $\gamma_2$-rays, which have a mean disintegration number of 0.88 (i.e. 88% of the $\gamma$-rays produced are $\gamma_2$-rays), the total number of $\gamma$-rays arriving to the detector will be:

$$0.00174 \times 10^6 \times 0.88 = 1530 \text{ rays per second} \tag{1.11}$$

However, when the total counts were measured with the counter by placing the source at 30 cm from the detector and taking the mean of several measurements performed over a short period of time, the answer obtained was 1012 counts per second. Therefore, the efficiency will be

$$\text{Efficiency} = \frac{1012}{1530} \times 100 = 66\% \tag{1.12}$$

The error introduced by the randomness associated to nuclear decay in this measurement is given by the square root of the sum of the total number of counts in all the measurements:

$$\sqrt{30372} = 174.3 \implies \left(\frac{174.3}{30372}\right) \times 100 = \pm 0.6\% \tag{1.13}$$

### 1.4 Automatic Gamma Counter

Together with the single sample gamma counter and the organ counter (thyroid uptake counter), the automatic gamma counter is the third type of gamma counter which can be found in a department of Nuclear Medicine.

*CHAPTER 1. Nuclear Medicine Technology and Quality Control*
The automatic gamma counter used in the Nuclear Medicine department at the WIG is a Packard Cobra Auto Gamma 5000 Series. In this type of counter, the radionuclide sample is mounted in a sample cassette which moves by being pushed by chain-driven pins that engage the sample cassette as it moves against the detector assembly. The sample is then loaded into the detector by an elevator that lifts the container into a through hole type scintillation crystal of 7.5 cm of diameter and shielded by 7.5 cm thickness of lead. A counterweight helps to guide the sample in and out of the detector. An optical tube sensor monitors the cassette and by passes missing tubes.

The next spectrum corresponds to a standard sample of $^{111}$In, which was counted for 300 seconds. This spectrum was plotted using the automatic ‘spectraview’ protocol. The labelling in the different peaks correspond to the following energies:

- noise (a)
- 23 keV $\text{K-}\alpha_1$ x-ray (44% yield), 23 keV $\text{K-}\alpha_2$ x-ray (23% yield) and 26 keV $\text{K-}\beta$ x-ray (14.6% yield) (b)
- 170 keV gamma radiation (90.2% yield) (c)
- coincidence sum peak of 170 keV gamma and 23 keV x-rays (d)
- 245 keV gamma radiation (94%) (e)
- coincidence sum peak of 245 keV gamma and 23 keV x-rays (f)
- coincidence sum peak of 170 keV gamma and 245 keV gamma (g)
Then, in order to compare the energy resolution of different types of counters, the same sample was measured on a single sample counter with a cylindrical detector. Every point of the following plot corresponds to the reading obtained by scanning the number of counts produced in a 10 mV electronic window placed across a voltage range between 0 and 220 mV. Each reading was obtained after 10 seconds of measurement.

Figure 1.27: \(^{111}\text{In}\) spectrum measured with a through hole detector.
In this last figure, the three peaks correspond to:

- 77 keV lead x-ray (a)
- 170 keV gamma radiation (90.2% yield) (b)
- 245 keV gamma radiation (94% yield) (c)
From these figures, it is possible to infer how in the case of the auto-gamma counter, its geometry can provide erroneous information. In this case, it is more likely that the light pulses produced by different gamma rays are taken as the light pulse produced by a single gamma ray with energy equal to the sum of the energy of the two gamma rays. In the case of the well detector, no coincidence peaks are detected as the detector is not surrounding the sample.
Chapter 2

Diagnostic Nuclear Medicine

2.1 Imaging tests

2.1.1 Myocardial Perfusion Imaging

Number of Scans I have performed: > 15

Protocol

<table>
<thead>
<tr>
<th>Radio-pharmaceutical</th>
<th>Activity- (ARSAC limit)</th>
<th>Effective Dose</th>
<th>Collimator</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{201}$Tl-Chloride</td>
<td>50 MBq- (80)</td>
<td>11.25 mSv</td>
<td>LEHS</td>
<td>64 × 64</td>
</tr>
</tbody>
</table>

Introduction

Coronary arteriography provides anatomical information about the site and the severity of the ischemic cardiac muscle, but gives no information about the functional impact of the lesion on myocardial blood flow, particularly during stress. Radionuclide imaging used in conjunction with other non-invasive assessments provides such physiological (functional) information of critical importance in the management of patients with coronary disease.
Myocardial perfusion imaging is used to image the supply of blood to the heart (blood flow) and, hence, the ability of the heart muscles to take up oxygen. Currently there are two groups of agents available for perfusion imaging, $^{201}$Tl and $^{99m}$Tc analogues. The department of nuclear cardiology at the Royal Infirmary, Glasgow (GRI) uses $^{201}$Tl in perfusion imaging while the department of nuclear cardiology at the Western Infirmary Glasgow (WIG) currently uses $^{99m}$Tc-Tetrofosmin. The use of a $^{99m}$Tc based agent ($T_{1/2} = 6\text{ hrs}$) allows a much higher activity to be given (because the radiation dose from $^{99m}$Tc agents is lower\(^1\) than from $^{201}$Tl). This is useful in reducing noise, which is particularly important when SPECT imaging is being used. $^{201}$Tl on the other hand has a better uptake (4% vs. 1.2%, see [7]) with the result that $^{201}$Tl is still widely used for perfusion imaging, particularly in departments where planar imaging is used. Once within the heart, the half-life elimination is 7 hours approximately. The use of $^{99m}$Tc or $^{201}$Tl is just one of the differences in the perfusion imaging techniques employed at WIG and at GRI. There are two other essential differences, which make their imaging techniques very different. WIG uses SPECT imaging while GRI uses planar imaging. Additionally GRI always does both a perfusion scan and a blood pool scan to study ventricular function. WIG only does perfusion scanning, unless a blood pool scan is specifically requested. I shall concentrate on the techniques used at GRI since it was here that I spent most of my time in Nuclear Cardiology. Nevertheless, I will briefly discuss SPECT imaging at the end of this section.

There are three components to an exercise thallium scan as it is performed in the department at GRI. Firstly, the patient goes through a full 12 lead ECG exercise test on an ergometer bike. Depending on the patient’s physical ability, exercise is carried out in three minute stages with workload starting at 50 W and increasing by 50 W after each stage (although this may be decreased if the patient is unable to manage 50 W). During the exercise test the patient’s ECG is continuously monitored and blood pressure is measured approximately every three minutes. While the exercise test gives some diagnostic information, the main reason for this

\(^1\)The effective dose of $^{99m}$Tc-Tetrofosmin is 0.0067 mSv per MBq administered, while in the case of the $^{201}$Tl-Chloride, the effective dose is 0.23 mSv per MBq

\textit{CHAPTER 2. Diagnostic Nuclear Medicine}
procedure is to increase the patient’s heart rate. Thallium \( ^{201}\text{Tl} \), which is injected into the patient’s blood stream (right arm) approximately 30 s before they finish exercising, is taken up by muscle through the cellular sodium-potassium channels as if it were potassium ions. If the cellular uptake is proportional to blood flow, the effect of the exercise is that uptake is improved. Therefore, exercising the patient on an ergometer bike increases heart muscle activity and hence increases \( ^{201}\text{Tl} \) uptake by the heart muscle. Patients are asked to aim for a target heart rate of \((220 - \text{Age}) \times 0.85\) bpm.

In the case of the patient being unable to exercise, due to peripheral vascular disease, artificial limbs or hypertension, their heart can be artificially stimulated using drugs. The most common of these is Dipyridamole, a vasodilator, this raises the pulse rate slightly without raising blood pressure. The dilation of the small arterioles in the heart increases thallium uptake by myocardial muscle and mimics the effects of exercise. When Dipyridamole is used the patients are still asked to exercise gently, either by light cycling or simply by lifting the arms a few times, as this reduces the amount of \( ^{201}\text{Tl} \) in the liver. Dipyridamole is contra-indicated in asthma, where Dobutamine is given instead. Exercise testing is used in the department because it is the safest. Mortality is about 1 in 10,000. This increases significantly when pharmacological stressing is used.

Stress imaging should begin within five minutes of injection and should be completed within 30 minutes to minimise the effects of redistribution. During this period, the distribution of thallium within the myocardium remains relatively fixed, and then starts to redistribute gradually. Thus, after the patient has finished the exercise test they are asked to lie on the imaging bed. A soon as the patient is on the bed, static images are taken from at least three standard views: anterior view, a left anterior oblique (40° LAO) view to optimise visualisation of the septum (usually) and left lateral view (75° LAO). For this last view, the patient lies supine on the couch with the left arm positioned so that it does not cause attenuation in any projection and so that the camera can be as close as possible to the chest wall. Redistribution of thallium is finished after 3 – 4 hours of administration, so the patient is asked to return in the afternoon to allow rest image acquisition of the same views.
Scan Interpretation

Since thallium uptake is proportional to blood flow, there will be high uptake where blood flow to the heart is good but uptake will decrease as blood flow gets progressively poorer. With knowledge of the anatomy of the heart and which arteries are supplying each muscle, it is possible from these images to determine whether a patient has coronary artery disease and indicate which arteries may be involved. However, precise determination of where the disease is located require an ‘educated guess’ based on the experience which is contrasted to the gold standard technique (coronary angiography) which allow to determine what artery is involved. Coronary angiography is invasive and is avoided when possible.

Two types of diseases can be presented: ischemia and infarction. Cardiac infarct tissue is that where cardiac cells are dead. Ischemic tissue is composed by alive cells, which receive non- or poor blood irrigation, and therefore potentially die. These two types of diseases are distinguishable by looking at images at different stages and study how the thallium is redistributed. Areas of ischemic heart muscle will show little or no \(^{201}\text{Tl}\) uptake in the morning views. In the afternoon \(^{201}\text{Tl}\) will have been distributed through all areas of muscle in the body which have a blood supply, no matter how poor, with the result that ischemic muscle will now show \(^{201}\text{Tl}\) uptake. This provides a means of differentiating between areas of ischemia and areas of infarction. These areas are then reported using a specific template for the purpose shown below.

Figure 2.1: Template used for reporting perfusion scans; schematic version of the heart as seen in three views: anterior, 40° LAO and 70° LAO.
2.1 Imaging tests

Imaging Technique

As it was said before, the imaging technique used in the GRI is the planar scan in ‘gated list mode’. Gated list mode acquisition consists of images gated to the electrocardiogram, which is acquired at the same time as the scan. The R-R interval for each beat is measured and divided into eight frames. The image from each frame is summed with the images in all the other equivalent frames for the entire scan. This gives eight images of the heart in different phases of beating. The collective counts for each of which is high enough to produce reasonable images. Gating the perfusion images removes the blurring caused by the beating of the heart.

If the images are displayed in sequence a ‘cine’ loop may be seen. This enables assessment of regional wall motion during the cardiac cycle.

WIG protocol

SPECT imaging is now a days a widely extended technique to monitor myocardial perfusion. This technique is used in the WIG, where a total dose of 1000 MBq $^{99m}$Tc-tetrofosmin is given to the patient. This dose is given on a one-day protocol basis, where the patients are administered with 250 MBq during the stress test in the morning, and then 750 MBq 4 hours later. Imaging occurs some time between 45 minutes and 3 hours after the first injection and 50 minutes after the second injection to allow as much liver clearance as possible.

