Development of a hybrid portable medical gamma camera

A thesis submitted for the degree of
Doctor of Philosophy

by

SARAH LOUISE BUGBY

Space Research Centre
Department of Physics and Astronomy

JULY 2015
Development of a hybrid portable medical gamma camera

Sarah Louise Bugby

Abstract

A novel small field of view medical gamma camera - the Compact Gamma Camera (CGC) - has been developed at the University of Leicester to provide portable, high-resolution gamma imaging for applications in nuclear medical imaging. The suitability of this camera for medical imaging is investigated through Monte Carlo simulation, phantom studies and preliminary clinical testing.

Quality assurance protocols are adapted for use with small field of view gamma cameras. These protocols are then used to provide a full characterisation of the CGC. The CGC is found to compare favourably to other small field of view systems in development. Phantom studies are described which show that the CGC is well suited to intraoperative imaging, particularly for use in sentinel lymph node biopsy.

A Monte Carlo model is described that is designed to simulate the response of a pinhole-collimated, scintillator-based gamma camera. The model is shown to accurately model sensitivity and spatial resolution. Previously derived analytical models are shown to be unsuitable for modelling finite source profiles and a new analytical model is described which addresses this shortcoming. This model is used to define appropriate test source sizes for the characterisation of small field of view systems.

A modified version of the CGC - the Hybrid Compact Gamma Camera (HCGC) - is described which includes an optical imager in a coaligned configuration. The HCGC allows for functional and anatomical images to be obtained simultaneously. The use of hybrid optical-gamma imaging is novel in small field of view cameras and offers new possibilities for assisting surgeons in localising the site of uptake in procedures such as sentinel node detection.
Acknowledgements

There a great many people who I would like to thank for their assistance throughout my PhD, foremost among them are Dr John Lees and Prof Alan Perkins. I have found John to be an invaluable mentor, both academically and professionally, and I have benefited enormously from his experience and expertise. Without Alan’s patience and comprehensive knowledge of medical physics this project would not have been successful. The encouragement, guidance and continual support I have received from both John and Alan have been indispensable and I feel extremely fortunate to have worked with them.

I am also fortunate to have undertaken this work at the SRC where I have found my colleagues - whether academic, technical or administrative - to be invariably generous with both their time and expertise. In particular, I would like to thank Dave Bassford - in many ways this project would not have been possible without him and his humour and technical ingenuity are greatly missed.

I am extremely grateful to the colleagues I’ve worked alongside, whether in subject or location - including but not limited to, Mohammed Alqahtani, Adam Bark, Bahadar Bhatia, Numan Dawood, Katie Dexter, Angaraj Duara, Layal Jambi, Simon Lindsay, Cedric Malherbe, Bill McKnight, Aik Ng, Cameron Scoular, Sean Tipper and Gauthier Torricelli - for being willing sounding boards. Particular thanks are extended to Dr Simon Lindsay for proofreading this thesis without any obligation to do so. I am also grateful to Elaine Blackshaw, Nottingham University Hospitals NHS Trust, who has been invaluable in patient recruitment, and to Helen Hill and David Monk, Leicester Royal Infirmary, for their generosity in time and resources.

I am appreciative, too, of Prof George Fraser, Prof Derek Raine, Prof Mark Sims and Dr Nigel Bannister for encouraging me to develop my research skills during my undergraduate career. I would also like to acknowledge the financial support of the Science and Technology Facilities Council in funding a studentship for this work.

I am incredibly thankful to my family and friends, for their encouragement and commiserations. Lastly, but by no means least, I would like to thank Benn, for his love and support and for never asking when my thesis was going to be finished.
# Contents

Abstract

Acknowledgements

Contents

Publications

1 Introduction

1.1 Motivation and Applications

1.2 Aims

1.3 Thesis Organisation

2 Principles of gamma detection

2.1 Attenuation

2.1.1 Photoelectric effect

2.1.1.1 Absorption edges

2.1.1.2 Fluorescence

2.1.1.3 Non-radiative transitions

2.1.2 Compton scattering

2.1.3 Rayleigh scattering

2.2 Detection mechanisms

2.2.1 Scintillation

2.2.2 Charge carrier generation

2.3 Summary

3 Devices for medical gamma imaging

3.1 A brief history of medical gamma imaging

3.2 Collimation

3.2.1 Pinhole collimators

3.2.1.1 Collimator Resolution

3.2.1.2 Collimator Sensitivity

3.2.2 Parallel hole collimators

3.2.2.1 Collimator Resolution

4 Conclusion

5 Appendix

6 References

7 Index
### Contents

3.2.2.2 Collimator Sensitivity ........................................ 29  
3.2.3 Other collimators ................................................. 29  
3.3 Indirect detection ................................................... 30  
  3.3.1 Scintillators ...................................................... 30  
  3.3.2 Photomultiplier tubes ........................................... 31  
  3.3.3 Photodiodes ...................................................... 32  
  3.3.4 Charge-coupled devices (CCDs) ................................ 32  
3.4 Direct detection .................................................... 33  
  3.4.1 Semiconductor detectors ....................................... 34  
3.5 Summary ............................................................. 35  

4 Compact Gamma Camera (CGC) design ............................... 36  
  4.1 Collimator .......................................................... 37  
  4.2 Scintillator ........................................................ 38  
  4.3 EMCCD ............................................................... 39  
  4.4 Shielding ........................................................... 41  
  4.5 Cooling .............................................................. 41  
  4.6 Casing ............................................................... 42  
  4.7 Image acquisition ................................................. 42  
  4.8 Image processing .................................................. 43  
    4.8.1 Hot pixel correction .......................................... 43  
    4.8.2 Blob detection ................................................. 43  
    4.8.3 Flat field correction .......................................... 44  
  4.9 CGC configuration summary ....................................... 44  

5 Monte Carlo simulation of the CGC ................................. 46  
  5.1 Definition of simulation environment ............................ 47  
  5.2 Photon generation ................................................ 49  
  5.3 Photon interaction ................................................ 50  
    5.3.1 Photoelectric effect .......................................... 51  
      5.3.1.1 Absorption edges ........................................ 52  
      5.3.1.2 Fluorescence .............................................. 53  
      5.3.1.3 Non-radiative transitions ................................ 54  
    5.3.2 Compton scattering ........................................... 55  
    5.3.3 Rayleigh scattering .......................................... 55  
  5.4 Scintillation ...................................................... 56  
    5.4.1 Generation of scintillation photons .......................... 56  
    5.4.2 Progression of scintillation photons through scintillator .. 58  
  5.5 CCD Processes .................................................... 60  
    5.5.1 Scintillation photon detection ................................ 60  
    5.5.2 Noise effects ................................................ 61  
  5.6 Summary .......................................................... 62
6 CGC collimator response
   6.1 Monte Carlo simulation ........................................... 64
   6.2 Sensitivity ......................................................... 64
   6.3 Spatial Resolution ................................................ 67
   6.4 Pinhole collimator response to finite sources ............... 72
      6.4.1 Analytical derivation of image profiles ................. 73
      6.4.2 Comparison to simulation .................................. 74
      6.4.3 Approximation of point sources using finite sources ... 76
   6.5 Optimisation of collimator design .............................. 78
      6.5.1 Requirements ................................................. 78
      6.5.2 Single-pinhole collimators ................................. 80
      6.5.3 Alternative collimator designs ......................... 81
         6.5.3.1 Parallel hole collimators ............................. 82
         6.5.3.2 Multi-pinhole collimators ......................... 83
   6.6 Conclusions and recommendations .............................. 84

7 CGC detector response ................................................... 86
   7.1 EMCCD performance ............................................... 87
      7.1.1 Photon transfer curves .................................. 87
         7.1.1.1 Calibration of ADU to electrons ..................... 89
         7.1.1.2 CGC measurements .................................. 90
         7.1.1.3 Charge collection .................................. 92
      7.1.2 Dark noise .................................................... 93
         7.1.2.1 Dark signal gradient ................................ 94
      7.1.3 Gain .......................................................... 96
         7.1.3.1 Temperature dependence .............................. 96
   7.2 Columnar CsI:Tl scintillator .................................... 101
      7.2.1 Spatial resolution and sensitivity ....................... 102
      7.2.2 Energy resolution .......................................... 104
         7.2.2.1 CCD effects .......................................... 106
      7.2.3 Scintillator-CCD coupling .................................. 107
   7.3 Conclusions and recommendations .............................. 109

8 Protocols for characterisation of SFOV gamma cameras ........ 111
   8.1 Intrinsic spatial resolution ................................... 112
      8.1.1 LFOV protocol and limitations ........................... 112
      8.1.2 Suggested SFOV protocol .................................. 113
      8.1.3 CGC method and results .................................. 114
   8.2 System spatial resolution ....................................... 116
      8.2.1 LFOV protocol and limitations ........................... 116
      8.2.2 Suggested SFOV protocol .................................. 117
      8.2.3 CGC method and results .................................. 117
   8.3 Spatial linearity .................................................. 119
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.3</td>
<td>8.3.1</td>
<td>LFOV protocol and limitations</td>
<td>119</td>
</tr>
<tr>
<td>8.3</td>
<td>8.3.2</td>
<td>Suggested SFOV protocol</td>
<td>119</td>
</tr>
<tr>
<td>8.3</td>
<td>8.3.3</td>
<td>CGC method and results</td>
<td>120</td>
</tr>
<tr>
<td>8.4</td>
<td>8.4.1</td>
<td>LFOV protocol and limitations</td>
<td>120</td>
</tr>
<tr>
<td>8.4</td>
<td>8.4.2</td>
<td>Suggested SFOV protocol</td>
<td>122</td>
</tr>
<tr>
<td>8.4</td>
<td>8.4.3</td>
<td>CGC method and results</td>
<td>122</td>
</tr>
<tr>
<td>8.5</td>
<td>8.5.1</td>
<td>LFOV protocol</td>
<td>121</td>
</tr>
<tr>
<td>8.5</td>
<td>8.5.2</td>
<td>Suggested SFOV protocol</td>
<td>123</td>
</tr>
<tr>
<td>8.5</td>
<td>8.5.3</td>
<td>CGC method and results</td>
<td>124</td>
</tr>
<tr>
<td>8.6</td>
<td>8.6.1</td>
<td>LFOV protocol</td>
<td>125</td>
</tr>
<tr>
<td>8.6</td>
<td>8.6.2</td>
<td>Suggested SFOV protocol</td>
<td>126</td>
</tr>
<tr>
<td>8.6</td>
<td>8.6.3</td>
<td>CGC method and results</td>
<td>126</td>
</tr>
<tr>
<td>8.7</td>
<td>8.7.1</td>
<td>LFOV protocol</td>
<td>127</td>
</tr>
<tr>
<td>8.7</td>
<td>8.7.2</td>
<td>Suggested SFOV protocol</td>
<td>128</td>
</tr>
<tr>
<td>8.7</td>
<td>8.7.3</td>
<td>CGC method and results</td>
<td>128</td>
</tr>
<tr>
<td>8.8</td>
<td></td>
<td>Comparison to other systems</td>
<td>129</td>
</tr>
<tr>
<td>8.9</td>
<td></td>
<td>Conclusion</td>
<td>133</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>HCGC and clinical tests</td>
<td>134</td>
</tr>
<tr>
<td>9.1</td>
<td></td>
<td>Hybrid compact gamma camera</td>
<td>135</td>
</tr>
<tr>
<td>9.1.1</td>
<td></td>
<td>Effect on CGC performance</td>
<td>136</td>
</tr>
<tr>
<td>9.1.2</td>
<td></td>
<td>Scale factor</td>
<td>138</td>
</tr>
<tr>
<td>9.1.3</td>
<td></td>
<td>Method for alignment of modalities</td>
<td>138</td>
</tr>
<tr>
<td>9.1.4</td>
<td></td>
<td>Image fusion</td>
<td>141</td>
</tr>
<tr>
<td>9.2</td>
<td></td>
<td>Clinical simulations</td>
<td>144</td>
</tr>
<tr>
<td>9.2.1</td>
<td></td>
<td>Detectability of image features</td>
<td>144</td>
</tr>
<tr>
<td>9.2.2</td>
<td></td>
<td>Thyroid simulation</td>
<td>146</td>
</tr>
<tr>
<td>9.2.2.1</td>
<td></td>
<td>Phantom specification</td>
<td>146</td>
</tr>
<tr>
<td>9.2.2.2</td>
<td></td>
<td>Image smoothing and detectability</td>
<td>147</td>
</tr>
<tr>
<td>9.2.2.3</td>
<td></td>
<td>Acquisition time and detectability</td>
<td>151</td>
</tr>
<tr>
<td>9.2.2.4</td>
<td></td>
<td>Comparison to LFOV systems</td>
<td>152</td>
</tr>
<tr>
<td>9.2.3</td>
<td></td>
<td>Sentinel lymph node simulation</td>
<td>154</td>
</tr>
<tr>
<td>9.2.3.1</td>
<td></td>
<td>Phantom specification</td>
<td>155</td>
</tr>
<tr>
<td>9.2.3.2</td>
<td></td>
<td>Lesion depth and detectability</td>
<td>156</td>
</tr>
<tr>
<td>9.2.3.3</td>
<td></td>
<td>Lesion separation and detectability</td>
<td>157</td>
</tr>
<tr>
<td>9.3</td>
<td></td>
<td>Patient images</td>
<td>158</td>
</tr>
<tr>
<td>9.3.1</td>
<td></td>
<td>Thyroid scan</td>
<td>159</td>
</tr>
<tr>
<td>9.3.2</td>
<td></td>
<td>Lacrimal drainage</td>
<td>159</td>
</tr>
<tr>
<td>9.4</td>
<td></td>
<td>Conclusion and recommendations</td>
<td>161</td>
</tr>
</tbody>
</table>
## 10 Summary, conclusions and future work

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.1</td>
<td>165</td>
</tr>
<tr>
<td>10.1.1</td>
<td>167</td>
</tr>
<tr>
<td>10.2</td>
<td>168</td>
</tr>
<tr>
<td>10.2.1</td>
<td>168</td>
</tr>
<tr>
<td>10.2.2</td>
<td>169</td>
</tr>
<tr>
<td>10.2.3</td>
<td>170</td>
</tr>
</tbody>
</table>

## A Description of blob detection algorithm

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.1</td>
<td>172</td>
</tr>
<tr>
<td>A.2</td>
<td>173</td>
</tr>
<tr>
<td>A.3</td>
<td>178</td>
</tr>
</tbody>
</table>

## B Camera configurations used in results

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.1</td>
<td>182</td>
</tr>
<tr>
<td>C.2</td>
<td>184</td>
</tr>
<tr>
<td>C.3</td>
<td>186</td>
</tr>
<tr>
<td>C.3.1</td>
<td>187</td>
</tr>
<tr>
<td>C.3.2</td>
<td>188</td>
</tr>
<tr>
<td>C.3.2.1</td>
<td>189</td>
</tr>
<tr>
<td>C.3.2.2</td>
<td>190</td>
</tr>
<tr>
<td>C.3.2.3</td>
<td>191</td>
</tr>
<tr>
<td>C.3.2.4</td>
<td>191</td>
</tr>
<tr>
<td>C.3.3</td>
<td>192</td>
</tr>
<tr>
<td>C.4</td>
<td>193</td>
</tr>
</tbody>
</table>

## D Curve fitting and statistical tests

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.1</td>
<td>195</td>
</tr>
<tr>
<td>D.2</td>
<td>196</td>
</tr>
<tr>
<td>D.3</td>
<td>197</td>
</tr>
</tbody>
</table>

## E Comparison of gamma camera performance characteristics

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.1</td>
<td>198</td>
</tr>
</tbody>
</table>

## Bibliography

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.1</td>
<td>200</td>
</tr>
</tbody>
</table>
Publications


Future publications


Chapter 1

Introduction

Diagnostic nuclear medicine employs radioactive tracers to investigate processes occurring within the body. Radiopharmaceuticals combine a radioactive material with a tagging molecule, tailored to the process being investigated. Following administration, the compound travels to the areas of interest within the body and an external gamma camera images the gamma radiation produced by the attached radioisotope. The targeting molecule, route of administration, and radioisotope used can all be tailored to suit the diagnostic need - resulting in a wide range of clinical applications.

The Compact Gamma Camera (CGC) has been developed at the Space Research Centre (SRC) at the University of Leicester in collaboration with Queen’s Medical Centre, Nottingham, and the University of Nottingham. The SRC has been able to bring its experience in X-ray astronomy instrument design to the development of a new portable high-resolution gamma camera with the capability for hybrid gamma and optical imaging.

The work described in this thesis characterises the CGC and its suitability for clinical imaging and describes a novel development - the Hybrid Compact Gamma Camera (HCGC).
1.1 Motivation and Applications

The CGC was designed as a portable device, providing greater flexibility for both staff and patients than the room-sized conventional gamma cameras currently in use. Conventional large field of view gamma cameras have spatial resolutions of around 7mm [1], with some portable small field of view systems improving this by an order of magnitude. In general, an improvement in spatial resolution is associated with a lower detection sensitivity and this is an important trade-off in gamma camera design.

In a clinical setting a large number of variables will have an effect on imaging quality. It is vitally important to fully understand CGC performance, theoretically and under a range of clinical conditions, in order to optimise its design and assess its utility for medical imaging. A complete simulation of the CGC (described in Chapter 5) allows for many parameters to be adjusted and the effects on image quality assessed - the results informing future design decisions. In this thesis, the effect of individual components on image quality is investigated (Chapters 6 and 7) and a detailed characterisation of the CGC (Chapter 8) has been carried out.

The small size of the CGC opens up the possibility of intraoperative imaging. Real-time gamma imaging during surgery could provide benefits for procedures such as tumour localisation and sentinel lymph node biopsy. Sentinel node imaging via lymphoscintigraphy has become an important technique for determining the stage of cancers and, in particular, whether the disease has spread from the primary tumour to the lymphatic system and beyond. The use of sentinel node biopsy can avoid the need for full lymphadenectomies in patients with cancer-negative nodes, reducing morbidity. Sentinel lymph node biopsies are regularly used in cases of breast cancer (1.7 million diagnoses worldwide in 2012 [2]) and melanoma (0.2 million diagnoses) with diagnostic benefits also shown in some vulvar, penile, thyroid, colorectal, gastric, head and neck, and oesophageal cancers [3].

 Sentinel lymph node biopsy requires the surgeon to locate and remove specific lymph nodes so they can be tested for cancerous material. Radiotracer-based sentinel lymph node biopsy is a commonly used protocol although exact methodology is variable [4].
In general terms, the position of the lymph nodes is found by injecting a short-lived radioactive substance (e.g. $^{99m}$Tc-labelled colloid albumin) into or around the tumour that will drain through the local lymph vessels and be collected in the nodes [3]. The sentinel nodes are those that the radioactive tracer reaches first - the nodes most likely to contain cancerous material. During surgery, the sentinel nodes are typically located using non-imaging gamma probes. A coloured dye may also be injected to allow visual identification during the surgical procedure [3, 4].

Intraoperative gamma imaging for sentinel lymph node biopsies has previously been investigated [5–8]. Olcott et al. [5] suggest that the improved spatial resolution of a portable gamma camera can assist in the detection of sentinel nodes close to the active injection site. Benefits may also be seen in procedures such as head and neck sentinel node biopsies where multiple small nodes are present, here the ability to survey larger areas while maintaining localisation could be advantageous [5].

Gamma images, such as those from single photon emission computed tomography (SPECT), show uptake of a radioisotope but are unable to image the surrounding anatomy. In some cases, a combined gamma camera and CT (computed tomography) image (SPECT-CT) is obtained prior to surgery; the CT scan showing anatomical detail and the gamma image indicating functional uptake in the sentinel nodes. Figure 1.1 shows an example image from this technique and illustrates the additional information that can be obtained through multi-modal imaging. Unfortunately, hybrid gamma-CT cameras are unavailable during surgery due to their large size and immobility and so any changes to node location after imaging cannot be assessed.

This thesis describes the introduction of a combination of the CGC and an optical camera (Chapter 9) - the HCGC - to provide simultaneous anatomical and scintigraphic information, combined into a single image. This may allow for more intuitive interpretation of gamma images and could aid surgeons in sentinel node localisation during surgery.
Chapter 1. *Introduction*

1.2 Aims

This thesis aims to determine the suitability of the CGC and HCGC for clinical imaging. To achieve this, system performance has been investigated through a Monte Carlo simulation and in phantom and clinical studies. These experiments explore potential uses to aid and inform future design decisions for improving localisation and visualisation of radionuclide sources.
Chapter 1. *Introduction*

### 1.3 Thesis Organisation

Chapter 2 provides the theoretical background to the interaction of gamma radiation with matter. Chapter 3 discusses the detector types commonly used in medical gamma imaging and Chapter 4 provides a full description of design of the CGC. Chapter 5 describes a Monte Carlo model developed to improve the understanding of the capabilities of the CGC and guide future design changes. Chapter 6 investigates the response of the pinhole collimator used, including a comparison of theoretical and modelled results and their implications, while Chapter 7 investigates the characteristics of the scintillator and CCD detector. Chapter 8 provides a full characterisation of CGC performance, using new protocols devised from the currently accepted standards for testing large field of view clinical devices. Chapter 9 describes the design of the optical component of the new Hybrid CGC (HCGC) and investigates its performance in clinical use. In Chapter 10, the overarching conclusions of this work are provided and possible directions for subsequent research are considered.
Chapter 2

Principles of gamma detection

In 1896, just four months after the discovery of X-rays by Wilhelm Conrad Röntgen, Henri Becquerel noticed that uranium salts produced radiation that could be detected by photographic plates [9]. This phenomenon was characterised by Marie Curie as ‘radioactivity’ in 1898. By mid-1902 Ernest Rutherford had classified emission from radioactive substances into three main types - α, β and γ radiation – with varying levels of penetration depth in matter [10]. In 1914 Rutherford, working with Edward Andrade, showed that gamma radiation could be diffracted and that it must therefore be comprised of electromagnetic waves [11], now known as gamma rays. Gamma rays can be defined as those photons emanating from processes within the nucleus [12]; this definition gives no set range for gamma ray energy, but for medical imaging energies of 30 keV to 400 keV are typical [1].

The energy of medical gamma rays means that they are highly penetrating, able to pass through many types of matter. This is a useful property as it allows the gamma photons to pass through the body and be detected by an external camera with minimal absorption or deflection, but it also makes them relatively hard to detect.
2.1 Attenuation

A gamma photon that travels through a material may be attenuated – either absorbed or scattered. Absorption processes transfer energy from the photon beam to the material while scattering processes change the direction of travel for individual photons. The main processes that contribute to gamma ray attenuation are the photoelectric effect, the Compton effect (or Compton scattering), and pair production. The proportion of energy lost due to each of these effects will depend on the initial energy of the gamma ray and the material it is passing through. Figure 2.1 shows the dominant attenuation process for different gamma ray energies and atomic numbers $Z$ of the absorbing material. As pair production is dominant only at energies far higher than those typically used in medical imaging it will not be discussed in this thesis.
When considering a beam of photons of initial intensity $I_0$ passing through a material, attenuation is described by the Beer-Lambert law [14]

$$I = I_0 e^{-(\mu/\rho)\rho x}, \quad (2.1)$$

where $\mu$ is the linear attenuation coefficient (a function of material and photon energy), $\rho$ is the density of the material, $x$ is the thickness of the material being traversed and $I$ is the intensity of the transmitted beam. The term $(\mu/\rho)$ is known as the mass attenuation coefficient and depends on the material and the energy of the interacting photon. The total mass attenuation coefficient for a material is the sum of the mass attenuation coefficients for each process contributing to attenuation. Mass attenuations can be calculated using XCOM – a web program that collates data from a number of published sources and interpolates this to generate mass attenuation coefficients for a given material and photon energy [13].

Based on the Beer-Lambert law, the proportion of photons $P$ that would be expected to interact after having travelled for a distance $\delta$ within a material is

$$P = 1 - e^{-((\mu/\rho)\rho \delta)}. \quad (2.2)$$

The proportion of interacting photons due to each process can be calculated using the appropriate mass attenuation coefficient for that process. Figure 2.2 shows the relationship between mass attenuation coefficients for the predominant processes over the energy range of medical X-rays, in this case for tungsten. The photoelectric effect (Section 2.1.1) is the clearly dominant process over this energy range although incoherent, or Compton, scattering (Section 2.1.2) and coherent, or Rayleigh, scattering (Section 2.1.3) also contribute to the total mass attenuation coefficient.

### 2.1.1 Photoelectric effect

The photoelectric effect occurs when an incident photon interacts with an electron in an atom and imparts enough energy to liberate the electron. The photon is entirely absorbed
by the electron during the process, and the emitted electron leaves a vacancy which can be filled through fluorescence or non-radiative transitions. These possibilities are illustrated in Figure 2.3 and discussed in more detail in Sections 2.1.1.2 and 2.1.1.3.

2.1.1.1 Absorption edges

Photoelectric absorption will not occur in an electron shell if a photon has insufficient energy to liberate that shell’s electrons. A photon with energy marginally less than the binding energy of a shell will not interact with that shell; a photon with energy marginally higher than that of the binding energy is able to do so. This leads to a discontinuity in the probability of photon absorption and so a discontinuity, or absorption edge, in mass attenuation coefficient, as seen in Figure 2.2. In the case of tungsten, these occur
Principles of gamma detection

2.1.1.2 Fluorescence

When an atom is left with an inner-shell vacancy, through photon interaction or otherwise, an electron transition will occur to return the atom to its lowest energy arrangement. This relaxation can occur through fluorescence or through a non-radiative transition. These are complementary processes; fluorescence yield $\omega_i$ is the probability that a vacancy in an inner shell $i$ will be filled through fluorescence, giving $1 - \omega_i$ as the probability that it will be filled through a non-radiative transition. Fluorescence yield increases with increasing $Z$ and increasing shell binding energies – for a given atom, the K-shell will always have the highest $\omega$ [15].

Fluorescence, as illustrated in Figure 2.3, occurs when an electron moves into a shell with a lower energy than its current position. During this process, a photon is emitted with a characteristic energy equivalent to the energy lost by the electron. This characteristic energy is specific to the transition that has occurred and the element it has occurred
Figure 2.4: Schematic of the highest probability allowable electron transitions for initial vacancies in the $K\text{-}$, $L_1\text{-}$, $L_2\text{-}$ and $L_3\text{-}$shells [15, 16]. Names for each emission line are shown in red.

in. This property of fluorescence has led to its widespread use in spectrometry, as the elemental makeup of a target can be determined by observing its fluorescence emission. Figure 2.4 shows some possible fluorescence transitions between energy shells, each of which will emit an X-ray photon of a specific energy. Certain transitions (e.g. $L_1 \rightarrow K$) are forbidden due to the required conservation of symmetry and angular momentum [17]. Transitions are categorised based on the shell of the original vacancy along with the emission line; for example, the leftmost transition shown in Figure 2.4, from $L_2 \rightarrow K$, is designated $K\text{-}\alpha_2$.

2.1.1.3 Non-radiative transitions

When an atom relaxes through a non-radiative transition, an electron moves to a lower energy shell to fill the vacancy. Whereas in fluorescence the energy lost by the transitioning electron is emitted as a photon, in a non-radiative transition this energy is transferred to a third electron which is then emitted from the atom (see Figure 2.3).
When a non-radiative transition occurs between different shells it is known as an Auger transition. When it occurs between different sub-shells of the same shell (e.g. $L_1$ and $L_2$) it is known as a Coster-Kronig transition [15]. The transition probability for Coster-Kronig transitions is considerably larger than that for Auger transitions due to their similar energy levels [18]. Non-radiative transitions to the $K$- or $L_3$-shells are always Auger transitions, as there are no higher energy sub-shells in which Coster-Kronig transitions can occur. Non-radiative transitions are typically referred to by the shell of the originating vacancy and the shells of the other electrons involved. For example, a transition designated $KL_1L_2$ indicates that an initial $K$-shell vacancy is filled by an electron from the $L_1$-shell while an electron from the $L_2$-shell is ejected from the atom.

### 2.1.2 Compton scattering

In incoherent (or inelastic) scattering, some proportion of the incident photon’s energy is transferred to the material with which it interacts. The scattered photon continues with a new direction of travel and an energy reduced by the amount imparted to the material. Although incoherent scattering may result from other processes (e.g. nuclear resonance scattering), it is predominantly due to Compton scattering and this is the sole form of incoherent scattering discussed in this thesis.

The Compton shift (the change in wavelength of a Compton scattered photon) is given by

\[
\lambda - \lambda_0 = \frac{h}{m_0c}(1 - \cos \psi),
\]

(2.3)

where $\lambda$ and $\lambda_0$ are the photon wavelengths after and before scattering respectively, $h$ is Planck’s constant$^*$, $m_0$ the mass of an electron$^\dagger$, $c$ the speed of light$^\ddagger$, and $\psi$ the scattering angle of the photon [19]. The term $h/m_0c$ is often referred to as the Compton wavelength $\lambda_c$. The scattering angle $\psi$ is defined as the angle between the photon’s initial direction and its scattered direction in the plane that contains the photon’s initial and scattered direction.

---

$^*$ $h = 6.626 \times 10^{-34}$ Js

$^\dagger$ $m_0 = 9.1 \times 10^{-31}$ kg

$^\ddagger$ $c = 3 \times 10^8$ m/s$^{-1}$
and the path of the scattered electron. Equation 2.3 shows that the Compton shift of a scattered photon depends only on $\psi$.

From Equation 2.3 it is possible to derive the energy of a scattered photon as

$$E = \frac{E_0}{1 + \frac{E_0}{m_0c^2}(1 - \cos \psi)},$$

which is dependent on initial photon energy $E_0$ alongside $\psi$ [20]. The relationship between scattering angle and change in energy is shown for a selection of initial photon energies in Figure 2.5. There is no energy loss without deflection (i.e. where $\psi = 0^\circ$) and maximum energy loss occurs at $\psi = \pm 180^\circ$. The proportion of energy lost for each angle is greater for larger initial photon energies. The energy lost is transferred to the electron involved in the scattering. For an incident photon of 141 keV the maximum possible energy loss due to Compton scattering is $\sim$50 keV. Compton scattering is typically defined for interactions with free electrons [20]. In practice, Compton scattering may also occur between a photon and a bound electron - this may result in shell vacancies if
FIGURE 2.6: Distribution of Compton scattering angles for a range of incident photon energies. All plots shown have been normalised to 1 at a scattering angle of 0°. The distribution for a 1 keV electron shows the case where $E \ll m_0c^2$.

enough energy is transferred to the bound electron [20, 21]. Where a vacancy is created, it will be filled by fluorescence or non-radiative transitions as in the photoelectric case.

During Compton scattering, the probability of a certain scattering angle occurring depends on the initial photon energy and the scattering material. The distribution of scattering angles is predicted by the Klein-Nishina formula for the differential scattering cross section $d\sigma/d\Omega$ [22],

$$
\frac{d\sigma}{d\Omega} = Zr_0^2 \left( \frac{1}{1 + \kappa (1 - \cos \psi)} \right)^2 \left(1 + \frac{\kappa^2 (1 - \cos \psi)^2}{(1 + \cos^2 \psi) [1 + \kappa (1 - \cos \psi)]} \right)
$$

(2.5)

where $\kappa = E_0/m_0c^2$ and $r_0$ is the classical electron radius$^5$. Atomic number $Z$ affects the total number of scattered photons but has no effect on the shape of the angular distribution.

$^5r_0 = 2.8 \times 10^{-15}$ m [20]
distribution. From the definition of $\psi$, angular distribution about the incident photon direction is uniform (solid angle $d\Omega = 2\pi \sin \psi \, d\psi$).

The distribution of scattering angles is shown in Figure 2.6 for a range of energies. The smaller the initial photon energy, the more likely it will be scattered through a large scattering angle. From Equation 2.5, at 141 keV approximately $2/3$ of photons will be forward scattered, with $1/3$ scattered by less than 30°.

### 2.1.3 Rayleigh scattering

In coherent (or elastic) scattering, photons change direction without an associated loss of energy. By definition this means that elastic scattering interactions cannot result in shell vacancies. The elastic scattering mechanism of concern for this thesis is Rayleigh scattering.

Rayleigh scattering, which occurs with bound electrons, can be thought of as a perturbation of Compton scattering for $E \ll m_0c^2$ ($\kappa \to 0$) [23]. The angular distribution in this case, for $E_0 = 1$ keV, is shown in Figure 2.6. From Equation 2.5, the Rayleigh cross section can be found to be [23]

$$
\frac{d\sigma_R}{d\Omega} = F(Z, \psi, \lambda) r_0^2 \left( \frac{1 + \cos^2 \psi}{2} \right),
$$

(2.6)

where $F$, the atomic form factor, is a perturbation of the simplified case from Equation 2.5.

The effect of the form factor in Rayleigh scattering is to increase the tendency for photons to scatter with small $\psi$, particularly at high energies and for high $Z$. The atomic waveforms used to determine $F$ can only be found analytically for H; approximations must be used for elements with higher $Z$ [24].
Chapter 2. *Principles of gamma detection*

2.2 Detection mechanisms

During attenuation, energy is transferred from impinging photons to the material they are travelling through. This can be an unwanted effect - attenuation within body tissues may be damaging or lead to a reduction of detected signal in medical imaging. This energy transfer, however, also allows for the detection of gamma rays when the energy is deposited within a detector.

In general, there are two principal types of gamma detection used in medical imaging. For direct imaging the gamma rays are absorbed by the detecting device; semiconductor detectors use this method. Indirect imaging requires an intermediate process - in the vast majority of medical gamma cameras, the gamma rays are first absorbed by a scintillator and it is the scintillation photons which are then detected. Detector design is described more fully in Chapter 3; the theory behind commonly used processes underpinning the detection methods used in medical imaging are described below.

2.2.1 Scintillation

Scintillators are materials which convert ionising radiation to optical or UV light. Scintillators have a long history of use in scientific research [25] and have been used in a medical context since the development of the earliest conventional gamma cameras [26] (see Chapter 3 for a brief history of medical gamma cameras). Of particular interest for this thesis is CsI doped with Tl (CsI:Tl) which is described, along with other commonly used scintillators, in Chapter 3.

Scintillators can be separated into two general types; organic and inorganic. For nuclear medicine, scintillating organic molecules are dissolved in a liquid solvent (although solid, plastic organic scintillators are also available) and are primarily used to assay radioactivity in *ex vivo* samples [1]. Inorganic scintillators are crystalline solids, these typically have a higher detection efficiency for penetrating radiation (such as gamma rays) than organic scintillators and are used for gamma imaging. In this work, only inorganic scintillators are considered. In inorganic scintillators, such as CsI:Tl, scintillation occurs due to the
movement of electrons between energy states of the crystal lattice of the material. An example of this energy state structure is shown in Figure 2.7. Electrons bound at lattice sites are said to be in the valence band; those that are free to move through the crystal are in the conduction band. An electron may move from the valence to the conduction band if it absorbs an energy sufficient to overcome the band gap. A conduction band electron may move to a vacancy within the valence band, emitting a photon in the process. In a pure crystal, transitions from conduction to valence bands are inefficient and typical band gaps result in high energy scintillation photons beyond the visible range [22].

To improve scintillator performance, inorganic scintillators are usually doped with a small amount of an impurity. The dopant molecules deform the area of the crystal lattice around them, creating what is known as a recombination centre (or alternatively a luminescent centre or activator site) [22]. At these sites, the band structure of the pure crystal is modified creating multiple energy states in the previously forbidden zone between the conduction and valence bands. This effect is illustrated in Figure 2.7. These additional energy states improve the efficiency of transitions from conduction to valence bands and also decrease the energy of emitted photons – typically bringing them within the absorption peak for standard detectors.
When ionising radiation passes through the scintillator it may be absorbed by a valence electron and cause it to transition to the conduction band. This leaves a hole in the valence band. Collectively, the excited electron and valence hole are known as an electron-hole (e-h) pair. If the freed electron has sufficient energy then it may itself create multiple e-h pairs.

The positive hole will drift towards a recombination centre (an area with a low ionisation energy) and ionise it. The electron is also free to migrate through the crystal and will do so until it reaches an ionised recombination centre. The electron will then transition between the energy states, either through production of scintillation photons or through non-radiative transitions. Non-radiative transitions, which may also occur away from recombination centres, reduce the efficiency of the ionising radiation to scintillation photon conversion; these processes are collectively referred to as quenching [22].

Decay time is the expected time taken for an electron to transition from an excited state to the valence band. It is not uncommon for a single scintillator to have multiple modes, or components, of decay. The fast component of decay is due to the electrons which transition directly from the conduction to the valance band. The slow component of decay occurs when an electron first drops into an energy state from which there is no allowable transition to the valence band. In this situation, the electron must first gain energy (typically through thermal excitation) to elevate it to a higher energy band from which transition to the valence band is possible. The effects of the slow component of decay are commonly referred to as afterglow.

The theoretical energy resolution of an inorganic scintillator is governed partly by photon statistics but must also take into account deviation from Poisson statistics due to non-proportional response of light yield to energy and variations within the crystal structure [27]. Recent tests have been able to derive a scintillation photon Fano factor (see Section 2.2.2) for some inorganic scintillators but this technique is not widespread [28]. Non-proportionality in energy response has been shown to correlate with the energy resolution of a detector [27]. In practice, it is difficult to experimentally separate the effects of scintillator non-linearity from multiple other factors that affect energy resolution, such as detector response.
2.2.2 Charge carrier generation

Modern gamma cameras detect photons by collecting the charge produced when they interact with a material within a detector. The specific details of each detector type are described in Chapter 3; this section provides an overview of the charge generation process.

When a photon deposits energy into a material, through any attenuation process, it may produce an e-h pair. The number of electron hole pairs produced by a given interaction is [14]

$$N_{e-h} = \frac{E}{w},$$

(2.7)

where $E$ is the deposited energy and $w$ is the ionisation energy - the energy required to create a single e-h pair. Ionisation energy will vary for different materials and materials under different conditions [14]. As charge generation is a stochastic process, $N_{e-h}$ will be expected to vary even for constant $E$. The variance in $N_{e-h}$ has been found to differ from a Poissonian distribution by a factor $F$ [29], the Fano factor, which is dependent on material and is typically found experimentally [23]. The variance in $N_{e-h}$ is then

$$\sigma^2_{e-h} = FN_{e-h}$$

(2.8)

which, when combined with Equation 2.7 and the full width at half maximum (FWHM) of a Gaussian curve (FWHM = $2\sqrt{2\ln2}\sigma$), gives an expected FWHM energy resolution of [23]

$$\text{FWHM} = 2.35\sqrt{wFE}.$$  (2.9)

2.3 Summary

Photons passing through matter may be attenuated - either absorbed or scattered - by a number of different processes. For the gamma photons of interest in this thesis (with energies $<200$ keV) the dominant attenuation process is the photoelectric effect. The energy deposited during scattering may be lost by fluorescence photons or electrons released in non-radiative transitions.
Attenuation is the basis of gamma detection. Some materials act as scintillators - generating photons of lower energies after absorbing a gamma photon. Direct detection relies on the conversion of deposited energy to charge. Both of these methods are in use in medical gamma cameras, and will be discussed in more detail in Chapter 3. The principles of photon-matter interaction described in this section are used to generate a Monte Carlo simulation of photon behaviour in Chapter 5.
Chapter 3

Devices for medical gamma imaging

Medical gamma imaging is now a widespread diagnostic technique which allows for the clinical and experimental study of many processes within the body. Over 100 different diagnostic procedures utilise gamma imaging techniques; processes that can be investigated include bone growth, lymphatic drainage, renal function, tissue perfusion, and the density of dopamine receptors in the brain [1].

The basic design of the conventional gamma camera used in hospitals has changed very little since the 1960s [1]. These are typically large, bulky devices, with a design emphasis on whole body scanning. More recently, portable gamma cameras have been developed. These have a wide variety of designs with smaller field of views (FOVs) than conventional gamma cameras [30].

Regardless of camera size, a medical gamma camera must have a high sensitivity; this allows low amounts of activity to be used therefore minimising the necessary radiation exposure to patients and staff. The camera must be able to differentiate between photons travelling directly from the source and those that have been scattered, either through collimation or energy discrimination. In addition, a camera must be able to produce an image with a high enough contrast and adequate spatial resolution to be clinically useful. Sensitivity and spatial resolution are discussed in more detail in Chapter 6 and image contrast is investigated in Chapter 9.
This chapter summarises the history and current state of medical gamma imaging.

### 3.1 A brief history of medical gamma imaging

The first X-ray image of a human was taken by Wilhelm Röntgen within weeks of his initial discovery of X-rays in 1896 [31]. Transmission images were also taken with gamma rays produced by naturally occurring radionuclides but the quality of these were easily surpassed by those taken using X-rays. Consequently, it was X-rays that became the standard for diagnostic imaging [1].

In 1924, George Hevesy established the possible benefit of using radioisotopes in medical imaging. Using naturally occurring radioisotopes of lead and bismuth, he was able to trace the circulation of these elements in plants and animal organisms [32]. Human tests were performed soon afterwards; in 1925, Herman Blumgart timed the circulation of a solution of $^{255}$Ra in a patient’s blood from one arm to the other [33]. This demonstrated the utility of radiotracers for functional imaging - observing processes within the body - as opposed to the structural imaging that can be obtained through the use of X-rays.

Nuclear medical imaging was initially limited by the amount and type of radioisotopes that were available. In 1934, Frédéric Joliot and Irène Curie produced the first artificial radioisotope [34]. In the early 1930s, the cyclotron was invented by Ernest Lawrence [35] making it possible to produce new radionuclides for medical imaging - including $^{99m}$Tc which is now commonly used in modern nuclear medicine. Cyclotron production of these radionuclides, however, was difficult to scale to sufficient quantities for widespread medical use. Around 1950, nuclear reactor facilities originally developed for the Manhattan Project began to be used for the production of medical radioisotopes (primarily $^{131}$I) and availability greatly increased [1].

Scintillators (Section 2.2.1) had been in use since the late 1800s – it was the scintillation of a zinc sulphide screen that allowed Rutherford to investigate the behaviour of $\alpha$-particles. Early nuclear medicine tests used Geiger-Müller counters to measure activity at various points of interest in the body. The 1940s saw the development of photomultiplier
tubes (PMTs), sensitive detectors of optical light, and the discovery of a range of newer scintillating materials (including thallium-activated NaI by Robert Hofstadter) [36]. This research allowed Benedict Cassen to develop a scintillation-based detector, 100 times more sensitive than a Geiger-Müller counter of the time [37].

In 1950, Cassen automated the motion of his detector, moving it in a raster pattern across the area of interest and combining counts at various positions into a map of radionuclide distribution [38]. The rectilinear scanner, as it was known, was mainly used to produce maps of the thyroid gland. It was also used to investigate functions in organs such as the liver and spleen which could not be imaged with X-ray technology, although the quality of these maps was poor [37].

The precursor of all modern medical gamma cameras was developed by Hal Anger, who finalised his design in late 1956 [39]. The Anger camera used a NaI:Tl scintillator coupled to an array of PMTs. Readings from across multiple tubes in the array were combined in calculations that allowed the exact position of the detected gamma ray to be recorded. With the Anger camera, it was possible to build an image of radionuclide distribution with a higher resolution and more quickly than with the rectilinear scanner, making dynamic functional studies possible [39].

Until the early 1960s, nuclear imaging was limited to the few specific organs that could be studied with the radionuclides available. In 1964, Paul Harper began imaging using the radioisotope $^{99m}\text{Tc}$ [1] and, at a similar time, $^{99m}\text{Tc}$ generators became commercially available [40].

A number of properties of $^{99m}\text{Tc}$ have led to its now ubiquitous use in nuclear medicine. With a physical half-life of 6 hours, $^{99m}\text{Tc}$ is within the required trade-off window between sufficient imaging time and minimising patient exposure. The gamma rays emitted by $^{99m}\text{Tc}$ have an energy of 141 keV, these can travel through tissue and be detected by an external camera. No harmful $\alpha$ or $\beta$ radiation is produced. In addition, it proved possible to label a wide variety of compounds with $^{99m}\text{Tc}$, allowing it to be used in studies for almost every organ within the body [1]. These features, coupled with generators which allow simple on-site $^{99m}\text{Tc}$ production, mean that approximately 80% of nuclear medicine studies carried out today use this isotope [41].
Gamma images were unable to give a 3-dimensional view of the body until after the invention of computed tomography (CT). CT is a reconstruction technique that allows planar images taken at many angles around the subject to be combined into a 3-dimensional representation. Developed by Godfrey Hounsfield, CT was first used to generate 3-dimensional X-ray images of a human in 1972. The benefits of CT were such that by the time Hounsfield was awarded the Nobel Prize for Medicine in 1979 X-ray CT systems were already in use in over 1000 hospitals [42].

In 1968, David Kuhl and Roy Edwards introduced the concept of reconstruction of source distributions from multiple conventional gamma images [38]. This would later become known as SPECT (single-photon emission computed tomography). In 1975, Michel Ter-Pogossian, Michael Phelps and Edward Hoffman applied Hounsfield’s algorithms to produce the first PET (positron emission tomography) scanner, which images the paired photons produced during annihilation of positron emissions from a radioisotope [38].

Although gamma imaging provides functional information unavailable with alternative imaging modes there may be a difficulty in relating this to anatomical information (see Figure 1.1) and image interpretation requires the skills of a highly trained medical specialist. One solution to assist interpretation is multimodal imaging - the simultaneous acquisition of multiple imaging types - which has become common practice. PET images are now invariably taken in combination with an X-ray CT [41]; the CT provides anatomical information and allows for attenuation correction while the PET can be used to analyse bodily processes. SPECT-CT is also routinely used, and hybrid nuclear/MRI (Magnetic Resonance Imaging) systems are now available for clinical use [41].

Today, medical nuclear imaging is widespread. The NHS (National Health Service) reports almost 0.6 million nuclear imaging procedures taking place in England in the year 2012-2013 [43].
3.2 Collimation

Gamma rays cannot typically be focussed in the traditional sense; due to their high energy it is not possible to create an optic to refract gamma rays in the same way that a glass lens might refract optical light [26]. In place of lenses, all imaging gamma detectors - whether using indirect (Section 3.3) or direct (Section 3.4) detection - require a collimator to produce an image.

Collimation is a method used to limit the directions at which a photon may impinge on the detector. If these are limited sufficiently then there will be an almost one-to-one relationship between the point where the photon is detected and where it was emitted, which allows an image to be built up [26]. Collimators are made from materials that are highly attenuating at the typical photon energies to be imaged and collimator design will vary depending on the type of imaging required. Some common collimator types for medical gamma imaging are discussed below.

3.2.1 Pinhole collimators

The pinhole collimator - a single hole in the dense shielding of a detector - has a long history in medical imaging, having been used in Anger’s original design [26]. Although the shape of the pinhole may vary, a circular knife-edge pinhole collimator (as illustrated in Figure 3.1) has been commonly used. Pinhole collimators are capable of both magnifying and demagnifying images. For a detector-collimator distance $t$ and a source-collimator distance $h$ the magnification of the image $M$ will be

$$M = \frac{t}{h}. \quad (3.1)$$

In the magnifying case $h < t$, this reduces the FOV of the camera but improves the object spatial resolution (Equation 3.2) of the image, making it ideal for small organ imaging [26].

*Gamma ray lenses have been developed and can be used under some conditions (e.g [44, 45]) but limitations such as inappropriate energy ranges, long focal lengths, energy non-linearity, small FOVs and difficulties in manufacture mean they are not currently practical for medical imaging.*
3.2.1.1 Collimator Resolution

If $M \neq 1$, the FWHM measured on the detector may not be directly comparable to resolution in terms of object size. The resolution in object space for a point source centred on the pinhole is given by

$$R_{\text{geom}} = d \left( \frac{1}{M} + 1 \right),$$  \hspace{1cm} (3.2)

where $d$ is the diameter of the pinhole [1]. $R_{\text{geom}}$ degrades with decreasing magnification. This is a geometric resolution and does not take into account the possibility of gamma ray penetration through the collimating material. To account for penetration through the collimator, Equation 3.2 may be modified by using an effective diameter $d_{\text{eff}}$ which includes the effects of the acceptance angle of the pinhole $\alpha$ and the linear attenuation coefficient $\mu$ for the energy and collimator material being investigated [46]. Although this effective diameter,

$$d_{\text{eff}}^2 = d \left( d + \frac{2 \tan \frac{\alpha}{2}}{\mu} \right) + \frac{2 \tan^2 \frac{\alpha}{2}}{\mu^2},$$  \hspace{1cm} (3.3)
is an imprecise approximation [47]. Alternative approximations, which can also account for source-collimator angle $\psi$, are discussed in Chapter 6.

### 3.2.1.2 Collimator Sensitivity

From Figure 3.1, the sensitivity $S$ - the fraction of incident photons which pass through the collimator - is geometrically

$$S_{\text{geom}} = \frac{d^2 \sin^3 \psi}{16h^2}.$$  \hspace{1cm} (3.4)

This approximation can be improved through use of the effective diameter from Equation 3.3 to replace $d$ [46]. Equation 3.3 tends to overestimate pinhole sensitivity. A more rigorous derivation that includes explicit calculations for the path length of oblique rays is given by Metzler et al [48] as

$$S = \frac{d^2 \sin^3 \psi}{16h^2} + \frac{\sin^5 \psi \tan^2 \frac{\alpha}{2}}{8h^2 \mu^2} \left( 1 - \frac{\cot^2 \psi}{\tan^2 \frac{\alpha}{2}} \right)^{\frac{1}{2}} \left[ 1 - \frac{\cot^2 \psi}{\tan^2 \frac{\alpha}{2}} + \frac{\mu d}{\sin \psi \tan \frac{\alpha}{2}} \right],$$  \hspace{1cm} (3.5)

which reduces to the effective diameter case of Equation 3.4 for $\psi = \frac{\pi}{2}$. The sensitivity of a pinhole collimator therefore decreases rapidly with increasing $h$.

A typical pinhole collimator for medical imaging will have a pinhole diameter in the region of 4 mm, a collimator-detector distance of approximately 250 mm, and is likely to be made out of lead [26]. Using these values as an example, at a source-collimator distance of 10 mm, the geometric resolution $R_{\text{geom}} = 4\text{ mm}$ from Equation 3.2 and the geometric sensitivity $S = 1\%$ from Equation 3.4. At $h = 100\text{ mm}$, this becomes $R_{\text{geom}} = 14\text{ mm}$ and $S = 0.01\%$.

### 3.2.2 Parallel hole collimators

A parallel hole collimator contains an array of uniform channels separated by thin walls of collimator material known as septa. Parallel hole collimators are used in the majority of all medical gamma cameras [1]. A conventional gamma camera will have
a selection of collimators available for use depending on the imaging procedure being carried out, typically these will include both a resolution optimised and a sensitivity optimised collimator [26]. Parallel hole collimators do not magnify; object size will be reproduced in the image on the detector face. A parallel hole collimator cross-section is shown in Figure 3.2.

### 3.2.2.1 Collimator Resolution

For a parallel collimator of length $T$ with square holes of width $d$, geometric resolution is given by

$$R_{\text{geom}} = d + \frac{d}{T} (h + t),$$

(3.6)

where $h$ and $t$ are source-collimator and detector-collimator distances respectively [26]. Gamma rays that penetrate through the septa of a parallel hole collimator can be accounted for.

---

†The distance $t$ in this case is more correctly the distance between the collimator and the point in the detector where a photon interacts. This distance will vary depending on photon energy although the effect of this is minimal relative to typical resolutions [1].

---

**Figure 3.2:** Illustration of cross-section of a square parallel hole collimator. The source-collimator distance $h$, collimator-detector distance $t$, hole width $d$, septal thickness $w$ and collimator length $T$ are defined as shown.
for by using the effective length

\[ T_{\text{eff}} = T - \frac{2}{\mu}, \quad (3.7) \]

where \( \mu \) is the linear attenuation coefficient, in place of \( T \) in Equation 3.6.

### 3.2.2.2 Collimator Sensitivity

The sensitivity of a parallel collimator accounting for penetration is

\[ S = K^2 \left( \frac{d}{T_{\text{eff}}} \right)^2 \left[ \frac{d^2}{(d + w)^2} \right], \quad (3.8) \]

where \( K \) is a constant dependent upon the shape and arrangement of holes \( (K = 0.28 \) for square holes in a square array [1]) and \( w \) is the septal thickness of the collimator [26].

Equation 3.8 implies that sensitivity is improved by an increase in the ratio \( \frac{d}{T} \) however, from Equation 3.6, this will cause a deterioration in spatial resolution. The trade-off between sensitivity and resolution informs collimator design.

A low energy all-purpose collimator may have parameters in the region of \( d = 3.4 \) mm, \( T = 36 \) mm, \( w = 0.5 \) mm and \( t = 9 \) mm [26]. This gives \( R_{\text{geom}} = 8.1 \) mm and \( S = 0.05\% \) (without penetration) at \( h = 10 \) mm. At \( h = 100 \) mm, sensitivity is unchanged however the resolution degrades to \( R_{\text{geom}} = 16.2 \) mm. A low energy high resolution collimator may have parameters in the region of \( d = 1.8 \) mm, \( T = 40 \) mm, \( w = 0.3 \) mm and \( t = 9 \) mm [26]. This gives \( R_{\text{geom}} = 4.1 \) mm and \( S = 0.01\% \) (without penetration) at \( h = 10 \) mm, at \( h = 100 \) mm sensitivity is unchanged and \( R_{\text{geom}} = 8.1 \) mm.

### 3.2.3 Other collimators

Although the parallel hole collimator is ubiquitous in medical gamma imaging, some procedures are better suited to adapted designs. Converging and diverging collimators are used to decrease or increase the FOV of a detector. Fan beam collimators - where
collimator holes converge towards a single focal point in one dimension - can expand the image of a small organ across an entire detector. These collimator variants are typically used for specialist tasks such as heart and brain imaging although in some instances these can be replaced by specialist imaging software.

### 3.3 Indirect detection

Indirect imaging is the most common detection method for medical gamma cameras as it generally has a higher sensitivity than direct methods. Gamma rays are first absorbed by a scintillator which then emits scintillation photons. These scintillation photons can then be recorded by a variety of different detectors.

#### 3.3.1 Scintillators

An ideal scintillator will have a high attenuation at the photon energies to be detected. It must convert from absorbed photons to scintillation photons with a high efficiency and a scintillation yield that is proportional to the energy absorbed. For an accurate response, particularly in a high flux environment, scintillation photons should be emitted near instantaneously after energy absorption (i.e. the scintillation should have a small decay time). In addition, the scintillator should be transparent to its own emission wavelengths to allow scintillation photons to be detected; ideally these emission wavelengths will fall into a region of high detection efficiency for the detector being used. Detection is aided if the scintillator has a refractive index similar to that of glass (∼1.5) to allow efficient coupling to detection optics [22].

Since Anger’s first design, the scintillator of choice for medical gamma imaging has been NaI:Tl which is relatively easy and inexpensive to grow into the large crystals needed [1]. Some small FOV (SFOV) cameras also make use of NaI:Tl scintillators [49, 50] while CsI:Tl [51–54] and CsI:Na [8] have also been used. Table 3.1 shows some relevant properties of these scintillators - since the level of doping has an effect on the properties
Chapter 3. Devices for medical gamma imaging

### Table 3.1: Properties of some scintillation materials used in medical imaging [1, 22, 27, 28, 36, 56–58]. Attenuation coefficients found using the XCOM database [13] using effective atomic number [1]. Percentages in decay time show the percentage probability for each mode of decay where this is known. Reported energy resolutions use different detection techniques and so are indicative but not directly comparable.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NaI:Tl</th>
<th>CsI:Tl</th>
<th>CsI:Na</th>
</tr>
</thead>
<tbody>
<tr>
<td>Density (gcm(^{-3}))</td>
<td>3.67</td>
<td>4.51</td>
<td>4.51</td>
</tr>
<tr>
<td>Attenuation coefficient at 141keV (cm(^2)g(^{-1}))</td>
<td>0.705</td>
<td>0.837</td>
<td>0.837</td>
</tr>
<tr>
<td>141keV absorption through 10 mm</td>
<td>92.5%</td>
<td>97.7%</td>
<td>97.7%</td>
</tr>
<tr>
<td>Photon yield (keV(^{-1}))</td>
<td>38-41</td>
<td>52-66</td>
<td>40</td>
</tr>
<tr>
<td>Poisson limited energy resolution at 141 keV</td>
<td>3.1%</td>
<td>2.6%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Reported energy resolution at 141 keV</td>
<td>9.4% [55]</td>
<td>7.4% [52]</td>
<td>32% [8]</td>
</tr>
<tr>
<td>Decay time (ns)</td>
<td>230 (91%)</td>
<td>680 (64%)</td>
<td>460</td>
</tr>
<tr>
<td></td>
<td>150000 (9%)</td>
<td>3340 (34%)</td>
<td>4180</td>
</tr>
<tr>
<td>Peak emission wavelength (nm)</td>
<td>415</td>
<td>550</td>
<td>420</td>
</tr>
<tr>
<td>Refractive index at peak emission</td>
<td>1.85</td>
<td>1.79</td>
<td>1.84</td>
</tr>
</tbody>
</table>

of the scintillator, the values given in Table 3.1 will vary for different doping levels but are broadly applicable.

Thicker scintillators will absorb a higher percentage of incident photons though an increase in scintillator thickness will cause an associated increase in FWHM resolution (a degradation in image quality). Within the scintillator, scintillation photons spread isotropically from the initial interaction point and the further they must travel to the detector the further they will spread from their true position in the image. As the photons are spread over a larger area, the signal-to-noise level will be decreased. This can be corrected if the depth of interaction (DOI) within the scintillator is constant; with thicker crystals this is not a valid approximation and image blurring results [26].

### 3.3.2 Photomultiplier tubes

A conventional gamma camera detects scintillation photons using an array of photomultiplier tubes (PMTs), a technique that is also used by some SFOV systems [49–51, 59]. The window of a PMT is coated with a photoemissive substance such as CsSb [1]; incident scintillation photons cause these compounds to emit electrons. The emitted photoelectrons are accelerated to a dynode at a positive bias within the PMT. The dynode
will be made of, or coated with, a substance that ejects multiple secondary electrons when
struck by a high-speed photoelectron - increasing the number of electrons in the PMT.
These electrons are then attracted to a second dynode where they are again multiplied - a
typical PMT might contain around 12 dynodes, leading to a total gain of around $10^8$ prior
to electron collection at the anode of the PMT [1]. The electron multiplication stages
result in a relatively large output current for a weak light signal.

The relative signals from each of the PMTs (with typical diameters of the order of 100 mm
[26]) within the array are used to determine the position of the original interacting gamma
photon [26]. The distribution over all PMTs is used to find the centre point (where the
original gamma photon is most likely to have interacted) and the total energy deposited.
Position sensitive PMTs (PSPMTs), which contain multiple anodes to provide the same
information usually provided by multiple PMTs, are typically used for compact gamma
cameras to reduce the bulk of a standard array [49–51, 59].

### 3.3.3 Photodiodes

Photodiodes are semiconducting devices governed by the physics described in
Section 2.2.2. In a photodiode, charge carriers are generated by the absorption of a
photon and a bias is applied in order to read out the generated charge. Photodiodes have a
higher quantum efficiency than PMTs but, with no integral gain, additional electronic
amplification is necessary for their use [26]. Photodiodes have been used in SFOV
systems, either in an array applying the same calculations as used in PMT arrays [8]
or as components within a pixelated detector [52].

### 3.3.4 Charge-coupled devices (CCDs)

A CCD is a Si-based pixel array which uses a series of metal-oxide semiconductor
capacitors to form each pixel. During image accumulation, incident photons are absorbed
and generate charge carriers within each capacitor. Capacitors are commonly arranged in
triplets‡, each triplet representing a single pixel on the final image. While accumulating an image, one capacitor will be held at a higher positive bias and surrounding capacitors are held at a lower bias. This creates a potential well that attracts electrons into the central capacitor and traps them there. Once accumulation is complete, the charge must then be transferred to the readout register of the CCD. The capacitors are closely spaced so that when the bias across adjacent pixels is equalised, charge will spread between them. The bias on the capacitor initially holding the charge can then be lowered, transferring the charge to the next capacitor. This allows charge to flow from one capacitor to another and, with multiple applications, allows serial readout of all CCD pixels. At readout, a voltage is generated for each pixel proportional to the signal charge transferred. This time-dependent voltage is used to construct an image of the initial light distribution [60].

CCDs can be designed with very small pixel dimensions, giving them excellent spatial resolution. The serial output of a CCD makes it vulnerable to thermal noise and CCDs must be cooled when used in low light conditions [14]. Noise effects on CCDs are described in more detail in Chapter 7. CCD detectors have been investigated for use with SFOV gamma cameras [54] and a new generation of electron multiplying CCDs (EMCCDs) with improved noise statistics have been included in SFOV designs including that of the CGC [53].

### 3.4 Direct detection

Direct imaging does not make use of a scintillator and gamma photons are detected directly from the production of charge carriers during absorption. CCDs are capable of directly imaging gamma rays, however poor sensitivity (due to the low Z-number of Si and therefore low absorption) makes them impractical for use at energies above $\sim 10$ keV [14]. Although direct detection typically has a lower sensitivity than indirect detection, it greatly improves energy resolution [30].

‡For three phase clocking. Two phase and four phase clocking CCDs, both of which require four capacitors per pixel, are also common.
3.4.1 Semiconductor detectors

Semiconductors such as CdTe or CZT (cadmium zinc telluride) have seen recent use in both specialised conventional [26] and SFOV camera systems [6, 61, 62]. These semiconductors are used as they have high atomic numbers (good absorption properties) and their large band gaps allow for room temperature operation [63]. Table 3.2 shows some relevant properties for these semiconductors; representative values are used as variation is expected for different semiconductor compositions.

Table 3.2 shows absorption through 10 mm of semiconductor material to allow direct comparison to the scintillators listed in Table 3.1. In practice, the useful thickness of a semiconductor detector is limited by its charge transfer properties. The average distance an electron or hole will travel through a semiconductor, the recombination length, is dependent on the properties of the semiconductor and the electric field that is applied across it. In practice, CdTe and CZT detectors have thicknesses of <5 mm [63, 64]. At this thickness, they have a theoretical absorption of 87% and 86% respectively.

The Fano limited energy resolutions of the semiconductors is significantly better than the Poissonian limited resolutions for scintillators. If the Fano factors of scintillators were taken in to account this difference would be even greater - for CsI:Na with a reported Fano factor of 3.2 [28] theoretical FWHM resolution increases from 3.2% in Table 3.1 to 5.6%. Despite these theoretical limits, there is not so distinct a difference between
reported experimental energy resolutions in scintillator and semiconductor based medical gamma cameras.

3.5 Summary

Medical gamma imaging is an important technique for a large number of diagnostic procedures. Spatial resolution and sensitivity are typically limited by collimator choice, and a trade-off exists between these parameters as improving one will generally have a negative effect on the other. A conventional medical gamma camera uses a parallel hole collimator with a NaI:Tl and PMT detector. SFOV cameras use parallel hole or pinhole collimators and a variety of different detectors. Modern developments in gamma camera design include the use of new scintillation materials (CsI:Tl, CsI:Na), new detectors for scintillation photons (photodiodes, CCDs) along with the direct imaging of gamma rays using semiconductor materials (CZT, CdTe). With current materials, scintillation detectors provide high sensitivities while semiconductor materials have improved energy resolutions.
Chapter 4

Compact Gamma Camera (CGC) design

The Compact Gamma Camera (CGC) was developed by the Space Research Centre, University of Leicester in collaboration with Radiological and Imaging Sciences at the University of Nottingham. The camera used in this work incorporated a number of improvements on the design previously described in the literature [68], particularly in terms of improved shielding and a new cooling system. Figure 4.1 provides an overview of the design of the CGC which will be described in more detail in the following sections.

The CGC was designed as a portable system - to be operated handheld or fixed in an adjustable support arm. The CGC itself has a mass of approximately 1.2kg. Readout electronics are housed separately to the CGC. Image acquisition is performed through an in-house designed software package written in IDL∗ (Interactive Data Language [69]).

The CGC consists of a 0.5 mm or 1.0 mm diameter pinhole with an acceptance angle of 60° in a 6 mm thick tungsten collimator. The detector is a 0.6 mm thick Tl doped CsI scintillator, consisting of multiple closely packed CsI:Tl columns each a few µm wide, coupled to an electron multiplying CCD (EMCCD).

∗Previous work carried out by Oliver Blake, Adam Bark and others at the Bioimaging Unit, University of Leicester.
Figure 4.1: Main: Schematic of Compact Gamma Camera (CGC). Inset: Image of CGC with protective cover removed to show pinhole collimator.

4.1 Collimator

The collimators of the CGC are manufactured from a 45 mm diameter, 6 mm thick tungsten disc. At 141 keV, transmission through 6 mm of W is $5 \times 10^{-10}$, so photon flux through the collimator material is negligible. A pinhole collimator was chosen as it allows the FOV of the CGC to extend beyond the dimensions of the detector used ($\sim 8 \text{ mm} \times 8 \text{ mm}$). A pinhole collimator also allows for a superior resolution to a parallel
Table 4.1: Geometric resolution (Equation 3.2) and sensitivity (Equation 3.3 and Equation 3.4 for a centred source) for different pinhole diameters and source-collimator distances used by the CGC. The collimator-detector distance has been fixed at 10 mm in all cases and the collimator material is W ($\mu$ = 36.22 cm$^{-1}$ for 141 keV incident photons).

4.2 Scintillator

CsI:Tl was chosen as scintillator for the CGC due to its high light yield (65 photons/keV [70]) and density. The peak scintillation photon wavelength of 550 nm is well matched to the response of the EMCCD used, which has a quantum efficiency of $\sim$ 92% at this energy [70, 71].

CsI:Tl can be produced with a columnar structure, with tightly packed narrow needles as shown in Figure 4.2 ranging in diameter from $\sim$5 $\mu$m to 15 $\mu$m) [72, 73]. The columns act as light guides within the scintillator - internal reflection will act to channel photons towards the CCD and reduce light spread within the scintillator.
4.3 EMCCD

Scintillation light is detected by a CCD97 from the L3Vision range of products from e2v technologies [71], chosen as it has been optimised for use with low illumination. This is an EMCCD, which differs from a standard CCD in that it has an on-chip gain stage. The incorporation of a gain stage reduces the effect of read noise on the image - a limiting factor for standard CCDs - to improve image quality. The CCD97 used is a back illuminated device and so has been back-thinned to reduce light absorption and improve sensitivity.