The distribution images are acquired with a triple head Picker gamma camera which enables simultaneous acquisition of transmission data on one head and emission data on the remaining two heads. One of the advantages of SPECT imaging is the presence of attenuation and scatter effects on the images, which can be corrected, although the correction techniques are a subject of current study.
2.1 Imaging tests

2.1.2 Blood Pool Ventriculography

Number of Scans I have performed: > 15

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Activity (ARSAC limit)</th>
<th>Resolution</th>
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<td>Effective Dose</td>
<td>3 mSv</td>
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<td>Acquisition</td>
<td>Gated list-mode</td>
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</tbody>
</table>

Blood pool ventriculography is performed as a means of measuring heart function, particularly ventricular ejection fraction. Although it is possible from a gated perfusion study to obtain a qualitative idea of the way in which a heart functions, an accurate quantitative measurement cannot be made. A patient’s thallium scan may show an effectively akinetic heart while the blood pool scan shows the patient to have an adequate ejection fraction (and vice versa). This makes it useful for both scans to be performed.

Blood pool imaging is the most common form of imaging in the department of Nuclear Cardiology (GRI), and almost all patients who receive exercise thallium scans also receive a blood pool scan. The patient is first given an IV dose of about 2.5 ml of pyrophosphate dissolved in saline solution. Pyrophosphate binds to red blood cells providing receptors to which 99mTc can attach, thus labelling the blood pool. Ten minutes after the pyrophosphate a dose (typically about 600 MBq) of 99mTc (pertechnetate) is given to complete the labelling of the red blood cells.

With the blood pool labelled, images of the cardiac chambers can be achieved. Imaging is performed in the LAO projection to provide the best separation of right and left ventricular activity. The heart should be positioned within the field of view. A caudal tilt of approximately 10° is applied to the camera. This minimises overlap of LV by LA. The closer the camera, the better the spatial resolution of the images.

During list mode acquisition the x-y co-ordinate of each scintillation event are
stored separately in computer memory along with the ECG gating signal and timing markers (images are acquired for 300 seconds). When acquisition is completed, a histogram of the cardiac beat lengths can be generated and a suitable R-R interval for the study selected. Acceptable beats will be used to generate images, which can be formed in the most appropriate timing interval for the type of analysis required. The list mode method of acquisition has the advantage, over other gated acquisitions (MUGA scans and variations on them), that no information is lost. The natural variation in R-R interval which is seen in a normally functioning heart has negligible effect on a list mode scan but can cause a blurring in the shape of the filling curve in a MUGA scan unless variations are removed by some other process, thus losing information. In this department, the blood pool images are boxed into 24 frames per cardiac cycle.

Quantification of radionuclide ventriculography is necessary for the estimation of left ventricular ejection fraction. A region of interest is drawn around the ventricle: identification of the edges of the blood pool at end-diastole and end-systole is performed manually. A time-activity curve for the LV at each frame in the cardiac cycle may then be generated.

![Time activity curve](image)

**Figure 2.2: Time activity curve.**

Calculation of EF is possible because there is a direct relation between ventricle activity and its volume. LV EF is calculated by dividing the background corrected difference in end-systolic and end-diastolic counts by the end-diastolic counts.
counts in the background area are normalised to the same area as the ventricle ROI. The ejection fraction is given by the following formula:

\[
EF = \frac{(\text{end diastole counts} - \text{bgd counts}) - (\text{end systole counts} - \text{bgd counts})}{\text{end diastole counts} - \text{bgd counts}}
\]

(2.1)

In practice, background correction is necessary because some counts within the left ventricle originate from tissue lying in front or behind the heart. It is impossible to measure these counts directly so it is usual to assume that the count density from an area inferolateral to the ventricle is a close approximation to that in front and behind the ventricle. Activity from extracardiac vascular organs such as liver and spleen should not be included within the background region of interest. In GRI, background correction is usually done by drawing a crescentic region of interest, close to, but outside the end-diastolic image.

Visual assessment of wall motion from a cine loop display is both reproducible and accurate in identifying regional dysfunction. Endless cine loop display allows evaluation of the heart throughout the entire cardiac cycle and regional wall motion can be assessed qualitatively.

Various images produced by the computer are also helpful. The stroke volume image is produced by subtracting the end systolic image from the end diastolic image, demonstrating the area of the ventricle that moves. The paradox image is the reverse of the stroke volume image and demonstrates areas that do not move. The accuracy of ejection fraction measurement is affected by a number of factors. Poor definition of the LV region of interest (ROI) may occur if there is patient movement, high background activity due to poor red cell labelling, or excess soft tissue attenuation. Because the left atrium fills as the ventricle empties, poor separation of left atrial enlargement may add counts to the LV ROI at end-systole, causing an underestimation of LV EF. Poor gating, attenuating artefacts over the LV and inappropriate background subtraction will also influence the accuracy of EF calculation (normal ejection fraction is greater than 40% in this department).
2.1 Imaging tests

2.1.3 MDP Bone Scan

Number of Scans I have performed: > 10

Protocol

<table>
<thead>
<tr>
<th>Radio-pharmaceutical</th>
<th>Activity (ARSAC limit)</th>
<th>Effective Dose</th>
<th>Collimator</th>
</tr>
</thead>
<tbody>
<tr>
<td>99mTc -Methylene Diphosphonate</td>
<td>600 MBq (600)</td>
<td>3 mSv</td>
<td>LEGP</td>
</tr>
</tbody>
</table>

Acquisition

Whole body (1024 × 256), 20 minutes acquisition and/or static point views (256 × 256), 400k – 1M counts. (Between injection and imaging patient drinks as much as possible. Bladder emptied immediately prior to imaging. All metal objects removed from field of view).

Resolution 256 × 256

Introduction

Bone scans are used for a wide range of investigations related to bone diseases, where regions showing increased activity can be interpreted as fractures, infections, tumours or areas where bone formation has accelerated due to bone repair. This low specificity associated with bone scans makes them useful for the assessment of any bone condition, only if they are interpreted together with a full clinical history and the relevant X-rays.

The radiopharmaceutical most widely used in this type of scan is Methylene diphosphonate (MDP) as it is rapidly excreted, producing a high bone to soft-tissue ratio at 3 – 4 hours post injection. 50 – 60% is taken up by bone while the rest is excreted by the renal system.
The clinical procedure for a bone scan followed in the GRI consists of 600 MBq in 3 ml of $^{99m}$Tc MDP administered 3 to 4 hours before the patient is imaged. During this time the patient is asked to drink 1.5 to 2 litres of water to aid in the renal excretion of excess $^{99m}$Tc MDP which is not taken up by bone. Immediately before a scan the patient is asked to empty their bladder, otherwise it will appear extremely hot with the result of loosing contrast in the rest of the image. Although images can be taken of the whole-body with a scanning camera, multiple spot views give better resolution. This has the risk of missing areas of high activity. To avoid this problem, great care is taken in positioning the patient and overlapping the images so no regions are missed in the scan.

**Image Interpretation**

1. *Normal Bone Scans*

   There are regions of natural high activity (e.g. sacro-iliac joints, the pedicles of the vertebral bodies, etc) in normal bone scans. An educated criterion will allow to recognise these regions as normal, classifying the scan as abnormal based on the appearance of hot spots in places not expected.

   The following pictures correspond to some of the normal bone scans I performed at the GRI.
2. Abnormal Bone Scans

Although there is number of situations where the uptake is either absent, diminished or apparently absent (e.g. osteolytic tumours, severe cardiac failure, presence of metal objects on or within the patient, etc), the most common situation is that where an increased uptake is related to an abnormality. The next images correspond to bone scans I performed, where, on the left, a metatarsal fracture on the right foot is demonstrable as a site of intense uptake. On the right, an scan showing an osseous reaction produced by a lymphoma.
However, during my placement at the GRI, I observed that the most predominant situation of abnormal scan correspond to bone metastases. In this case, small hot spots randomly placed will appear in the diseased region, which may extend to the whole skeleton as I found in one of the scans I performed in the GRI.

Figure 2.5: Bone scans presenting areas of intense uptake due to bone abnormalities.
Figure 2.6: Bone scan presenting extended bone metastases in ribs. The hot spot on the left arm correspond to the injection site.
Whole skeleton metastases arrive to its extreme situation in the so-called ‘superscan’, where the uptake in all the skeleton is so high that the kidneys cannot be seen in the scan.

Figure 2.7: Bone super scan.
2.1.4 Bone Marrow Scans

Number of Scans I have performed: > 5

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Activity- (ARSAC limit)</th>
<th>Effective Dose</th>
<th>Collimator</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-pharmaceutical</td>
<td>$^{99m}$Tc -colloid</td>
<td>4000 MBq- (400)</td>
<td>4 mSv</td>
<td>LEGP</td>
</tr>
<tr>
<td>Acquisition</td>
<td>Entire skeleton 30 min after injection - total of 300−400000 counts per image.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abnormalities in a bone narrow scan might be associated to diseases such us:

1. haematogical diseases
2. sarcomas to show focal increase in uptake
3. osteomyelitis to show focal increase in uptake

The radiopharmaceutical used at the GRI to image the bone marrow is nanocolloid, which consists of albumin millimicrospheres of 30 – 100 nm in diameter, with 95% of them less than 80 nm. This one is injected intravenously and then imaging starts 20 – 30 minutes after injection.

The imaging protocol is similar to the bone scans, where the bladder is emptied just before the scan. However, an additional problem to the bone scan is found with bone marrow imaging. This is the very high uptake by the liver and spleen (72% and 7.5%, respectively, 30 minutes after injection), which obscures the lower ribs and often the lower two dorsal and upper two lumbar vertebrae. This effect is minimised by positioning the patient so the field of view is selected to minimise liver and spleen visibility.
2.1.5 Renogram

Renograms are used at the GRI and WIG to assess renal function. A renogram is the time activity curve resulting from the dynamic acquisition of the count-rate produced by each kidney after a radiopharmaceutical has been injected into the patient intravenously. The radiopharmaceutical used in both hospitals is $^{99m}$Tc MAG3 injected IV.

$^{99m}$Tc MAG3

Number of Scans I have performed: 3

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Radio-pharmaceutical $^{99m}$Tc-MAG3</th>
<th>Activity- (ARSAC limit) 100 MBq- (100)</th>
<th>Effective Dose 0.7 mSv</th>
<th>Collimator LEGP</th>
<th>Resolution $128 \times 128$</th>
</tr>
</thead>
</table>

MAG3 is a $^{99m}$Tc labelled radiopharmaceutical mainly cleared by tubular filtration (80%) while the reminder is cleared by glomerular filtration.
At the WIG, 750 ml of water are given to the patient 20 minutes before the scan is started. Then a bolus of 100 MBq of $^{99m}$Tc MAG3 is injected to the patient after being asked to empty their bladder immediately before the scan starts. The patient lies supine on the bed (prone, at GRI) with the camera placed under (over, at GRI) the bed such that the bottom edge of the patient’s rib cage is in line with the centre of the line mark of the gamma camera. The patient should be lying centrally within the field of view of the camera. The radionuclide is then injected and the scan starts lasting for 15 – 40 minutes. In a normal renogram, like the one shown below, curves are similar showing their maximum uptake 3 – 5 minutes after injection (normal transit time).
Once MAG3 is injected intravenously, the individual function of the kidney can be monitored with the aid of a dynamic study of the renal function. During this
study, the arrival, uptake and secretion of the radiopharmaceutical from the kidney is assessed throughout a ‘renogram curve’. This is a time-activity curve where the count rate is plotted versus time. The different features of this curve are associated with the three phases indicated above:

1. Vascular or perfusion phase, represented by a sharp rise and corresponding to the arrival of the radiopharmaceutical to the kidney.

2. Secretary or functional phase, represented by a slower rise of the activity and corresponding to the phase where the kidney takes up the radiopharmaceutical.

3. Drain or excretory phase represented by a falling slope of the curve and corresponding to the excretory phase of the process.

This curve is obtained by summing the total counts from selected regions of interest (ROI) around the kidneys within each dynamic frame of the investigation. Both the WIG and the GRI uses the same clinical protocol but with different number of frames used in this dynamic investigation. In the first case, the data is acquired at 80 frames of 30 seconds each; whereas in the second case, the data is acquired in a succession of frames of different length. This is, at 30 frames of 2 seconds each, then 16 frames of 15 seconds each and finally 50 frames of 30 seconds each.

At both, GRI and WIG, a whole kidney renogram is obtained in order to investigate the pelvic/uretric junction. This is the situation observed in the next renogram I performed on a patient with normal renal function.
2.1 Imaging tests

Figure 2.8: *Different ROIs considered in a renogram.*

Figure 2.9: *Transit curves obtained from the ROIs shown in Figure 3.8.*
In Figure 3.8, there is a ROI surrounding each kidney. This region is selected in order to correct the renogram for the radioactivity present in tissues over and under each kidney, i.e. these are background ROIs. The counts enclosed by these areas are subtracted from the total counts obtained from the kidneys. This is known as background subtraction. The selection of these areas changes with the institution, but popular sites are below and between the kidneys.

Finally, another region of interest appears in the upper part of the scan. This corresponds to the heart. The reason this ROI is selected refers to the dependency of the shape of the renogram not only on the perfusion, function and drainage of each kidney but also on the rate at which the radiopharmaceutical arrives at the kidneys. This rate will depend on bolus quality and site of injection as well as conditions unrelated to renal function such as cardiac failure.

In a mathematical context, a renogram can be mathematically reproduced by taking this input rate as an input function and convoluting it with an impulse response function (or retention function), which will transform the input function into the renogram taking into account the factors above mentioned. The retention function is the renogram that would be obtained if the input function were an idealised infinite narrow peak (‘delta’ function). It is argued that if the renogram were to be presented in the form of the response to the delta function as a standard input function, then intercomparison of renograms would be more reliable and reporting more objective.

Thus, the renogram \( K(t) \) which results from an input function \( I(t) \) is given by this function convolved with the retention function:

\[
K(t) = I(t) \times R(t)
\]  

(2.2)

This is normally calculated over a period of time \( t \) using the convolution integral

\[
K(t) = \int_0^t I(T)R(t-T)dt
\]  

(2.3)

where \( T \) is a dummy variable.

Knowing \( I(t) \) and \( K(t) \) from the ROIs selected in the scan, \( R(t) \) can be found using the inverse of convolution, that is deconvolution. The main features of this curve are an initial spike followed by a plateau and then a fall off to zero (in a
normal kidney). The retention function allows renogram parameters such as transit times to be calculated. The main parameter is the mean transit time (MTT) which is given by the area under the curve divided by the height of the plateau:

$$K(t) = \frac{\int_0^t R(t)dt}{R(0)}$$

(2.4)

This parameter is also included in the report sheets used at the WIG. The next figure shows the retention function for each kidney on Figure 2.8:

![Retention function](image)

Figure 2.10: *The Retention function, R(t), showing normal kidney function. The areas under both curves divided by their height represent the MTT for each kidney.*

As the initial spike of the retention function is caused by the vascular phase, it is usual to extrapolate the plateau back to time 0, as shown.

Finally, the other two parameter normally reported in the GRI and WIG refer to differential renal function. These will represent the contribution of each kidney to the total renal function and is obtained by summing the counts accumulated in each kidney during part of the functional phase of the renogram. The period selected for this measurement can only last for about a minute, since it must be after the vascular phase but before the onset of drainage (i.e. 3 – 5 minutes after injection). The relative function in each kidney is usually expressed as a percentage of the total renal functioning mass, i.e.:
Relative function in right kidney = \left( \frac{\text{counts in right kidney} - \text{background}}{\text{total counts in both kidneys} - \text{background}} \right) \times 100 \quad (2.5)

Thus, the parameters associated with the renogram shown above were

<table>
<thead>
<tr>
<th></th>
<th>Left Kidney</th>
<th>Right Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uptake</strong></td>
<td>51%</td>
<td>49%</td>
</tr>
<tr>
<td><strong>Residual Activity</strong></td>
<td>17%</td>
<td>20%</td>
</tr>
<tr>
<td><strong>Peak Time</strong></td>
<td>3 minutes</td>
<td>3 minutes</td>
</tr>
<tr>
<td><strong>MTT</strong></td>
<td>3.74 minutes</td>
<td>3.49 minutes</td>
</tr>
</tbody>
</table>

Table 2.1: Results of Renogram

The uptakes in this renogram show a normal functioning of both kidneys, with full contribution by each one to the total renal function. Both, peak and mean transient times are also within the normal range (3 to 5 minutes). Residual activity refers to the activity left in the kidney at the end of the renogram. Ideally, these should be as close as possible to 0% although the percentages obtained in this study can be considered normal.
2.1 Imaging tests

2.1.6 $^{99m}$Tc DMSA

Number of Scans I have performed: 16

<table>
<thead>
<tr>
<th>Protocol</th>
<th>$^{99m}$Tc -DMSA</th>
<th>Activity- (ARSAC limit)</th>
<th>80 MBq- (80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-pharmaceutical</td>
<td>$^{99m}$Tc</td>
<td>Activity- (ARSAC limit)</td>
<td>80 MBq- (80)</td>
</tr>
<tr>
<td>Effective Dose</td>
<td>0.7 mSv</td>
<td>Collimator</td>
<td>LEHR</td>
</tr>
<tr>
<td>Acquisition</td>
<td>Static</td>
<td>Resolution</td>
<td>$256 \times 256$</td>
</tr>
</tbody>
</table>

$^{99m}$Tc -dimercaptosuccinic acid (DMSA) is taken up by the cortex (proximal convoluted tubular tissue) of the kidney where it will be held for about 6 hours following injection. This makes it an excellent agent for renal imaging not renography as the case of $^{99m}$Tc MAG3. Due to its uptake characteristics, $^{99m}$Tc DMSA is useful for looking at size, shape and positioning of the kidneys. But an important application of this type of scan is to demonstrate scarring and narrowing of the renal cortex in pyelonephritis. I performed $^{99m}$Tc DMSA scans at the WIG to assess the divided function of the kidneys.

The imaging process starts 2 hours after injection of 80 MBq of $^{99m}$Tc DMSA. The images acquired will be a posterior, anterior, both posterior oblique, both anterior oblique and some times the lateral views. When assessing renal failure, the relative uptake of the kidneys in each view gives a reference of their function. This relative uptake is obtained from the counts corrected for background. These counts are obtained drawing ROIs for each kidney and another one for the background. If the distance of each kidney to the detector is different, the attenuating tissue between the kidney and the detector will be different. In order to make the relative uptake of each kidneys independent of this distance, the geometrical mean of the relative uptake of each kidney in anterior and posterior views has to be obtained.

The next is the result of one of the $^{99m}$Tc DMSA scans I performed.

CHAPTER 2. Diagnostic Nuclear Medicine
2.1 Imaging tests

Figure 2.11: *Anterior and posterior views of a DMSA scan.*

With relatives uptakes:

<table>
<thead>
<tr>
<th>Posterior View</th>
<th>Counts (BG) corrected</th>
<th>Relative Uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Kidney</td>
<td>78271.5</td>
<td>52%</td>
</tr>
<tr>
<td>Left Kidney</td>
<td>727286</td>
<td>48%</td>
</tr>
</tbody>
</table>

| Anterior View  | Right Kidney | 55863 | 57% |
|                | Left Kidney  | 41769 | 43% |

| Geometrical Mean Correct. | Right Kidney | 66125 | 54.5% |
|                           | Left Kidney  | 55138 | 45.5% |

Table 2.2: *Results of test*

These results looked normal to me (corrected relative uptakes close to 50% on each kidney) from where I inferred that both kidneys were functioning normally, with no apparent scarring present at the images.

*CHAPTER 2. Diagnostic Nuclear Medicine*
2.1.7 Lung Ventilation and Perfusion (VQ) Scans

Number of Scans I have performed: 21

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Activity- (ARSAC limit)</th>
<th>Effective Dose</th>
<th>Collimator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-pharmaceutical $^{99m}$Tc - Tecnegas</td>
<td>20 MBq- (40)</td>
<td>0.3 mSv</td>
<td>LEGP</td>
</tr>
<tr>
<td>Acquisition</td>
<td>Resolution</td>
<td>Counts</td>
<td></td>
</tr>
<tr>
<td>Radio-pharmaceutical $^{133}$Xe</td>
<td>370 MBq- (400)</td>
<td>0.37 mSv</td>
<td>LEGP</td>
</tr>
<tr>
<td>Acquisition</td>
<td>Dynamic (Time)</td>
<td>Resolution</td>
<td></td>
</tr>
<tr>
<td>Radio-pharmaceutical $^{99m}$Tc - MAA</td>
<td>100 MBq- (100)</td>
<td>1 mSv</td>
<td>LEGP</td>
</tr>
</tbody>
</table>

The aim of a VQ scan is the search for pulmonary embolism (PE). PE is produced when a thrombus (or clot), originated somewhere in the body by any given circumstance (e.g. surgical or traumatic injury to a vein), flows to the right side of the heart and from there to the lungs via the pulmonary trunk, blocking one or more pulmonary arteries.

A VQ scan is divided in two parts: perfusion imaging and ventilation imaging. Different radiopharmaceuticals can be used to perform each of these two. At the GRI Tecnegas is preferred for ventilation imaging while, at the WIG, $^{133}$Xe and $^{81m}$Kr are used for the ventilation. In both departments $^{99m}$Tc human albumin
2.1 Imaging tests

Macroaggregates ($^{99m}$Tc MAA) is used for the perfusion imaging. $^{99m}$Tc MAA consists of micro-particles of 10 – 40 mm in diameter which once injected, they impact in the terminal arterioles and other precapillary vessels. The number of particles required to obtain an image of the lung is 200,000 particles. When the patient imaged is suspected of having pulmonary hypertension, the number of particles imparted should be reduced by 50%. For pregnant women the activity is halved and in the case of children, the activity should be reduced by a factor proportional to the body weight. In this case, this practice will lower the radiation level burden to acceptable levels.

Dual isotope ventilation-perfusion scan using $^{81m}$Kr and $^{99m}$Tc MAA

General set-up considerations

To understand the procedure followed at the WIG to perform VQ scans using $^{81m}$Kr, it is important to know some technical aspects related to this isotope. $^{81m}$Kr is a noble gas obtained from the decay of $^{81}$Rb (4.6 hours half-life). $^{81m}$Kr decays emitting 190 keV gamma rays with a half-life of 13 seconds. There are particular technical issues associated with the use of the $^{81m}$Kr generator and image acquisition. The combination of short half-life and physiological turnover of gas in the lungs, means that the distribution of inhaled $^{81m}$Kr provides an image of regional ventilation of the lungs. I will comment these issues as I describe my experience in VQ scans at the WIG.

A dual isotope ventilation-perfusion scan is performed in a double-headed PICKER Gamma Camera with the patient laying down on the couch. A portable $^{81m}$Kr generator besides the bed is used to produce the isotope. One of the main characteristics of this generator is the shielding required to attenuate the high-energy gamma rays emitted during the decay of $^{81}$Rb. The generator used in the WIG is introduced in a thick lead container to avoid leakage. If the generator is well shielded, it should not be placed far from the bed site so losses of activity due to decay from the generator to the patient is minimal. In the case of the WIG the length of the generator outlet line used is 2 m.

The $^{81m}$Kr gas is imparted to the patient through a face-mask (although mouth
masks are also used in conjunction with clips to obstruct the nasal airway). A one-way valve is connected to the mask, and the generator outlet line is connected to the inlet side of the valve. Each side of the valve is connected to 1m of bore corrugated tubing. The inlet tubing forms a reservoir system. The generator output (\(^{81m}Kr\)) is stored in this tubing while the patient breathes out through the other tubing, taking the exhaled \(^{81m}Kr\) away from the camera.