The EMCCD (schematic shown in Figure 4.3) comprises an imaging region of $512 \times 512$ $16 \mu m$ square pixels. An image is accumulated, then transferred to a storage area which allows simultaneous integration and readout; this is then clocked into the serial readout

---

In most cases. For further details see Section 7.2.3.
Figure 4.3: Simplified schematic of EMCCD sensor. Charge collection occurs as in a standard CCD. Electron multiplication occurs in the multiplication register. Each multiplication element contributes a small gain in signal; this becomes significant over the entire multiplication register of 536 stages.

Register as in a standard CCD. Before the final readout, charge is transferred through 536 elements in the multiplication register.

On-chip pixel binning (4 × 4 if not otherwise stated) was used to improve readout speed. This gives an effective pixel size of 64 µm, a reasonable size given the expected spatial resolution of the system (of the order 100 µm [75]). In this mode, rows are binned as they are transferred to the serial register and so pass through the multiplication register already binned. Column binning occurs after multiplication, during the readout stage.

The multiplication process in the EMCCD gain register is due to impact ionisation. Prior to the multiplication stage, charge is transferred in the same way as in a standard CCD. Clocking voltages control the movement of charge from one capacitor to the next in the imaging and storage regions and in the serial register.

In the multiplication register, one of the typical transfer steps is given a clocking voltage far higher than usual (around 50 V compared to typical clocking voltages of less than
12 V). The large potential drop, over a small distance, produces electric fields of the order $10 \times 10^7 \text{ V m}^{-1}$ [76]. Electrons in these fields may gain enough energy to excite an electron from the valence band of the material into the conducting band, generating a new electron-hole pair [77]. This has a small effect in each clocking stage with typical gains of the order 1.01 [78] which, over many stages, can result in gains of several orders of magnitude. The gain accumulated depends on the magnitude of the clocking voltage (see Chapter 7).

The readout electronics and voltages used were configured to the manufacturer’s suggested specifications unless otherwise stated. The CCD is operated in an inverted mode to reduce dark current [60]. In this mode, the biases applied to the CCD are inverted - this creates a large population of holes along the surface, where thermal noise is predominately generated, which act to ‘mop up’ the thermal current produced [60].

The detector is housed within a small vacuum chamber (typical pressures of the order 1 Pa) to improve cooling and protect the detector from dust and moisture (CsI:Tl is slightly hygroscopic [1]). The vacuum chamber is made from 4 mm thick Al. A 20 mm diameter entrance window, integral to the housing, has been thinned to a thickness of 1 mm to reduce attenuation of photons passing through the pinhole.

### 4.4 Shielding

The front of the detector chamber is shielded by the 6 mm thick W collimator. Surrounding all other sides is 3 mm thick W shielding with an expected transmission of $5.6 \times 10^{-10}$ for 141 keV gamma photons.

### 4.5 Cooling

The CCD is cooled using a thermoelectric cooler (TEC) device coupled to a paraffin-based phase-change material (PCM). This cools the CCD to between 260 K to 275 K, depending on operating conditions. The use of the PCM allows for cooling without the need for either
an air intake or a water cooling connection, preferable for use in a clinical environment where the risk of infection must be minimised.

### 4.6 Casing

In a clinical environment, devices should be easy to sterilise with smooth surfaces. For handheld use, it is also important that devices are ergonomically designed. For certain procedures, the CGC needed to be easily and securely mounted to an adjustable support arm. The casing of the CGC currently in use was designed at De Montfort University to fulfill these criteria. The additive manufactured case has a smooth surface and separate clip-on attachment for easy mounting. Figure 4.4 shows the CGC in clinical use with the black case body and white case cap clearly visible.

### 4.7 Image acquisition

A full image can consist of numerous frames, each of which takes \( \sim 0.1 \) s to acquire. Images are stored in a propriety event record format, which separates each image frame to allow for image processing. The image format records the x-position, y-position and signal for each pixel in the frame which exceeds a preset threshold signal level. This threshold is typically set at a value equal to the mean of the noise peak plus \( 5\sigma \).
4.8 Image processing

The following image processing steps occur post-acquisition but could, with software adaptation, be completed in real time. The image processing steps aim to convert the scintillation counts detected on the CCD to an image that displays the magnitude and position of deposited energy throughout the acquisition time.

4.8.1 Hot pixel correction

In a CCD it is common for there to be non-uniformity in the response of different pixels to the same signal level. For this thesis, hot pixels were defined as those recording counts above expected thermal noise in more than 5% of frames in a dark image. Designated hot pixels are replaced with the average signal value of their four nearest neighbours. This is carried out individually for each frame during post-processing, prior to blob detection.

4.8.2 Blob detection

Each gamma ray absorbed in the scintillator gives rise to a large number of scintillation photons reaching the CCD. The number of photons reaching the CCD will depend on the interaction depth, the spread within the scintillator, the quality of the scintillator material, the coupling efficiency of the scintillator to the CCD and the efficiency of the CCD at the wavelength of the optical photons. In practice the CCD records a “light splash” which extends over a number of pixels.

The spread of the light is partly determined by where in the scintillator it is absorbed. Gamma rays interacting far from the CCD produce a greater spread and hence a lower peak intensity. The number of photons created by a gamma ray absorbed in a scintillator is proportional to its energy, so the total intensity measured by the CCD will give an indication of the incident gamma energy.

To calculate total intensity, a method known as automatic scale selection, or blob detection, is used [79]. The mathematics of this process are described in more detail in
Appendix A but the objective is to find the best fit of a Gaussian distribution to each individual light splash. This is done for every light splash in a frame and for every frame within an image. Each gamma interaction can be characterised by a representative Gaussian distribution with a peak amplitude $A$ and a standard deviation $\sigma$. An energy spectrum histogram, which uses the total number of counts within each light splash, as energy is equal to $2\pi A\sigma^2$ for each scintillator event.

After blob detection, an image can be displayed in two modes. In the centre point display mode, a light splash on the image is replaced by a single event, representing the initial gamma photon, at the centroid of the light splash. In the cumulative display mode, the light splashes are reconstructed as Gaussian distributions with a peak amplitude $A$ and a standard deviation $\sigma$.

### 4.8.3 Flat field correction

Flat field correction is applied after blob detection is completed.

A flood image is acquired, either with a point source at a large distance (for intrinsic measurements) or with a uniform flood source (for extrinsic measurements). A dark image, with no incident illumination, is also needed. A master flat image is then created by subtracting the dark image from the flood image (corrected for any difference in exposure time) and then normalising the resulting image to its maximum value. Images are then corrected for flat field effects by subtracting a dark image and dividing by the master flat image.

### 4.9 CGC configuration summary

A number of different CGC units were used throughout this thesis, designated A, B, C and D, each with an identical design but some minor differences in assembly. Some difference in performance between devices is expected. The design of the CGC is summarised in Table 4.2 and differences between the units are identified where appropriate.
### Table 4.2: Summary of CCD configuration for the CGC units (A, B, C and D) used throughout this thesis.

These configurations are referenced throughout this thesis where CGC results are presented. The CGC configuration and the diameter of the pinhole used for each dataset is also summarised in Appendix B.
Chapter 5

Monte Carlo simulation of the CGC

This chapter describes a new Monte Carlo model, developed in IDL [69], that was specifically designed to simulate the response of a pinhole-collimated scintillator-based gamma camera to incident photons. This model was developed to allow greater flexibility in both input and output information than proprietary software packages. The aim of this simulation was to fully understand the responses of the components of the CGC and to use simulation results to guide future development of the CGC.

A Monte Carlo simulation allows for the modelling of stochastic processes by assigning probabilities to particular outcomes and using a pseudo-random number generator to test against these probabilities*. Use of Monte Carlo simulations in the investigation of pinhole collimator [80–84], scintillator [85–89], and CCD [90–94] response is well established. A number of off-the-shelf software packages offer general Monte Carlo simulation (e.g. GEANT4 [95], MCNP [96], and EGS4 [97]) while other packages offer simulation of SPECT and PET imaging systems (e.g. SIMIND [98], EIDOLON [99] and GATE [100]).

The model developed in this work simulates X-ray attenuation from photoelectric absorption (Section 5.3.1), Compton scattering (Section 5.3.2) and Rayleigh scattering (Section 5.3.3). In addition, fluorescence (Section 5.3.1.2) and non-radiative transitions

*Hereinafter the term ‘random’ will be used in place of ‘pseudo-random’. For more information on the pseudo-random number generator used see Appendix C.1.
Chapter 5. *Monte Carlo simulation of the CGC*

(Section 5.3.1.3) due to shell vacancies are modelled. Within the scintillator, energy deposition and transport (including reflection effects) have been modelled (Section 5.4). A simulated image is formed based upon the detection of scintillation photons in the CCD, along with the modelled effects of noise from the CCD and associated electronics (Section 5.5). Final results may be viewed in real time or recorded for further analysis.

Figure 5.1 provides an overview of this model. Each simulated process is described in more detail in the appropriate subsections of this chapter.

### 5.1 Definition of simulation environment

The CGC as simulated consisted of a W pinhole collimator, an Al window, a CsI:Tl scintillator and a Si-based CCD. The default size and configuration of these components aimed to represent the current iteration of CGC design as described in Chapter 4 and shown in Figure 4.1.

The Al window thickness (1 mm), collimator diameter (45 mm), frame rate (10 s\(^{-1}\)) and scintillation material (CsI:Tl) were fixed at the values appropriate to the CGC. Source type, source activity, source position, collimator thickness, pinhole diameter, pinhole acceptance angle, pinhole-scintillator distance, scintillator thickness, detector size, pixel size and imaging time were all adjustable through a Graphical User Interface (GUI).

Simulated frames could be viewed as they were generated, either displaying each individual frame or an accumulated image combining all simulated frames. Simulated images could also be recorded in an event record format (see Section 4.7) – in this case the simulation would run for an appropriate number of ‘seconds’ and the file produced could be analysed in the same manner as CGC acquisition data.
Chapter 5. Monte Carlo simulation of the CGC

Figure 5.1: Flow diagram of Monte Carlo simulation. The top chart gives an overview of the entire simulation. Black outlines indicate deterministic processes and blue outlines indicate stochastic processes. Red circles indicate deterministic processes. The bottom chart shows the full interaction routine given by a single process (red circle) in the overview chart. Figure created using Gliffy Online [101].
5.2 Photon generation

In the simulation, a source was defined by its size, position, activity and the energy of the photons it produced (assuming a circular source of negligible thickness). Source activity was defined in MBq; the number of photons to be produced by the source for each frame was calculated by dividing the source activity by the frame rate.

Simulated sources were considered to be monochromatic. To model a polychromatic source, the simulation could be run multiple times with different source energies. To accurately simulate a polychromatic source, the amount of activity would need to be varied so that the relative number of photons generated at each energy matches the expected spectrum of the source.

Along with the selected energy, each photon was randomly assigned an initial x- and y-position within the defined source and the initial z-position was set at 0. The starting direction of the photon was defined by two angles: inclination $\theta$ and azimuth $\phi$. These were used to calculate the x-, y- and z-position of a photon after it had travelled a distance $r$ as shown in Figure 5.2. These directional angles $\theta$ and $\phi$ were randomly sampled from a distribution so as to simulate isotropic illumination; this process is described more fully in Appendix C.2.

After generation, photons were immediately moved to the z-position of the first object within the simulation. The x- and y-positions of the photon were calculated from its direction of travel and any photons with x- or y- positions outside the bounds of the simulation were removed. Throughout the rest of the simulation, photons were moved in 0.01 mm steps except for photons within the scintillator material, where the steps were 0.005 mm. A step size of 0.01 mm showed good agreement with theoretical and experimental values for resolution and sensitivity. The step size within the scintillator was reduced as changes made to scintillator properties during testing were of the order 0.01 mm (see Chapter 7).
5.3 Photon interaction

For each step of the simulation, the position of all photons was compared to the locations of objects within the simulation environment. If a photon was within a material (W, Al, CsI) it was assumed that the entire step took place within that material. This assumption was considered valid as the chosen step size was small compared to the thickness of the objects considered. For each material, attenuation coefficients for photoelectric absorption, incoherent (Compton) scattering, coherent (Rayleigh) scattering, and total attenuation were obtained from the NIST XCOM database [13]. The energy resolution of the attenuation coefficients was 0.1 keV over a range of 1 keV to 200 keV.

The Beer-Lambert law (Equation 2.2) was used to calculate the probability of each type of interaction. To determine which, if any, interaction occured, a random number, \( 0 < R < 1 \), was generated and compared to the cumulative interaction probabilities.
Table 5.1: Example of application of cumulative comparison method. This method required the probabilities for all considered outcomes to be normalised to 1. Arbitrary probabilities have been used in this example.

Table 5.1 gives an example of this cumulative comparison method and this methodology was used throughout the simulation.

For compounds, a random number check against probability was performed to determine with which element the interaction would occur. For a photon interacting with CsI, for example, the probability of the photon interacting with a Cs atom is

\[ P_{Cs} = \frac{W_{Cs} \left( \frac{\mu}{\rho} \right)_{Cs}}{\left( \frac{\mu}{\rho} \right)_{CsI}} \]

where \( W_{Cs} \) is the weight fraction of Cs in CsI [19]. For the energies 1 keV to 200 keV, the probability of interaction with a Cs atom ranges from 0.517 – 0.536 (and therefore 0.483 – 0.464 for I). The probability of interaction with a Tl atom was not considered as doping levels of 0.04 - 0.07 mole percent are typical [73] and therefore the probability of interaction is negligible \((2.7 \times 10^{-3}\) at most).

### 5.3.1 Photoelectric effect

When a photon interacts through the photoelectric effect it will transfer energy to an electron within one of the atom’s shells. The electron is ejected, leaving a vacancy in the shell with may be filled through fluorescence or non-radiative transitions. When a simulated photon interacted through the photoelectric effect it was removed from the simulation. The shell in which it interacted was determined (Section 5.3.1.1) and any secondary effects were investigated (Section 5.3.1.2 and Section 5.3.1.3). If secondary effects gave rise to one or more fluorescence photons, these were created with the
appropriate energy and travelling in a randomly determined direction as described in Section 5.2. Fluorescence photons were then treated identically to other photons within the simulation and could be absorbed or scattered by the materials in the model and detected through interaction with the scintillator.

5.3.1.1 Absorption edges

To determine the shell vacancy produced by an absorbed photon, the photon’s energy was first compared to the binding energies of the relevant element’s low energy shells (the K, L₁, L₂, L₃ and M shells were all considered in this model). A photon that does not exceed the binding energy for a shell cannot produce a vacancy in that shell. A photon with energy exceeding the binding energy for a shell may cause a vacancy in that shell but also has a small probability of producing a vacancy in a shell of lower binding energy.

The mass attenuation coefficient for individual shells may be derived from the total mass attenuation of the atom as

\[
\left( \frac{\mu}{\rho} \right)_{\text{shell}} = \frac{J - 1}{J} \left( \frac{\mu}{\rho} \right)_{\text{tot}},
\]

where \( J \) is the jump factor for the edge in question [19] (see Section 2.1.1.1).

Equation 5.2 extrapolates attenuation for energies below the absorption edge to energies beyond the absorption edge; this is then subtracted from the total attenuation after the edge so as to obtain the attenuation for the shell alone. As such, this is an approximate method which is most accurate close to the edges when attenuation may be extrapolated with confidence. Figure 5.3 shows this process graphically.

Equation 5.2 was calculated for each shell with binding energies lower than the photon energy. The Beer Lambert law - Equation 2.2 - was then used to calculate absorption probabilities which were normalised to 1. The cumulative comparison method was used to determine which shell the photon interacted with and so which shell the initial vacancy was created in.

Jump factors and absorption edges for each element were taken from Brunetti et al. [102].
5.3.1.2 Fluorescence

If photoelectric interaction resulted in an inner-shell vacancy, a random number check was performed against the fluorescence yield $\omega$ for that shell. In a random number check a random number is generated and compared to a test value, $\omega$ in this case. Two outcomes are possible - if the random number is less than or equal to the test value the test outcome is ‘true’ (the vacancy causing fluorescence in this case), if the random number is greater than the test value the outcome is ‘false’ (i.e. the vacancy will be filled through a non-radiative transition). Random number checks were used in this manner throughout the simulation.

Fluorescence yields used throughout the model were obtained from Brunetti et al. [102] for K-, L$_{1}$-, L$_{2}$- and L$_{3}$-shells and Öz et al. [103] for M-shells. These are detailed in
Appendix C.3.1. The model considered only transitions to these shells and, in addition, all M-shells were collapsed into a single shell.

If a vacancy was found to be filled through a radiative process it was then necessary to determine which transition had occurred. The transitions considered in this model are illustrated in Figure 2.4 and also tabulated in Appendix C.3.2. The relative intensities of each fluorescence line, along with their energies, have been drawn predominantly from Thompson et al. [15], with Kaye & Laby absorption tables [16] used for initial L\(_1\) and M vacancy transitions.

As only relative intensities were available, these were converted to transition probabilities by normalising to 1 for each shell. This disregards the effect of any transitions not explicitly considered, but the rates of these were small enough to be considered negligible [16]. The cumulative comparison method was used to determine which transition occurred for each instance of fluorescence.

Any new fluorescence photon was generated with the appropriate energy for the transition. This photon continued to progress through the model and could undergo further interactions. In addition, a vacancy was created in the shell the electron transitioned from. This vacancy was treated identically to the initial vacancy and could cause further fluorescence or non-radiative transitions. In this manner, vacancies could cascade outwards through atomic shells.

For both fluorescence and non-radiative transitions, shells with binding energies lower than that of the M-shells (e.g. N-shells) were not considered. Any transitions to shells of very low binding energy would have a very low energy (<1 keV) and so would not affect the results of the simulation.

5.3.1.3 Non-radiative transitions

If a vacancy is not filled through fluorescence, it will be filled through a non-radiative transition. When this occurs, the initial vacancy will be filled and two new vacancies will be created (see Figure 2.3). These vacancies may then be filled through further fluorescence or non-radiative transitions.
Non-radiative transition probabilities for each shell [18, 104–106] were normalised to 1. The cumulative comparison method was used to determine which transition occurred and new vacancies were created in the appropriate shells. Transitions considered in the model are tabulated in Appendix C.3.3.

5.3.2 Compton scattering

A Compton scattered photon interacts with an electron in an atom, transferring a proportion of its energy to the electron and changing the photon's direction of travel. When a photon was determined to have been Compton scattered, it was removed from the program and replaced with the scattered photon. The angular distribution of scattered photons was found using the Klein-Nishina formula (Equation 2.5). Probabilities were derived from this distribution at 0.1° intervals. These were normalised, and the cumulative comparison method used to determine the direction of scatter. Once the direction of scatter was known, Equation 2.4 was used to calculate the energy of the scattered photon. A new photon was then created, travelling at the previously determined scattering angle with the calculated energy. Compton scattered photons continued through the simulation and could undergo further interactions.

It is possible for a photon to undergo Compton scattering through interaction with an inner-shell electron. In these cases, a vacancy can be created which may then cause fluorescence or non-radiative transitions as the atom relaxes; however, studies on Compton scattering by inner-shell electrons are relatively scarce [21] and for simplicity this was neglected in the model. This was considered to have a minimal effect as discussed in Appendix C.4.

5.3.3 Rayleigh scattering

When a photon is determined to have been Rayleigh scattered, its energy remains unchanged but the direction of travel must be adjusted based on the theoretical distribution of Rayleigh scattering angles (see Section 2.1.3).
The Rayleigh scattering angle was determined similarly to the Compton scattering angles as described in Section 5.3.2. The differential scattering cross section was calculated from Equation 2.6 and, after normalisation, cumulative comparison was used to determine the scattering angle. Rayleigh scattering differs from Compton scattering in that its angular distribution is also dependent upon the material within which the scattering occurs. For a Rayleigh scattered photon, the material it interacts with determines the form factors $\mathcal{F}$ which will be used in Equation 2.6 - all form factors used being those tabulated by Hubbell and Øverbø [107]. These are approximations which match experimental data sufficiently for these purposes [24]. Where necessary, these form factors were interpolated to allow an angular resolution of $\sim 0.1^\circ$.

## 5.4 Scintillation

Within the scintillator, photons may interact through the photoelectric effect or by scattering. Any scattered or fluorescence photons produced by these interactions continued through the simulation and could interact elsewhere. In addition to this, the energy deposited through interaction with the scintillator was recorded so that scintillation photons could be generated.

### 5.4.1 Generation of scintillation photons

A photon that loses energy through any interaction within the material will cause scintillation. If the photon has interacted due to the photoelectric effect, the initial energy it deposits will be the difference between the initial photon energy and the binding energy of the electron it interacts with. For non-radiative transitions, additional energy is deposited as electrons are released. This energy $E_{dep}$ is calculated from

$$E_{dep} = B_h - B_{trans} - B_{emit},$$

(5.3)

where $B_h$ is the binding energy of the shell containing the initial vacancy, $B_{trans}$ the binding energy of the shell from which an electron will transition to this vacancy and
For simplicity, it was assumed that the scintillation photons were generated instantaneously; this is a reasonable assumption as integration time for each frame (e.g. 0.1 s) was approximately five orders of magnitude larger than the slow component of decay time for CsI:Tl (3.3 µs) [22].

All scintillation photons were generated at the point at which the original photon was absorbed as photoelectron range is assumed to be smaller than the detector resolution. For a maximum energy of 200 keV, the photoelectron range is 180 µm (based on the continuous slowing down approximation [109]).

Energy response was assumed to be invariant - for each keV of energy absorbed, 65 scintillation photons are expected [22]. The Fano factor for scintillation photons in inorganic scintillators is strongly dependent upon scintillator material [28]. In the absence of experimental data, the Fano factor of CsI:Tl was estimated to be 3.2, the same as that for CsI:Na [28]. This is a key assumption in this model which has been included as it provided a greatly improved reproduction of experimental results than when the number of scintillation photons generated was derived solely from Poisson statistics. For an absorbed energy \( E \) in keV, the number of photons generated was drawn from a Gaussian distribution with a mean of \( 65E \) and a standard deviation of \( \sqrt{3.2 \times 65E} \). These photons were generated with a randomised initial direction of travel as described in Section 5.2.
Figure 5.4: Illustration of possible scintillation photon paths through columnar scintillator. CsI:Tl columns (green shaded) of diameter $d$ are separated by a vacuum gap (unshaded) of width $\delta$. Scintillation photons are generated on the left side of the image with an angle of inclination $\theta$, and must travel a perpendicular distance $D$ through the scintillator to reach the detector. Ray splitting at boundaries indicates the possible paths of a photon. Dotted paths show reflection at the vacuum-CsI:Tl boundary; continuation of these paths has been omitted for clarity.

5.4.2 Progression of scintillation photons through scintillator

The CsI:Tl scintillator was modelled with a columnar structure (Figure 4.2). These columns were assumed to be cylindrical with a diameter of $d$. Columns ran vertically through the entire thickness of the scintillator and were modelled in a regular square-packed configuration. Columns were separated by a vacuum gap, a reasonable assumption for the CGC (Section 4.3), with a minimum separation of $\delta = 0.1 \mu m$. Figure 5.4 shows a two dimensional representation of this configuration.

All scintillation photons generated by a single interaction were created at the same starting position. Each scintillation photon was randomly assigned an angle of inclination $\theta$, assuming isotropic radiation, along with an azimuth $\phi$. Scintillation photons were stepped from boundary to boundary within the modelled scintillator. Due to the range of directions, the path length for each photon for each step was not fixed. For each step, a random number check was used to determine whether a scintillation photon was absorbed (using the Beer-Lambert law - Equation 2.2 - and a linear self-attenuation coefficient for CsI:Tl of $0.387 \text{ cm}^{-1}$ [110]) and, if so, the photon was removed from the simulation.
Chapter 5. Monte Carlo simulation of the CGC

For each scintillator boundary, the normal vector of the scintillator surface was calculated. To provide results consistent with experimental values roughness of the scintillator surface was simulated [88, 111], each component of the normal vector was varied by a randomly determined amount drawn from a normal distribution with a standard deviation of 15% of the component vector size. The angle of incidence $\theta_i$ was then calculated from the dot product of the surface normal vector and the photon’s directional vector. The angle of refraction $\theta_r$ could then be calculated by Snell’s Law.

Assuming unpolarised light [112], the probability of transition through a boundary, $T$, can be calculated from Fresnel’s equations [113];

$$r_\parallel = \frac{\tan(\theta_i - \theta_r)}{\tan(\theta_i + \theta_r)}, \quad (5.4a)$$

$$r_\perp = -\frac{\sin(\theta_i - \theta_r)}{\sin(\theta_i + \theta_r)}, \quad (5.4b)$$

$$T = 1 - \frac{1}{2}(r_\parallel^2 + r_\perp^2), \quad (5.4c)$$

where $r_\parallel$ and $r_\perp$ are the reflectance for light polarised parallel and perpendicular to the surface respectively.

CsI:Tl has a refractive index of 1.79 [114], so if the angle of incidence $\theta_i$ is greater than $\sin^{-1}(\frac{1}{1.79})$, $\sim 34^\circ$, the photon will undergo total internal reflection and $T = 0$. The probability of transition through the boundary (either CsI:Tl-vacuum or vacuum-CsI:Tl) is calculated and a random number check performed. The photon was then either reflected by or refracted through the boundary, and was then stepped towards the next boundary travelling in its new direction. The probability of a transition between columns was up to $\sim 85\%$ for small $\theta_i$.

The back surface of the scintillator is modelled as perfectly reflective, simulating the mirrored substrate. Scintillation photons were propagated through the simulation until they either reached the modelled CCD described below or left the region defined as the scintillator, at which point they were removed from the simulation.
5.5 CCD Processes

Within the CCD, scintillation photons could be detected and noise effects were applied. Although in practice a CCD may detect gamma rays directly if they pass unimpeded through the scintillator, this has not been considered in this model. The probability of absorbing gamma rays directly with the CCD are low (for 5 µm of Si, absorption is 0.02% at 200 keV). The detection probability of lower energy photons, such as fluorescence X-rays, is higher (for 5 µm of Si, absorption is 83.9% at 10 keV - although a higher proportion of these will be captured by the scintillator - but these will also be excluded from modelled results. The process of blob detection, however, already removes many of these events in experimental images (see Appendix A).

The EMCCD was modelled as a standard CCD with an additional gain stage. Values used in this section of the simulation were determined experimentally, with a gain voltage of 43.5 V and a temperature of −12 °C assumed - ideal operating conditions for the CGC. Experimental procedures and results are described in Chapter 7.

5.5.1 Scintillation photon detection

Scintillation photons were treated as identical optical photons. The quantum efficiency $Q$ of the CCD was taken to be 90% - this being the mean quantum efficiency for the EMCCD used [64] across the emission spectrum for CsI:Tl [70]. The quantum efficiency of a system is the proportion of incident photons that are detectable, and so includes the absorption of the CCD material. At a mean wavelength of 550 nm (2.25 eV), each scintillation photon may produce a single electron-hole pair in the CCD [60]. The Fano factor $F$ for Si is 0.16 [67]. For $N_p$ incident scintillation photons, the number of electron-hole pairs generated was drawn from a Gaussian distribution with a mean of $QN_p$ and a standard deviation of $\sqrt{FQN_p}$ and was always an integer value.

From manufacturer’s specifications, full well capacity of the EMCCD is $1.3 \times 10^5 e$ for each 16 µm square pixel [71]. This was assumed to scale linearly with pixel area and acts as a cutoff for total number of electrons within a pixel. As the full well limit is not
reach either experimentally or during simulation, the effect of charge spreading was not considered.

To simulate gain, the charge in each pixel is multiplied by a factor of 40 (see Section 7.1.3). In the multiplication stage, saturation occurred at $8 \times 10^5 e$ [71]. During simulated readout, the number of electrons were converted to ADU (analogue-to-digital units) by applying a factor of 2 (see Section 7.1.1.2).

5.5.2 Noise effects

The dominant noise effect in the CGC is dark (or thermal) noise. This is due to electrons within the CCD gaining enough thermal energy to move into the conduction band without the need for an incident photon. Noise parameters in this section have been derived experimentally in Chapter 7.

Experimentally, dark noise was measured to be approximately $0.6 e \mu m^{-2} s^{-1}$ (Section 7.1.2) which could be applied to pixels of any chosen size. This gave a mean value for dark noise, with individual dark noise values for each pixel drawn from a Gaussian distribution with this mean and a standard deviation of $0.2 e \mu m^{-2} s^{-1}$ (Section 7.1.2). Dark noise was then added to signal in each pixel, prior to the simulated gain stage. Unless otherwise stated, the time for each frame was calculated from frame rate i.e. readout time was assumed to be negligible.

The multiplication stage itself has an excess noise factor $F_{ex}$ (identical in effect to a Fano factor) of 2 [115]. For a signal $S$ a gain factor of 40 resulted in a mean signal of $40S$ with a standard deviation of $\sqrt{80S}$.

Readout noise occurs as each pixel’s signal level is read out into recording electronics. As this occurs during readout, this noise was added after the gain stage of the CCD. Readout noise was found to have a mean of $35 e$ pix$^{-1}$ (Section 7.1.1.2), with individual readout noise values for each pixel drawn from a Gaussian distribution. This was negligible compared to signal and dark noise but was included to allow for investigations into gain effects at a later date.
5.6 Summary

The Monte Carlo model described in this chapter uses theoretical and experimental parameters in order to model the collimator, scintillator and CCD response along with that of the CGC as a whole. The output of the model is a simulated image which may be recorded and analysed in the same manner as experimental CGC data. This model is used in Chapter 6 and Chapter 7 to investigate the components of the CGC and inform future design choices.
Chapter 6

CGC collimator response

The effectiveness of a medical gamma camera can be described using a range of different parameters (for further discussion on this subject see Chapter 8). Sensitivity and spatial resolution are particularly important factors as they strongly influence the features that may be imaged by the camera and therefore its utility in medical imaging. Collimator design is the dominant factor affecting both sensitivity and spatial resolution in medical gamma cameras.

For a pinhole collimator, sensitivity and spatial resolution are dependent upon the pinhole diameter \(d\), the pinhole acceptance angle \(\alpha\) and the collimator material (through the linear attenuation coefficient \(\mu\)). The response of a pinhole collimator to a source will also depend on the source-pinhole angle \(\psi\) which is defined as 90° when the source is centred on the pinhole axis. These parameters are illustrated graphically in Figure 3.1. The parameter \(\mu\) is also dependent upon the energy of the photons produced by the source.

The sensitivity and resolution of pinhole collimators have been investigated both experimentally and theoretically [46, 48, 116–119]. Conventionally a point source model is used to evaluate pinhole performance theoretically and small sources are used to approximate point sources when characterisation is carried out experimentally. The response due to finite sources is less well understood although some finite source models have been developed to investigate pinhole sensitivity e.g. [120].
In this chapter, the response of pinhole collimators is investigated both analytically and through a simplified version of the Monte Carlo model described in Chapter 5. Image profiles for finite sources are investigated analytically and through simulations, and the appropriateness of point source approximations is investigated. The suitability of the pinhole collimators currently in use with the CGC are discussed along with possible design improvements.

### 6.1 Monte Carlo simulation

Unless otherwise stated, this chapter uses a reduced version of the simulation described in Chapter 5. This is in order to isolate pinhole response effects from detector effects and allow a direct comparison to analytical models of pinhole response.

In the simplified simulation, scintillator and CCD interactions are not included. These have been replaced by a single detector area with 100% detection efficiency. The detection of fluorescence or scattered photons of lower energies has not been considered. The pinhole-detector distance $t$ was fixed at 10 mm and the collimator thickness to 6 mm, to match the dimensions of the CGC. Collimator diameter has been extended across the full width of the simulation area. Unless otherwise specified, a finite square detector of width 8.192 mm was used to properly simulate CGC response. In some cases an infinitely large detector has been modelled for better comparison with theoretical models.

### 6.2 Sensitivity

The sensitivity of a collimator describes the number of photons produced by a source which may pass through it and reach the detector. The sensitivities stated in this chapter are given as the proportion of photons, produced by a point source, that pass through the collimator and impinge on the detector. In practice, the system sensitivity will be lower than the sensitivity of the collimator in isolation - this will be discussed further in Chapters 7 and 8.
The sensitivity of the pinhole may be calculated analytically using the effective diameter method (Equation 3.3 [46] and 3.4) or the method described by Metzler et al. (Equation 3.5 [48]).

Figure 6.1 shows a comparison between the Metzler and effective diameter methods (which are equivalent in this case as $\psi = 90^\circ$) and sensitivities from the simplified Monte Carlo simulation. Unlike the sensitivity of a parallel hole collimator, Figure 6.1 shows a strong dependence on source-collimator distance $h$. As would be expected, higher sensitivities are found for larger pinhole diameters $d$. Sensitivity also increases for larger $\alpha$ (not shown).

There was generally good agreement between the analytical results and those found
Figure 6.2: Relationship between sensitivity and source-pinhole angle $\psi$. Solid lines show analytical sensitivities calculated using the effective diameter method (black) and the Metzler method (red). Solid lines with points show sensitivities from $10^9$ iterations of the simplified Monte Carlo method. The simulation was run with a finite square detector of sides 8.192 mm (blue) and with an infinite detector (green), in each case $t = 10$ mm. The dimensions used for the W pinhole collimator were $h = 50$ mm, $\alpha = 60^\circ$ and $d = 0.5$ mm. The Metzler method is defined only for $\psi = 90^\circ \pm \alpha/2$.