The rate of gas flow administered to the patient will depend on the ability of the patient to breathe. The more gas the patient is able to inhale, the greater the rate will be, with an ideal value estimated at 1 l/min. Nevertheless, the most important parameter to control when giving the activity to the patient is the number of counts. The WIG protocol establishes a minimum of 600 Kcounts for both perfusion and ventilation. The diagnostic reference level established by ARSAC for \(^{81m}Kr\) is 6000 MBq (equivalent effective dose 0.2 mSv). However the activity administered in the WIG is approximately 2000 MBq.

**Gamma Camera Issues**

In order to produce dual isotope VQ scans using \(^{81m}Kr\) in conjunction with \(^{99m}Tc\) MAA, it is necessary to ensure the compatibility of the camera with the simultaneous use of these two isotopes. The fact that the two isotopes in use have different gamma emission allows simultaneous perfusion and ventilation acquisition. This will imply a quicker way to perform VQ scans giving the opportunity to increase the throughput of patients. However, there are also some disadvantages such as the component of the Compton down-scatter from \(^{81m}Kr\) into the \(^{99m}Tc\) energy window. This can be assessed by comparing the resultant studies obtained from separate \(^{99m}Tc\) and \(^{81m}Kr\) single views of a patient and simultaneous views using dual acquisition mode.

Other parameters relative to the camera that should be checked before using a camera for dual isotope imaging for the first time are collimator resolution and sensitivity. The gamma energy of \(^{88m}Kr\) is normally outside the recommended energy specification of low energy collimators. However, the design of some low energy collimators is such that they are acceptable for \(^{81m}Kr\) lung imaging. The issue is the septal penetration in the collimator. This can be assessed if the
parameters of the collimator are known. This penetration will be given by

\[ l \approx \frac{sh}{(2r + s)} \]  \hspace{1cm} (2.6)

Hence, the septal attenuation will be given by:

\[ S = (1 - e^{-\mu l}) \times 100\% \]  \hspace{1cm} (2.7)

Where \( \mu \) is the linear attenuation coefficient. An acceptable value of septal attenuation for \(^{88m}\text{Kr} \) lung imaging is 90%.

Sensitivity is also important. The collimator used should have an acceptable sensitivity for both \(^{99m}\text{Tc} \) and \(^{88m}\text{Kr} \) lung imaging.

In the case of the WIG, a low-energy ultra-high resolution (LEUHR) collimator is used.

**Imaging protocol**

Patients are asked to lie down on the couch. Chains or any metallic object are removed from the patient. If the patient wears glasses, these are removed as well. Then the person performing the scan spends some time explaining the procedure to be carried out to obtain the images of the lungs.

Immediately before starting to image, 100 MBq of \(^{99m}\text{Tc} \) MAA are injected into the patient. The patient is placed under the camera and the collimators are placed...
as close as possible to the patient, bearing in mind that some room has to be left to apply the mask to the patient. The perfusion image is then started. To start the $^{88m}\text{Kr}$ acquisition, the operator holds the face-mask firmly against the face of the patient to avoid leakage of gas. Then, using a remote control, the operator activates the generator and adjusts the rate of gas flow. By looking at the display of the image, the operator can determine the number of counts acquired. The perfusion image requires a longer period of time to acquire the same number of counts than the ventilation image.

Once the perfusion image is finished, the heads are rotated and the process starts again. Six images in total are acquired: posterior, anterior, both posterior oblique, and both anterior oblique.

Following these lines there is a VQ scan I performed at the WIG using $^{99m}\text{Tc}$ -MAA and $^{88m}\text{Kr}$ . The images show evidences of mismatch between the perfusion and ventilation images indicating high risk of pulmonary embolism.

![Figure 2.13: Anterior and posterior views of a ventilation perfusion scan: (a) anterior $^{99m}\text{Tc}$ -MAA image, (b) matched anterior $^{88m}\text{Kr}$ image, (c) posterior $^{99m}\text{Tc}$ -MAA image, (d) posterior $^{88m}\text{Kr}$ image.](image)
Ventilation scans using $^{133}$Xe

Although it is an excellent imaging agent, the short half-life of the generator (4.5 h) and its cost make $^{88m}$Kr a very inaccessible source only used twice a week at the WIG.

The rest of the lung scans performed in this department use $^{133}$Xe as the imaging agent for the ventilation scans. One of the major disadvantages when using this agent is the inferior image quality obtained due to its low gamma photon energy (81 keV with a half-life of 5.3 days). For this reason, the imaging technique with this agent involves a single intake of $^{133}$Xe where usually only posterior views are taken.

The ventilation examination when using $^{133}$Xe consist of three phases:

1. Breath hold.

2. Equilibrium. After approximately 3 to 5 minutes the alveolar gas has a uniform xenon concentration and the regional activity is a measure of regional alveolar volume.

3. Wash out. After the patient is disconnected from the spirometer circuit, the wash-out of activity is recorded. Poorly ventilated areas have slower wash out.
2.1 Imaging tests

Figure 2.14: $^{133}$Xe lung ventilation image, acquired as a series of dynamic frames in the posterior-anterior (PA) view.
2.1 Imaging tests

Ventilation scans using $^{99m}$Tc -Technegas

$^{99m}$Tc -Technegas is a carbonated aerosol produced by heating a graphite crucible, filled with $^{99m}$Tc -Pertechnetate in normal saline at a temperature of 2500°C in an atmosphere of pure Argon. This results in a $^{99m}$Tc -labeled carbon-argon suspension, which has to be inhaled within 10 minutes by the patient. The particle size of the gas is a factor of relevance relative to the efficiency of the aerosol imaging. In the case of the $^{99m}$Tc Technegas, the particle size is 5 – 30 nm in cross section and 3 nm thick allowing alveolar deposition. But even at that particle size, deposition mechanisms are very inefficient so most of the inhaled particles are exhaled.

**Imaging protocol**

$^{99m}$Tc -Technegas is the radiopharmaceutical administered to patients undergoing VQ scans at the GRI. During the first part of the scan, the ventilation image is acquired. In this case, 20 MBq of $^{99m}$Tc are imparted to the patient who breathes the gas in order to rise the count rate up to 1.2 kcps. This represents one fifth of the count rate produced during the perfusion scan with $^{99m}$Tc MAA.

The ventilation image is taken with the patient sitting down in front of the gamma camera with the collimator positioned as close as possible to the chest cavity. Once all the ventilation views have been taken (eight views are taken with the posterior view to a count of 200k the others to counts of 100k each), the patient is asked to lie down in the imaging bed, where 100 MBq of $^{99m}$Tc MAA are injected intravenously. The reason the patient is positioned supine is to provide a more even distribution of perfusion. A much higher activity for the perfusion is used to minimise the contribution of Technegas to the perfusion imaging. Other way to avoid the ‘shine through’ effect produced by the Technegas onto the perfusion image is to wait one hour between the ventilation and perfusion images, so the Technegas contribution would be reduced by the time the perfusion images are taken.

The next figure shows a ventilation Technegas scan I performed at the GRI.
Figure 2.15: Normal ventilation $^{99m}$Tc-Technegas with uniform distribution across the anatomy of the lungs.
2.1 Imaging tests

2.1.8 Thyroid

Number of Scans I have performed: 5

Protocol

<table>
<thead>
<tr>
<th>Radio-pharmaceutical</th>
<th>Activity- (ARSAC limit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc-Pertechnetate</td>
<td>40 MBq-(80)</td>
</tr>
</tbody>
</table>

Effective Dose 0.5 mSv  
Collimator Pin Hole

Acquisition Static to Counts  
Resolution $256 \times 256$

The thyroid gland is part of the endocrine system of the human body. It consists of two conical lobes weighting about 25 g with a rich blood supply (80 – 120 ml per min). One of its major functions is the clearance of iodine from the blood stream to produce thyroxine and triiodothyronine hormones. This function makes possible to image and measure the gland activity using iodine radionuclide, which can be detected by a gamma camera or an organ counter. The aim in this study is to investigate thyroid disorders such as thyrotoxicosis, goitre and nodular physiology. In this section I will focus in the imaging process of the thyroid as I followed it during my placement at the GRI. In the following section I describe the non-imaging technique used to investigate thyroid disorders, i.e. radio-iodine thyroid uptake.

Thyroid Imaging

Functional as well as anatomical information is obtained from a thyroid scintigram. In particular, localisation and assessment of the size and shape of the gland, as well as identification of the active and non-active thyroid nodules, is the information obtained from a thyroid scan. To obtain this information, three different types of isotopes might be used: $^{131}$I, $^{123}$I and $^{99m}$Tc-Pertechnetate. The higher energy and higher radiation dose of $^{131}$I, as well as the cost and less readily availability of $^{123}$I make them less desirable agents than $^{99m}$Tc-Pertechnetate. This is the isotope used in the GRI.
$^{99m}$Tc Pertechnetate is trapped in the thyroid through the active transport mechanism, which traps iodine. However it is not subsequently organified resulting in a build-up of concentration.

The collimator used at the GRI to acquire the image is the pinhole collimator, which consists of a small aperture (3 − 5 mm diameter) at the end of the conical lead shield containing sufficient attenuating material to minimise photon penetration for energies up to 500 keV.

![Sketch of a typical pinhole collimator](image)

The use of this collimator has two advantages. Firstly, image of the thyroid can be magnified, obtaining more information from the image. Secondly, due to the shape of the neck, the pinhole collimator provides more accessibility to the thyroid.

In order to perform a thyroid scan, the patient will have to stop taking the thyroid medication four days before the scan, so the gland is scanned under its normal activity. Once the patient is sitting in the imaging bed, 40 MBq of $^{99m}$Tc Pertechnetate are injected intravenously. Immediately after the injection, the collimator aperture is positioned at $\approx 3$ cm anterior from the patient neck. The scan is started and a minimum of 200000 counts is acquired.

Different types of diseases can be assessed in a thyroid scintigram. The next image shows an example of a scan I performed where a cold area reflects a cyst in the left thyroid gland.

**CHAPTER 2. Diagnostic Nuclear Medicine**
2.2 Non-Imaging tests

2.2.1 Pre-radioidine therapy uptake measurement using $^{99m}$Tc-Pertechnetate

Number of Scans I have performed: 12

<table>
<thead>
<tr>
<th>Protocol</th>
<th>$^{99m}$Tc-Pertechnetate</th>
<th>Activity- (ARSAC limit)</th>
<th>Effective Dose</th>
<th>Detector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radio-pharmaceutical</td>
<td></td>
<td>8 MBq- (40)</td>
<td>0.1 mSv</td>
<td>Thyroid</td>
</tr>
<tr>
<td>Counter</td>
<td></td>
<td></td>
<td></td>
<td>Counter</td>
</tr>
</tbody>
</table>

In this case, only a quantitative measurement of the amount of $^{99m}$Tc-Pertechnetate uptake by the thyroid is performed using the organ gamma counter.

CHAPTER 2. Diagnostic Nuclear Medicine
described in section 2.3. The aim of this measurement is to estimate the treatment activity of $^{131}$I required in the treatment of hyperthyroidism.

Again, as in the case of the thyroid scans, the patient has to stop taking thyroid medication 4 days previous to his visit to the Nuclear Medicine department. Between 8 – 9 MBq in 1 ml of $^{99m}$Tc -Pertechnetate are administered intravenously to the patient 20 minutes before the uptake measurement. After the 20 minutes uptake, the collimator opening is placed on the neck and then two measurements lasting for 40 seconds are made. As it is difficult to estimate the position of the gland, in the second reading the detector is moved 1 cm downwards to make sure the entire gland is included into the field of view. The mean of the two readings obtained is then compared with counts produced by a standard source of 2% of the same activity administered, contained in a neck phantom. From these measurements and from background count (measured during 40 s previous to the test), the percentage of the activity given which is taken up by the thyroid can be measured. Typically there will about a 2% uptake of $^{99m}$Tc in a normal patient. The result are then passed to the clinician who decides what activity of $^{131}$I the patient should be given.

The next figure corresponds to one of the thyroid uptake worksheet of the uptake tests I performed at the GRI.
### 2.2 Non-Imaging tests

#### Thyroid Uptake Worksheet: 99mTc - 20min uptake

<table>
<thead>
<tr>
<th></th>
<th>Counts (40 secs)</th>
<th>Mean Counts</th>
<th>Background Subtracted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Background</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Standard 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(O/50)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Standard 2</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(O/50)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patient</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) 73.22</td>
<td></td>
<td>1374.5</td>
<td>13675.5</td>
</tr>
<tr>
<td>(2) 14161</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Percent Uptake = \( \frac{\text{Patient counts} \times 100}{\text{Dose counts}} \)  

Time from injection to measurement: 50 mins 99mTc Uptake = \( \frac{7}{2} \)
2.2 Non-Imaging tests

2.2.2 Glomerular Filtration Rate (GFR)

This test provides quantitative information of the glomerular function of the kidneys. This information is obtained on the basis that $^{51}$Cr Ethylene diamine tetra-acetic acid (EDTA) is only cleared from plasma by glomerular filtration via the kidneys. Thus, the determination of $^{51}$Cr EDTA clearance rate from the bloodstream of a patient will provide a very close figure to the glomerular filtration rate. The rate at which $^{51}$Cr EDTA is cleared from the bloodstream is obtained by measuring the activity of $^{51}$Cr EDTA in plasma samples taken at 2, 3 and 4 hours after IV injection. Then a Log plot of counts versus time is obtained to calculate the clearance rate constant ($\lambda$) and the counts at time zero. This number of counts are used to calculate the volume of dilution ($V_D$) at time zero, which in turn depends on some other factors:

$$ V_D = \frac{C_S}{C_P} \times D \times \frac{P}{S} \quad (2.8) $$

where,

- $C_S$ = Net counts of a standard source
- $C_P$ = Net counts of plasma sample @ $t = 0$ s
- $D$ = Dilution factor
- $P$ = Activity given to patient
- $S$ = Activity in standard source

Once this volume is being calculated, the clearance rate is given by the product:

$$ \text{Clearance Rate (GFR)} = \lambda \times V_D(t = 0 \text{ sec}) \quad (2.9) $$

I obtained the parameters defining the dilution volume in a GFR tests I performed at the WIG, from a 2 MBq $^{51}$Cr EDTA in 5 ml source, 4 ml were injected IV, flushing through the syringe with saline to make sure all the activity is administered to the patient. The time the activity was imparted was noted. Previous to this injection, a base blood is taken to act as a patient background. From the remaining 1 ml, standard doses are prepared by withdrawing 0.5 ml into a flask, adding sodium hydroxide (to prevent sticking to the glass) and diluting.
into 500 ml with water. This is mixed and three 2.5 ml aliquots are withdrawn into three counting tubes serving as standard sources.

Two, three and four hours after the injection, 10 ml of blood are collected from the opposite arm. These are centrifuged for ten minutes to separate the plasma and 2.5 ml samples of the plasma are withdrawn into counting tubes. The plasma samples, the base line sample and the three standards together with empty vials for machine background are placed in an auto-gamma counter and counted for ten minutes each.

The automatic counter computes the net sample counts, the GFR between two correlative measurements, the volume of distribution, and the overall GFR. The results of the test were:

<table>
<thead>
<tr>
<th>Sample</th>
<th>Actual Time (min)</th>
<th>Actual Volume (ml)</th>
<th>CPM (Gross)</th>
<th>Background subtraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background</td>
<td></td>
<td></td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>$^{51}$Cr</td>
<td></td>
<td></td>
<td>3503</td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td></td>
<td></td>
<td>3460</td>
<td></td>
</tr>
<tr>
<td>$^{51}$Cr</td>
<td></td>
<td></td>
<td>3492</td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base</td>
<td></td>
<td></td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>$2^{nd}$hour</td>
<td>119</td>
<td>2.5</td>
<td>328</td>
<td>286</td>
</tr>
<tr>
<td>$3^{rd}$hour</td>
<td>184</td>
<td>2.5</td>
<td>250</td>
<td>208</td>
</tr>
<tr>
<td>$4^{th}$hour</td>
<td>248</td>
<td>2.5</td>
<td>188</td>
<td>146</td>
</tr>
<tr>
<td>background</td>
<td></td>
<td></td>
<td>47</td>
<td></td>
</tr>
</tbody>
</table>

Computing:

\[ GFR = 124.72 \text{ ml/min} \]

Volume of dilution, \( V_D = 25733.59 \text{ ml} \)

Gradient of best-fit line, \( \frac{dy}{dx} = -0.005211 \)

Correlation Coefficient, \( r = 0.9994 \)
To prove these results were correct, I obtained the above values independently. The next logarithmic plot shows the negative gradient of the best-fit line corresponding to the variation of the counts with time.

![Graph](image.png)

Figure 2.18: *GFR measurements at the 2nd, 3rd and 4th hours after IV injection of 4 ml of 2 MBq $^{51}$Cr EDTA.*

Using the equation given for $V_D$ in (2.8), I calculated a volume of dilution of 26923 ml. The glomerular filtration rate is then obtained from

$$GFR = 0.93 \times \lambda_{GFR} \times V_D = 0.93 \times (\lambda_{eff} - \lambda) \times V_D$$  \hspace{1cm} (2.10)

where $\lambda_{eff}$ (which is the measured clearance rate constant from the Log plot) is related to physical and biological clearance rate constants by

$$\lambda_{eff} = \lambda_{GFR} + \lambda$$  \hspace{1cm} (2.11)

This effective clearance rate corrects for the decay of the source during the four hours due to physical decay and biological metabolism. The 0.93 factor corresponds to the correction of the overestimation of the GFR when calculated.
with this method [3]. The resultant GFR I obtained following these calculations was

\[ GFR = 123.66 \text{ ml/min} \]  

(2.12)
Chapter 3

Common artefacts in Nuclear Medicine procedures

Image artefacts can degrade image quality or counting measurements to the extent where the test is unreportable or, catastrophically, the wrong diagnosis is made. This section discusses common image artefacts and artefacts in non-imaging tests. Examples of artefacts I have had experience with during my training are shown.

3.1 Artefacts in Nuclear Medicine images

3.1.1 Camera artefacts

The gamma camera has various components and failure of a component in isolation or in combination may lead to image artefact. Quality assurance checks as discussed in section 2 are performed to ensure that changes in the camera are known. An obvious fault is PMT failure, which would leave a hole in the image. Another artefact which may occur, particularly important in quantitative studies, is the problem of count losses at high count rate. This will happen when the interval between events is comparable to the system dead time or resolving time (for modern gamma cameras, this should not occur below approximately 40 kcounts/s). Thus, this is unlikely to be a problem for the common diagnostic tests. Pixel overload may also occur. This is when more counts are detected in an
3.1 Artefacts in Nuclear Medicine images

individual pixel than the computer can record. This may happen if there is intense activity over a small area e.g. thyroid uptake.

In the next images it is shown an artefact produced by a air bubble in a flood source.

![Figure 3.1: Cold area on the corners of these flood images due to the presence of an air bubble within the flood source.](image)

Although this is not an artefact strictly produced by the gamma camera, the alteration on the flood image will alter the uniformity correction made on the images, and this effect could lead to artefacts on the images.

### 3.1.2 Foreign object artefacts

Foreign object artefacts occur when an object in the field of view produces photon absorption or is itself radioactive. A common artefact is metal objects, belts or jewellery in the field of view producing cold areas in the image. Artefacts may be caused by radioactive contamination including urine contamination, tissue injections and injection drips.
Figure 3.2: Different types of foreign object artefacts: (a) MDP whole body bone scan showing a large cold spot in the rib cage. This is a result of a removable breast prosthesis attenuating the radiation; (b) MDP whole body bone scan showing lots of drips from the injection; (c) MDP whole body bone scan showing a cold area on the left hip due to a hip replacement; (d) MDP whole body bone scan showing a urine bag overlying the right pelvis.
3.1 Artefacts in Nuclear Medicine images

3.1.3 Physiological artefacts

These are the most common artefacts. Physiological artefacts can result from non-uniform attenuation or overlap of areas (e.g. scapula and ribs) of increased uptake, which may appear as a hot spot. Breast attenuation is a particular problem in cardiac imaging and may result in the presence of a false defect. Patient movement also produces an artefactual image.

Figure 3.3: (a) MDP whole body bone scan in which the patient has been unable to lie still. (b) MDP whole body bone scan showing increased uptake in the upper chest area. This was found to be lung tumour uptake rather than bone uptake.
3.1.4 Radiopharmaceutical artefacts

Poor quality $^{99m}$Tc products can result in the presence of the pertechnetate ion in the patient’s body. In this situation, the salivary gland, thyroid and stomach would be visible on the final image. This is the situation in the following cardiac planar image, where free pertechnetate ions have gone to the kidney, obscuring the rest of the image.

![Cardiac planar image with free pertechnetate ions in the liver and kidney](image)

Figure 3.4: Free pertechnetate ions accumulate in the liver due to poor labeling of the radiopharmaceutical ($^{99m}$Tc -Pertechnetate).

3.1.5 Artefacts in non-imaging tests

Artefact in non-imaging data may occur as a result of the presence of foreign radioactive substances, of faults in the counter, of positioning errors in the counter or again saturation.

Counter saturation artefacts are caused by a ‘tailing off’ in the linear response of...
3.1 Artefacts in Nuclear Medicine images

recorded count with true count rate. Counting in nuclear medicine is usually used to determine concentration of a radioactive material in a substance, for this to be effective it is important that count rate is representative of the concentration, and hence that the true count rate is detected. It is therefore important to ensure that the activity of a sample is kept within the region of linear response of a counter. The presence of foreign radioactive substances in a sample are likely to lead to an artefactually increased count rate due to cross over, the spread of detected counts from one energy window into another (e.g. a GFR following another radionuclide test is not uncommon).

CHAPTER 3. Common artefacts in Nuclear Medicine procedures
Chapter 4

Therapeutic Nuclear Medicine

4.1 Radio Iodine Therapy

Radioiodine therapy is the choice of treatment for thyroid diseases such as Graves’ disease and toxic nodular goitre (thyrotoxicosis). In these cases, a hyperactive thyroid is suggested from an elevated radioiodine thyroid uptake (see section 3.2.1). I attended a radioiodine therapy session given to an adult female while I was at the GRI.

The effectiveness of radioiodine treatment for hyperthyroidism is due to radiation-induced cellular damage resulting from high-energy beta emission, the magnitude of which is directly proportional to the radiation dose received by the thyroid gland. As an average, the activity administered to adult patients is 400 MBq approximately, although different activities will be given depending on different factors such as age, gland size, etc. Many physicians will administer a larger activity of radioiodine to patients who have been previously treated with antithyroid medications.

One of the main complications of radioiodine therapy is the incidence of early post-\textsuperscript{131}I hypothyroidism. Hypothyroidism is only a problem if not adequately treated, and many practitioners will initiate thyroxine replacement therapy at the earliest indication of post-therapy hypothyroidism.

At the GRI there is a special room dedicated to thyroid treatment. During the treatment session I attended, the patient was sat in front of a tray containing the
vial with the activity. This vial was contained in a lead pot to protect the technical staff administering the activity from radiation. Before the administration of the activity, the person carrying out the treatment checked out the patient details. The patient was explained that after taking the radioactive drink she must observe certain precautions in order to avoid radiation hazards to members of her family and to the public. All the questions were relevant to three basic principles:

- **Distance**: avoiding sleeping with or have prolonged physical contact with others (especially children and pregnant women). The patient should always keep the maximum distance from others.

- **Time**: radiation exposure depends on how long the patient remain in close contact to others. The patient should always be the minimum time in contact with others. Depending on the activity received and the nature of work, the patient will have to wait for a number of days before returning to normal life.