Computationally. For $d = 2.0$ mm the analytical model overestimated the sensitivity of the system at small $h$. This is due to the fixed detector size and collimator-detector separation $t$ which makes it possible in some cases for photons to pass through the pinhole without impinging upon the detector. The CGC was designed with an intended pinhole diameter of 0.5 mm and $t$ was optimised for use with this; the modelled 0.5 mm diameter pinhole sensitivities do not deviate from those calculated analytically even with small $h$. Although the deviation from theoretical sensitivity seen for $d = 2.0$ mm is small, it shows that $d$ cannot be enlarged indefinitely without further CGC design considerations.

Figure 6.2 shows the dependence of sensitivity upon source-pinhole angle $\psi$. All methods produce similar results at $\psi = 90^\circ$, with the effective diameter method overestimating sensitivity for off-axis sources as was previously shown by Metzler et al. [48]. Sensitivity
decreases for offset sources as fewer photons pass through the collimator; this decrease is most pronounced for a pinhole with small $d$ or large $\alpha$ (with changes in $\alpha$ having a relatively minor effect when compared with changes in $d$). As would be expected, the discrepancy between finite and infinite detector simulation results increases with increasing $d$ and $\alpha$; finite and infinite detector results are identical when $t$ is adjusted to an appropriate value for each collimator’s dimensions.

The effective diameter method consistently overestimates sensitivity when compared to alternative methods as previously described [48]. This overestimation decreases for large $d$, particularly for large offsets outside the expected FOV of the pinhole. For small offsets, even at large $d$ the effective diameter method overestimates sensitivity and, if an analytical calculation is required, the Metzler method is preferable.

Metzler sensitivities would be expected to match simulated sensitivities with an infinitely large detector. This is shown in Figure 6.2 to be true for small source offsets ($\psi$ close to $90^\circ$) but at larger offsets the Metzler sensitivity underestimates compared to that found through simulation. This discrepancy is more pronounced for small $\alpha$, for $\alpha > 120^\circ$ there is no statistically significant difference between the methods.

The Metzler method approximates a pinhole as two back-to-back cones. This approximation does not take collimator thickness into account and so causes an underestimation of sensitivity at large source offsets. When the simulation is adjusted to treat the collimator as infinitely thick as in Metzler’s approximation, the discrepancy between the models disappears. This would need to be taken into consideration when using the Metzler method to calculate sensitivity, particularly when investigating systems with small $\alpha$, large source offsets or thin collimators.

### 6.3 Spatial Resolution

The spatial resolution of a system determines its ability to separate closely spaced sources. The spatial resolution of medical gamma cameras is defined as the FWHM of a point spread function (PSF) - the intensity profile through the image of a point source. The
spatial resolution of a system as a whole will be larger (implying a poorer ability to resolve sources) than the spatial resolution of the collimator in isolation - this will be discussed further in Chapters 7 and 8.

The spatial resolution of the pinhole may be calculated analytically using the geometric resolution (Equation 3.2) - that of an infinitely attenuating pinhole collimator - and an effective diameter (e.g. Equation 3.3) which accounts for photons which penetrate through the collimator material. The effective diameter in Equation 3.3 has been derived for sensitivity calculations and has been shown to provide a poor fit for experimental resolution data [47]. Accorsi and Metzler [119] provide a resolution-equivalent effective diameter of

\[
d_{\parallel} = d + \Delta L_k \left( \tan^2 \frac{\alpha}{2} - \cot^2 \psi \right) \cot \frac{\alpha}{2} \sin \psi, \quad (6.1a)
\]

\[
d_{\perp} = \sqrt{\left( d + \Delta L_k \tan \frac{\alpha}{2} \sin \psi \right)^2 - \Delta L_k^2 \cos^2 \psi}, \quad (6.1b)
\]

where \(d_{\parallel}\) is the effective diameter parallel to the plane containing the source and pinhole normal and \(d_{\perp}\) is the effective diameter perpendicular to this. The parameter \(\Delta L_k\) is the path length through the collimator material associated with an attenuation factor \(k\). For a FWHM measurement, the width of the profile at half its height is required and \(k = 0.5\) [119]. The path length \(\Delta L\) can be derived from the Beer-Lambert law (Equation 2.1) as

\[
\Delta L_k = -\frac{\ln k}{\mu}. \quad (6.2)
\]

For W, this equates to \(\Delta L_k = 0.191\)mm for 141keV photons when \(k = 0.5\).

The pinhole resolution was also found computationally using the simplified Monte Carlo simulation. A simulated image such as that in Figure 6.3 is generated, and profiles taken in the horizontal (parallel) and vertical (perpendicular) planes. The FWHM can then be calculated from the profile. Stochastic irregularities such as those seen in the profile peak in Figure 6.3 can have a large effect on FWHM measurements. These irregularities can be reduced by increasing the number of counts contributing to the profile.
The analytical calculation does not take scattered photons into account, so this were excluded from simulation results. This would be expected to result in an underestimate of spatial resolution. For the simulation shown in Figure 6.3 approximately 1% of the photons reaching the detector were scattered. If these scattered photons were included in the image, background signal increased but had no significant effect on profile width was seen.

Figure 6.4 shows a comparison between theoretical and simulated resolutions for a selection of $h$ and $d$. Resolution is also dependent on $\alpha$; collimators with small $\alpha$ have a smaller (better) resolution than those with large $\alpha$ - this is discussed in more detail in Section 6.5.2.

The resolutions calculated with the effective diameter method from Equation 3.3, shown as dashed lines in Figure 6.4, are overestimates compared both the simulation and calculations based on Accorsi effective diameters. This overestimation is present over all parameters and is largest for large $\alpha$.

Figure 6.4 shows good agreement between the Accorsi resolutions from Equation 6.1 and simulated resolutions. The Accorsi resolutions were marginally smaller than simulated resolutions for large $h$ but these differences were within the estimated error for simulated
values of resolution. The simulated resolutions were calculated from a PSF, a profile taken through a two dimensional image (see Figure 6.3). The image slice used to create the profile has a finite width - 0.064 mm in this case - which will slightly reduce the measured resolution, particularly for small source projections, and is the cause of the discrepancies at large $h$.

The Accorsi formula predicts a variation in resolution depending on source angle $\psi$. This is due to the drop-off in sensitivity over the FOV of the camera as shown in Figure 6.2. Figure 6.5 shows the expected variation in FWHM resolution over the FOV for a selection of pinhole diameters, for profiles taken in the direction parallel to source.
FIGURE 6.5: Relationship between FWHM resolution and source-collimator angle $\psi$ for W knife-edge pinhole collimators of diameter $d = 0.5$ mm (black), 1.0 mm (red) and 2.0 mm (blue). Solid lines show theoretical Accorsi resolutions from Equation 6.1. Points show Monte Carlo resolutions taken from profiles of a point source with $10^{12}$ photons generated. In all cases $h = 50$ mm and $\alpha = 60^\circ$. Errors were estimated assuming Poissonian statistics, these are too small to be readily visible.

For Figure 6.5, a finite detector ($8.192 \times 8.192$ mm) was used in the simulation. Edge effects reduce FOV to a usable region for resolution measurements, beyond which PSFs extend past the imaging area. The reduction in FOV where resolution is measurable depends on the collimator resolution; for $\alpha = 60^\circ$ and $h = 50$ mm the effective acceptance angle is $\alpha_{eff} = 54^\circ$ - reducing the effective FOV from $50$ mm $\times$ $50$ mm to $45$ mm $\times$ $45$ mm for spatial resolution measurements.

There was again good agreement between the Accorsi and simulated resolution values with a slight trend for the Accorsi method to underestimate resolution for large source offsets. Again, these differences were within expected errors. As the Accorsi effective diameters use the same double-cone approximation as Metzler sensitivity calculations.
described in Section 6.2, this is an expected result. The offset indicated by $\psi$ has a greater relative effect on FWHM resolution for small $d$, as shown in Figure 6.5, and for small $\alpha$.

### 6.4 Pinhole collimator response to finite sources

The analytical methods described above are limited to the measurement of response of a pinhole collimator to a point source. For standard gamma cameras, a source is considered a point source when it has a diameter of less than $1/50$ of the usable field of view of a system [121], $\sim 8$ mm for a conventional gamma camera. Adopting this criteria for the CGC would require a source to be $< 0.8$ mm in diameter for a typical imaging distance, and sources of this size may be difficult to manufacture and use [122]. This makes procedures for the measurement of resolution, which require a point source, difficult to translate to SFOV systems.

As a further example, lymph nodes measured during SLNB for breast cancer range in size from 2.4 mm to 10 mm [123]. For a conventional camera, these can generally be considered to be point sources with behaviour that can be determined analytically. For the CGC, the response to sources of this size cannot be assumed to be identical to that for a point source. It is therefore important to understand the response of a pinhole collimator to finite sources.

Finite source profiles could be estimated if they were modelled as the sum of a series of point source profiles. This method would not be exact for offset sources as PSF shape varies with $\psi$. A finite source will always have some amount of offset so this method is not suitable. In this section, pinhole collimator response to finite sources was investigated using the simulation described in Section 6.1 and numerically from equations derived in Section 6.4.1.
6.4.1 Analytical derivation of image profiles

Although a robust method for determining collimator response, a Monte Carlo simulation can be computationally intensive. As an alternative, an analytical model of expected image profiles was developed with the aim of producing comparable profiles. Figure 6.6 shows the configuration and geometry used in the derivation with the necessary variables defined. The aim of the model is to calculate the relative photon flux at each position on the detector \( p \), over all possible generated photons.

Simple trigonometry shows that

\[
    r = h \tan \theta + s , \quad (6.3)
\]

and that

\[
    p = (h + t) \tan \theta + s . \quad (6.4)
\]
When $|r| > \frac{d}{2}$, photons travel a distance $\Delta L$ through the pinhole material and transmission $T$ may be calculated from the Beer-Lambert law (Equation 2.1). When $|r| \leq \frac{d}{2}$, $\Delta L = 0$ and photons will pass through the pinhole unimpeded giving $T = 1$. From the sine rule,

$$\Delta L = \left( |r| - \frac{d}{2} \right) \cos \frac{\alpha}{2} \left[ \csc \left( \frac{\alpha}{2} - \theta \right) + \csc \left( \frac{\alpha}{2} + \theta \right) \right], \quad (6.5)$$

which may then be substituted into the Beer-Lambert law to give $T$. For a given distance $p$, and a source that extends from $s_{\text{min}}$ to $s_{\text{max}}$, $\tan \theta$ must be in the range

$$\frac{p - s_{\text{max}}}{h + t} < \tan \theta < \frac{p - s_{\text{min}}}{h + t} \quad (6.6)$$

and transmission rates may be calculated from

$$T = e^{-\mu K \left( p - t \tan \theta - \frac{d}{2} \right)} \quad \text{for} \quad \tan \theta < \frac{p - \frac{d}{2}}{t}, \quad (6.7a)$$

$$T = 1 \quad \text{for} \quad \frac{p - \frac{d}{2}}{t} \leq \tan \theta \leq \frac{p + \frac{d}{2}}{t}, \quad \text{and} \quad (6.7b)$$

$$T = e^{-\mu K \left( t \tan \theta - p - \frac{d}{2} \right)} \quad \text{for} \quad \tan \theta > \frac{p + \frac{d}{2}}{t}, \quad (6.7c)$$

where $K = \cos \frac{\alpha}{2} \left[ \csc \left( \frac{\alpha}{2} - \theta \right) + \csc \left( \frac{\alpha}{2} + \theta \right) \right]$. The relative photon flux at point $p$ is then the sum of $T$ over all possible $\theta$. It may be possible to solve this through integration but in practice it proved simpler to solve numerically.

### 6.4.2 Comparison to simulation

Figure 6.7 shows a comparison between image profiles collected from the Monte Carlo simulation and the analytical model described in Section 6.4.1 for circular sources of differing diameter $s$. There was generally good agreement between the two calculation methods. Further results discussed in this chapter have been derived from the analytical profile method.
Chapter 6. CGC collimator response

Figure 6.7: Example image profiles for a range of source size $s$. Red lines show the analytical model described in Section 6.4.1. Points show results from simulation described in Section 6.1. Errors have been estimated based on Poissonian statistics. In all cases, $h = 50$ mm, $t = 10$ mm, $d = 1.0$ mm and $\alpha = 60^\circ$.

The analytical model described does model the pinhole as infinitely thick and so should not be used for very large source offsets, results in this chapter have been constrained to offsets where this variation is within expected errors.

The differences in shape for different source sizes seen in ?? is due to the variation in sensitivity at different positions within the FOV. The shape of the image profile is also strongly dependent on the source-collimator angle $\psi$ as demonstrated by Figure 6.8. A clear asymmetry can be seen in the profile shape of an offset source as photons originating at the side of the source furthest from the detector will be more significantly attenuated.

Variation in source shape, either due to source size or source offsets, will have an effect on the detectability of the source. Detectability of sources is discussed in Chapter 9.
Figure 6.8: Example image profiles showing the change in profile shapes for offset sources. The solid black line shows a centred source of $s = 10$ mm ($\psi = 90^\circ$), then dashed blue line shows an identical source at $\psi = 68^\circ$ (20 mm offset). Intensities have been normalised to the maximum intensity for the centred source. In all cases, $h = 50$ mm, $t = 10$ mm, $d = 1.0$ mm and $\alpha = 60^\circ$.

6.4.3 Approximation of point sources using finite sources

It is sometimes necessary when quantifying camera response to use a phantom that approximates a point source. This may be done by using a phantom that is small compared to the detected camera resolution (e.g. [124]) or by correcting for the use of a finite source (e.g. [125]).

One method for source correction is to subtract the source size $s$ in quadrature [125]. The expected resolution would be

$$ R^2 = S^2 - s^2, \quad (6.8) $$

where $S$ is the FWHM of the image in object space. This method assumes Gaussian blurring [47], which is not the case for the profiles shown in Figure 6.7, and can result in considerable underestimation of spatial resolutions.
Figure 6.9 shows the relationship between $S$ and $s$ for profiles from the analytical model. Two distinct regions can be seen. For small $s$, measured FWHM varies very little from the FWHM at $s \to 0$ mm (the resolution of the system). At large $s$, blurring effects are negligible relative to source size $s$ and image size tends towards source size. Figure 6.9 also shows that Equation 6.8 is not valid for these profiles.

By taking the double differential of the curve shown in Figure 6.9 the inflection point, i.e. the position of the transition between the two regimes, could be found. This inflection point occurs when the source is the same size as the geometric resolution (as given in Equation 3.2), and is therefore dependent on $d$ and $h$. For sources where $s \leq R_{geom}$, the source is entirely subtended by the pinhole. When $s > R_{geom}$ the source extends beyond the pinhole and no longer behaves similarly to a point source. The position of the
inflection point does not vary with $\alpha$ or $\mu$ so is not related to the true resolution of the collimator with penetration taken into account.

At the inflection point, the FWHM of the image profile is larger than the FWHM of a PSF. This is a more significant effect for smaller pinholes. For example, if $d = 0.25$ mm, the FWHM of a source of size $s = R_{geom}$ is 12% larger than that of a point source whereas if $d = 1.5$ mm this difference is reduced to 2%.

When using a finite source to simulate a point source, the smaller the source the more accurate the result will be. Sources used should be smaller than the geometric resolution for the pinhole for the smallest distance $h$ to be investigated. This is a more forgiving limit than that derived from $\frac{1}{50}$ of the usable FOV - 1.5mm as opposed to 0.3 mm for $d = 0.5$ mm and $h = 20$ mm. The limiting requirement $s = R_{geom}$ provides the best accuracy for large $d$ but all measurements with finite sources will overestimate the true resolution of the pinhole.

The subtraction in quadrature method (Equation 6.8) is not applicable to pinhole collimators and may significantly underestimate the resolution of a system.

## 6.5 Optimisation of collimator design

The CGC used in this thesis can be used with W pinhole collimators with pinhole diameters $d = 0.5$ mm or $d = 1.0$ mm, both with $\alpha = 60^\circ$. These collimators can be used across a number of clinical procedures, including those described in Chapter 9.

This section discusses possibilities for future collimator design with the aim of optimising the CGC for use in the intraoperative detection of sentinel lymph nodes.

### 6.5.1 Requirements

It is desirable for CGC parameters to be compared to those for a LFOV conventional gamma camera, typically used prior to surgery, and for a non-imaging gamma probe of the kind currently used intraoperatively.
The amount of activity administered to a patient during sentinel lymph node biopsy varies depending on the location of the procedure, the type of radiopharmaceutical used and even the institution where the procedure is carried out [4]. For surgical procedures in breast cancer, administered activities of 5 MBq to 30 MBq are typical [4]. Although also showing significant variation, the median uptake by a sentinel node is approximately 0.3% of the injected activity [126]. This puts a low-end estimate on node activity of around 18 kBq. An ideal intraoperative gamma camera would be able to detect this level of activity within a relatively short period of time. Node depths have been measured from 15 mm to 85 mm [127]. In this section source-collimator distance $h = 50$ mm is used as an estimate of depth for a relatively deep-seated node [127].

Lymph nodes within the region of the body of interest for SLNB for breast cancer range in size from 2.4 mm to 10 mm [123]. Lymph nodes can be at very close proximity to one another (<5 mm separation [128]), although no studies investigating the typical separation of sentinel lymph nodes (if more than one are present) could be found.

The FOV of a conventional gamma camera is relatively large - around 200 mm $\times$ 200 mm [55, 129] - which allows nodes to be identified in a large area in a single image. Depending on the collimator used, typical collimator sensitivities can range from $1 \times 10^{-4}$ to $5 \times 10^{-4}$ with resolutions of 5.9 mm to 11.6 mm at $h = 50$ mm.

Typical non-imaging probes have total angular FOVs of 40° to 60° [130] (18 mm to 30 mm at a depth of 50 mm, although sensitivity varies widely across this FOV. At $h = 50$ mm, sensitivities are in the region of $5.8 \times 10^{-5}$ to $3.8 \times 10^{-4}$ with resolutions of 40 mm to 58 mm [131]*.

Sensitivities in the following sections were investigated for $R = 2.4$ mm (minimum node size) and $R = 6$ mm (the same resolution as a LFOV camera). Resolutions were investigated for $S = 5 \times 10^{-4}$ (10 detected counts per second for an 18 kBq node) and $S = 5 \times 10^{-5}$ (1 detected count per second). The node-collimator distance $h$ will be set at 50 mm in all cases.

*Note that these are values for the gamma probe system as a whole and so should not be compared directly to the collimator-only parameters discussed in this section. They have been provided as a first approximation only. In addition, these values have been determined through 50 mm of tissue equivalent medium. Sensitivities through air would be expected to be $\sim 20\%$ higher than those stated here [130].
6.5.2 Single-pinhole collimators

At $h = 50\,\text{mm}$, the current CGC collimators have resolutions of $3.7\,\text{mm}$ and $6.7\,\text{mm}$ and sensitivities of $1.2 \times 10^{-5}$ and $3.4 \times 10^{-5}$ for the $0.5\,\text{mm}$ and $1.0\,\text{mm}$ pinhole diameters respectively.

Figure 6.10 shows maps of the resolution and sensitivity values achievable with a single-pinhole collimator for a source distance of $h = 50\,\text{mm}$. It is clear that the ideal (smallest) resolutions and the ideal (highest) sensitivity cannot be obtained using the same pinhole parameters.

For sensitivity, $d$ has a far larger effect than $\alpha$ - although the effect of $\alpha$ on sensitivity will be greater for offset sources. The best tradeoff between resolution and sensitivity occurs for small $\alpha$; however a small $\alpha$ results in a small FOV.

Table 6.1 gives some specific values for pinhole parameters of interest. The pinholes investigated had $\alpha = 20^\circ$ (best overall response from Figure 6.10), $\alpha = 44^\circ$ (a FOV of approximately $40\,\text{mm}$, similar to a gamma camera that has been previously used for sentinel lymph node biopsies [51]) and $\alpha = 60^\circ$ (its current dimension in the CGC). The
Table 6.1: Required pinhole diameters for a range of set $R$ or $S$ responses, optimised to give the best imaging quality. Sensitivity has been calculated from Equation 3.5 and resolutions from Equation 6.1. In each case $t$ has been optimised for the parameters used. Approximate FOVs are given as these vary slightly with $d$.

<table>
<thead>
<tr>
<th>$\alpha$ (degrees)</th>
<th>FOV (mm)</th>
<th>$d$ (mm)</th>
<th>$R$ (mm)</th>
<th>$S$</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>~20</td>
<td>0.9</td>
<td>2.4</td>
<td>$2.1 \times 10^{-5}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.1</td>
<td>6.0</td>
<td>$1.1 \times 10^{-4}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.0</td>
<td>5.6</td>
<td>$1.0 \times 10^{-4}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.4</td>
<td>15.4</td>
<td>$5.0 \times 10^{-4}$</td>
</tr>
<tr>
<td>44</td>
<td>~40</td>
<td>0.4</td>
<td>2.4</td>
<td>$7.9 \times 10^{-6}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.2</td>
<td>6.0</td>
<td>$4.0 \times 10^{-5}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.9</td>
<td>10.1</td>
<td>$1.0 \times 10^{-4}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.4</td>
<td>30.0</td>
<td>$5.0 \times 10^{-4}$</td>
</tr>
<tr>
<td>60</td>
<td>~60</td>
<td>0.3</td>
<td>2.4</td>
<td>$5.8 \times 10^{-6}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.8</td>
<td>6.0</td>
<td>$2.5 \times 10^{-5}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.8</td>
<td>13.5</td>
<td>$1.0 \times 10^{-4}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.3</td>
<td>39.8</td>
<td>$5.0 \times 10^{-4}$</td>
</tr>
</tbody>
</table>

As expected, the best overall response occurs for $\alpha = 20^\circ$, which has a resolution similar to that of a general purpose LFOV collimator and a sensitivity similar to that of a high resolution LFOV collimator when $d = 2$ mm. However, the FOV of the camera using this collimator would be in the region of 20 mm. This would reduce one of the benefits of using the CGC over a non-imaging probe, although imaging with this FOV may still be beneficial for some procedures. With $\alpha = 44^\circ$, which gives a more typical FOV, smaller pinhole diameters are required to reach the same resolutions and so sensitivities are poorer. When $\alpha = 60^\circ$, this performance degrades further (although FOV is enhanced).

### 6.5.3 Alternative collimator designs

Section 6.5.2 shows that it is not possible to achieve an ideal sensitivity, resolution and FOV simultaneously for a single pinhole collimator. An alternative collimator design may provide a more favourable tradeoff between these parameters.
One advantage of a single pinhole collimator is the magnification it provides - this allows for FOVs far larger than the area of the detector. The EMCCD used in the CGC is currently limited to an active area of 8.192 mm × 8.192 mm. Although it may be possible to tile multiple EMCCDs, this would increase the complexity of the electronics within the CGC to a prohibitive level for the current design. Larger EMCCDs can be custom-built but only at significant cost.

This problem can be solved with the use of a tapered fibre optic connecting a large area collimator/scintillator to a small area detector (e.g. [75, 132]) although this requires multiple optical couplings which may be difficult to implement (see Chapter 7). In addition, fibre optic tapers have been shown to reduce the contrast-to-noise ratio with this effect increasing for greater tapering ratios [53] and the intrinsic resolution of the detector will have a far greater effect on system resolution. Due to this, comparisons made here between pinhole and other collimator responses are approximate.

### 6.5.3.1 Parallel hole collimators

The FOV of a parallel hole collimator depends on its dimensions (defined in Figure 3.2) only. The resolution of a parallel hole collimator will degrade with increasing $h$, though to a lesser extent than for a pinhole collimator. For parallel hole collimators, $S$ is independent of $h$.

Table 6.2 allows for direct comparison with pinhole response in Table 6.1. For the purposes of these calculations, the detector has been assumed to be directly behind the collimator (i.e. $t = \frac{T}{2}$ where $T$ is the collimator length). Holes are taken to be square, with a septal thickness $w = 0.2$ mm, and the collimator is assumed to be constructed from W. To allow direct comparison to Table 4.1, $h = 50$ mm in all cases and the same example values for $R$ and $S$ have been used.

These results are promising when compared to the pinhole collimators described in Section 6.5.2; however there is difficulty in manufacturing W to this level of precision. Layering etched W foil has produced collimators of similar dimensions [133] though this requires great precision when stacking layers. Recent advances in additive manufacturing
Table 6.2: Required parallel hole collimator dimensions for a range of set $R$ or $S$ responses, optimised to give the best imaging quality. Resolution is determined by Equation 3.6 and sensitivity from Equation 3.8 which in both cases use an effective thickness from Equation 3.7.

<table>
<thead>
<tr>
<th>$d$ (mm)</th>
<th>$T$ (mm)</th>
<th>$R$ (mm)</th>
<th>$S$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>9.0</td>
<td>2.4</td>
<td>$3.6 \times 10^{-5}$</td>
</tr>
<tr>
<td>0.5</td>
<td>6.0</td>
<td>6.0</td>
<td>$4.0 \times 10^{-4}$</td>
</tr>
<tr>
<td>0.4</td>
<td>7.5</td>
<td>3.5</td>
<td>$1.0 \times 10^{-4}$</td>
</tr>
<tr>
<td>0.6</td>
<td>6.0</td>
<td>6.6</td>
<td>$5.0 \times 10^{-4}$</td>
</tr>
</tbody>
</table>

(e.g. [134]) may solve this problem in the near future but current tolerances are of the same order as the dimensions required. The FOV of a parallel-hole collimated system will be limited by the dimensions of the collimator used, this may also introduce difficulties for portable systems.

### 6.5.3.2 Multi-pinhole collimators

Imaging systems with multiple single pinhole collimating detectors have heritage in SPECT imaging [1]. A number of multiplexing single detector SPECT system designs have been previously investigated. These have the benefit of improved sensitivity over a single-pinhole collimator whilst maintaining excellent resolution [135, 136]. The required image reconstruction may lead to a reduction in signal to noise ratios [135]. Planar imaging with small $h$ causes difficulties in image reconstruction including the introduction of artifacts when sources at different depths are imaged simultaneously [137]. Systems without multiplexing require less complex image reconstruction but may be difficult to achieve with a single small detector.

Multi-pinhole collimators have potential for future use with the CGC and should be investigated further. The simplicity of the CGC design has a number of benefits and this should be maintained as much as possible. For CGC work in the near future, multi-pinhole collimation is not appropriate.
6.6 Conclusions and recommendations

In this chapter, the Monte Carlo pinhole collimator simulation (a component of the model described in Chapter 5) was shown to provide an accurate model of pinhole collimator response when compared to previously derived analytical models. The simulation showed that the analytical models were inaccurate for large source offsets (for both sensitivity and resolution) as the finite thickness of the collimator is not accounted for. The simulation has shown that these inaccuracies are negligible for the collimator dimensions currently used by the CGC.

A new analytical model that describes the image profile of finite sources has been derived and shows good agreement to results from the Monte Carlo simulation. The shape of the image profile varies for different source sizes and becomes asymmetric when a source is offset from the pinhole.

Using the analytical model, it was found that a finite source may be considered as a point source, for the purpose of determining resolution, if the size of the source is less than the geometric resolution of the collimator used. Resolution measurements will be more accurate when smaller sources are used.

All collimator designs require a trade off between spatial resolution and sensitivity. The current CGC collimators provide excellent spatial resolution at the expense of some sensitivity. For sentinel lymph node biopsies where low activities are common, the 1.0 mm diameter pinhole should be used - giving a 6.7 mm resolution and a sensitivity of $S = 3.4 \times 10^{-5}$ (a count rate of approximately 0.7 s$^{-1}$ for a low activity node).

Future collimator designs should be made with input from clinicians or clinical studies and it may be appropriate to use different collimators for different procedures. If, for example, greater sensitivity is required; in the short term, the CGC design may be adjusted slightly to increase $t$ to 13 mm. This will allow a collimator with $\alpha = 44^\circ$ and $d = 1.9$ mm to be fitted. This will increase sensitivity to $S = 1.0 \times 10^{-4}$ at $h = 50$ mm (a count rate of approximately 1 s$^{-1}$ for a low activity node) which is more inline with similar cameras in development [8, 51]. This will however degrade resolution to $R = 10$ mm.
It is suggested that future investigations should be carried out into non-multiplexing multi-pinhole collimators as these may be able to increase sensitivity while maintaining the resolution of a single pinhole. For the best possible resolution/sensitivity trade-off a small pinhole acceptance angle should be used.
Chapter 7

CGC detector response

In the CGC, incident gamma rays are converted to optical photons in a CsI:Tl scintillator. These scintillation photons are then detected by an EMCCD, and a reconstruction algorithm (described in Appendix A) converts light splashes into the energy and position of the original gamma photon.

The dimensions of the scintillator affect the size of the light splashes as well as the sensitivity and spatial resolution of the system. The energy resolution of the system is dependent on the performance of the blob detection algorithm and so is a function of the shape of the light splashes arriving from the scintillator, and of the noise performance of the CCD.

In this chapter, experimental and modelled results are used to investigate the performance of the CGC detector and to determine the theoretical spatial resolution, energy resolution and sensitivity. The fundamental performance of the CCD is investigated under standard operating conditions, using camera configuration D. The Monte Carlo simulation described in Chapter 5 is then used to investigate scintillator performance.
7.1 EMCCD performance

An EMCCD can be considered as a standard CCD with an additional gain stage. The magnitude of the gain can be adjusted by varying the voltage applied during this gain stage $\Phi_{HV}$ (see Section 7.1.3). If the gain voltage is set to a low value $\Phi_{HV} < 20$ V, the EMCCD behaves as a standard CCD.

In this section, the noise performance of the EMCCD with a low gain voltage is investigated through the use of photon transfer curves. The gain performance of the EMCCD is also discussed.

7.1.1 Photon transfer curves

A common method of investigating the response of CCDs is to use a photon transfer curve (PTC) [60]. This test compares signal to noise in CCD images taken at a range of illumination levels, typically varied logarithmically to cover the full dynamic range of the CCD. To produce the PTC, mean signal (minus the electrical offset found in the overclocked region) and standard deviation in signal are calculated for each image and plotted on a log-log graph. An example PTC can be seen in Figure 7.1. From Janesick [60], PTC curves will contain three noise regimes; these have been labelled in Figure 7.1.

At low signal levels, read noise ($\sigma_R$) is dominant. Read noise is due to the readout electronics and will be added as each pixel is read out from the CCD. Read noise is added to each pixel independent of the signal stored within that pixel. As read noise remains constant with signal level, the curve in this region is expected to have a gradient of 0. Read noise is small compared to typical signal levels, so is dominant only under very low signal conditions.

At mid-range signal levels, shot noise ($\sigma_S$) dominates. Shot noise is the random noise associated with a stochastic process (such as electron generation). For a stochastic process, a signal of $N$ would be expected to have noise of $\sqrt{N}$. Hence, the curve in this region is expected to have a gradient of $\frac{1}{2}$. 
Figure 7.1: Example PTC curve for the EMCCD. Points of different colours represent different data sets, obtained under different initial illumination levels. Three regions of behaviour can be seen: $\sigma_R$ (read noise) dominated, $\sigma_S$ (shot noise) dominated and $\sigma_F$ (fixed pattern noise) dominated. Full well capacity occurs at a signal level of approximately 6000. Signal and noise are in arbitrary units. Dotted grey line shows an example theoretical curve.

At high signal levels, fixed pattern noise ($\sigma_F$) is dominant. Fixed pattern noise is due to nonuniformity in pixel response - typically arising from irregularities in manufacture. Fixed pattern noise of this type results in noise that is proportional to the signal level and so the PTC would be expected to show a gradient of 1.

At very high signal levels, full well capacity is reached. Although the output signal remains high, individual pixel wells become saturated and unable to hold any additional charge. Additional charge then leaks to surrounding pixels. This has a smoothing effect and lowers the noise value creating a drop off as seen in Figure 7.1. Note that the drop-off in Figure 7.1 (at a signal level of approximately 6000) does not show the true full well capacity of the EMCCD but a cut off due to read out electronics. As it is proportional to signal, fixed pattern noise is only significant for high signal levels.
Fixed pattern noise will typically be corrected for when the CCD is in use. When creating a PTC, fixed pattern noise may be eliminated if two images are taken for each illumination level with the mean signal of both images used. One image is then subtracted from the other and noise is the standard deviation in the subtracted image divided by $\sqrt{2}$ to take the two sources of noise into account. The resulting PTC with fixed pattern noise removed is sometimes referred to as the classic PTC [60], an example of which is shown in Figure 7.2.

7.1.1.1 Calibration of ADU to electrons

The classic PTC is useful for determining the calibration between electrons in the CCD and output signal. First it must be assumed that a number of photons $P$ will produce a
signal in arbitrary digital units $S$ of

$$S = \frac{P}{K},$$  \hspace{1cm} (7.1)

where $K$ is a camera gain constant. If it is further assumed that each photon can free a single electron in the detector - a valid assumption when optical photons are used - then $K$ is the required conversion factor from arbitrary analogue-to-digital units to number of electrons with units $e \text{ ADU}^{-1}$. The expected variance in $S$ is then [60]

$$\sigma_S^2 = \left(\frac{\sigma_P}{K}\right)^2 + \sigma_R^2.$$  \hspace{1cm} (7.2)

For randomly arriving photons $\sigma_P = \sqrt{P}$, and so

$$K = \frac{S}{\sigma_S^2 - \sigma_R^2},$$  \hspace{1cm} (7.3)

or, taking the logarithm,

$$\log K = \log S - \log [\sigma_S^2 - \sigma_R^2].$$  \hspace{1cm} (7.4)

This equation may now be solved using the classic PTC (Figure 7.2). For regions of the curve where $\sigma_S^2 \gg \sigma_R^2$, Equation 7.4 may be approximated as

$$\log K \approx \log S - \log \sigma_S^2.$$  \hspace{1cm} (7.5)

To determine $K$, Equation 7.5 is fitted to the shot noise limited region of the log curve.

### 7.1.1.2 CGC measurements

A PTC is typically recorded with low energy incident light, usually in the optical region, so that each absorbed photon may be expected to produce a single electron. However, once placed in the CGC the EMCCD is sealed in a vacuum chamber and cannot be illuminated optically. In practice, the EMCCD will also be covered with a scintillator. This makes the typical method for PTC measurement impossible when the EMCCD is in situ. An
alternative method is to use the thermal noise on the EMCCD in place of an optical signal. This is a theoretically equivalent method, although pixel-to-pixel non-uniformity in dark current is approximately 10 times greater than non-uniformity in pixel sensitivity [60] so results are expected to be less accurate.

For an EMCCD within the CGC, a signal was generated with dark current. As temperature affects internal gain in an EMCCD, it was kept fixed within 10\% at $-10^\circ \text{C}$. The signal was then varied by adjusting the integration time for each image. In each case, high voltage gain stage was set to a gain of 1 (see Section 7.1.3).

To obtain a traditional PTC measurement for comparison, an EMCCD was placed into a vacuum chamber separate from the CGC. An LED, also placed within the chamber, was powered through a signal generator, allowing the LED to be turned on and off with an accuracy of 2 ms ($\frac{1}{20}$ frame time). The current supplied to the LED could also be varied, giving greater control of illumination. In this test, illumination is varied while acquisition time remains fixed.

Table 7.1 compares results using each method. Although different EMCCDs were used in each case, the readout electronics used were identical and results were expected to be comparable using both methods. The results in Table 7.1 are consistent with this expectation. Although the optical signal method provided a more precise measurement for $e \text{ADU}^{-1}$, both methods produce results that were the same within errors.

During analysis the EMCCD image was split into 16 regions to provide additional data points - reducing the number of regions used in future tests and covering a wider range of signal levels will improve the statistics of the results. When the thermal signal

### Table 7.1: Comparison of PTC results using the optical photon signal and thermal current signal (in situ) methods. Note that maximum signal level is limited by the digital readout electronics rather than the capability of the EMCCD and occurs before full well capacity is reached.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Optical signal</th>
<th>Thermal signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>$e \text{ADU}^{-1}$</td>
<td>$2.0 \pm 0.3$</td>
<td>$2.3 \pm 0.5$</td>
</tr>
<tr>
<td>Read noise (ADU)</td>
<td>$17.2 \pm 0.3$</td>
<td>$17.3 \pm 0.3$</td>
</tr>
<tr>
<td>Maximum signal (ADU)</td>
<td>16383</td>
<td>16383</td>
</tr>
</tbody>
</table>
tests used four regions per image, the calculated number of electrons per ADU was 2.1 ± 0.3 e ADU\(^{-1}\).

Based on the calculated ADU to electron conversion, read noise was found to be 34.4 ± 6.0 e pix\(^{-1}\) frame\(^{-1}\). This value is in agreement with experimental and theoretical read noise values reported in literature [71, 78, 138, 139].

The maximum charge per pixel that can be read out is approximately 37 600 e. This is approximately 30% of the manufacturer’s suggested value. This is not the true full well capacity but occurs when signal reaches the maximum digital value of the readout electronics at 2\(^{14} - 1\).

#### 7.1.1.3 Charge collection

For further characterisation, a PTC was also created through illumination of the CGC with a \(^{109}\)Cd source, with no coupled scintillator in place. This source produces high energy photons and so a single photon, when absorbed by the EMCCD, would be expected to produce a large number of electrons. When high energy photons are used to produce a PTC, the signal level at which shot noise is equal to 1 now represents the number of photons per ADU. This is related to the quantum yield of the device by

\[
J = \frac{K}{\eta} \tag{7.6}
\]

where \(J\) is the number of photons per ADU, \(K\) the number of electrons per ADU and \(\eta\) the quantum yield [60].

A fit to the \(^{109}\)Cd PTC gives \(J = [4.796 \pm 0.007] \times 10^{-4}\) photons ADU\(^{-1}\). Assuming that \(K = 2 e\) ADU\(^{-1}\) from Table 7.1, this gives \(\eta = 4200 \pm 600 e\) photon\(^{-1}\). Gamma photons emitted by \(^{109}\)Cd will have energies ranging from 21.99 keV to 25.51 keV [15]; taking into account their relative probabilities this gives a mean photon energy of 22.624 keV and so a mean expected electron yield of 6250 e (based on an ionisation energy of 3.62 eV for Si). This suggests that on average approximately 30% of the deposited energy is not collected
by the CCD in each photon interaction; this may be due to escaping fluorescence photons, charge transfer inefficiency or pixel spreading.

### 7.1.2 Dark noise

A typical CCD under optimal conditions will be read noise limited, meaning that it cannot accurately measure signals below this level. Due to the gain stage, which is applied before the addition of read noise, EMCCDs are able to extend this useable range and are instead dark noise limited.

Dark signal occurs due to the natural thermal generation of charge carriers. This thermal signal will increase with temperature and integration time as more carriers are generated. An additional dark noise component exists due to clock induced charge - spurious signal generated as electrons are transferred through the device - which is independent of integration time [140].

The dark signal on the CGC’s EMCCD was measured at a range of possible operating temperatures. Results are shown in Figure 7.3 alongside the manufacturer’s expected values for dark signal [71]. The experimental results show a higher level of dark signal than is typical but are within the range expected.

For a 16 µm square pixel, the manufacturer provides typical dark signal values of $400 \, e \, pix^{-1} \, s^{-1}$ and maximum dark signal values of $800 \, e \, pix^{-1} \, s^{-1}$ at 20°C [71]. Experimental values at 14°C were around $560 \, e \, pix^{-1} \, s^{-1}$. At typical operating temperatures of between −10°C and −5°C, dark signal varied from $21 \, e \, pix^{-1} \, s^{-1}$ to $28 \, e \, pix^{-1} \, s^{-1}$. In most cases the CGC is operated with $4 \times 4$ pixel binning in place - noise per binned pixel under typical operating conditions is therefore $330 \, e \, pix^{-1} \, s^{-1}$ to $450 \, e \, pix^{-1} \, s^{-1}$. Dark signal non-uniformity was also in agreement with the manufacturer’s stated values - approximately $60 \, e \, s^{-1}$ for a 16 µm square pixel with fixed pattern noise removed.
7.1.2.1 Dark signal gradient

Alongside the dark signal non-uniformity described above, there is a fixed pattern component in dark signal, the magnitude of which is strongly dependent on signal level. Fixed pattern dark signal is common in CCDs due to pixel variations introduced in manufacturing [60]. In the CGC, there is a systematic variation of dark signal, with higher dark signals recorded at the bottom of the image. Figure 7.4, which records the mean dark signal in each row across the image, shows this non-uniformity. Note that although there is also variation across the CCD when looking at the mean signal in each column, this does not show as clear a trend and is not significant when compared to the row by row variation.

Variation over these rows is to be expected as rows read out first have a lower integration time, in terms of dark signal, than those read out last. In this case, the relationship between
row number and dark signal should be linear and this does provide a reasonable fit to the data ($R^2 > 0.998$).

At $-9.5^\circ C$, dark signal was 40 times higher in the bottom row of the image when compared to the top row. This level of variation can cause a number of problems for imaging. With such a large range in noise, thresholding (typically set at the mean of the noise peak plus $5\sigma$) will exclude some valid signal electrons at the top of the image and include unwanted dark signal at the bottom. As this variation is sensitive to temperature, it also creates difficulties when applying flat field correction to images. Optimum results may only be reached when the flood image used for flat field correction is taken at exactly the same temperature as the image to be corrected. As very deep images are used for flat field correction, it is common for the temperature of the CCD to vary during the acquisition of the flood image so it is unlikely that temperature changes will be replicated. Further work should be carried out to determine the best method for reducing the impact
of this dark signal variation, although it may be minimised by decreasing readout times so they become less significant when compared to integration times.

### 7.1.3 Gain

The gain of the EMCCD was varied by changing the gain clocking voltage $\Phi_{HV}$. Illumination was provided by an $^{241}$Am source with peak emission at 59.5 keV. The potential applied prior to the high voltage step was set at $\Phi_{DC} = 2.5$ V [71]. A bias voltage of $\Phi_{HV} = 20$ V was assumed to produce no gain in the system as stated by the manufacturer [71] and the recorded signal at this level was used as the baseline for each temperature. Gain was calculated by dividing recorded signal for each $\Phi_{HV}$ by the baseline signal. The dependence of the total multiplication gain $G$ on the individual gain for each stage $g$ is given by

$$G = g^S$$  (7.7)

where $S$ is the number of impact ionisation stages*. For the EMCCD used with the CGC, $S = 536$ [71]. A stage gain of $g = 1.01$, for example, would therefore result in a total gain of $G = 207$. Equation 7.7 was used to convert the recorded gain $G$ to the gain per stage $g$ which could then be compared to models derived from avalanche multiplication theory.

#### 7.1.3.1 Temperature dependence

The variation of gain $G$ with $\Phi_{HV}$ was investigated at temperatures ranging from 266 K to 297 K. As discussed in Section 7.1.2, noise within the EMCCD is temperature dependent and would be expected to change significantly over this temperature range [140]. This will not affect the results described in this section as signals at $\Phi_{HV} = 20$ V were found separately for each temperature.

*This assumes that $g$ is constant for all gain stages. In practice, the increase in charge in each successive step will act to change the electric field properties and so the gain of future steps [141]. This effect is assumed to be negligible for this work as no non-linearity between input and output charge was seen over the ranges tested.
Gain was found to vary exponentially with the applied voltage across each gain stage $V$ (calculated by $\Phi_{HV} - \Phi_{DC}$), with higher gains found at lower temperatures. The gains recorded in this investigation were similar in magnitude to those found in other investigations of EMCCD performance [90, 138] although slightly lower than those reported by the manufacturer [71]. The maximum gain was 230 at a temperature of 266 K and a gain voltage of $\Phi_{HV} = 46$ V, although at this point some pixels were saturated. The lower experimental gain compared to the manufacturer’s stated value is unlikely to be due to saturation as it occurs in fitted curves even when saturated points are removed. The gain performance of EMCCDs is known to degrade with time [142] which is a more likely cause of the discrepancy.

Miller [143] gives an empirical equation for gain over a set of p-n step junctions as

$$g = \frac{1}{1 - \left(\frac{V}{V_B}\right)^m}$$

(7.8)

where $V$ is the junction voltage, $V_B$ is the breakdown voltage (where impact ionisation multiplies infinitely) and $m$ is an empirical parameter related to material properties such as doping concentrations [143]. Miller finds values of $m$ between 1.4 and 4 for a range of Si junctions, with $m = 4$ occurring for the highest breakdown voltage tested, $V_B = 47.5$ V[143].

Figure 7.5 shows experimental gain data for a number of temperatures, with Equation 7.8 fitted to each data set†. Equation 7.8 was first fitted to the data with $m$ and $V_B$ varied to find the best fit. The parameter $m$ showed no temperature dependence so the mean value of $m = 9.33 \pm 0.2$ was used for all fits shown in Figure 7.5.

$V_B$ was found to be proportional to temperature and varied from $70.13 \pm 0.04$ V at 266 K to $71.39 \pm 0.04$ V at 297 K. A linear fit to $V_B$ ($R^2 = 0.984$) showed a variation of 0.073% per degree, similar to the the 0.1% variation previously reported [77], although only five

†For clarity, the full range of data is not shown in Figure 7.5. The full range of data extends from 20 V to 50 V in 1 V increments and fits were performed over this entire range. Saturated data points were defined as those where more than 1% of pixels had signal levels equal to 16383 - the readout electronics limited maximum for this device (see Section 7.1.1.2). This occurred at different points for different temperatures e.g. after 40.5 V at 274 K and after 39.5 V at 266 K. Saturated data points were excluded from the fits shown.
Figure 7.5: Relationship between applied voltage $V$ across the gain stage junction ($\Phi_{HV} - \Phi_{DC}$) and gain per stage $g$. The Miller gain model (Equation 7.8) has been fitted to each data set with $m = 9.33$ fixed and $V_B$ varied to provide the best fit. In all cases, $R^2 > 0.9995$. Note that for clarity the full range of data is not shown and data points with high levels of saturation have been removed.

Data points were available. The Miller equation varies significantly from experimental data for junctions with higher breakdown voltages where multiplication varies rapidly for small changes in field [143]. The values for $V_B$ calculated here are significantly higher than those in Miller’s experiment, as is the calculated value for $m$. This suggests an acceptor concentration in the region of $7.6 \times 10^{15}$ cm$^{-3}$ [77], approximately an order of magnitude less than in the devices used by Miller [143].

The dependence on $V_B$ seen in Equation 7.8 arises as $V_B$ is inversely proportional to the ionisation rates of electrons and holes in a material - with ionisation rates in turn being temperature dependent [144]. Gain can be determined by integrating the ionisation rate across the width of the junction.

A variety of analytical models for impact ionisation exist which have been reviewed elsewhere [145], almost all of which take their starting point from Chynoweth [141] who
gives an expression of ionisation rate of electrons as

\[ \alpha = Ae^{-bE}, \]  

(7.9)

where \( E \) is electric field strength and \( A \) and \( b \) are empirically determined values [141]. \( A \) is a constant whereas \( b \) is temperature dependent [145]. An equivalent set of constants exists for the ionisation rate of holes. As this experiment measured total current, with contributions from both holes and electrons (although the majority of holes are expected to diffuse into the substrate layer), the values calculated can be thought of as effective constants (\( A_{\text{eff}} \) and \( b_{\text{eff}} \)) combining both electron and hole effects.

The Spirito equation for avalanche multiplication, which is based on the assumption that \( g \leq 1.2 \), is [146]

\[ g = \frac{1}{1 - \frac{2A}{b}Ve^{-b(\frac{K}{2V})^2}} \]  

(7.10)

where \( K \) is related to the distribution of the electric field within the junction. When \( E \) is linearly dependent on distance, this relationship is

\[ K = \frac{W}{E_{\text{max}}} \]  

(7.11)

where \( W \) is the width of the junction and \( E_{\text{max}} \) the maximum electric field [146]. Reasonable estimates for these parameters are \( E_{\text{max}} = 10^7 \text{ V m}^{-1} \) and \( W = 1 \mu\text{m} \) [76], which give \( K = 10^{-13} \text{ m}^2 \text{ V}^{-1} \).

As with Miller’s expression (Figure 7.5), values for \( K \) and \( A \) were initially allowed to vary - as these parameters are independent of temperature, the means of each were calculated. These parameters were fixed at their mean value, \( K = (6.9 \pm 0.4) \times 10^{-13} \text{ m}^2 \text{ V}^{-1} \) and \( A = (2.8 \pm 0.5) \times 10^{11} \text{ m}^{-1} \), and curve fitting was used to more accurately determine \( b \). \( K \) was therefore of the same magnitude as was estimated from Equation 7.11, so a linearly dependent electric field appears to be a reasonable approximation of the true field shape within the CCD junctions. The Spirito model provided a better fit to experimental results than the Miller model with \( R^2 > 0.9998 \) in all cases.
Figure 7.6: Relationship between $b$ and $T$ calculated by fitting Equation 7.10 to the experimental results shown in Figure 7.5 with $K = (6.9 \pm 0.4) \times 10^{-13}$ m$^3$ V$^{-1}$ and $A = (2.8 \pm 0.5) \times 10^{11}$ m$^{-1}$. $R^2 = 0.98$ for the fitted line.

The relationship between $b$ and $T$, plotted in Figure 7.6, was $([6.0 \pm 0.2] \times 10^4) T + ([1.663 \pm 0.006] \times 10^8)$ V m$^{-1}$. Table 7.2 compares these values to impact ionisation values for holes $p$ and electrons $n$ from the literature.

<table>
<thead>
<tr>
<th></th>
<th>$A_n$</th>
<th>$A_p$</th>
<th>$b_n$</th>
<th>$b_p$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>×10$^7$ (m$^{-1}$)</td>
<td>×10$^8$ (Vm$^{-1}$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moll and Overstraeten [147]</td>
<td>1.6</td>
<td>0.55</td>
<td>1.65</td>
<td>1.65</td>
</tr>
<tr>
<td>Grant [148]</td>
<td>6.2</td>
<td>20</td>
<td>1.05 + 0.0013$T$</td>
<td>1.95 + 0.0011$T$</td>
</tr>
<tr>
<td>Massey et al. [149]</td>
<td>4.43</td>
<td>11.3</td>
<td>0.966 + 0.0005$T$</td>
<td>1.71 + 0.0011$T$</td>
</tr>
<tr>
<td>Ershov and Ryzhii [150]</td>
<td>7</td>
<td>-</td>
<td>1.04 + 0.0006$T$</td>
<td>-</td>
</tr>
<tr>
<td>Woods et al. [151]</td>
<td>9.2</td>
<td>2.4</td>
<td>1.45</td>
<td>1.64</td>
</tr>
<tr>
<td>Effective parameters</td>
<td>27500</td>
<td></td>
<td>1.663 + 0.0006$T$</td>
<td></td>
</tr>
</tbody>
</table>

Table 7.2: Simulated (Ershov and Ryzhii) and experimental (all others) values for impact ionisation constants in a range of differently fabricated Si diodes. Temperature ranges cover 15 K to 450 K. Woods et al. performed experiments at 300 K only. Effective parameters from this work were measured over 266 K to 297 K.
Table 7.2 shows the range of values that may be expected for ionisation rates in Si with differing doping concentrations and profiles. The value for $b$ calculated in this work is of a similar magnitude, although slightly larger, than those given for electrons in Table 7.2, with temperature dependence consistent with previously determined values. Although hole multiplication in a charge-coupled device is thought to be 5-10 times lower than electron multiplication [76] this is not negligible. The discrepancy between experimental values in this and other work is likely due to the combined effects of holes and electrons being measured simultaneously. The parameter $b$ is thought to be related to the ionisation energy and the mean free path of carriers between ionising collisions [141] - as these are dependent on doping levels [144], this may also be the cause of some variation between results.

The parameter $A$ is variable across all experiments, but the value calculated in this investigation is significantly higher than other reported values. This difference may partly be due to the combined contribution of holes and electrons in this experiment, although it would not be expected for this to have so large an effect. A larger value for $A$ results in a higher gain for the same electric field, suggesting that gain performance of the EMCCD is better than in the diodes tested in Table 7.2.

### 7.2 Columnar CsI:Tl scintillator

The CGC currently uses a 600 µm thick scintillator, on a 500 µm thick mirrored amorphous carbon substrate, with columnar structures ranging in diameter from $\sim$5 µm to $\sim$15 µm [72, 73]. To improve sensitivity, a thicker scintillator may be used although due to depth of interaction (DOI) effects, this will have implications for spatial and energy resolution [152]. In this section, the behaviour of a columnar scintillator is investigated through the Monte Carlo simulation described in Chapter 5. Light splashes generated by the simulation are analysed using the standard blobbing algorithm described in Appendix A to determine the total energy deposited in each case.
Figure 7.7: Absorption of gamma photons through a CsI scintillator for a range of photon energies [13]. Absorption edges can be seen at 33 keV (I) and 40 keV (Cs).

7.2.1 Spatial resolution and sensitivity

The expected absorption for CsI layers of several thicknesses is shown in Figure 7.7. The current CGC uses a 600 µm thick scintillator, with an expected absorption of 0.205 for 141 keV photons. A 1500 µm thick scintillator - available through the same manufacturer as the scintillator currently used [70] - would increase this to 0.436. Increasing the scintillator thickness would also reduce the effects of the K-absorption edges at 40 keV and 33 keV - this would be of benefit if the camera was used to image lower energy radioisotopes such as $^{125}$I (35.5 keV).

The 100 µm and 300 µm thick scintillators have expected absorptions of 0.037 and 0.108 respectively at 141 keV. These have been investigated as CsI:Tl has successfully been grown directly onto a CCD at these thicknesses [153]. The possible benefits of this technique are discussed in Section 7.2.3; however the low absorption rates shown here
Table 7.3: Sensitivity and FWHM spatial resolution of simulated columnar CsI:Tl of varying thickness. Simulated pixel size is 64 µm square. Theoretical sensitivities are indicative of the maximum possible sensitivity of the scintillator and experimental values are expected to be lower. 5000 detected events were simulated for each scintillator thickness.

<table>
<thead>
<tr>
<th>Thickness (µm)</th>
<th>Maximum theoretical sensitivity</th>
<th>Simulated sensitivity</th>
<th>Simulated photopeak sensitivity</th>
<th>Spatial Resolution (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>0.037</td>
<td>0.035</td>
<td>0.016</td>
<td>49.9</td>
</tr>
<tr>
<td>300</td>
<td>0.108</td>
<td>0.103</td>
<td>0.046</td>
<td>56.7</td>
</tr>
<tr>
<td>600</td>
<td>0.205</td>
<td>0.193</td>
<td>0.083</td>
<td>59.8</td>
</tr>
<tr>
<td>1500</td>
<td>0.436</td>
<td>0.412</td>
<td>0.170</td>
<td>59.3</td>
</tr>
</tbody>
</table>

mean that it would not be practical for the CGC unless far greater thicknesses could be grown.

Table 7.3 compares the simulated sensitivity and spatial resolution for this range of scintillator thicknesses. Sensitivity has been calculated based on the number of inelastic interactions of 141 keV photons with the scintillator. Photopeak sensitivity has been defined as the amount of deposited events with calibrated energies of 100 keV or higher to include the escape peak (see Section 7.2.2).

Simulated sensitivity provided a good match to theoretical sensitivity with differences due to instances Rayleigh scattering where no energy is deposited and scattering was not sufficient for the photon to leave the simulation. When Rayleigh and Compton scattering are removed from calculations, it was found the the photopeak sensitivity of each scintillator (based on the above criterion) was approximately 50% of its calculated theoretical value. This indicates that the blobbing algorithm is not always successful in reconstructing energy, this is discussed in more detail in Section 7.2.2 but is thought to be due to simulated light splashes having smaller scales than those seen experimentally.

Simulated spatial resolutions are lower than those seen experimentally for the CGC but similar to those reported by other CsI:Tl/CCD based systems [154]. The discrepancy here is likely because the simulation allows for a perfect point source for measuring resolution whereas experimental results are limited by CGC design (see Chapter 8). Thicker scintillators have larger spatial resolutions however, this increase is not significant compared to the increase seen in sensitivity for thicker scintillators.
7.2.2 Energy resolution

The energy of each light splash can be determined through blob detection. An example energy spectrum (Figure 7.8), derived after the simulation of 141 keV photons incident on an 600 µm thick CsI:Tl scintillator is shown below. This has been calibrated based on the position of the 141 keV photopeak.

Along with the 141 keV photopeak, escape peaks can be seen at \( \sim 110 \text{ keV} \). The peak at \( \sim 30 \text{ keV} \) is a combined fluorescence peak from the K-shell fluorescence of both Cs and I. In the region between 60 keV to 100 keV, a low level of counts are seen - these appear to be artifacts of blobbing algorithm as there were no energy depositions of these values during the simulation. As the energy reconstruction is based on the maximum count value within a feature it is susceptible to cases where similar high counts are spread
across two or more pixels. Below 50 keV, there were some expected depositions due to Compton scattering. The uptake in counts at very low energies (<20 keV) is also an effect of blobbing, in some cases this was due to the incorrect identification of a feature around a local maxima within a larger feature and in some cases this was due to incorrect fitting.

It is worth noting that, in this simulation, the scales of individual light splashes more closely matched those seen experimentally. This is due to double events (such as originally deposited energy and that from a fluorescence photon recaptured nearby) being detected as a single light splash. Despite this, the modelled results are significantly different from experimental spectra such as that shown in Figure 7.8.

Counts at low energies (<20 keV) are elevated in experimental data when compared to simulated results. This is to be expected, partly due to low energy fluorescence photons from material not modelled in this example (e.g. Al and W shielding) and partly due to detector noise which has also not been modelled. In experimental data, energy resolution is degraded at high energies to the point at which the photopeak and escape peaks are combined into a single peak. As the energy resolution is measured as the FWHM of the photopeak, this would artificially inflate the measured resolution.

The separate and significant escape peak may also be a feature of the simulation. In the simulated images, fluorescence photons are typically absorbed very close to the initial photon absorption. In this simulation, scintillation light splashes are consistently smaller than those seen experimentally. This means that original energy depositions and those from fluorescence photons are reconstructed as separate events if they are separated by a single pixel. With larger light splashes, such as those seen experimentally, these separate events would be reconstructed as a single event with energy within the photopeak. Rebinning to pixels of size 0.5 mm reduces both the escape and fluorescence peaks to levels similar to those reported experimentally [155], although energy resolution remains significantly better than measured elsewhere. The possibility that this is a CCD effect is discussed below.
7.2.2.1 CCD effects

One possible cause of the discrepancy between the energy resolutions of experimental and simulated data is CCD noise. CCD noise was simulated as described in Chapter 5 and applied to the same data as in Section 7.2.2. The largest difference between the simulated spectra produced was the large number of events seen with energies of less than 5 keV - this suggests that its presence in the experimental data is due to CCD noise.

There was also a slight increase in the measured photopeak FWHM - from 6.57 keV to 7.29 keV - once simulated CCD noise was added but this was still significantly smaller than for the CGC. Sensitivity was unchanged. Even when the amount of thermal noise present on the CCD was increased by a factor of 20 - equivalent to warming the CCD from a standard operating temperature to around 14°C - noise levels could not account for the degradation in resolution seen in experimental data.

The effect of the coupling efficiency between the CCD and scintillator was also investigated. Reducing the coupling efficiency to 50% (the maximal expected efficiency between a scintillator and PMT [14]) increased FWHM energy resolution to 7.3 keV. At 5% coupling efficiency this was 12.2 keV, at 0.5% efficiency the escape peak and photopeak are no longer resolved and FWHM energy resolution was measured to be 61 keV (Figure 7.9). Although the resolution is more similar to experimental results in this case, the escape peak is seen to be significant.

Coupling has a large impact on energy resolution and the optical coupling in the CGC is not yet optimised (Section 7.2.3). In addition to poor coupling, variation in coupling efficiency across the detector face would be expected to degrade resolution further. The current scintillation model produces light splashes less Gaussian in shape than those seen experimentally; if gaps are present between the CCD and scintillator these may smooth out scintillation light - this should be investigated further.
7.2.3 Scintillator-CCD coupling

The scintillator-CCD coupling in the CGC is variable between camera models. Two different techniques have been used in practice; the optical grease method uses a thin layer of optical grease [74] spread on the scintillator surface both to bind the scintillator to the CCD and to optically couple the two elements. In the direct contact method, the scintillator is placed directly onto the CCD and secured with small plastic spacers and Kapton tape.

The direct contact method is a straightforward process to implement and it is relatively quick and simple to detach and reattach the scintillator as needed. The optical grease technique is far harder to complete successfully - great care must be taken to spread...
the grease evenly and attach the scintillator with no air bubbles. If the process is not successful, the scintillator must be removed and the CCD cleaned thoroughly and dried before a second attempt can be made - there will however always be some grease still on the scintillator so if the same piece is reattached it becomes even more difficult to achieve uniform coupling.

As shown in Figure 7.10, both methods introduce non-uniformity to the detector response. In the optical grease coupled example, a number of features can be seen in the flood image. These are due to inconsistency in the spreading of the optical grease or to small air bubbles introduced when the scintillator was attached. These features initially vary rapidly with time, and can be seen to be shifting over 1 h to 2 h of imaging time. The non-uniformity features caused by this method tend to be relatively small and distinct. In the image in Figure 7.10, it can also be seen that the scintillator is not perfectly aligned with the imaging area of the CCD, with a region on the bottom of the image that is not covered by the scintillator. This type of misalignment is trivial to correct when the direct contact method is used but would be time consuming with the optical grease binding method and may introduce further inefficiencies upon recoupling.

The use of optical grease does provide superior optical coupling when compared to the direct contact method. In the right hand image of Figure 7.10, the central bright spot is believed to be due to a small amount of optical grease still present from a previous
coupling attempt. The non-uniformity when direct contact is used tends to occur over larger areas and is less discrete. It is still difficult to achieve uniform contact across the detector. At the top of the image, particularly in the corners, the scintillator has become decoupled to such an extent that no counts are detected. This ‘curling up’ of corners of the scintillator is fairly common, most likely as they are cut from a larger piece of scintillator, which weakens the bond to the substrate. The non-uniformity seen with direct coupled scintillators is, however, more consistent over time and so at present provides the best solution to the coupling problem.

An alternative method of CCD-scintillator coupling is to grow the scintillator directly onto the CCD (e.g. [153]) however previous investigation into this technique within the Bioimaging Unit, University of Leicester has found it prohibitively time consuming, expensive and the thickness that could be achieved was limited to $\sim 200 \mu m$.

Poor coupling will effect the sensitivity and uniformity of the detector but also has implications for energy resolution and is believed to be a significant factor in the poor energy resolution of the CGC in its current form (see Section 7.2.2.1).

### 7.3 Conclusions and recommendations

The noise and gain characteristics of the EMCCD have been investigated over temperatures of $-12^\circ C$ to $25^\circ C$. Empirical dependencies have been found by combining theoretical relationships and experimental results, allowing these quantities to be estimated for a wider range of temperatures. The EMCCD was found to be operating within the manufacturer’s typical performance specifications with some room for improvement. The tests described here should be performed on a second EMCCD to determine the variability between devices.

The dependence of dark signal and variation in dark signal on temperature has been shown to degrade camera performance. This is an area with room for improvement without major adjustments in camera design. A feedback system should be implemented for better temperature stability. Decreasing operating temperature will improve performance; this
could be achieved through multi-stage TEC, although the ability of the phase change material to dissipate heat should also be investigated. The effect of dark signal variation could be minimised by increasing the readout speed for each frame, by increasing pixel binning for example, although this will have implications for other areas of camera performance.

The Monte Carlo simulation of the CsI:Tl scintillator was shown to match theoretical calculations for sensitivity and experimental measures of spatial resolution. The energy resolution of the simulated scintillator were better than those seen experimentally.

The light splashes produced by simulated scintillation photons were smaller than those seen experimentally with the CGC. This may be due to optical coupling effects which aren’t currently simulated or may indicate that the model of the scintillator itself is insufficient. It may be that the regular array of columns is not a reasonable representation or that photoelectrons travel significant distances, for example. In its current form, the model suggests that the benefit to sensitivity from increasing scintillator thickness outweighs the small loss in spatial resolution.

To improve the simulation, the true response of the scintillator should be investigated more fully. Experimental techniques such as that described by Korevaar et al. [152] would allow a direct comparison between DOI and light spread profile to be made. In addition, an air gap between the CCD and scintillator should be modelled, as this would allow the effect of poor coupling between the scintillator and the CCD on energy resolution to be more thoroughly investigated.

The optical coupling has been shown to be variable and nonuniform - suggesting that its efficiency is also poor. This should be addressed in future design iterations, initially by including a method for fastening a direct contact scintillator more closely to the CCD. For the best efficiency, optical grease is recommended although a new application technique should first be developed.
Chapter 8

Protocols for characterisation of SFOV gamma cameras

Standardised procedures for assessing the performance characteristics of medical gamma cameras have generally been based on the original standards published by the US National Electrical Manufacturing Association (NEMA) [156]. In the UK and Europe a comprehensive description of procedures to be carried out in clinical departments has been developed by the Institute of Physics and Engineering in Medicine (IPEM) [121]. However, these tests are designed for use with standard LFOV gamma cameras and are not necessarily applicable to SFOV systems. The term SFOV itself is ambiguous, and has been used for cameras with FOVs between 400 mm × 400 mm (e.g. [157]) and 40 mm × 40 mm (e.g. [30]). For cameras at the higher end of this range, the IPEM standards can be applied directly. For cameras with FOVs at the lower end of this range, these standards may not be applicable and the procedures may in some cases even be impossible to perform.

In this chapter, current LFOV standards are outlined and the necessary adjustments to these for use with SFOV cameras are given. These standards are then applied, in full, to the CGC, fully characterising its performance for the first time*. Performance

*Two CGC systems with identical designs were used. Camera A was used for resolution and sensitivity measurements and Camera C was used for all other tests (see Section 4.9. For a full characterisation of a single system, using preliminary versions of the protocols described in this section, see Bugby et al. [158].
characteristics are then compared to those of several standard LFOV systems currently in clinical use, and to a number of SFOV cameras in development.

8.1 Intrinsic spatial resolution

Intrinsic spatial resolution is defined as the FWHM of a line spread function (LSF) or PSF without an imaging collimator installed. A FWTM measurement is typically also stated as the PSF or LSF may deviate from a Gaussian profile [121]. In some cases, intrinsic resolution is defined as the point at which the modulation transfer function (MTF) - which allows comparison of image contrast in frequency space - has dropped to a certain percentage of its maximum value. Bar patterns cease to be visible at around the 10% point of the MTF, so this value may be reported for the resolution (5% or 3% values are also occasionally reported). A MTF plot can provide more detailed information about detector behaviour than a FWHM measurement can but is not typically supplied by manufacturers.