- **Hygiene**: the patient is explained that radio-iodine is excreted through urine, and therefore it is important to flush the toilet two or three times after each use as well as clean the hands with soap and plenty of water. It is important not to share eating utensils for the first few days and wash them separately to reduce the chance of contamination.

After the patient checklist was completed, and the patient consented to be treated, the activity was given to the patient. This is done through a tube attached to a needle punctured through the rubber septum of the vial, followed by a glass of water to clear the radioactive fluid remaining in the mouth and throat.
Chapter 5

Radionuclide Dispensary

5.1 Design of the building

As part of my training, I spent five days in the radiopharmacy at the Western Infirmary, Glasgow. This radiopharmacy provides a centralised service to the whole of the West of Scotland, comprising a complex dedicated to the production of radiopharmaceuticals, where more than 40 000 patient dose are prepared every year.

Such a complex requires a particular design in order to ensure the sterility of the radiopharmaceutical production and radiation protection as recommended by the British legislation [8, 9, 10].

In Figure 5.1 it is shown the floor plan corresponding to the Radiopharmacy at the Western Infirmary, Glasgow.

One of the main features of this plan is the separation of the laboratory (aseptic) area from the service area through a first change area which gives access to the preparation laboratory. Within the laboratory area, six laboratories are used for different purposes:

- Laboratory 1 → Closed procedures
- Laboratory 2 → Generator storage
- Laboratory 3 → Open procedures
5.1 Design of the building

Figure 5.1: Ground floor plan of the radiopharmacy at the Western Infirmary, Glasgow.

- Laboratory 4 \(\rightarrow\) Non-parenteral lab
- Laboratory 5 \(\rightarrow\) Preparation area
- Laboratory 6 \(\rightarrow\) Quality Control lab

The production and the preparation area are separated by a second change area. The doors of each change area utilize electromagnetic locks and are interlocked with a 20 sec time delay to maintain air pressure differentials. In each of the previous labs a particular over-pressurised atmosphere is established to prevent the access of dirty air from outside. This maintains a sterile environment. The pressure established in each of these areas is listed in Table 5.1.

The different air classes refer to the characteristics of the environment required in clean areas for the manufacture of sterile products. Each manufacturing operation requires an appropriate environmental cleanliness level in the operational state in order to minimise the risks of particulate or microbial contamination of the product or materials being handled.

CHAPTER 5. Radionuclide Dispensary
5.1 Design of the building

<table>
<thead>
<tr>
<th>Area Type</th>
<th>Room</th>
<th>Area ($m^2$)</th>
<th>Air Pressure (Pa)</th>
<th>Air Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aseptic Area</td>
<td>Laboratory 1</td>
<td>17</td>
<td>+60</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>Laboratory 2</td>
<td>14</td>
<td>+60</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>Laboratory 3</td>
<td>11.5</td>
<td>+60</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>2\textsuperscript{nd} Change</td>
<td>$2 \times 4.5$</td>
<td>+40</td>
<td>A</td>
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<td>37</td>
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</tr>
<tr>
<td></td>
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<td></td>
<td>1\textsuperscript{st} Change</td>
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<tr>
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<td></td>
</tr>
<tr>
<td></td>
<td>Waste Store</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Washup</td>
<td>11.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 5.1: Schedule of accommodation

In order to meet ‘in operation’ conditions these areas should be designed to reach certain specified air-cleanliness levels in the ‘at rest’ occupancy state. The ‘at rest’ state is the condition where the installation is complete with production equipment installed and operating but with no operating personnel present. The ‘in operation’ state is the condition where the installation is functioning in the defined operating mode with the specified number of personnel working.

The four grades above mentioned are described as follow:

\textbf{Grade A}: The local zone for high risk operations, e.g. filling zone, stopper bowls, open ampoules and vials, making aseptic connections. Normally such conditions are provided by a laminar air flow work station. Laminar flow systems should provide an homogeneous air speed of $0.45 \pm 20\% \text{ ms}^{-1}$ (guidance value) at the working position.

\textbf{Grade B}: In case of aseptic preparation and filling the background environment for grade A zone.
Grade C and D: Clean areas for carrying out less critical stages in the manufacture of sterile products.

The airborne particulate classification for these grades is given in the following table.

<table>
<thead>
<tr>
<th>Grade</th>
<th>at rest</th>
<th>in operation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Maximum permitted number of particles/m³ equal to or above</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt; 0.5µm</td>
<td>&gt; 0.5µm</td>
</tr>
<tr>
<td>A</td>
<td>3500</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>3500</td>
<td>0</td>
</tr>
<tr>
<td>C</td>
<td>350 000</td>
<td>2 000</td>
</tr>
<tr>
<td>D</td>
<td>3 500 000</td>
<td>20 000</td>
</tr>
</tbody>
</table>

Table 5.2: Airborne particulate classification

Another aseptic measure of the laboratory areas is a continuous airflow throughout the building. The air supply is obtained from an air-conditioning plant located in the subbasement and contains panel and bag prefilters followed by a high efficiency particulate (HEPA) filter in order to prolong the life of the terminal room filters. The supply is fed though a duct situated in the tower to the roof space, where it is ducted to terminal absolute HEPA filters immediately above the room intakes. The room extracts are sited at the floor level, ducted back into the roof space and routed into the upper portion of the tower for discharge. Finally, together with the circulating air through out the building, laminar flow cabinets are used as work station for radiopharmaceutical production. Here, air is circulated vertically with 70% of air recirculated and 30% being extracted on each cycle.
5.2 Production of $^{99m}$Tc labelled Radiopharmaceuticals

The production and dispensing of $^{99m}$Tc labelled radiopharmaceuticals consists of the following major processes:

1. Production of $^{99m}$Tc by elution of a $^{99}$Mo-$^{99m}$Tc generator.

2. Production of the radiopharmaceutical by binding the eluted $^{99m}$Tc to a specific compound.

3. Sterile dispensing of the radiopharmaceutical.

5.2.1 Production of $^{99m}$Tc

$^{99m}$Tc is the daughter radionuclide of $^{99}$Mo, where the first has a half life of 6.02 hours and the second one decays with a half life of 67 hours. $^{99m}$Tc is obtained from a $^{99}$Mo-$^{99m}$Tc generator. There are different types of radionuclide generators, but the one from which I eluted $^{99m}$Tc is the Amersham International generator (Amertec II), which is a negative pressure generator, that is the collection vial used is an evacuated vial.

The operating principle is fairly straightforward. A vial containing solvent fluid (NaCl) is placed over the eluting input needle. Then, one of the sterile evacuated vials supplied with the generator is placed within a lead pot over the eluant output needle. This will produce a negative pressure on the input vial, which will draw the saline solution through the generator column. In this column, the $^{99}$Mo is chemically absorbed from the eluted volume onto an aluminium oxide core ($\text{Al}_2\text{O}_3$-alumina) while the $^{99m}$Tc produced by decay of the $^{99}$Mo (85% of $^{99m}$Tc and 15% of $^{99}$Tc) will be dissolved in the saline. A maximum $^{99}$Mo contamination of 1 part over 1000 is allowed in a sample of $^{99m}$Tc, and this should be measured in the first elution of each day (see section 6.3.2).

The activity of $^{99m}$Tc obtained from this process depends on the time of elution with respect to the time the $^{99}$Mo source was produced. As the $^{99}$Mo source decays, the activity of $^{99m}$Tc increases, and at approximately four half lives of...
5.2 Production of $^{99m}$Tc labelled Radiopharmaceuticals

$^{99m}$Tc, i.e. $\approx 24$ hours, parent and daughter radionuclide achieve the same activity. This point is called the ‘equilibrium point’, and from here, both radionuclides appear to decay at the same rate. At this equilibrium time, the amount of activity eluted from the generator will be maximal, as we can see in the next figure.

Figure 5.2: The build-up of activity of the daughter product with time for a typical ($^{99}$Mo/$^{99m}$Tc) radioisotope generator.

At present, the Radionuclide Dispensary (WIG) buys two generators per week (75 GBq and 60 GBq), which provides the activity necessary for the dispensing of approximately 700 patient doses per week.

5.2.2 Production and sterile dispensing of the Radiopharmaceutical

$^{99m}$Tc is eluted from a $^{99m}$Tc generator in the form of sodium pertechnetate ($\text{NaTcO}_4$). In this form it is used for a large number of scans including transplant renograms, thyroid scans, and first pass blood pool imaging. However, in order to visualise other organs and tissues the $^{99m}$Tc must be attached (labelled) to another chemical to achieve the required biological distribution. These labelling procedures are accomplished through the use of a ‘kit’. Kits are commercially manufactured, and in general consist of a vial containing sterile lyophilised powder with sufficient ingredients for the preparation of several patient doses.

To prepare a radiopharmaceutical from a kit, the required volume of $^{99m}$Tc...
5.2 Production of $^{99m}$Tc labelled Radiopharmaceuticals

Pertechnetate is withdrawn from the generator eluate and injected into the kit. The vial is then shaken and allowed to incubate at room temperature for a few minutes during which the $^{99m}$Tc complex is formed. The length of this incubation period is determined by the pharmaceutical used.

One of my experiences in producing radiopharmaceuticals in the radiopharmacy was the production of 600 MBq of $^{99m}$Tc-tetrofosmin from a MYOVIEW kit. The kit is a lyophilised powder contained in a vial under nitrogen atmosphere and sealed with a rubber septum. The vial was placed in a shielding container and the rubber septum was sanitised with alcohol swabs. Then, using a 10 ml syringe, 4 – 8 ml of $^{99m}$Tc obtained from the generator eluate was added to the vial. Before removing the syringe from the vial, a volume of gas equivalent to the volume of the eluate added to the vial was withdrawn in order to normalise the pressure inside the vial.

Then the vial was shaken for 10 seconds to ensure complete dissolution of the powder and then incubated at room temperature for 15 minutes. The kit is stored at 2 – 8°C before and after reconstitution and the finished preparation stored at 15 – 25°C and discarded after 8 hours. The patient dose should be used within 2 hours of its reference time.

In order to ensure that no bacterial contamination occurs during this process, I was told to wear sterilised clothes with hat, mask and gloves. Bacterial contamination is monitored using incubating broths, where the person preparing the radiopharmaceutical has to sweep both hands once dispensing is finished. The broths are sent for bacterial contamination analysis on a regular basis.

The production process was carried out in a laminar flow cabinet. The main purpose of this process is to calculate the required activity at the time at which the dose is drawn up to achieve the desired activity at a specific reference time. This calculation is based on the exponential decay formula, where the exponential will be positive in this case as we need to calculate how much to increase the source activity to get the activity $A_t$ at a time $t$, i.e.

$$A_d = A_t \cdot e^{\lambda t} = A_t \cdot e^{\left(\frac{0.693}{T_{1/2}}\right)t}$$

(5.1)

where $A_d$ is the activity to be prepared, and $T_{1/2}$ is the half life of the radionuclide.
5.3 Quality assurance of radiopharmaceuticals

To ensure optimum quality, the following properties of a radiopharmaceutical must be considered.

5.3.1 Particulate contamination testing

After elution from the generator and prior to its use in compounding injections, the eluate must be free from any gross particle contamination. In the radionuclide dispensary, before proceeding with the $^{99}$Mo breakthrough test, the vials are viewed through an Allan viewer (a polarising filter with back lighting) to check for particulate suspension.

5.3.2 Radionuclidic Purity

This is defined as the ratio, expressed as a percentage, of the radioactivity of the radionuclide concerned to the total radioactivity of the source.

There are three main sources of radionuclidic impurities in radionuclides:

1. the manufacturing process
2. daughter radionuclides
3. parent radionuclides

These impurities will increase the dose given to the patient and affect the imaging processes.