8.1.1 LFOV protocol and limitations

Standard methodologies for LFOV gamma cameras (e.g. [121, 156]) use a capillary line source containing approximately 40MBq activity, with a maximum internal diameter 20% less than the expected resolution. LFOV cameras have expected intrinsic resolutions of the order 3 mm [55, 129]. To satisfy NEMA criteria a camera of this type would require a line source with a width of, at maximum, 2.4 mm and so the use of a 0.5 mm width line source clearly falls within these guidelines. Capillary tubing of this size are common and can be easily filled with the required radioisotope solution.

Typically a line source will be masked with parallel Pb blocks, limiting its width to 0.5 mm. The line source is imaged parallel to the principal orthogonal axes of the camera, and images are taken across the FOV of the camera. If a point source is used instead, it is also be masked to a diameter of approximately 0.5 mm, and images are taken across the entire FOV. Resolution may also be measured qualitatively, such as with an Anger or bar phantom, as typical LFOV gamma camera collimators have holes of 2 mm to 5 mm and
small changes in intrinsic resolution will simply act to reduce image contrast. In all cases, the sources used are placed directly onto the detector crystal.

At the time of writing, SFOV cameras currently in development can achieve far better intrinsic resolutions than their LFOV counterparts. A camera with an expected intrinsic resolution of, for example, 100 µm [75] would require a line source with a width of less than 80 µm, preferably even smaller. At these widths, the difficulty in manufacture and filling of phantoms without specialist equipment becomes a limiting factor [122, 159].

8.1.2 Suggested SFOV protocol

Intrinsic spatial resolution may also be calculated using an edge response function (ERF) method - this method eliminates the need for very small sources.

A mask with a machined edge, manufactured from a material with low transmission for the gamma energies being used, is required. The edge should be perpendicular to the mask surface and straight to an accuracy of at least 10% of the expected resolution. The mask thickness should at a minimum be sufficient to attenuate 99% of gamma photons, with thick masks preferable to exclude divergent photons.

The mask should be placed as close to the scintillator crystal as camera design allows. To ensure uniformity, illumination is provided by a point source at a distance of at least 100 times its diameter. Measurements are required with the mask in alignment with both the x- and y-axes of the detector array.

During processing an ERF is calculated; this is a plot of the distance from the edge of the mask on the image plane against normalised signal. If the edge is not perfectly aligned with the camera axes, this must be taken into account using a line of best fit when creating the ERF. The ERF is then differentiated to give a LSF - which can then be analysed in the usual manner. Intrinsic resolution should be reported as the mean FWHM and mean FWTM of the LSF.
8.1.3 CGC method and results

A 5mm thick Pb block, with a 3 mm × 20 mm machined slit, was placed directly on the uncollimated camera face. Due to the camera design (see Chapter 4), this placed the slit at a distance of 7 mm from the detector. The slit was illuminated with a $^{99m}$Tc source, 3 mm in diameter. The source contained an activity of 10 MBq and was positioned a distance of 325 mm from the camera face. 30000 frame images were taken, giving approximately 34000 counts/pixel within the slit region.

Figure 8.1 shows an example image taken for intrinsic resolution measurement and the associated analysis steps. Figure 8.1a has been rotated by 90°; the brighter background signal on the left hand side of the image is due to the higher dark signal at the bottom of the CCD as discussed in Section 7.1.2.1.
Figure 8.1b shows the normalised ERF of the slit. A large amount of variation in signal can be seen, particularly at high signal levels within the slit\(^\dagger\). A clear step can be seen between background count levels and counts within the slit. Well within the slit, the signal remains level - indicating that the slit width is sufficient for it to be considered as two separate edges.

Figure 8.1c shows the normalised LSF - the derivative of the ERF from Figure 8.1b. The two peaks are from the rising and falling edges of the slit profile.

Figure 8.1d shows the modulation transfer function (MTF), which is found by performing a fast Fourier transform on the LSF (in this case the LSF of the right hand edge). A MTF allows investigation of detector response in frequency space; a higher function value indicates a better ability to resolve lines at the associated separation. MTFs are best used to compare the response of multiple systems and are rarely used for quantitative measures of a single camera.

Parameters derived from Figure 8.1 are tabulated in Table 8.1. The CGC resolution is approximately 2 to 3 pixels (each pixel being 64 µm) which is reasonable, particularly considering that the transmission mask was not placed directly onto the detector.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSF FWHM</td>
<td>158 ± 15 µm</td>
</tr>
<tr>
<td>LSF FWTM</td>
<td>289 ± 27 µm</td>
</tr>
<tr>
<td>ERF 90% to 10%</td>
<td>170 ± 50 µm</td>
</tr>
<tr>
<td>10% MTF</td>
<td>0.79 ± 0.3 LP/mm</td>
</tr>
<tr>
<td></td>
<td>630 ± 270 µm</td>
</tr>
</tbody>
</table>

**Table 8.1**: Intrinsic resolution measurements for the CGC configuration A. Mean values of vertical and horizontal measurements are shown. Errors are large on some measurements due to nonuniformity, these measurements have been included for completeness.

\(^\dagger\)The magnitude of variation suggests that the uniformity of Camera A is poorer than that of Camera C which was tested in Section 8.4.
8.2 System spatial resolution

System, or extrinsic, spatial resolution is the FWHM of a LSF or PSF measured when the imaging collimator is in place. Separate system spatial resolution measurements should be reported for each collimator that will be used. System spatial resolution is a more clinically relevant parameter than intrinsic spatial resolution, as it will naturally take intrinsic resolution effects into account and is measured with the camera in the configuration that will be used in practice.

To increase practicality, spatial resolution measurements can also be quoted for a range of camera-source distances, with scattering media (such as Perspex or water) placed in the intervening space to emulate source depth within a patient. It is common for system spatial resolutions to be reported for sources on the collimator face and at a distance of 100 mm through scattering material.

8.2.1 LFOV protocol and limitations

For LFOV systems a line source or point source with a diameter of around 0.5 mm is used. The source is imaged at the appropriate distance (i.e. on the collimator face or at 100 mm distance) and the FWHM and FWTM values calculated from the produced image.

Similarly to intrinsic spatial resolution measurements, for SFOV cameras with far smaller expected resolution measurements than typical LFOV systems it is preferable to use smaller line or point sources, which are difficult to manufacture and fill. It may be possible to use a point or line source of a known size and then deconvolve the expected profile from the resultant image to determine resolution; this is not ideal and requires specific knowledge of the expected profile of the source which, as shown in Section 6.4.3, is not necessarily a trivial task.

In addition, many SFOV cameras use pinhole collimators. For a pinhole collimator, a line source imaged at the collimator face would appear as a flood source in the resultant image - making resolution measurements impossible. Resolution will vary significantly with
source distance so measurement at a single point will not provide complete information of the camera response. For a more detailed description of pinhole effects see Chapter 6.

8.2.2  Suggested SFOV protocol

A line source of no greater than 0.5 mm diameter should be imaged at the collimator face for parallel hole collimators. For pinhole collimators, measurement should be made at the non-magnifying point and source widths should be limited by the geometric resolution of the pinhole at the non-magnifying point (see Section 6.4.3). Measurements are to be repeated at five or more distance intervals to a maximum distance of 100 mm from the collimator face; in each case the space between the camera and the source should be filled with scattering material such as Perspex or water.

The FWHM and FWTM should be recorded at each distance. These values should be corrected for magnification if applicable; for example a FWHM of 1 mm recorded for a distance giving a magnification of 0.2 has a FWHM in object space of 5 mm. A line of best fit should be calculated for both distance versus FWHM and distance versus FWTM. These relationships should be reported along with the range over which they were measured.

8.2.3  CGC method and results

A 0.55 mm internal diameter butterfly cannula was filled with approximately 50 MBq of $^{99m}$Tc (0.3 MBq mm$^{-1}$). This was used as a line source, and was imaged at a range of distances from the camera, with Perspex placed in between the source and camera as a scattering medium. This was performed for both the 0.5 mm and 1.0 mm diameter pinhole collimators.

Figure 8.2 shows a plot of calculated resolution measurements against Perspex depth for both the 0.5 mm and 1.0 mm diameter pinhole collimators. As would be expected, resolutions degrade with increasing depths of Perspex. At greater thicknesses, unscattered counts are reduced and scattered counts act to enhance the background noise level. The
Figure 8.2: System resolution measurements for CGC configuration A using pinhole collimators with $d = 0.5$ mm and $d = 1.0$ mm. FWHM (red) and FWTM (green) measurements are shown along with lines of best fit for a range of Perspex depths.

<table>
<thead>
<tr>
<th></th>
<th>Fitted parameters</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$m$</td>
<td>$c$</td>
</tr>
<tr>
<td>$d = 0.5$ mm</td>
<td>FWHM</td>
<td>$0.054 \pm 0.003$</td>
</tr>
<tr>
<td></td>
<td>FWTM</td>
<td>$0.126 \pm 0.009$</td>
</tr>
<tr>
<td>$d = 1.0$ mm</td>
<td>FWHM</td>
<td>$0.095 \pm 0.002$</td>
</tr>
<tr>
<td></td>
<td>FWTM</td>
<td>$0.139 \pm 0.003$</td>
</tr>
</tbody>
</table>

Table 8.2: Fitted gradient $m$ and constant offset $c$ for the linear relationship between depth of scattering material and resolution. These parameters have been fitted for depths of scattering material up to 50 mm.

The overall effect is larger on FWTM values, where signal is already relatively low. Similarly, the lower sensitivity of the 0.5 mm diameter pinhole collimator resulted in poorer photon statistics and so larger error in the results.

The FWHM resolutions at the non-magnifying position (a distance of 10 mm) was $1.48$ mm and $2.57$ mm for $d = 0.5$ mm and $d = 1.0$ mm respectively, with FWTM values of $2.7$ mm and $3.5$ mm. Resolution varies according to the linear relationship between distance through scattering medium $x$ and resolution - the fitted relationships in Figure 8.2 are tabulated in Table 8.2.

The results in Table 8.2 are of the order of the geometric resolution of a pinhole (see Chapter 6), with the discrepancy coming from scatter, leakage through the collimating material and photon spreading within the scintillator.
8.3 Spatial linearity

Spatial linearity is a measure of how accurately event positions are mapped to the resulting image. This is quantified by investigating the difference between the image of a line and a true straight line. Reported values are the absolute linearity (maximal deviation from line) and the differential linearity (mean and standard deviation from line).

8.3.1 LFOV protocol and limitations

Spatial linearity measurements may be taken with phantoms specifically designed for this purpose. An ortho-hole transmission phantom (OHTP) is a regular array of holes drilled through Pb. A parallel line equal spacing (PLES) transmission phantom uses regular, parallel machined grooves instead of holes. Ideally these phantoms will extend across the entire detector area (400 mm × 400 mm) and feature widths range from 2 mm to 10 mm [160]. In either case the test pattern is placed on the uncollimated face of the camera, with features carefully aligned to the rows and columns of the image matrix. A small source of activity is placed a suitable distance above the test phantom and an image is acquired.

A least-squares fit is performed the image, either along a PLES phantom groove or a line connecting centre points of OHTP holes. The distance, in pixels, between the fitted line and line image is measured at 10 mm intervals across the face (PLES phantom) or at each hole position (OHTP). These measurements are converted to millimetres and the maximal, standard and mean deviations recorded.

This method can, in principle, be applied directly to SFOV cameras. Due to the small detector size typical in SFOV cameras, the phantoms used would need to be scaled down to some extent.

8.3.2 Suggested SFOV protocol

If an appropriate transmission mask can be created, SFOV methodology will be identical to that for a LFOV system. If this is not possible, a single-slit transmission mask may be
used. For each row or column (depending on slit orientation) of the slit image, the centre-point should be found. A least-squares fit should be produced and the deviations (the distance between the expected and actual centre positions) found for each row or column. The mean and maximal deviations and the standard deviation in deviations (differential linearity) should be reported.

### 8.3.3 CGC method and results

A 10 mm thick Pb block with a 2 mm × 20 mm slit was positioned 40 mm in front of the uncollimated camera face (47 mm from the detector). A 3 mm diameter tube containing 14 MBq $^{99m}$Tc liquid source was placed 200 mm above the slit. For each row, a Gaussian function was fitted to the slit profile and the centroid of this taken to be the centre of the slit. Rows where a centre position could not be found due to low signal to noise ratios were excluded from this analysis with 26 of 113 rows removed. Results from this test on the CGC are shown in Table 8.3. CGC response can be said to be linear to within 2 pixels (128 µm) - less than the intrinsic resolution of the detector.

### 8.4 Uniformity

Uniformity is a measure of variations in camera detection performance across the detector face. Incident photons from a uniform source would be expected to produce a uniform image; differences in spatial linearity and energy response across the detector lead to variations the number of counts recorded in different areas of the image.
There are a number of quantitative measures of spatial uniformity used in the quality control of medical gamma cameras. Standard measurements include the coefficient of variation (the ratio of standard deviation in counts to mean counts quoted as a percentage), integral uniformity and differential uniformity. IPEM Report 86 [121] recommends that at least one integral and one differential value should be quoted with preference given to the coefficient of variation and the spread of differential uniformity as the most effective methods. In all cases, a lower uniformity measurement indicates a more uniform detector response.

Integral uniformity is defined as

\[ U_{\text{int}} = \frac{C_{\text{max}} - C_{\text{min}}}{C_{\text{max}} + C_{\text{min}}} \times 100\% \]  

where \( C_{\text{max}} \) and \( C_{\text{min}} \) are the maximum and minimum number of detected counts per pixel respectively. This gives an indication of global uniformity but does not account for local variations and is not robust when outlying pixels are present. An alternative measure of \( U_{\text{int}} \) is the coefficient of variation (CoV) - the ratio of standard deviation in counts to mean counts.

For local variations, differential uniformity \( U_{\text{diff}} \) is required. This can be calculated by using Equation 8.1 for a localised group of pixels. IPEM standards suggest calculating differential uniformity 10 times for each pixel, using the five nearest pixels in a row and a column, across an entire image [121]. The mean differential uniformity is then reported.

### 8.4.1 LFOV protocol and limitations

Uniformity measurements are carried out with either a point source (at sufficient distance for incident photons to be considered uniform) or a flood source with a coefficient of variation of less than 1% in contact with the camera face. The measured uniformity is strongly dependent upon the total number of counts detected. At low count densities apparent non-uniformity may be caused by large statistical noise; at least \( 10^7 \) counts are advised (roughly 10000 per pixel) to reduce this statistical variation. Any uniformity
correction that will be applied in clinical use is also applied when the uniformity of the system is calculated.

This methodology is directly applicable to SFOV systems; in most cases it will be far easier to use a point source at a suitable distance than it is for LFOV cameras, and so a flood source is not necessary.

### 8.4.2 Suggested SFOV protocol

A flood image should be accumulated using a uniform source of activity. Integral uniformity should be reported as the coefficient of variation. The mean differential uniformity should also be reported.

### 8.4.3 CGC method and results

Spatial uniformity was measured with a number of flood images obtained using a 3 mm diameter source containing 25 MBq $^{99m}$Tc liquid source at a distance of 250 mm from the uncollimated detector face. Approximately 12000 counts/pix were recorded so statistical non-uniformity is expected to be <1%.

Uniformity results are shown in Table 8.4.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coefficient of variation</td>
<td>1.58</td>
</tr>
<tr>
<td>Integral uniformity</td>
<td>8.5</td>
</tr>
<tr>
<td>Mean differential uniformity</td>
<td>1.32</td>
</tr>
</tbody>
</table>

**Table 8.4**: Spatial uniformity measurements for CGC configuration C. Flat field correction has been applied prior to analysis.

Differential uniformity was lower than integral uniformity suggesting that there may be some systematic variation across the detector - likely due to the dark signal gradient discussed in Chapter 7. As the coefficient of variation, which is also an integral measurement, does not show as large a discrepancy, it is more probable that a single
pixel with very high or very low number of counts has disproportionately affected the calculation of integral uniformity.

8.5 Sensitivity

Sensitivity is a measure of the proportion of photons incident on the camera which are detected. This is stated both without a collimator (intrinsic) and with a collimator in place (system or extrinsic).

8.5.1 LFOV protocol

A source with known amount of radioactivity is imaged, and the ratio of expected count rate on the detector to actual count rate detected is reported. This method is directly applicable to SFOV systems although for intrinsic measurements a correction should be applied if the entirety of the source is not subtended by the detector.

8.5.2 Suggested SFOV protocol

For both intrinsic and system sensitivities a point source of known activity is required. For intrinsic measurements, sensitivity should be reported as the ratio of detected to incident counts to allow for easy comparison between detectors of different sizes. Incident counts are calculated using solid angle formulae - assuming a source is centred at a distance $h$ from a rectangular detector of dimensions $\alpha \times \beta$ the solid angle subtended will be

$$\Omega = 4 \tan^{-1} \frac{\alpha \beta}{2h\sqrt{4h^2 + \alpha^2 + \beta^2}}.$$  \hspace{1cm} (8.2)

The proportion of photons emitted from an isotropic point source that are incident on the detector is $\frac{\Omega}{4\pi}$.

System sensitivity should be reported at at least two distances from the camera: the non-magnifying point (for pinhole collimators) or the collimator surface (parallel hole
collimators) and at a distance of 100 mm through a scattering material. Ideally, a plot showing the relationship between distance and sensitivity should also be produced. System sensitivities should be reported in terms of cps MBq\(^{-1}\) for a point source. Flat field corrections should not be performed on images taken for sensitivity measurements.

### 8.5.3 CGC method and results

For intrinsic measurements, a 3 mm point source with an activity of 30 MBq of \(^{99m}\)Tc was positioned 325 mm from the camera face to produce flood images. Equation 8.2 was used to calculate the intrinsic sensitivity of the CGC, which was found to be 6±0.5%. Theoretically, 600 \(\mu\)m of CsI:Tl has an expected absorption of 20% for 141 keV photons. Approximately 4% of photons are expected to be attenuated by the 1 mm thick Al window (although many of these will be scattered), so this should have a minimal (<1%) effect on intrinsic sensitivity results. This suggests that inefficiencies in coupling in the detector and other losses account for a large decrease in sensitivity.

System measurements were taking using the same source with Perspex filling the space between the camera and the source. System measurements were taken with the 1.0 mm pinhole collimator in place. The relationship between sensitivity and depth of Perspex is shown in Figure 8.3, along with theoretical sensitivities from Chapter 6 assuming an intrinsic sensitivity of 6%.

The theoretical sensitivities do not take the effect of scattering media into account so it is expected that these will be greater than the experimental values. The ratio between theoretical and experimental sensitivities was used to determine the linear attenuation coefficient of the Perspex used. This was found to be \(0.19 \pm 0.20\) cm\(^{-1}\) - which is the same as the expected theoretical value [58]. At this photon energy, attenuation coefficients for fat, muscle and bone have been found experimentally to be 0.11 cm\(^{-1}\), 0.16 cm\(^{-1}\) and 0.24 cm\(^{-1}\) respectively [161]. The sensitivity measured here is therefore likely to be an underestimate of the sensitivity that may be achieved clinically, where fat is the typical scattering medium.

Sensitivity results are tabulated in Table 8.5.
Figure 8.3: Experimental (points) and theoretical (dashed line) system sensitivities for a range of depths of Perspex. Camera configuration A was used with a 1.0 mm diameter pinhole.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrinsic sensitivity</td>
<td>6±1%</td>
</tr>
<tr>
<td>System sensitivity at non-magnifying point</td>
<td>40 ± 1 cps MBq⁻¹</td>
</tr>
<tr>
<td>System sensitivity at 50mm</td>
<td>0.8 ± 0.1 cps MBq⁻¹</td>
</tr>
</tbody>
</table>

Table 8.5: Sensitivity measurements for CGC configuration A.

### 8.6 Count rate capability

An ideal detector would show observed count rate increasing linearly with incident count rates. In practice, saturation or dead time effects mean for many detectors this is not the case at high count rates. Count rate capability is a measure of the range in which the detector response is linear. This is expressed quantitatively as the incident count rate at which observed count rate is 10% or 20% less than would be expected from extrapolating the linear portion of the graph. The maximum achievable counts are also recorded.
8.6.1 LFOV protocol

A source is placed above the uncollimated detector and count rates recorded at intervals as the source decays. IPEM Report No. 86 [121] suggests using a distributed source with an active width of 150 mm, with 50 mm of scattering medium and no more than a 20 mm air gap between the activity and the detector face. The observed count rate is then plotted against source activity as the source decays or as known activities of stock solution are added to the source. This is used to calculate the required parameters.

8.6.2 Suggested SFOV protocol

A $^{99m}$Tc point source of known activity should be placed at a distance of at least 100 times its diameter from the uncollimated camera face. Activity should be greater than expected clinical activities. The source should be imaged at regular time intervals until it has decayed to an undetectable level. Incident counts are calculated from the initial activity of the source, the time the image was taken and the solid angle subtended by the detector (Equation 8.2). Measured counts should be plotted against incident counts and a line of best fit calculated for the linear region. The maximum measured count rate should be reported, along with the incident count rate at which measured count rate deviates from the line of best fit by more than 10%.

8.6.3 CGC method and results

A 20 MBq $^{99m}$Tc source, set at a distance of 350 mm from the detector was imaged at 30 min intervals over 24 h. The count rate response curve is shown in Figure 8.4.

A straight line was fitted to the proportional section of the curve ($R^2 = 0.9996$) indicating that the sensitivity of the detector is linear until an incident count rate of at least 1200 s$^{-1}$. Testing on a similar detector - with identical design but lower sensitivity - has shown measured values began to vary by more than 20% from this fitted line at 2200 s$^{-1}$ incident. This was due to the nature of the blob detection algorithm which requires distinct light
FIGURE 8.4: Count rate capability of CGC configuration C normalised to an integration time of 1 s.

splashes for fitting. Where more than one light splash overlaps, the algorithm is unable to resolve these as separate events and this leads to ‘saturation’. The maximum observed count rate (i.e. the y-axis of Figure 8.4) of 30 s\(^{-1}\) corresponds to approximately 3 events per frame and this is clearly below the saturation threshold.

### 8.7 Energy resolution

Energy resolution is an important parameter as it indicates the ability of a system to discriminate true events from scattered events and so improve the spatial resolution and signal to noise ratio of images, or discriminate between photon energies for dual radionuclide tests. Energy resolution is defined as the FWHM of the photopeak of the principal emission energy of the radionuclide being imaged.


8.7.1 LFOV protocol

Energy spectra are accumulated using a point source of activity. Measurements should be performed for all radionuclides that will be used with the camera. Energy resolution measurements should be repeated regularly to ensure stability in detected photopeak energy over time.

8.7.2 Suggested SFOV protocol

A point source should ideally be placed at a distance of at least 100 times its diameter from the uncollimated camera face. The activity of the source used should be within the count rate capability of the detector. At least two radioisotope sources are needed for calibration of the energy spectrum, one of which should be $^{99m}$Tc. Energy resolution for $^{99m}$Tc is reported as the FWHM of the photopeak profile as a percentage of its peak energy (141 keV).

8.7.3 CGC method and results

An 18 MBq $^{99m}$Tc point source was placed at a distance of 45 mm from the camera and the energy spectrum recorded using the blob detection algorithm. Similarly, a 4 MBq $^{109}$Cd source at a height of 5 mm was used to produce a second spectrum - this was closer to the camera than is ideal but was necessary to obtain the required number of counts in a reasonable time period due to the low activity of the source used. Flat field correction was not applied for these tests. The resultant spectra are compared in Figure 8.5.

$^{109}$Cd produces photons of 22.16 keV and 24.94 keV; photons of both energies contribute to the single peak in Figure 8.5 at $\sim$23 keV. As FWHM of the $^{109}$Cd peak is 20.4 keV, it was not expected that the separate peaks of the $^{109}$Cd spectrum would be resolvable.

The FWHM of the $^{99m}$Tc peak, at 141 keV, is 82.4 keV; an energy resolution of 58%. At the lower energy end of the $^{99m}$Tc spectrum a large noise tail is present, along with a peak
Figure 8.5: Spectral data for $^{99m}$Tc (red) and $^{109}$Cd (blue) sources (configuration B).

at approximately 30 keV. This peak can be identified as the overlaid fluorescence peaks from the scintillator (Cs-K at 31 keV, I-K at 28 keV).

8.8 Comparison to other systems

The full characterisation of the CGC is collated in Table 8.6; for comparison purposes results with the 1.0 mm diameter pinhole collimator have been used where applicable. It is now possible to compare both LFOV cameras currently in clinical use and SFOV cameras being developed for imaging in the future, and a selection of these have been included in Table 8.6. For systems using PMTs, values are usually available for both the Usable Field of View (UFOV) and the Central Field of View (CFOV) to account for variation towards the edges of the detector matrix. In Table 8.6, CFOV measurements have been used exclusively when provided. A dash indicates information was not available. For the CGC, a source distance of 10 mm was used for distance dependent values. When multiple
### Table 8.6: Comparison of performance characteristics for a range of gamma cameras [5, 6, 8, 49–55, 61, 129, 157, 162–164]. This table is replicated in a larger size in Appendix E.

<table>
<thead>
<tr>
<th>Field of view</th>
<th>CGC a</th>
<th>LFOV scintillator/PMT detectors</th>
<th>SFOV scintillator/PSPMT detectors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal (mm)</td>
<td>40 × 40</td>
<td>370 × 210</td>
<td>210 Ø</td>
</tr>
<tr>
<td>Intrinsic spatial FWHM (mm)</td>
<td>0.16</td>
<td>2.6</td>
<td>5.6</td>
</tr>
<tr>
<td>resolution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>System spatial resolution</td>
<td>2.6</td>
<td>7.1</td>
<td>7.8</td>
</tr>
<tr>
<td>Spatial linearity</td>
<td>Absolute (mm)</td>
<td>0.12</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td>Differential (mm)</td>
<td>0.09</td>
<td>0.18</td>
</tr>
<tr>
<td>Intrinsic spatial uniformity</td>
<td>Integral uniformity (%)</td>
<td>8.5</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
<td>Differential uniformity (%)</td>
<td>1.32</td>
<td>1.9</td>
</tr>
<tr>
<td>Count rate capability</td>
<td>Maximum counts (kBq)</td>
<td>&gt; 1.2</td>
<td>200</td>
</tr>
<tr>
<td>Energy resolution</td>
<td>FWHM at 141 keV (%)</td>
<td>58</td>
<td>9.7</td>
</tr>
<tr>
<td>Intrinsic (%)</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrinsic (cps/MBq)</td>
<td>40</td>
<td>144</td>
<td>122</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>1.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrinsic (cps/MBq)</td>
<td>40</td>
<td>290</td>
<td>112</td>
</tr>
<tr>
<td>Energy resolution</td>
<td>FWHM at 141 keV (%)</td>
<td>58</td>
<td>32</td>
</tr>
</tbody>
</table>

* CsI:Tl scintillator
* NaI:Tl scintillator
* CsI:Na scintillator
* CdZnTe semiconductor
* CfFe semiconductor

The intrinsic spatial resolution of the CGC compares favourably to most other systems. This is mainly due to the use of a CCD detector as opposed to PMTs – CCDs have naturally better resolution due to the smaller pixel size. A camera that uses a similar detection system, the UGC, reported an intrinsic resolution of approximately 50% of that found for the CGC (60 µm to 90 µm) despite having a similar design. However, the UGC resolution was measured at the crystal face, whereas the CGC resolution was measured with the camera assembled for clinical imaging and so approach to the crystal was limited to 7 mm. In practice, the intrinsic resolution of a detector is small compared to the system resolution and acts to reduce contrast in an image taken with a collimator in place. For values for resolution were present in literature, the value at the distance closest to 10 mm was chosen. Where multiple collimator values were found in the literature, the collimator that gave the best performance for the parameter in question was chosen.
this reason, a comparison of system spatial resolution provides a better indication of how a camera will behave in practice.

System spatial resolution also compared favourably to other systems, with a FWHM similar to the majority of SFOV systems. It is worth noting that this is the resolution at the non-magnifying point and that resolution will degrade at greater values. Resolution will also degrade with increasing distance for other systems; the POCI camera has a resolution varying from 3.2 mm FWHM at the collimator face to 7.5 mm through 50 mm of a scattering medium [8]. For comparison, the CGC has a calculated resolution of 6.4 mm through 50 mm of a scattering medium. The difference in proportional variation is simply due to the different behaviour of pinhole (CGC) and parallel hole (POCI) collimation. Some systems in Table 8.6 showed lower resolutions than the CGC with the lowest being 1.2 mm (although this was not recorded at the non-magnifying point of the pinhole). If the CGC is fitted with a 0.5 mm diameter pinhole collimator a resolution of 1.48 mm was found, which is more in line with this value.

From the measurements made it has been shown that the CGC detector has a spatial linearity well within the range expected for clinical systems. The CGC detector is significantly smaller than that of LFOV systems so it is to be expected that linearity measurements, particularly absolute linearity, are lower than these systems.

Integral uniformity for the CGC is higher than that of other cameras, with only one other camera being less uniform. Integral uniformity, however, is a less robust method of quantification than the coefficient of variation (1.58% for the CGC) which is the IPEM suggested parameter – it is excluded from Table 8.6 as it is not typically given for other systems. The SSGC does provide the coefficient of variation as its integral uniformity. The SSGC integral uniformity of 4.5% [62] is higher than that of the CGC. The comparatively high integral uniformity for the CGC in Table 8.6 is therefore more likely to be due to the method of calculation of integral uniformity, not the integral uniformity itself. The CGC has the lowest spatial uniformity when this parameter is measured by the spread of differential uniformity. Chapter 7 discusses the non-uniformity caused by the current CCD-scintillator coupling method; improved coupling techniques should be investigated for future iterations of the CGC.
At the time of writing, count rate capability of the CGC was a factor of 100 lower than other systems, although at this level of activity the full count rate capability of the detector has not been reached. It is expected that a camera with a larger detecting area will have a higher count rate capability. Considering count rate per detector area, the CGC would have a capability of $>1.9 \text{ kBq cm}^{-2}$, compared to the Solomobile, with a capability of $0.5 \text{ kBq cm}^{-2}$.

Count rate capability of the CGC is limited by the ability to resolve different light splashes on the detector. A similar set up was seen to saturate at approximately 3 events per frame. The current CGC runs at $10 \text{s}^{-1}$ (i.e. 30 resolvable events per second). A CCD of the same type has achieved a frame rate of $180 \text{s}^{-1}$ [165]. Were the CGC able to run at rates of even half this, it would be able to resolve approximately 270 events per second. Assuming the relationship of incident to observed counts remains consistent over this range, the CGC should be able to achieve count rate capabilities in the range of approximately 20 kBq. This is a factor that is expected to be improved upon in further iterations of the electronic systems used by the CGC.

The extrinsic sensitivity measured here compared poorly with other systems. As discussed in Chapter 6, system sensitivity is largely dependent on collimator design - the cameras tabulated in Table 8.6 use parallel hole collimators except in the case of the MediPROBE which uses a single pinhole collimator. However, theoretical calculations (and the performance of the MediPROBE system) indicate that the sensitivity of the CGC could be brought inline with other systems if intrinsic sensitivity was to be improved.

The energy resolution of the CGC was considered to be poor compared to the other cameras in Table 8.6. Theoretically, the energy resolution of a detector is limited by photoelectron statistics, themselves limited by the quantum efficiency of the detector, the energy conversion efficiency of the scintillator, and the light collection efficiency in the coupling between the scintillator and detector, along with impurities and imperfections in the scintillating crystal. Chapter 7 discusses improvements to CGC design that may bring energy resolution closer to its theoretical limit. Semiconductor detectors report energy resolutions of less than 10%; it is expected that these cameras will have a better
energy resolution than scintillator cameras due to the direct conversion of gamma energy to electronic signal [30].

8.9 Conclusion

The protocols described in this chapter were successful in translating LFOV standards to methods applicable to high resolution SFOV cameras. Application of these protocols allows for measurement of intrinsic and system spatial resolution, intrinsic and system sensitivity, spatial linearity, uniformity, count rate capability and energy resolution for high resolution systems where standard LFOV protocols are inappropriate. These protocols also suggest reporting parameters to encourage standardisation and allow for direct comparisons between SFOV systems.

SFOV cameras are often designed for specific purposes such as sentinel lymph node biopsy, parathyroid gland surgery and radioimmunoguided surgery [30]. In addition to the transfer of LFOV protocols described here, standardised tests should be established for the specific procedures where a SFOV camera may be used. Protocols designed to determine the suitability of a camera for intraoperative sentinel lymph node biopsy are currently in development.

The characterisation of the CGC undertaken in this thesis demonstrates that it has potential to provide high-resolution clinical images with an acceptable level of uniformity. These preliminary results show areas for improvement for future design iterations which, based on theoretical calculations, will bring the CGC in line with other systems in terms of sensitivity, count rate capability and energy resolution.
Chapter 9

HCGC and clinical tests

It is well established in medical imaging that hybrid systems combining different modalities can provide additional diagnostic information to clinicians and improve patient care. The popularity of hybrid imaging such as PET-CT and SPECT-CT has led to more recent developments such as PET-MRI [166]. In all these examples, nuclear techniques - which provide functional information - have been combined with techniques that provide detailed anatomical information which must otherwise be gathered by other means.

To provide anatomical context, an optical imaging component* has been combined with the CGC. With this adaptation, the hybrid CGC (HCGC) can image in both gamma and optical modalities with the optical image providing anatomical information. The development of the optical component is discussed in this chapter, and hybrid images are presented.

In Chapter 8 the performance of the CGC was shown to be comparable to other SFOV systems in development, a number of which have begun clinical and surgical evaluations [5, 162]. In this chapter, bench tests are described which aim to simulate specific clinical procedures and investigate the imaging performance of the HCGC. Images from

*Designed alongside Dave Bassford, Adam Bark, John Lees and others at the Bioimaging Unit, University of Leicester. The optical component discussed in this work is of a new configuration using a mirror. A different hybrid design, with an optical camera placed directly in front of the pinhole, has been previously investigated [167].
Figure 9.1: Schematic showing an optical mirror mounted in front of the pinhole collimator of the CGC. High energy gamma photons pass through the mirror while optical photons are reflected towards an optical camera.

A preliminary clinical evaluation of the HCGC, carried out at Queen’s Medical Centre, University of Nottingham, are also presented.

### 9.1 Hybrid compact gamma camera

A schematic of the HCGC design is shown in Figure 9.1. In the HCGC, a small mirror is placed at an angle of 45° in front of the pinhole of the CGC collimator.

Photons incident on the camera from a radioisotope source will include gamma photons, emitted from decay within the source, and optical photons from ambient light. The gamma photons will pass directly through the mirror (with a small amount of attenuation,
discussed below) and are imaged just as in the standard CGC. Optical photons do not have enough energy to pass through the mirror and so will be reflected towards an optical camera mounted off-axis. Both optical and gamma photons can thus be imaged simultaneously. If the correct camera positions are used, the FOV of each detector will also be identical, independent of the source distance (the alignment process is discussed in Section 9.1.2).

Figure 9.2 shows the prototype HCGC. For testing, an optical rig was designed that slots over the existing CGC body. The mirror and the optical camera (in this case a webcam) can both be seen. The prototype rig was designed to be flexible and the position of both the mirror and the camera is easily adjustable. The optical mechanism added bulk to the prototype with the mirror and optical camera having larger dimensions than would be used in a clinical model. Throughout this chapter, this design has been used as a proof of concept of the HCGC.

Figure 9.2: Prototype HCGC comprising an optical rig fitted over the CGC. The optical camera is mounted to the left with the mirror centred above the pinhole of the collimator. The position of both components can be adjusted independently.

9.1.1 Effect on CGC performance

Placing material between a source and the collimator of the CGC, in this case a mirror, would be expected to degrade gamma camera performance. The mirror was made from soda lime glass and was 3 mm thick. For gamma rays perpendicular to the collimator face, the distance travelled through the glass would be 4.24 mm. Figure 9.3 shows the theoretical transmission of gamma photons through the mirror for perpendicular gamma rays over a range of energies. Transmission is also shown for a 1 mm thick mirror (distance travelled of 1.41 mm) as these are readily available and would be expected to transmit a higher proportion of photons.
At 141 keV, transmission is approximately 0.86 and so a sensitivity loss of approximately 14% is expected. In practice, the incident angle of the gamma rays means that some will travel through more than 4.24 mm of glass and some through less. A $^{99m}$Tc source was imaged with the HCGC, both with and without the mirror positioned in front of the pinhole. The sensitivity loss when the mirror was in place was found to be $(10.4 \pm 0.4)\%$ within a central region of interest (ROI). This is slightly lower than the theoretical sensitivity loss; a number of the photons not considered to be transmitted theoretically are likely (due to the low Z of the glass components) to have been Compton scattered and, as no energy windowing was used for the CGC, some of these will have been recorded. Scattered photons (those outside the ROI) increased by $(12 \pm 10)\%$ with the mirror in place which is consistent with this explanation, although the low count level means this result is not conclusive. A 1 mm thick mirror has a theoretical absorption of 5% and so would be a more appropriate component for future cameras.
9.1.2 Scale factor

The accuracy of alignment between the two imaging modalities is dependent on the arrangement of the mirror and optical camera in relation to the pinhole collimator. The magnification of the image seen by the optical camera is dependent on the distances from the source to the camera lens and the lens to the camera. Similarly, the magnification of the gamma camera is dependent on the distances from the source to the pinhole and the pinhole to the detector. For the modalities to be coaligned at any source distance, the ratio between their magnifications must be independent of source distance.

The magnification $M_g$ of the pinhole gamma camera is $M_g = \frac{t}{h}$ (Equation 3.1), where $t$ is the collimator-detector distance and $h$ is the source-collimator distance. The magnification of a camera with a lens $M_o$, such as the optical camera used here, is

$$M_o = \frac{-f}{f-s}, \quad (9.1)$$

where $f$ is the focal length of the lens used and $s$ is the distance between the source and the lens. The scale factor $F$ between the images is

$$F = \frac{p_g M_o}{p_o M_g}, \quad (9.2)$$

where $p_g$ and $p_o$ are the pixel sizes of the gamma and optical detectors respectively. For automatic image alignment $F$ must be independent of source distance $h$. As $M_g \propto \frac{1}{h}$, this requires $s = h + f$ which will result in $M_o \propto \frac{1}{h}$ and so a constant $F$.

9.1.3 Method for alignment of modalities

The mirror should be positioned so that a point directly above the pinhole of the collimator is aligned with the centre of the optical camera. This would be possible through accurate measurement but is easiest to achieve with a laser pointer. Initially, the laser pointer is directed into the pinhole of the collimator. The optical mount can then be attached to the camera and the mirror adjusted until the reflected laser point is centred on the optical image.
Chapter 9. *Hybrid and clinical imaging*

**Figure 9.4:** Example of alignment testing. Optical image (left) and gamma image (centre) of hot spot phantom with centre and second diagonal 2 mm holes filled with $^{99m}$Tc. Filled wells are marked with red crosses. Combined image (right) uses the mean scale factor from each pair of hot spots to correctly match image size. Camera configuration A was used.

detector. Small translational misalignments can be corrected during image processing, after calibration using a phantom such as that shown in Figure 9.4. If the required shifts are large it is more appropriate to return to the initial alignment stage.

An accurate measurement of the distance between the optical camera and the mirror is difficult to achieve as it is dependent on the exact position of the lens within the camera casing. The process described here allows for correct camera positioning relative to an arbitrary initial position.

A phantom consisting of a series of small spots of activity (see Figure 9.4) was imaged with both the gamma and optical cameras. These images were overlaid, and the size and position of the gamma image were adjusted by inspection to provide the best match to the optical image. The scale factors found for different source distances are shown in Figure 9.5. Errors in scale factor are significant, particularly at large distances where the resolution of the gamma camera has degraded.

The distance $s$ has been chosen to be defined as $h + \delta$, where $\delta$ is an unknown displacement which may be positive or negative. The red dashed line in Figure 9.5 shows a fit of Equation 9.2 to the data presented. For the optical camera used in this example, $p_o = 6 \mu m$ and $f = 3.5 \text{ mm}$. The resulting fit gives $\delta = -10.3 \pm 0.2 \text{ mm}$.

For $F$ to be independent of $h$, $s = h + f$ and therefore this requires $\delta = f$. An adjustment from $\delta = -10.3 \text{ mm}$ to $\delta = f = 3.5 \text{ mm}$, requires the optical camera to be be moved
Figure 9.5: Scale factor required to align gamma and optical images with an arbitrarily positioned optical camera for a range of phantom-collimator distances (points). The red dashed line shows a fit of theoretical scale factor (Equation 9.2) to the data ($R^2 = 0.945$). Camera configuration A was used.

approximately 13 mm further away from the mirror from its initial arbitrary position for coalignment independent of source distance. The scale factor required to align images may then be calculated from Equation 9.1 and Equation 9.2, $F \approx 3.7$ for the example discussed here.

Once calibration is complete, Equation 9.2 provides a robust measure of the required scale factor. This is demonstrated by Figure 9.6 where the gamma image is aligned with the known source of activity at distances varying from 2.5 cm to 2.5 m - which is far beyond the distance range required for clinical use.
9.1.4 Image fusion

The introduction of a second modality introduces challenges for image display. Images from each modality may be displayed individually (as in the first two images of Figure 9.4) but for the full benefit of hybrid imaging they should be combined (as in the final image of Figure 9.4). When combining the images, the loss of detail from either modality should be minimised while maximising contrast between the imaging types so that the contribution of each is clear.

A large number of fusion methods can be applied to combine images such as these, examples include Brovey transform, high-pass filtering and principal component analysis [169]. Figure 9.7 shows examples of four common techniques for image combination, chosen as they require minimal processing, applied to a co-aligned image from the HCGC. The same colour table has been used in each case. A background with bright and dark areas, including a bright light source, was chosen as an extreme form of some of the common challenges that might occur clinically. Each combination technique relies on comparing the pixel values between each image, and using the results of this comparison to produce a new image. These techniques are described in more detail below;
Chapter 9. *Hybrid and clinical imaging*

**Figure 9.7**: Hybrid image of a cross phantom comprising multiple wells of 2 mm diameter filled with $^{99m}$Tc. The phantom had a total activity of 50 MBq and was imaged for 100 s at a distance of 150 mm from the HCGC. The presence of a bright light source can overwhelm gamma data in the combined image. Camera configuration A was used.

**Pixel addition** For each pixel, channel values for each image are summed to produce the combined image. As both images are in colour, this is performed for the red, green and blue channels of each image independently.

**Hue and saturation replacement** Images may be described by their red, green and blue channel values (RGB method) or, alternatively, by their intensity, hue and saturation (IHS method). The values of $I, H$ and $S$ in terms of the channel values $R, G$ and $B$...
(normalised between 0 and 1) are given by [170]

\[ I = R + G + B, \]  \hspace{1cm} (9.3a)

\[ H = \frac{G - B}{I - 3B}, \]  \hspace{1cm} (9.3b)

\[ S = \frac{I - 3B}{I}. \]  \hspace{1cm} (9.3c)

The intensity of an image indicates how light or dark it is, with a high \( I \) giving a light pixel. Hue determines the colour of the image and saturation the vibrancy or brightness of these colours. When using this method, the final image was constructed from the intensity of the optical image - essentially converting it to greyscale. The hue and saturation of the final image were then the hue and saturation of the gamma image - essentially meaning that colour was taken from the gamma image. This IHS image was converted back to RGB for display.

**Pixel replacement** For each pixel, channel values for each image are compared. The final image is constructed from the highest channel value in each pixel. As both images are in colour, this is performed for the red, green and blue channels of each image independently.

**Pixel difference** For each pixel, channel values in the gamma image are subtracted from those in the optical image. The difference in channel values is used to create the final image. As both images are in colour, this is performed for the red, green and blue channels of each image independently.

From Figure 9.7, it can be seen that very bright regions in the optical image can overwhelm gamma data in the combined image. Gamma information can only be clearly seen in the brightest region for the pixel difference method of image combination, although this method does not provide as accurate a depiction of the gamma information as do alternative methods. In particular, the darker regions of the optical image act to increase the apparent activity in these regions. Hue and saturation replacement provides the clearest contrast between gamma and optical information; this method would also
be suitable for use with a wider array of colour tables as similarities between colours in optical and gamma images do not create a problem. However, the desaturation of the optical image would not be ideal in situations where this could provide additional information, such as when using blue dye in sentinel lymph node biopsy. Pixel addition and pixel replacement methods show fairly similar results, with the gamma image clearer in pixel addition and the optical image slightly clearer in pixel replacement.

For the rest of this chapter, the pixel addition method of image combination has been used. Future clinical trials will determine the ideal method for future use.

### 9.2 Clinical simulations

The tests outlined in Chapter 8 provide a good indication of camera performance and allow for comparisons with other devices. However, how the parameters from Chapter 8 will effect camera performance for specific tasks is not necessarily intuitive. To investigate camera performance in a way that is directly relevant to clinical work, a number of phantom studies were performed.

#### 9.2.1 Detectability of image features

Whether a particular structure is visible in an image is relatively subjective and will depend strongly on the observer and the display conditions. Detectability is a quantitative measure, related to visibility, which relates the number of counts within a particular structure or ROI and the number of counts in the area surrounding this ROI. Detectability can be used as a comparative measure between different images and image features, but a single calculated detectability is not indicative of whether a particular feature will be identifiable in an image.

A number of parameters are used as measures of detectability. Fractional contrast is defined as

\[ FC = \frac{M_{ROI}}{M_{background}}, \]  

(9.4)
where $M$ is the mean counts per pixel in the specified region. Contrast is defined as

$$C = \frac{M_{ROI} - M_{background}}{M_{background}}.$$  \hspace{1cm} (9.5)

For comparison between hot and cold spots, the numerator in Equation 9.5 is reversed for cold spots [171]. These measures can be applied either using known activity in the source (subject contrast) or the counts recorded in each pixel (image contrast).

Signal to noise ratio (SNR) is defined as

$$\text{SNR} = \frac{(M_{ROI} - M_{background}) A_{ROI}}{\sigma_{background} \sqrt{A_{ROI}}},$$  \hspace{1cm} (9.6)

where $A$ denotes an area and $\sigma$ standard deviation [1]. This measure takes into account the effect of noise on detectability in addition to the contrast between ROI and background counts. To determine whether a feature is detectable, a threshold in SNR is used. Typically this SNR threshold, as defined by Rose [172], is taken to be 5 although this comes with a number of caveats as the Rose criterion is strongly dependent on the size of the image and the size of the lesion (or test element) being investigated. Rose calculates this threshold by choosing a value for which the expected number of false positives in the image falls below one. For a general case, the SNR threshold can be given as [172]

$$k = \sqrt{-2 \ln \left(\frac{\sqrt{2\pi} N_{ROI}}{N_{pix}}\right)},$$  \hspace{1cm} (9.7)

where $N_{pix}$ and $N_{ROI}$ are the number of pixels in the image and ROI respectively. Equation 9.7 is derived from the expected probability distribution of noise and takes into account that a large structure can have a lower SNR to be visible when compared to a small structure (which is more likely to have arisen from random noise fluctuations in the background) [172]. If an feature has a SNR higher than the threshold $k$, the ROI in question can be said to be detectable by this measure.

When calculating contrasts and SNRs, the positioning of the lesion ROI and background ROI can have a significant impact on the results. For consistency, these regions were
always defined in the following manner in this work. The size of the lesion ROI was determined by the expected size of the object, with theoretical magnification and resolution taken into account. These lesion ROIs were always circular, and were aligned with the centre of the lesion by inspection. Where the phantom and camera placement was not varied between images, lesion ROI positions were kept constant.

The background of a lesion ROI was taken to be a ring centred over the ROI with the two areas separated by half the lesion ROI radius. The area of the background ROI was chosen to be approximately three times the area of the lesion ROI - this was to allow for representative background calculations for even the smallest lesion ROIs and was small enough that background ROIs never extended beyond the phantom boundaries.

### 9.2.2 Thyroid simulation

The thyroid is a superficial gland positioned in the neck. Gamma imaging is often used to investigate thyroid function as anatomical features such as size are not always a good indication of thyroid function. Imaging is typically performed using $^{123}$I-sodium iodide (gamma emission energy of 159 keV) or $^{99m}$Tc-pertechnate. For radiotherapy and metastatic imaging, $^{131}$I (gamma emission energy of 364 keV) is also used [173]. A large number of thyroid conditions can be investigated through gamma imaging; in general clinicians are looking for regions of unusually high or low radioisotope uptake.

A thyroid phantom, described in more detail below, was used to investigate the ability of the HCGC to successfully perform thyroid imaging. In addition, results from this phantom were used to investigate signal-to-noise ratio in the presence of background activity and the effects of image smoothing on detectability.

#### 9.2.2.1 Phantom specification

The Picker thyroid phantom (Figure 9.8) is widely available in nuclear medicine departments and allows direct comparisons to be made with previously published studies. This phantom contains a number of structures which simulate features that may be seen
in clinical images including uneven uptake in each side (lobe) of the thyroid and both hot (high activity) and cold (low activity) areas (known as nodes). In the phantom, the left hand ‘hot’ lobe has a depth of 18.4 mm, the right hand ‘cold’ lobe has a depth of 9.6 mm. Within these lobes are three cold nodes with no activity present ranging in size from 12 mm to 6 mm diameter. There is also a hot node, 12 mm in diameter, which has a depth of 18.4 mm in the cold lobe. The size of the entire phantom is approximately 60 mm × 60 mm, roughly 50% larger than a typical patient thyroid, with a fillable volume of 35 ml.

Typically, a $^{99m}$Tc thyroid scan will require administration of 185 MBq to 370 MBq of activity with expected uptake of 1% to 5% [173]. This gives expected thyroid activity ranging from 1.85 MBq to 18.5 MBq. Planar imaging is usually undertaken, taking about 5 min per view [173].

### 9.2.2.2 Image smoothing and detectability

Figure 9.9 shows a single image of the thyroid phantom displayed using three different methods. In all cases the blob detection algorithm was applied. Figure 9.9a shows a
Figure 9.9: Image of thyroid phantom with activity of 300 MBq at a distance of 100 mm from the HCGC (with a 0.5 mm pinhole collimator) using three different display methods. a. Centre point image, b. Centre point image with a 2 pixel radius Gaussian filter applied, c. Cumulative image. Camera configuration A was used.

centre point reconstructed image, Figure 9.9b the same centre point image with a 2 pixel radius Gaussian filter applied and Figure 9.9c the cumulative reconstructed image (see Appendix A for more details about this process).

Although the raw data for each image is identical, features in the processed images have different levels of detectability. This has been tabulated for the 12 mm hot node (which has a subject fractional contrast of 2 and a subject contrast of 1) in Table 9.1. In all images, the SNR is significantly higher than the required threshold from Equation 9.7 of $k \approx 3$. In practice, the colour table would be adjusted to provide a better visibility than is seen in Figure 9.9.

<table>
<thead>
<tr>
<th>Image</th>
<th>Fractional Contrast</th>
<th>Contrast</th>
<th>SNR</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>1.2897</td>
<td>0.2897</td>
<td>14.63</td>
</tr>
<tr>
<td>b</td>
<td>1.2476</td>
<td>0.2476</td>
<td>32.00</td>
</tr>
<tr>
<td>c</td>
<td>1.3505</td>
<td>0.3505</td>
<td>28.45</td>
</tr>
</tbody>
</table>

Table 9.1: Detectability measurements for 12 mm hot node for images in Figure 9.9.

Both contrast and SNR are significantly higher in the unprocessed cumulative image (Figure 9.9c) compared to the unprocessed centre point image (Figure 9.9a). Smoothing the centre point image reduced contrast but significantly increased SNR due to the reduction in random noise fluctuations. This increased SNR, however, will vary
depending on the size of the smoothing filter applied and will come at the expense of spatial resolution.

To investigate the effects of smoothing on image quality, Gaussian filters of varying widths were applied to the image shown in Figure 9.9a. The SNR of each node was calculated, with the ROI size and position determined from the image with no blurring. These are compared in Figure 9.10.

The SNR threshold described by Equation 9.7 was exceeded for all nodes, even when no blurring was applied. This would suggest that even the 6 mm cold node was detectable in all images - although subjectively this does not appear to be the case in Figure 9.9a. Exceeding the SNR threshold shows that the image feature is statistically likely to be real rather than due to random noise fluctuations however it does not necessarily mean that this feature will appear visible to an operator.
Of all the nodes, the 12 mm cold node had the highest SNR, which was expected as it had a higher subject contrast than the 12 mm hot node which provides the closest comparison. This was true except for those images with a filter width of less than 1 applied - in these cases variation in background noise was more significant and this was higher in the hot lobe (which contained the 12 mm cold node) than the cold lobe (which contained the 12 mm hot node). All data follow a similar pattern, with an initial increase in SNR for increasing filter widths, a peak SNR and then a more gradual decline. The position of the peak varied between each node and appears to be a function of both lesion size and subject contrast.

Although smoothing improves image quality in terms of SNR it will also degrade image quality in terms of spatial resolution. To investigate this, the node profiles were considered approximately Gaussian, a reasonable assumption for large source-camera distance $h$. The convolution of two Gaussian functions will also be Gaussian with standard deviation $\sigma = \sqrt{\sigma_1^2 + \sigma_2^2}$, where $\sigma_1$ and $\sigma_2$ are the standard deviations of the component Gaussians. This may be used to calculate the change in FWHM of a node when a given Gaussian blur is applied.

For a filter width of 1.5 pixels - which showed the best collective response in Figure 9.10 - this would cause a change in FWHM of $\sim 2\%$ for a 12 mm diameter lesion, $\sim 3\%$ for a 9 mm diameter lesion and $\sim 7\%$ for a 6 mm diameter lesion when imaged from this distance. As this is an upper limit for expected image distance, this suggests that the benefit that a smoothing filter of width 1.5 pixels has for SNR outweighs the negative effect it has on resolution for lesions of this size. For smaller lesions, or greater imaging distances, the ideal filter width will be reduced.

A large number of image processing techniques have been developed for medical imaging (including interpolation techniques and PSF deconvolution [174–176]) and the appropriate smoothing for HCGC images will likely vary depending on the organ and radiopharmaceutical used and according to operator preferences. These methods will be determined in collaboration with clinical and technical staff during the planned clinical evaluation.
9.2.2.3 Acquisition time and detectability

From Equation 9.6, it is expected that SNR will be proportional to the root of the total signal (as statistically $\sigma = \sqrt{M}$). As photon statistics improve, relative noise is decreased leading to an improvement in SNR. As such, SNR was expected to be dependent on any factor that acts to vary photon counts, including source activity, camera sensitivity and imaging time. As imaging time is a trivial parameter to vary, the dependence upon this parameter was investigated.

The thyroid phantom was filled with an activity of $\sim 15$ MBq of $^{99m}$Tc solution, within the typical uptake range for a thyroid undergoing clinical imaging. The phantom was imaged over $10^5$ frames, resulting in a total imaging time of approximately 3 h. Images were analysed in cumulative increments of 2000 frames (200 s) in each case the mean counts in the image and the SNR of each node were calculated. A selection of images taken over this period are shown in Figure 9.11 with SNR results shown in Figure 9.12.

In this test, the 12 mm cold node no longer showed the highest SNR but was exceeded by that of the 12 mm hot node. This node was in the lower activity lobe which suggests that, at low counts, background levels are more significant - a result which is implied by Equation 9.6.

With this lower level of activity, counts were reduced and SNRs are considerably smaller than those in Figure 9.10. This was true even when the mean counts in the image exceeded those in results from the previous section. This indicates that image quality cannot be determined from count rates alone. The proposed model of $\text{SNR} \propto \sqrt{M}$ from
Equation 9.6 does not provide a good fit to this data. The fitted model either strongly overestimates (for high counts if low count values are used for fitting) or underestimates (vice versa) SNR. This effect is likely to be due to the decay of the phantom activity over the imaging time (expected to be $\approx 30\%$) and so background counts would be expected to increase relative to signal counts over this time period. This would be particularly significant for the 6\,mm cold node the SNR of which was seen to decline for long acquisition times.

### 9.2.2.4 Comparison to LFOV systems

Seret [177] performed a contrast study on 52 camera heads, from commercially available conventional LFOV cameras, using the Picker thyroid phantom. The phantom was filled with $74 \pm 12$ MBq of $^{99m}$Tc solution and imaged at a source-camera distance of 100\,mm from the camera heads. Contrast, as defined in Equation 9.5, was calculated for individual nodes in the phantom. The images had a stop condition of $10^6$ counts over $256 \times 256$ pixels, with the required imaging time ranging from 8 min to 20 min.
Attempts were made to recreate this methodology for the HCGC. The Picker phantom was filled with 300 MBq of $^{99m}$Tc and imaged from 100 mm. An acquisition time of approximately 30 min resulted in an image with $2.4 \times 10^5$ counts; this is lower than the accumulated counts used by Seret due to the lower sensitivity of the HCGC. Contrast values, which do not take into account variation in background, are not expected to be related to the total number of counts in the same way as SNR although a higher background level relative to signal would have an effect. Seret also acquired images of $2.5 \times 10^5$ counts and found the results of these did not differ significantly from longer accumulations. Seret used energy windows of 15-20% whereas no windowing was used for the HCGC data, this would be expected to degrade rather than enhance the contrast in HCGC images.

To ensure a direct comparison, the method of analysis was kept as similar as possible; Seret used ROI diameters of 12 pixels for the background, 8 pixels for the 12 mm nodes and 6 pixels for the 9 mm node. From the pixel sizes given [177], this indicates ROIs of 10.2 mm, 6.8 mm and 5.1 mm respectively. Taking the magnification of the HCGC into account, ROIs of the same size can be achieved using diameters of 19, 11 and 8 pixels respectively. In addition to these, the 6 mm node was included in the HCGC analysis with a ROI diameter of 6 pixels. The background ROIs were positioned in the middle of each lobe, avoiding any hot or cold nodes. The ratio between the counts in each lobe was also calculated.

Table 9.2 shows contrast values for each node in the phantom alongside the mean and range of values found in Seret’s study. These take into account results from both high-resolution and ultra-high-resolution collimators used by Seret covering 30 repeats in total. A blurring filter was not applied before analysing contrast. The significant levels of error are due to the nature of the calculation and are indicative of the poorer photon statistics when compared to Seret’s measurements.

Contrasts recorded for the HCGC and conventional LFOV cameras are broadly similar. The lobe ratio and 12 mm cold node contrast are lower than those from the conventional cameras, while the 12 mm hot node contrast is within the range recorded by Seret but lower than the mean contrast for LFOV systems. The 9 mm cold node contrast is almost
identical to the LFOV mean. That the 9 mm cold node contrast showed the closest approach to LFOV values suggests that the resolution of the HCGC (≈5.5 mm compared to ≈7 mm) increases the contrast for smaller nodes.

In all of the cameras tested, Seret found that the 12 mm cold node had a higher contrast than the 12 mm hot node - which was also true of the subject contrast. This was not the case for HCGC results, indicating that there was a higher background count level than in a conventional camera - the most likely cause of which is the lack of energy windowing for HCGC results. Removal of a mean background value, taken in the central region of the phantom between the two lobes, results an increase in all contrast values - by 22% for nodes in the hot lobe and by 43% for nodes in the cold lobe - so this is a significant effect. The impact of energy windowing should be investigated for further iterations of the HCGC acquisition software.

### 9.2.3 Sentinel lymph node simulation

One of the main applications of the HCGC is for use in intraoperative sentinel lymph node localisation. For this procedure a $^{99m}$Tc nanocolloid solution, sometimes supplemented with a blue dye, is injected in the region of a tumour. This colloid drains via the lymphatic system and becomes trapped in the first lymph node or nodes draining the tumour - the sentinel lymph nodes – enabling localisation of the lymph node for biopsy. The ability to detect all sentinel nodes is essential for sentinel lymph node imaging. Small, low activity nodes must be distinguishable from the high level of background activity from the injection site where a large amount of activity will remain. This section describes
FIGURE 9.13: Main: Schematic of lymph node phantom with wells shaded grey. Each well has a depth of 6 mm in 8 mm thick Perspex. Concentric circles show 10 mm steps from the centre of the central well. Inset: Model of lymph node phantom. Not shown is a 4.5 mm thick Perspex cap which is attached to the top of the phantom, sealing it.

preliminary phantom testing to investigate the suitability of the HCGC for sentinel lymph node imaging.

9.2.3.1 Phantom specification

The lymph node phantom was designed to investigate the specific case where a sentinel node is very close to the injection site. This is of interest as this is one of the scenarios where non-imaging gamma probes are known to have difficulty detecting nodes.

The phantom (Figure 9.13) consists of a series of wells drilled to a depth of 6 mm in 8 mm thick Perspex. The well diameters range from 8 mm, for the central well, and then decrease in increments of 1 mm down to a 1 mm diameter. The central well is used to simulate the injection site, with smaller wells used to simulate sentinel nodes. The
arrangement is such that wells of each size are positioned in 10 mm increments (centre to centre) at 10 mm to 50 mm from the central well. The flexibility of the phantom comes from filling only certain wells for each test. The phantom also has an optional flood source positioned below all the wells, for simulation of background activity in the tissue, and can be sealed with a 4.5 mm thick Perspex cap.

9.2.3.2 Lesion depth and detectability

The lymph node phantom was used to investigate the effect of depth of scattering material on detectability. In practice, the HCGC will be placed as close to the patient as possible – the distance to the source will then effectively also be the thickness of scattering tissue. The 8 mm diameter central well was filled with \( \sim 32 \) MBq of \(^{99m}\)Tc and the innermost 2 mm diameter well with \( \sim 2 \) MBq. This gave an activity ratio of approximately 1:16 - this is at the lower end of ratios that are expected to occur in surgical practice [126].

The centre to centre distance of the wells was 10 mm. Images of 2000 frames (200 s acquisition) were taken. In all cases, the 0.5 mm diameter pinhole was used.

The phantom was imaged through Perspex depths ranging from 4.5 mm to 100 mm; with the camera positioned at a distance of 13 mm from the Perspex used. The distances shown in figures in this section are the total source–camera distance. For this test, the movement of the camera (along with the varying magnification at different distances due to the pinhole) meant that a new ROI was required for each image. This was fitted by inspection to each hot spot, with the background defined as described in Section 9.2.1. For images at larger distances \( (h > 70 \text{ mm}) \), the two spots became difficult to resolve and background regions overlapped with the ROIs of the spots themselves – this is expected for a simulation of very closely spaced sources.

Figure 9.14 shows SNR results for both wells as a function of phantom depth. As would be expected, the 8 mm diameter source had a far higher SNR than the 2 mm diameter source and was easily detectable at depths of 100 mm. For the 2 mm diameter source, measurements were only possible up to \( \sim 80 \text{ mm} \) total distance. Past this point, the sentinel node was not resolved from the larger injection site. The 2 mm diameter source was detectable, based on Rose’s criterion (Equation 9.7), to a depth of 65 mm.
In both cases the root of expected signal - based on the attenuation due to depth of Perspex and the geometric sensitivity at each distance - has been calculated. This was fitted to SNR for both sources ($R^2 = 0.969$ for the 8 mm diameter source and $R^2 = 0.833$ for the 2 mm diameter source). This is a better fit to the $\sqrt{M}$ relationship than was seen in Section 9.2.2.3. This may indicate that this model is only applicable for large SNRs - note that the lower SNRs in the 2 mm diameter source data appear to be deviating from the model in the same way as described in Section 9.2.2.3, though the large scatter in data points means this is not conclusive.

### 9.2.3.3 Lesion separation and detectability

The simulated injection site and sentinel node used in Section 9.2.3.2 were separated by a centre-to-centre distance of 10 mm, or an edge-to-edge separation of 5 mm. The resolution of the HCGC system used for these tests, as a function of scattering medium depth, has previously been investigated [158] and the relationship found to be

$$\text{FWHM} = 0.0432x + 0.727,$$  \hspace{1cm} (9.8)
where $x$ is the source-camera distance through scattering material. From the same data, the FWTM of a line source was found to be

$$\text{FWTM} = 0.0819x + 1.300. \quad (9.9)$$

From this, it would be expected that the FWHM limit of resolution for a 10 mm separation would occur at $x = 98.9$ mm and the FWTM limit at $x = 45.2$ mm. In Section 9.2.3.2, the 2 mm diameter sentinel node became unresolvable before the FWHM limit was reached but somewhat after the FWTM limit. Mean pixel counts in the injection site ROI remained consistently five times higher than that of the sentinel node ROI, suggesting that the FWTM intensity of the injection site will have a similar magnitude to the FWHM intensity of the sentinel node. From the known camera spatial resolutions, this overlap will occur at approximately 64 mm distance – very similar to the cut-off value of 65 mm found in Section 9.2.3.2. This suggests that resolvability limits can be calculated directly for any separation and activity ratio as long as the appropriate resolution measurements are available. Further tests over a greater range of separation and activity ratios are required to verify this result.

The detectability of deep-seated nodes and those close to the injection site will be a limiting factor for intraoperative gamma cameras. This result suggests that, although sensitivity is an important parameter to optimise, improvements in resolution will also enhance the detectability of these nodes which are difficult to locate with traditional gamma probes.

### 9.3 Patient images

Ethical approval was granted for clinical evaluation of the HCGC in the Nuclear Medicine Clinic at Queen’s Medical Centre. For this evaluation, patient diagnosis and radioisotope administration were not affected. Patients undergoing a nuclear imaging procedure were asked if they would like to take part in the evaluation. If formal consent was obtained, HCGC images were taken at times which would not interfere with conventional imaging.
9.3.1 Thyroid scan

Figure 9.15 shows patient thyroid scan images taken with the HCGC and a conventional LFOV gamma camera. For this test, 80 MBq $^{99m}$Tc was administered to the patient. The LFOV image shown was accumulated over 300 s. From the LFOV image, it was estimated that uptake within the thyroid was $\sim 2\%$ (1.6 MBq). HCGC images were accumulated for 2000 frames (around 200 s), and the 1.0 mm diameter pinhole collimator was used. Cumulative reconstructed images are shown.

These figures show that the low sensitivity of the 1.0 mm pinhole collimator means that a longer acquisition time would be required to match the quality of the image from the LFOV camera. Despite the low count rates, the HCGC was able to match areas of higher activity with the expected location of this activity in the optical image.

9.3.2 Lacrimal drainage

A nuclear lacrimal drainage scan is a non-invasive study that uses a low radiation dose introduced to the eye to assess the performance of the nasolacrimal drainage system. This procedure can be important for pre-operative planning, to determine the position of an obstruction, and post-operatively for surgical evaluation.