The method used in the WIG to determine the $^{99}$Mo level present in the first elution of the morning is based on the principle that a specified thickness of lead will attenuate practically all $\gamma$-rays from $^{99m}$Tc while producing much less attenuation on the higher energy $\gamma$-rays from $^{99}$Mo. The thickness of the lead pot used in the radiopharmacy at the WIG is 6 mm, which produces an attenuation of the $\gamma$-rays from $^{99m}$Tc by a factor of $10^6$ whereas only 65% of the $^{99}$Mo radiation is...
5.3 Quality assurance of radiopharmaceuticals

attenuated. The vial activity is measured in the radionuclide calibrator with and without the lead pot. The ratio of the two measurements gives a ratio of $^{99}$Mo to $^{99m}$Tc present in the vial. The measurements of $^{99}$Mo breakthrough I performed during my visit to the radiopharmacy were all less than 0.01%, which is within the specifications of the manufacturer (Amersham).

5.3.3 Radiochemical Purity

This is defined as the ratio, expressed as a percentage, of the radioactivity of the radionuclide concerned that is present in the source in the chemical form declared to the total radioactivity of that radionuclide present in the source.

There are a number of competing reactions that result in impurities being produced within the kit vial. These competing reactions make it important to routinely check the radiochemical purity of the radiopharmaceuticals produced in the radiopharmacy.

To determine the radiochemical purity of a radiopharmaceutical, it is necessary to separate the various radiochemical forms present in the radiopharmaceutical. This is achieved by using planar chromatography. There are different techniques used in planar chromatography, but in the paragraphs below I describe a thin layer chromatography I performed using $^{99m}$Tc-tetrofosmin.

The test is performed by placing a few microlitres of the radiopharmaceutical being tested near the bottom (origin) of the chromoplate. This corresponds to the stationary phase, which is followed by the mobile phase where the chromoplate is placed in a solvent ensuring that is not immersed in the solvent. In this way, the solvent is allowed to migrate along the chromoplate (by absorption and capillary action) separating the chemical species present. The different species distribute themselves between the mobile and stationary phases, with the most soluble moving faster. When the solvent has moved the desired distance along the chromoplate then it is removed from the solvent and allowed to dry.

Then the chromoplate is placed in an autoradiography auto imager, which will separate the developed image of the chromoplate into different regions of interest and count the activities enclosed in these ROIs. The next figure shows the results obtained from the test.

CHAPTER 5. Radionuclide Dispensary
5.3 Quality assurance of radiopharmaceuticals

The image above is called chromatogram, where the ROIs are selected to measure the counts. As a result, a count per unit of length representation (chromatograph, shown below) gives us the counts produced by each radioactive specimen, as each one will travel different distances.

In the table shown in Figure 6.4, the first row represent the counts and relative purity of the $^{99m}$Tc-Tetrofosmin segment (ROI). The second row corresponds to the origin where free sodium pertechnetate is placed. The third row represents the

CHAPTER 5. Radionuclide Dispensary
information relative to the total chromoplate. The last row represents background. The test shows a purity factor of 99.0% of $^{99m}$Tc-tetrofosmin, which is within the manufacturer specifications of 90%.

### 5.3.4 Chemical Purity

This test checks for possible Al$^{3+}$ impurities in the vial originated in the generator column during the absorption process of the $^{99}$Mo on to the alumina column. The Al$^{3+}$ can affect the stability of some colloidal radiopharmaceuticals.
Chapter 6

Safety and Radiation Protection

6.1 Radiation protection principles and regulations applying in Nuclear Medicine

In a Nuclear Medicine department, where radioactive materials are routinely used for imaging and therapy procedures, radiation protection plays an important role to ensure the safety and welfare at work of workers and members of the general public. This is achieved by applying rigorously the legislation concerning the administration and handling of radioactive sources. It is the responsibility of the Hospital Trust to ensure the compliance of the provided radiation protection with this legislation. This is achieved through a radiation safety committee, which monitors feedback from the radiation protection advisors (RPAs) and informs the Hospital Trust of the state of radiation protection arrangements.

Radiation Protection arrangements are based on the fact that external radiation can be reduced by: limiting the duration of an exposure period (time), increasing the distance between the external radiation source and the person (distance), and placing a shielding material between the external radiation source and the person (shielding). Personnel monitoring, site monitoring and testing for radioactive contamination are useful means of assessing radiation protection arrangements.

With the objective of checking the compliance with the radiation protection regulations, I performed different audits on the doses received by patient and staff in the Nuclear Medicine department at the GRI for different types of studies.
6.1 Radiation protection principles and regulations applying in Nuclear Medicine

6.1.1 Regulations

The following statutory requirements apply to work with radioactive substances:

4. The Radioactive Material (Road Transport) Regulations 1996.
5. Administration of Radioactive Substance Advisory Committee (ARSAC) - Notes for the guidance on the administration of radiopharmaceuticals and the use of sealed radioactive sources (Dec ’98 Update).
6. The Ionising Regulations (Protection of persons undergoing Medical Examination or Treatment) Regulations 1988 (POPUMET) - now superseded by IRMER 2000.
7. The Ionising Radiation Regulations 1999 (IRR 99)

6.1.2 The Health and Safety at Work Act 1974 (HSW)

This act concerns the health, safety and welfare at work of all employees, establishing the rules, which ensure satisfactory working conditions for the employee. The compliance with these rules is a responsibility of both the employer (NHS Trust) and the employee, being controlled by the Health and Safety Executive who operate through a network of local inspectors. Employing authorities must have a written safety policy that covers all aspects of the HSW Act.
6.1 Radiation protection principles and regulations applying in Nuclear Medicine

6.1.3 Medicines (Administration of Radioactive Substances) Act 1978

The diagnostic and therapeutic uses of radiopharmaceuticals are controlled by this act. Clinical procedures involving the use of radioactive substances can only be carried out under the supervision of a person holding a certificate issued by the Administration of Radioactive Substances Advisory Committee. Maximum administered activities are defined for each type of investigation or application.

6.1.4 Radioactive Substances Act 1993

It governs how the radioactive material must be contained and used, and how the radioactive waste must be kept and disposed. It requires:

- That all users of radioactive materials must be registered with the Scottish Environmental Protection Agency (SEPA) in Scotland, or the Environment Agency in England.
- Be in possession of an authorisation to accumulate and dispose of radioactive waste, producing records of the date, activity and route of every disposal.

Compliance with the Act and withdrawal of authorisation to use radioactive material lies under the responsibility of a chief inspector appointed by the Secretary of State.

6.1.5 Transportation of radioactive Substances

Two regulations govern the transportation of radioactive substances:

1. Radioactive Material (Road Transport) Regulations 1996.

These regulations establish the amounts and activities of radioactive material that can be transported by road, and the types of container in which they must be transported. At the same time, these regulations require the appropriate training.
of the drivers to ensure that no injury to health or damage to property or the environment should occur while the material is in transit. The vehicles used for transporting radioactive material should display placards and carry a notice detailing emergency procedures inside the vehicle.

As the Radionuclide Dispensary at the WIG provides radioactive material to the whole West of Scotland, certain requirements for packaging, the amount of material which may be carried and the labelling of each package have to be accomplished. Two types of packages are transported: ‘Excepted’ and Type A packages. The difference between these two types of packages is that Excepted packages contain smaller amounts of activity than Type A packages.

Both types of package use different labels. Excepted packages do not require external warning labels, but a ‘Radioactive’ marking should be enclosed in such a way that it is obvious on opening the package. The surface dose rate for an excepted package must be less than $5 \mu Sv/h$. Packages containing less than 400 MBq of $^{99m}$Tc in a lead pot, fall into the excepted category.

However, Type A packages must have the appropriate external labelling, which will be one of the next three categories:

<table>
<thead>
<tr>
<th>Category</th>
<th>Colour of Label</th>
<th>Surface Radiation Level</th>
<th>Transport Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>White</td>
<td>$&lt; 5 \mu Sv h^{-1}$</td>
<td>$&lt; 1$</td>
</tr>
<tr>
<td>II</td>
<td>Yellow</td>
<td>$&gt; 5 \mu Sv h^{-1}$ but $&lt; 500 \mu Sv h^{-1}$</td>
<td>$&lt; 1$</td>
</tr>
<tr>
<td>III</td>
<td>Yellow</td>
<td>$&gt; 0.5 mSv h^{-1}$ but $&lt; 2 mSv h^{-1}$</td>
<td>$&gt; 1$ but $&lt; 10$</td>
</tr>
</tbody>
</table>

Where the transport index represents the way in which it is transported and it is calculated by measuring the maximum level of radiation at a distance of 1m from the surface of the package in $mSv h^{-1}$. This value is then divided by 10 and rounded up to the first decimal place.

The enforcement body of these regulations is the Department of Transport.
6.1 Radiation protection principles and regulations applying in Nuclear Medicine

6.1.6 Administration of Radioactive Substance Advisory Committee (ARSAC) - notes for the guidance on the clinical administration of radiopharmaceuticals and the use of sealed radioactive sources

This document reviews the legislation that applies to Nuclear Medicine. The document starts with an explanation of the conditions required for the granting of the ARSAC certificate, which allows the holder to perform tests and therapies. This certificate is valid for five years and it is obtained after having completed adequate training and experience. ARSAC certificate holders must be clinical personnel but other staff may act under their written direction. The certificate can also be obtained for research purposes. In this case, the certificate will be only valid for two years and ARSAC establishes the requirements for approval by a local ethics committee. ARSAC also establishes the dose limits and the way the dose should be given to (potentially) pregnant women and children, including possible use of sedation.

In the Appendix 1 of the document, ARSAC issue the recommended activity limits for radiopharmaceuticals used in diagnostic procedures in Nuclear Medicine. The limits for both sealed and unsealed sources when they are used for therapeutic purposes are a matter of clinical judgement and ARSAC gives advice on methods of dose calculation.

6.1.7 The Ionising Radiation Regulations

The IRR 99 regulations come under the HSW Act and are specific regulations to minimise radiation exposure to employees. IRR 99 supersedes IRR85 (to comply with the Basic Safety Standard European Directive). The regulations comprise the three principles specified in the ICRP 60 document of the International Commission for Radiological Protection:

- *Justification*, no practice shall be adopted unless its introduction produces positive net benefit.

*CHAPTER 6. Safety and Radiation Protection*
6.1 Radiation protection principles and regulations applying in Nuclear Medicine

- **Optimisation**, all exposures should be as low as reasonably as achievable economic and social factors being taken into account (the ALARA principle).

- **Limitation**, there should be control over risk of exposure and the dose equivalent for the individual shall not exceed the limits recommended for the appropriate circumstances.

The limits on annual dose in different circumstances established in IRR 99 are summarised in the next table.

<table>
<thead>
<tr>
<th></th>
<th>Classified staff</th>
<th>Trainees and non-classified staff</th>
<th>Members of the public</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective Dose</td>
<td>20 mSv*</td>
<td>6 mSv</td>
<td>1 mSv</td>
</tr>
<tr>
<td>Equivalent Dose to the lens of the eye</td>
<td>15 mSv</td>
<td>50 mSv</td>
<td>15 mSv</td>
</tr>
<tr>
<td>Equivalent Dose to the skin</td>
<td>500 mSv</td>
<td>150 mSv</td>
<td>50 mSv</td>
</tr>
<tr>
<td>Equivalent Dose to an individual organ</td>
<td>500 mSv</td>
<td>150 mSv</td>
<td>50 mSv</td>
</tr>
</tbody>
</table>

* An employee can receive up to 50 mSv in any one year but no more than 100 mSv in any 5 years.

A classified worker is an employee who receives 30% or more of the maximum permissible annual dose limit. Classified workers must undergo regular medical examinations and detailed records are kept of the doses they receive. These records must be retained for 50 years after the death of the employee. The reduction of dose limits introduced by IRR99 required consideration of classified workers, since it was possible that more employees would need to be classified. Such employees may include technicians working in the radiopharmacy and sealed source technicians.
It is likely to be the dose to the hands or fingers which necessitates the classification of a worker. This is because there has been a change to the way in which the dose to the hands is defined. In IRR85, the hand dose was averaged over an area of 100 cm$^2$, under IRR99 the dose must not exceed the limit of 150 mSv in any 1 cm$^2$ area.

The regulations also include classifications of areas where radiation exposure is likely. These areas are physically demarcated with suitable signs as being either ‘Controlled’ or ‘Supervised’. A controlled area is an area where the effective dose received by an employee working in the area may exceed 6 mSv/yr. Work in a controlled area is restricted to classified persons or persons working under a written system of work described in the local rules. A supervised area is an area where the effective dose received by a member of staff may exceed 1 mSv/yr.

IRR 99 regulations require every employer who undertakes work with ionising radiation to make an assessment of the hazards associated with that work. Employers are required to make contingency plans for dealing with foreseeable incidents and in some circumstances to submit them to the Health and Safety Executive.

The regulations impose duties on the manufacturer and installers of radiation equipment and require the employee to maintain equipment used in connection with medical exposure. Furthermore the employer must investigate and notify the HSE of any confirmed incident in which a patient receives a dose much greater than intended.

For the purpose of work with ionising radiation to be carried out in accordance with these regulations, every radiation employer must produce in writing such local rules as are appropriate to the radiation risk and the nature of the operations undertaken.

The radiation employer must appoint a suitable radiation protection advisor (RPA) to ensure these regulations are observed. One or more suitable radiation protection supervisors (RPS) must also be appointed for the purpose of securing compliance with these regulations and must be included in the local rules.
6.1 Radiation protection principles and regulations applying in Nuclear Medicine

6.1.8 The Ionising Radiation (Medical Exposure) Regulations 2000

These regulations (IRMER 2000) replace POPUMET. The concept of the clinical and physical direction has now been replaced by the referrer, the practitioner and the operator. The referrer requests that a medical exposure be undertaken for a particular diagnostic or therapeutic purpose. It is up to him/her to provide sufficient evidence to allow the practitioner to decide whether the medical exposure can be justified. The practitioner decides whether the requested procedure is the best suited to answer the referrer’s question and whether the risk involved in the medical exposure is of net benefit to the patient. The operator will then perform the medical exposure, using the minimum amount of radiation exposure to obtain the relevant information.

Some of the new requirements of IRMER 2000 include:

- The legal responsibility for a medical exposure is on the employer.
- It is the responsibility of the employer to ensure that each practitioner and operator who is employed is fully trained for his/her task and undertakes continuing education and training after qualification.
- Written procedures must be in place for medical exposures.
- Referral criteria for medical exposures including radiation doses must be established.
- Quality assurance programs must be established.
- Overexposure of a patient to ionising radiation must be reported to the appropriate authority and investigated (this exists in IRR99 for overexposures due to equipment malfunction).

The enforcing body for these regulations in Scotland will be the Scottish Executive who will appoint inspectors.

CHAPTER 6. Safety and Radiation Protection
6.1.9 Local Rules

It is a requirement in the ionising radiation regulations that every employee should have read and understood the local rules governing work with radiation. The safety provisions and emergency plans are detailed in the rules. These include the actions to be taken in the event of fire, accidents involving unsealed sources, overexposure and medical emergencies involving a patient to whom unsealed sources have been administered.

The local rules of the department must embody the requirements of radiation safety legislation. They are designed to ensure that ionising radiation is used safely and with as little risk to the operator as can reasonably be achieved.

The local rules specify the duties of the radiation protection supervisor (RPS) who is responsible for supervising radiation dose monitoring, providing staff with training and for overseeing the quality assurance program. All classified staff in designated areas within nuclear medicine and required to wear personal dosimeters. The rules specify for how, when, where and for how long they should be worn.

The nuclear medicine department has designated controlled or supervised areas, defined in the local rules, where diagnostic and therapeutic procedures are undertaken. Anyone working in these areas can do so under Systems of Work, which are specified, for each group of employees, in the local rules.

The local rules are designed to be as complete as possible, defining the procedures which should be followed in any foreseeable situation. The rules are detailed and specific defining how even the most basic procedures should be carried out.

6.2 Audits on patient and staff dose levels for different studies

In the context of the ARSAC and IRR99, I performed different audits of the activities injected to patients in different types of study at the GRI. The audits were relevant to $^{201}$TI for Myocardial imaging (Nuclear Cardiology) and $^{99m}$Tc MDP used for bone and $^{99m}$Tc MAA for lung scans (Nuclear Medicine).
6.2 Audits on patient and staff dose levels for different studies

In terms of therapeutic procedures, I audited the residual activities of $^{131}\text{I}$ left in the vial after the administration of the dose for thyroid treatment.

6.2.1 Thallium activities administered to patients in cardiac studies

ARSAC establishes tabulated diagnostic reference levels of activity for diagnostic purposes. These levels are issued for typical examinations for groups of standard sized patients or phantoms for broadly defined types of equipment. These levels are expected not to be exceeded for standard procedures when good and normal practice regarding diagnostic and technical performance is applied. In each adult investigation ARSAC recommends that the practitioner note the diagnostic reference level for each investigation. In some cases and for clinical reasons, greater activities than those prescribed by ARSAC might be necessary. However, the guiding principle for the investigation of any subject is that the activity administered should be the minimum consistent with acquiring adequate information from the investigation concerned. ARSAC recommends that the total activity administered to patients during myocardial perfusion studies should not exceed 80 MBq for $^{201}\text{Tl}$ scans. However, the Nuclear Cardiology department at the GRI administer activities no higher than 70 MBq for myocardial imaging conserving a good specificity and sensitivity.

The audit was performed for the two different wards (wards 7 and 64) where this type of study is carried out. The activities were obtained from the counts given by the gamma camera used for the study by placing the syringe with the activity on the collimator and counting for 10 seconds. This is done before injecting the activity IV. The next plots show the distribution of activities administered during the month of September 2001.
6.2 Audits on patient and staff dose levels for different studies

Figure 6.1: Distributions of activities administered to patients during cardiac studies found when auditing Ward 7 (upper) and Ward 64 (lower).
The resultant means and standard deviations from these distributions are

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ward 7</td>
<td>54.32 MBq</td>
<td>4.16</td>
</tr>
<tr>
<td>Ward 64</td>
<td>48.98 MBq</td>
<td>5.93</td>
</tr>
</tbody>
</table>

In both plots it is possible to observe there is a significant number of individuals at 44 MBq in Ward 7 and 36 MBq in Ward 64. ARSAC establishes that the activity administered to any patient should be the minimum consistent with obtaining a diagnostic result. Based in this principle, ARSAC recommends that the normal activities administered to adults should be used as a guide to the activity to be administered to children weighting less than 70 kg. Therefore, in practice, only a fraction of the adult activity is administered so the same count density is obtained for both adult and children patients. This was the situation for the low activities administered in both wards.

### 6.2.2 $^{99m}$Tc activities administered to patients for bone scan

In this case the activities were measured using a radionuclide calibrator just prior to the IV injection. The limit established by ARSAC is 600 MBq. Next figure shows the resultant distribution I obtained from the audit.
6.2 Audits on patient and staff dose levels for different studies

Figure 6.2: Distribution of $^{99m}$Tc MDP activities administered to patient during bone scans. These represent the activities corrected for the activities left in the syringes. The mean of the activities left in the syringe was 17 MBq. The right tail of the distribution still shows administered activities over the ARSAC limit.

These are the activities administered to patients corrected for the activity left in the syringe. This correction was made by measuring the activities of the syringe and the needle separately and correcting their readings for the source decay from the time of injection to the time of measurement:

$$pre = post \times e^{0.001925 \cdot t}$$  \hspace{1cm} (6.1)

Where, $pre$ correspond to the activity at the time of injection, $post$ correspond to the activity at the time of measurement, 0.001925 is the decay factor of $^{99m}$Tc and $t$ is time between activity administration and measurement of activity remaining in the syringe-needle. After subtracting the mean of the activity left in the syringe (17 MBq) from the individual activities, some of the resultant activities administered to patients were still above the limit of 600 MBq, but the mean value
6.2 Audits on patient and staff dose levels for different studies

was 582 MBq.

The administration of activities higher than 600 MBq does not comply with ARSAC and it was reported for further investigation.

6.2.3 $^{99m}$Tc MAA administered for lung scan

In this case the activities were obtained again from a calibrator and previous administration via IV. The ARSAC limit for $^{99m}$Tc MAA scans is 100 MBq although this activity has to be reduced in the case of pregnancy or patients with history of pulmonary hypertension. The next plot shows the activity distribution obtained.

![Bar chart showing activity distribution](image)

Figure 6.3: Distribution of $^{99m}$Tc MAA activities administered to patients for lung scans. The right tail of the distribution shows administered activities over the ARSAC limit.

Again, higher activities than allowed were reported for further investigation.
6.2 Audits on patient and staff dose levels for different studies

6.2.4 Activity left in $^{131}$I vials for radio iodine therapy

One of the difficulties I observed when treating overactive thyroids with $^{131}$I is the source of inaccuracy produced by the residual activity left in the vial. I audited this activity in order to determine if the procedure followed is correct or, however, it can lead to undertreatment of patients going through this therapy.

The overall residual activity was obtained as a percentage of the total sum of activities considered in the study, i.e.

$$\text{Overall average} = \frac{\sum \text{residue}_{activity}}{\sum \text{activity}} \times 100$$

(6.2)

The resultant overall average was 1.42% with a maximum residual of 14.97 MBq for a 400 MBq therapy (3.74%), and a minimum residual of 0.70 MBq for a 500 MBq therapy (0.7%). Therefore, the residual activity left in the vials was found insignificant to produce a change on the outcome of the therapy.

6.2.5 Audit on effective doses received by Nuclear Cardiology staff in $^{201}$Tl Myocardium imaging

In order to observe the compliance with IRR99 regulations, an audit on the effective doses received by the staff in Nuclear Cardiology at GRI during $^{201}$Tl Myocardium imaging was performed. IRR99 establishes that the maximum effective dose received by an employee should not exceed the 20 mSv per calendar year. To estimate the effective dose received by the Nuclear Cardiology staff operating the camera, I measured the effective dose rates at different distances from the imaging bed produced during $^{201}$Tl Myocardium studies. These distances were always measured perpendicular to the couch axis and on the right hand side of the patients, at the level of the head (see diagram).
Figure 6.4: Diagram showing the disposition in which the dose rate measurements were taken.

Due to the limited availability of the dose meter, I measured the dose rates only in the direction indicated in the diagram. Nevertheless, I thought the results of this measurement would be significant as this ‘path’ is the most occupied by the staff when setting up the patient on the camera. The next picture shows the behaviour of the dose rates I measured at 0.5, 1, 1.5, 2 and 3 meters from the patient.
6.2 Audits on patient and staff dose levels for different studies

Figure 6.5: Resultant dose rates measured at 0.5, 1, 1.5, 2 and 3 meters from the imaging bed during Myocardial Perfusion Imaging.

In the department of Nuclear Cardiology at the GRI, a technical staff composed of three MTOs attends 3000 patients (i.e., each MTO attends ≈ 1000 patients). Each scan last for 20 minutes and in the worst case scenario, the MTO carrying out the scan would stand during this time at a meter away from the patient in the direction indicated in the diagram of Figure 7.4. From Figure 7.5, the dose rate measured at one meter for both, stress and rest scans, is ≈ 0.90 µSv h⁻¹. Therefore, the dose received per year by the staff when they stand at one meter from the bed would be:

\[ 1000 \text{ patients} \times \frac{1}{3} \text{h} \times 0.9\mu\text{Sv h}^{-1} = 300\mu\text{Sv} \]  

(6.3)

This is several units under the limit established by IRR99 (20 mSv) and yet, it represents the worst case scenario as MTOs are always at a minimum distance of ≈ 5 meters from the imaging bed during the scans. This result shows the compliance of the department with the IRR99.
Bibliography