Figure 9.16 compares a HCGC and a conventional LFOV image of a patient undergoing a lacrimal drainage investigation. 1 MBq of $^{99m}$Tc nanocolloid was introduced to each eye. The patient was first imaged with the conventional gamma camera with an acquisition
time of 200 s; HCGC images were taken approximately 1 h later after all standard tests had been completed. Due to this time difference, it is not expected for drainage patterns to be identical between the images as further draining will have occurred and the administered activity will have decayed to some extent. HCGC images were accumulated over 2000 frames (around 200 s), and the 0.5 mm diameter pinhole collimator was used. Cumulative reconstructed images are shown.

There was good registration between the gamma and optical images which provide anatomical context not available in the LFOV images. There was also good agreement between the conventional gamma camera and the HCGC, with the patient’s right eye showing better drainage when compared to the left.

Despite having a lower activity in the regions imaged than in the thyroid scan described above, and being taken at a similar distance, these images are higher quality than for the thyroid scan - likely because background activity was minimal and the structure imaged was less diffuse.

A second patient, undergoing an identical procedure, was also imaged with the HCGC. In this case, the HCGC was fitted with the 1.0 mm diameter pinhole collimator and the left and right eyes were imaged separately to allow the HCGC to be brought closer to the patient. Each image was taken over 3000 frames (around 5 minutes). In addition, the gamma component of the images displayed in Figure 9.17 were reconstructed using
the centre point technique, with a Gaussian smoothing filter with width 1.5 pixels applied (shown to give the best detectability for the phantom study in Section 9.2.2.2).

These images appear visually to be of higher quality than those in Figure 9.16, predominantly due to the larger number of counts accumulated. This test also demonstrated an additional benefit of hybrid imaging: during the course of image acquisition the patient often shifted in position, with only gamma images available this shift would be impossible to rectify without optical context. By comparing optical images taken at the start and the end of the acquisition period, it was possible to determine the extent of patient motions. In some case, images could be rejected due to large patient motion visible in the optical images. In the future, this effect could be used to allow real time motion correction of gamma images using the optical information.

9.4 Conclusion and recommendations

The HCGC is an adaptation of the CGC that allows for coaligned hybrid optical/gamma imaging. Through calibration, the optical camera may be positioned in such a way that the gamma and optical data show good registration across a wide range of imaging distances. The HCGC system allows for gamma and optical images to be fused and displayed simultaneously, providing additional anatomical information when compared to a conventional LFOV gamma camera. A fully functioning prototype HCGC has been constructed and used for preliminary clinical evaluation and in bench tests to determine its suitability for both thyroid and lymph node imaging.
The introduction of a 3 mm thick mirror reduces the sensitivity of the CGC by around 13% in the current prototype. This is significant for the performance of the HCGC, particularly as sensitivity is the area in which there must be the most improvement for intraoperative imaging. The sensitivity loss could be reduced to 4% if a 1 mm thick mirror was used. As thin a mirror as possible should be used in future designs.

For the HCGC to be used intraoperatively, a number of currently post-processed steps - such as hot pixel removal and blob detection - must be applied in real time. While these processes have been established and tested with the current system, the acquisition software should be adapted to include them. In addition, the ideal display method for fused images and the appropriateness of image smoothing are yet to be determined. Final decisions on these points should be made after discussion with end-users such as surgeons and clinicians.

A thyroid phantom was used to investigate the effect of image smoothing and acquisition time on SNR. A lymph node phantom was used to investigate the effects of lesion depth on SNR. The combined results suggest that SNR is proportional to the root of the number of counts in an image, but that this relationship does not hold for small SNRs ($< 100$). Contrasts from thyroid studies were shown to be similar, although slightly lower, to results from conventional LFOV cameras. This comparison suggests that energy windowing is an important factor in detectability and should be developed for the HCGC.

Initial tests with a sentinel lymph node phantom have shown that a node is detectable at a tissue depths of $>50$ mm with a node-injection site separation of 10 mm and node-injection site activity ratio of 1:16. These results are consistent with theoretical detectabilities based on camera spatial resolution. This testing should be continued prior to clinical evaluation of the HCGC for sentinel lymph node imaging (scheduled for 2015). A number of adaptations to the test described should be investigated, including using larger activity ratios, background activity and superficial injection sites with sentinel nodes at depth. Testing should be carried out with the 1.0 mm pinhole collimator as discussed in Chapter 6.

A small number of patient images have been acquired with the HCGC prototype. These show the that the hybrid system can provide both functional and anatomical imaging.
Images were taken during lacrimal drainage and thyroid imaging procedures. The thyroid imaging was less successful due to the diffuse nature of the source and the large level of background activity - higher sensitivity collimation should be used with future images to overcome this. For lacrimal drainage imaging, the HCGC was able to successfully image low levels of activity in a clinical setting. The optical component was particularly useful for this test, as it allowed the matching of areas of activity with anatomical landmarks. In addition, the optical images could be used to determine the extent of patient motion. The possibility of using this to correct for either patient or operator motion should be investigated further.

Clinical evaluation is ongoing. In addition to thyroid and lacrimal drainage scans, it is hoped that the HCGC will be tested with a range of procedures including bone scans and lymphatic drainage studies. Intraoperative evaluation is currently undergoing ethical approval and a HCGC unit appropriate for intraoperative use is now in development.
Chapter 10

Summary, conclusions and future work

The CGC has been developed to provide portable, high-resolution gamma imaging for medical applications. In this thesis, the suitability of the CGC for medical nuclear imaging has been investigated. To fully describe CGC response, a Monte Carlo simulation was developed and has been shown to accurately reproduce experimental results - allowing future design changes to be optimised before implementation.

Phantom studies have been used to investigate the performance of the CGC for a variety of clinical applications. Particular focus was given to the possibility of intraoperative use for sentinel lymph node biopsy. This is a vital procedure for cancer staging, for which existing localisation techniques have been shown to be inadequate in some cases [5]. For direct comparison between SFOV systems commercially available and in development, a new set of characterisation protocols were developed which aim to allow consistency in reporting for future work.

This thesis also describes the HCGC, an adaptation to the CGC which allows for simultaneous and co-aligned gamma and optical imaging. This combination of modalities results in fused images that may aid the localisation of regions of high activity. A fully functioning prototype has been constructed and used for preliminary evaluation in patients.
This chapter describes the overarching conclusions of this thesis, and their implications for HCGC design and the field of SFOV gamma imaging.

10.1 Conclusions

A Monte Carlo simulation was used to investigate pinhole collimator response under a number of conditions. Previously derived analytical models were shown to accurately represent pinhole response to sources directly centred on the pinhole and for large pinhole acceptance angles. These models are derived from the assumption of an infinitely thick collimator, a limitation which means that these models underestimate source sensitivity and spatial resolution at large offsets. This underestimation was shown to be small but consistent and should be considered when using these models.

For SFOV cameras, improved spatial resolutions mean that many small sources that may have previously been treated as point sources must instead be treated as finite sources. Source size is commonly measured in terms of the FWHM of the image profile of the source; however this does not take into account the variation in profile shape seen for finite sources of differing sizes. An analytical model was developed to calculate profile shape for finite sources, and this was shown to reproduce the profiles derived through Monte Carlo modelling. Variation in profile shape was significant, particularly for sources at small distances from the collimator and with large offsets. Using the analytical model, it was found that a finite source may be considered as a point source for the purpose of determining resolution if the size of the source is less than the geometric resolution of the collimator used. In addition, it was shown that the subtraction in quadrature method of measuring spatial resolution is not appropriate for pinhole collimators. These factors should be considered when measuring the spatial resolution of SFOV pinhole collimated gamma cameras.

The use of SFOV gamma cameras for medical imaging is a relatively new field when compared with that of LFOV cameras. For LFOV cameras, standardised procedures for assessing performance characteristics are well-established and it can be assumed that measurements performed in different institutions and on different imaging systems will
have occurred under similar conditions and so be directly comparable. These existing procedures cannot be directly applied to SFOV cameras. A number of groups developing SFOV cameras have independently adapted portions of these protocols or used alternative methods. Without consistency in measurement techniques, however, it is difficult to directly compare parameters between devices.

In this thesis a new and complete set of characterisation protocols, applicable to SFOV systems, have been described and successfully tested with the CGC. Application of these protocols allows for measurement of intrinsic and system spatial resolution, intrinsic and system sensitivity, spatial linearity, uniformity, count rate capability and energy resolution for high resolution systems where standard LFOV protocols are inappropriate. These protocols also suggest reporting parameters to encourage standardisation and allow for direct comparisons between SFOV systems.

Using phantom studies, it was shown that image smoothing can be beneficial for SFOV systems with benefits in detectability exceeding the disadvantages from degradation in spatial resolution. The preferred level of smoothing, however, is strongly dependent on the structures being imaged and may lead to misleading results if applied incorrectly. The Rose criterion was shown to be a poor measure when determining whether a structure is visible for a typical viewer, although it does allow for quantitative comparison between images. For high SNRs (> 100), SNR was seen to follow a root-signal relationship. This relationship significantly overestimates SNR for lower SNRs where background activity becomes more dominant. When a low SNR image is expected, it is more beneficial to attempt to decrease background (for example by using energy thresholding) than to attempt to increase recorded counts (for example by increasing imaging time).

The detectability of deep-seated nodes and those close to the injection site will be a limiting factor for intraoperative cameras. Preliminary results have shown that the ability to resolve nodes from injection sites, for a range of depths, can be estimated when sensitivity and spatial resolution of the camera is known at the depths investigated. The high resolution of SFOV systems will enhance the detectability of nodes which can be difficult to locate with traditional gamma probes.
10.1.1 HCGC performance

The complete characterisation of the CGC undertaken in this thesis demonstrates that it has potential to provide high-resolution clinical images. These preliminary results show areas for improvement for future design iterations (described below) which, based on theoretical calculations, will bring the CGC in line with other systems in terms of sensitivity, count rate capability and energy resolution.

The spatial resolution of the CGC at the non-magnifying point was found to be 1.5 mm when using a 0.5 mm diameter pinhole collimator and 2.6 mm when using a 1.0 mm diameter pinhole collimator, a considerable improvement over typical values for LFOV systems and comparable with other SFOV systems. The size of the CGC will allow it to be brought into closer proximity to the patient than is typical for LFOV systems, further improving its spatial resolution performance. Initial tests with a sentinel lymph node phantom have shown the CGC can detect a node at a tissue depths of more than 50 mm with a node-injection site separation of 10 mm and node-injection site activity ratio of 1:16. SNR results obtained from thyroid phantom imaging were shown to be comparable with those from LFOV cameras despite significantly lower accumulated counts than in the LFOV images.

The sensitivity of the system characterised in this thesis was found to be limited by a low intrinsic sensitivity of 6% at 141 keV. This parameter varied greatly for different CGC units and, in some cases, at different positions across the detector face. Simulations have shown that CCD noise has a minor effect on sensitivity but this cannot explain the variation seen and so it is probable that non-optimal scintillator-CCD coupling is significantly reducing the sensitivity of the camera. Improving the intrinsic sensitivity to its theoretical value would bring the CGC in line with other SFOV devices. For low activity levels, and for fast imaging, an adaptation to the existing collimator design to improve sensitivity would be beneficial.

The HCGC is an adaptation of the CGC that allows for coaligned hybrid optical/gamma imaging. Fused images were able to display both visual and functional information on gamma uptake. The coalignment between modalities was shown to be robust for imaging
distances up to several metres. Preliminary clinical evaluation has shown that the HCGC is able to localise areas of activity within the patient and that imaging results were improved when a higher sensitivity collimator was used. In addition, the optical image provided information about patient motion during imaging.

10.2 Further work

Opportunities for further work in this area of research are considerable and have clear implications for improved patient care. For clarity, this section has been subdivided into three broad categories of future work; simulation, experimental and developmental. There is, however, overlap between these sections and a number of topics should be pursued concurrently.

10.2.1 Simulation

The Monte Carlo simulation described in this model has been shown to predict a number of trends replicated in camera operation. A number of adaptations should be considered to give a more true representation of the HCGC.

In its current form, the simulation does not include W shielding around the detector or the optical component of the HCGC, both of which should be included. The response of the columnar CsI:Tl scintillator should be investigated experimentally to allow currently estimated values within the simulation to be quantified, particularly the surface roughness and Fano factor of the CsI:Tl crystal. Experimentation could also investigate whether simplifications made in the current model, such as limiting photoelectron range to zero and simplified optical transport, have an impact on the simulated results. In addition, the modelling of the CCD should be updated so that it is able to directly detect high energy photons passing through the shielding or scintillator as the effects of these are yet to be quantified.
To decrease the computation time required, the efficiency of the simulation should be improved - convergent testing can be used to investigate the most efficient number of steps required and in some cases code optimisation will result in significant improvements.

In the first instance, the simulation should be used to determine the extent of the effect of poor optical coupling between the scintillator and CCD, initially through modelling a small vacuum gap between these components and optical transfer effects. The simulation should also be used to investigate a range of possible collimator designs, particularly multiple pinhole collimators with responses that are difficult to determine analytically, and a range of alternative scintillator materials.

### 10.2.2 Experimental

Throughout this work a number of differences in the performance of theoretically identical camera units have been noted. To investigate this further, a full characterisation should be performed with every unit built. Characterisations should also be performed at regular intervals for each unit to determine the consistency of performance over time.

The possibility of using the optical imaging of the HCGC to correct for motion, from either the patient or the operator, in final images should initially be investigated through bench tests. Video stabilisation is a well established field with a number of approaches [178, 179] and the use of these in conjunction with multi-modal image correction techniques [180] should be investigated.

With a view to using the HCGC for sentinel lymph node imaging, further phantom studies should be carried out to determine its efficacy in this area. The bench tests described in this work should be expanded to include more challenging situations. Results of these should be used to compare the performance of the HCGC with that of non-imaging gamma probes. These tests may be developed into a set of protocols for investigating and comparing SFOV and non-imaging probe performance, specifically for SNLB, across a number of devices.
Preliminary patient imaging should continue, with the 1.0 mm diameter collimator used in preference to the 0.5 mm diameter collimator in the short term. As large a range as possible of imaging procedures should be carried out (e.g. bone scans, lymphoscintigraphy and brain scans) and ideally this should extend to imaging with isotopes other than $^{99m}$Tc. The extent of this testing depends on patient availability and the possibility of extended ethics approval for this study, or resubmitting as a multicentre study, is being investigated to increase the possible patient pool.

Ethical approval has been obtained for clinical evaluation of the HCGC for intraoperative sentinel lymph node imaging (scheduled for 2015). This will be performed with a new generation of HCGCs and full characterisations and testing will be performed on them beforehand. In addition to the tests outlined in this thesis they must also undergo electrical and other safety tests prior to operating in the theatre.

### 10.2.3 Developmental

In the short term, the developmental focus of the HCGC will be in optimisation of the current design. A number of improvements that would be trivial to implement have been described in this report; using a thinner optical mirror, increasing collimator-detector separation to allow a pinhole collimator with $\alpha = 44^\circ$ and $d = 1.9$ mm to be fitted, improvement of the scintillator-CCD coupling technique and implementation of a feedback loop to the TEC. The Monte Carlo model adapted, to allow a number of different scintillation materials to be tested. Prior to intraoperative use, software should be updated so that currently post-processed steps - such as hot pixel removal and blob detection - are applied in real time. Consultation with surgeons should also determine the appropriate method of image fusion and degree of image smoothing - although requirements may change once surgical evaluation begins. In the long term, changes may be made to collimator design, cooling technique and scintillator type depending on the results of simulations.

There are a number of directions in which future HCGC development could proceed. Fluorescence markers are an emerging technology in SLNB with markers in development...
which are lymph specific - an improvement over the non-specific dye currently used intraoperatively. Combined radio and fluorescence tracers are now being tested [181, 182] which combine the benefit of targeted high-resolution fluorescence dyes with the superior depth penetration of gamma imaging. An adaptation of the optical component of the HCGC would allow for concurrent fluorescent and gamma imaging. This would be extremely beneficial in the initial testing currently being undertaken where non-integrated fluorescence and gamma cameras are currently being used. If these markers prove beneficial for SLNB, a hybrid fluorescence-gamma camera based on the HCGC design may be hugely beneficial in surgery.

Estimation of the depth of radiolabelled nodes and tumours prior to operating is not possible with current SFOV gamma cameras. Some facilities use SPECT imaging prior to surgery to gain depth information, particularly for more difficult procedures such as head and neck SLNB, but this typically requires an additional patient dose and there are reports that nodes may shift within the patient between imaging and surgery. By combining two HCGC heads with a small separation, stereoscopic images could be taken. This has been shown to be feasible in bench tests when a single camera head was translated by a few centimetres [183]. This would require significant development work, both in determining the optical camera design and in developing a means to display stereoscopic images with quantified depth information. The introduction of stereoscopic imaging intraoperatively could have huge benefits for patients undergoing more complex procedures.
Appendix A

Description of blob detection algorithm

This appendix details the blob detection algorithm which has been used for image processing throughout this work.

A.1 Purpose of blob detection

A single gamma photon interacting with the CGC scintillator will produce a light splash on the CCD. This light splash will be formed from a number of scintillation photons; the total counts within the splash is expected to be proportional to the energy of the interacting gamma ray. In order to calculate the energy deposited in the scintillator, an automated process was required that was able to detect these light splashes and then calculate the total number of counts within each one.
Appendix A. Description of blob detection algorithm

An example of a single frame CGC image is shown in Figure A.1. A large number of light splashes can be seen, some of which appear to overlap. There is also a significant variation in the sizes of the light splashes - this was to be expected, as scintillation photons from an interaction at the top of the scintillator will spread further than those from an interaction at the bottom.

Blob detection is a method for finding features, or 'blobs', in images when both the position and the size of the features are unknown. This makes it ideal for detecting light splashes from scintillation photons. Once individual features are identified, the deposited energy for each light splash and its centre point are calculated and can be used to reconstruct the image and to create an energy spectrum.

A gamma photon may also interact directly with the CCD. In this case a single pixel (assuming no pixel spreading) will contain the charge generated by the photon. The charge within the pixel will be proportional to the gamma photon energy.

A.2 Blob detection process

The blob detection algorithm which was used to analyse CGC images is described in detail below. The algorithm is applied on a frame-by-frame basis to each image. Images are thresholded for noise during acquisition; pixels which are not illuminated will therefore have a signal $S = 0$.

The first step of the blob detection algorithm is to determine the position of light splash events. Row and column segments where $S > 0$ are found. Where these overlap, they are combined into a region of interest (ROI) fully containing the light splash. When multiple ROIs overlap these are combined into a larger ROI containing multiple light splashes. This is continued until all pixels of $S > 0$ are included within a ROI. A single frame may result in 0, 1, or multiple ROIs, each ROI containing a single light splash or multiple light splashes*. Figure A.2 shows an example of a single light splash from Figure A.1.

*The blob detection algorithm does work when full image frames are used so this step is not necessary for an image to be processed. Partitioning the frame in this way, however, greatly improves the efficiency of the algorithm.
In order to calculate the deposited energy in each light splash, the signal within it must be summed. To do this it is first necessary to determine the size of the light splash - the number of pixels with contributing signals. Each light splash is approximately circular with a size described by its scale, $\sigma_s$. The goal of the following process is to determine $\sigma_s$ and use this to calculate the total signal within each light splash.

In two dimensions, a Gaussian distribution is defined as

$$G(x, y, \sigma_k) = \frac{1}{2\pi \sigma_k^2} e^{-\frac{x^2+y^2}{2\sigma_k^2}}$$  \hspace{1cm} (A.1)$$

where $\sigma_k$ is the standard deviation, now referred to as scale, of the distribution - the radius that contains 68.3% of the total distribution. A two dimensional Gaussian distribution may also be described by a matrix which is known as a kernel when convolved with an image during processing.

To determine $\sigma_s$ for each light splash, the image is convolved with a series of Gaussian kernels of varying scales $\sigma_k$. A Gaussian kernel is used as this allows determination of
scale independent of the shape of the image feature [184]. The scales used in this case are

\[ \sigma_k = \frac{e^{n \ln 50}}{10} \quad (n = 0, 1, \ldots, 19) , \]  

(A.2)

where \( n \) has been chosen so that \( \sigma_k \) varies from 0.1 to 5 pixels in exponential steps - covering the full range of \( \sigma_s \) seen in CGC images. For an image \( I \), a scale-space image \( L(x, y, \sigma_k) \) is produced through convolution with the Gaussian kernel;

\[ L(x, y, \sigma_k) = G(x, y, \sigma_k) * I(x, y) . \]  

(A.3)

In practice, the image is convolved by a one-dimensional Gaussian kernel in both x and y directions - this produces an identical result to Equation A.3 and is more computationally efficient.

Convolution is performed with kernels of widths covering the full range of \( \sigma_k \). Example results of these convolutions are shown in Figure A.3. These images are combined to form a three dimensional (x-position, y-position, and scale \( \sigma_k \)) scale-space stack.

Figure A.4 shows the relationship between pixel value and \( \sigma_k \) for an arbitrary pixel in image \( L \), where \( L \) is Figure A.3. For small \( \sigma_k \), the pixel value remains constant and the Gaussian convolution has only a minor effect on the image. As \( \sigma_k \) increases, the pixel value also increases as the kernel becomes wider and more pixels contribute to each application of the kernel. At large \( \sigma_k \), the kernel extends beyond the feature, and so additional contributing pixels will have signal levels of 0 and so not have any effect on the convolved image. The second vertex of the graph (dashed line in Figure A.4), the point of greatest curvature after the inflection point, is the point at which the kernel size matches the scale of the feature.

This scale-matching point is at the minimum of the scale-normalised double differential. This minimum point will be in a different position for each pixel - the true scale can be found from the global minimum of the double differential across the image stack which also indicated the at the x and y-position of the centroid of the feature.
The scale normalised double differential of the image stack is given by its Laplacian defined as [79]

$$J(x, y, \sigma_k) = \sigma_k^2 \left( \frac{\partial^2 L}{\partial x^2} + \frac{\partial^2 L}{\partial y^2} \right)$$  \hspace{1cm} (A.4)

which, similarly to the Gaussian distribution, is applied as a Laplacian convolution kernel. The relationship of $J$ to $\sigma_k$ for the pixel is also shown in Figure A.4 with the minimum showing the point at which $\sigma_k = \sigma_s$.

The minimum of $J$ in terms of $x$, $y$, and $\sigma_k$ is found. Using the minimum $x$ and $y$ position, the minimum for $\sigma_k$ is interpolated iteratively to an accuracy in $n$ of approximately $\frac{1}{210}$. In the case of the feature in Figure A.2, the true minimum occurs at $n = 13.2174$ and so the scale of the light splash $\sigma_s$ is found to be 1.52 pixels$^\dagger$.

$^\dagger$This is not the same as the minimum shown in Figure A.4 which does not represent values for the central pixel.
Figure A.4: Relationship between $\sigma$ and pixel value for a single pixel in image $L$ (left) and image $J$ (right). Dashed red lines show point where kernel size matches the scale of the feature.

Figure A.5: Image (left) and surface plot (right) of reconstructed light splash after blob detection algorithm has been applied to Figure A.2.

The peak intensity is taken from the central pixel of the detected feature - $A = 148$ for the feature in Figure A.2. A reconstructed feature may then be created, which assumes a Gaussian shape with the appropriate $\sigma$ and $A$ such as that shown in Figure A.5.
Appendix A. Description of blob detection algorithm

A.3 Modes of display

A map of $\sigma_s$ against $A$, such as Figure A.6, can be created, allowing for visual investigation of the blob detection results. The horizontal line of points at high peak intensities in Figure A.6 can be attributed to hot pixels or direct gamma interactions - these typically have high peak intensities and very low scales as they occur within a single pixel.

The total energy of an event can be estimated from $A$ and $\sigma_S$ as

$$E = 2\pi A\sigma_S^2.$$  (A.5)

Interaction events at the top of the scintillator will have a smaller $A$ and larger $\sigma_S$ with the converse being true for interactions closest to the CCD. The product $A\sigma_S^2$ should be constant for identical deposited energies.
After blob detection is complete, the image may be reconstructed in two ways, results of which are shown in Figure A.7. Prior to reconstruction it is possible to place thresholds, both high and low, on the energies to be reconstructed. This allows for energy windowing in displayed images.

In cumulative mode (left hand side of Figure A.7), the light splashes have been reconstructed from their fitted values. In this mode a single pixel count does not relate to a single gamma event, so quantitative comparisons are more difficult. Images produced in this mode, however, exhibit higher SNRs and so can aid in localisation of activity.

In centre point mode (right hand side of Figure A.7), the location of gamma events are displayed. The signal within each light splash is reduced to a single pixel count at the centroid position. Light splashes of all energies are treated identically as it is assumed that events will have already been filtered through energy windowing. This view is equivalent to that typically shown by conventional LFOV camera systems. This mode allows for quantitative comparison of counts between different regions of interest.
Appendix B

Camera configurations used in results

This appendix details the camera configuration used for each set of results discussed in this thesis. The CGC configurations used are shown in Table B.1 which has been reproduced from Section 4.9.

<table>
<thead>
<tr>
<th>Component</th>
<th>Parameter</th>
<th>CGC Configuration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detector</td>
<td>Material</td>
<td>W</td>
</tr>
<tr>
<td></td>
<td>Pinhole diameter</td>
<td>0.5 mm or 1.0 mm</td>
</tr>
<tr>
<td></td>
<td>Pinhole acceptance angle</td>
<td>60°</td>
</tr>
<tr>
<td>Pinhole collimator</td>
<td>Coupling to CCD</td>
<td>Direct</td>
</tr>
<tr>
<td></td>
<td>Material</td>
<td>CsI:Tl [70]</td>
</tr>
<tr>
<td></td>
<td>Thickness</td>
<td>600 µm</td>
</tr>
<tr>
<td>Scintillator</td>
<td>Model</td>
<td>Back illuminated CCD97 [71]</td>
</tr>
<tr>
<td></td>
<td>Active image area</td>
<td>8.192 mm × 8.192 mm</td>
</tr>
<tr>
<td></td>
<td>Effective pixel size</td>
<td>64 µm × 64 µm</td>
</tr>
<tr>
<td></td>
<td>Effective pixel number</td>
<td>128×128</td>
</tr>
<tr>
<td></td>
<td>Operating temperature</td>
<td>−12 °C to −6 °C</td>
</tr>
</tbody>
</table>

**TABLE B.1:** Summary of CCD configuration for the CGC units (A, B, C and D) used throughout this thesis.

Table B.2 lists each section of this thesis where results are presented. In each case the camera configuration and pinhole diameter (where applicable) are given.
<table>
<thead>
<tr>
<th>Section</th>
<th>Configuration</th>
<th>Pinhole diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section 7.1</td>
<td>D</td>
<td>N/A</td>
</tr>
<tr>
<td>Section 7.2.2</td>
<td>B</td>
<td>0.5</td>
</tr>
<tr>
<td>Section 7.2.3 Figure 7.10 LHS</td>
<td>C</td>
<td>None</td>
</tr>
<tr>
<td>Section 7.2.3 Figure 7.10 RHS</td>
<td>A</td>
<td>None</td>
</tr>
<tr>
<td>Section 8.1</td>
<td>A</td>
<td>None</td>
</tr>
<tr>
<td>Section 8.2</td>
<td>A</td>
<td>0.5 and 1.0</td>
</tr>
<tr>
<td>Section 8.3</td>
<td>C</td>
<td>None</td>
</tr>
<tr>
<td>Section 8.4</td>
<td>C</td>
<td>None</td>
</tr>
<tr>
<td>Section 8.5</td>
<td>A</td>
<td>1.0</td>
</tr>
<tr>
<td>Section 8.6</td>
<td>C</td>
<td>None</td>
</tr>
<tr>
<td>Section 8.7</td>
<td>B</td>
<td>0.5</td>
</tr>
<tr>
<td>Section 9.1</td>
<td>A</td>
<td>0.5</td>
</tr>
<tr>
<td>Section 9.2.2</td>
<td>A</td>
<td>0.5</td>
</tr>
<tr>
<td>Section 9.2.3</td>
<td>B</td>
<td>0.5</td>
</tr>
<tr>
<td>Section 9.3.1</td>
<td>A</td>
<td>1.0</td>
</tr>
<tr>
<td>Section 9.3.2 Figure 9.16</td>
<td>B</td>
<td>0.5</td>
</tr>
<tr>
<td>Section 9.3.2 Figure 9.17</td>
<td>A</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**TABLE B.2:** Camera configuration used for each set of results presented in this thesis.
Appendix C

Verification and validation of Monte Carlo model

This appendix expands on some of the procedures used in the Monte Carlo simulation described in Chapter 5.

C.1 Random number generation in IDL

The simulation described in this thesis was written in IDL version 8.2.2 which utilises the Mersenne Twister (MT19937) algorithm first described by Matsumoto and Nishimura [69, 185]. This is a pseudo-random number generator in that, although its output is statistically indistinguishable from a truly random sequence, the algorithm used is entirely systematic.

The Mersenne Twister is based on a generalized feedback shift register (GFSR) which uses the following linear recurring equation [186]

\[ x_{l+n} = x_{l+m} \oplus x_l \quad (l = 0, 1, \ldots) \quad (C.1) \]

\( x_l \) in this case is a ‘word’ (a binary number of \( w \) bits), \( n \) indicates the number of words, \( m \) is a constant (\( m < w \)) and \( \oplus \) is a bitwise exclusive-or operation. Although this is a
fast generator with a long period (the length of the sequence before sequence repetition occurs), a GSFR sequence can be shown to have poor randomness and the level of randomness is largely dependent upon the initial seeds used [186]. To combat this, a twisted GSFR (TGFSR) was introduced with the form

\[ x_{l+n} = x_{l+m} \oplus x_{l}A \quad (l = 0, 1, \ldots) \]  

(C.2)

where \( A \) is a \( w \times w \) matrix with components of 0 or 1, which acts to increase the order of the polynomial relationship arising from the GFSR thus increasing the appearance of randomness [186]. The period of a TGFSR sequence can attain the theoretical limit of \( 2^{nw} - 1 \) when appropriate \( n, m \) and \( A \) values are chosen.

The Mersenne Twister (MT) algorithm is a particular implementation of a TGFSR, modified to have a Mersenne-prime period (of the form \( 2^a - 1 \) where \( a \) is a prime number) [185]. The linear recurrence used in this case is

\[ x_{l+n} = x_{l+m} \oplus (x_{l}^{u} | x_{l+1}^{u}) A \quad (l = 0, 1, \ldots) \]  

(C.3)

the \((x_{l}^{u} | x_{l+1}^{u})\) term is a concatenation of the upper \((w-r)\) bits of \( x_{l} \) with the lower \( r \) bits of \( x_{l+1} \). The required constants are therefore \( n, w, m (1 \leq m \leq n), r (0 \leq r \leq w - 1) \) and the matrix \( A \). For MT19937, the implementation used in IDL 8.2.2, these constants are \( w = 32, n = 624, m = 397 \) and \( r = 31 \) with the matrix \( A \) chosen primarily for speed of multiplication [185]. This gives the MT algorithm a period of \( 2^{19937} - 1 \) (\( \sim 10^{6000} \)). For comparison, the period of the algorithm used in IDL version 8.1 is \( \sim 10^{9} \). This is significantly higher than the \( \sim 10^{7} \) iterations required for the Monte Carlo simulation described in this work and so the sequence would not be expected to repeat over even several thousand iterations of the model.

Although a large period is preferable in a random number generator, it is not alone indicative of quality. The ‘k-distribution’ test is commonly used to measure the uniformity of the sequence over many iterations [187]. If \( k \) truly random numbers are plotted in \( k \)-dimensional space then the points would appear uniformly distributed. In practice, pseudo-randomly generated numbers lie on discrete \((k - 1)\)-dimensional planes when
this test is performed [187]. For $v$ bits, a sequence is said to be $k$-distributed if each of $2^{kv}$ boxes in $k$-space contains the same number of points.

The $k$-distribution of the linear recurrence described in Equation C.3 is improved by multiplying each generated word by a tempering matrix [185]. After tempering, results from the MT algorithm are uniformly distributed in up to 623 dimensions for 32-bit accuracy [185]. For comparison, the upper bound value of the algorithm used in IDL version 8.1 was 25 dimensions for 32-bit accuracy [69, 188, 189].

For the model described in Chapter 5, the MT19937 algorithm provides a sufficiently long period and degree of randomness.

C.2 Uniform spherical distributions

The direction of travel for a photon is described by an angle of inclination, $\theta$ and an azimuth $\phi$ - the x, y, and z components may be calculated from spherical to Cartesian mapping (see Figure 5.2).

In order to describe a full sphere, the angles used should range between $0 \leq \theta \leq \pi$ and $0 \leq \phi \leq 2\pi$. To generate an isotropic distribution, it may appear logical to simply randomise these values within the appropriate range. Figure C.1 shows the distribution of points on an arbitrary sphere obtained using this method; the generated points are clearly non-uniformly distributed. This non-uniformity arises because the points are uniformly distributed by angle whereas the required result is that points are uniformly distributed by area.

In spherical coordinates the derivative of a solid angle is given by

$$d\Omega = \sin \theta \, d\theta d\phi.$$  

(C.4)
Appendix C. Verification and validation of Monte Carlo model

Figure C.1: Side-on (left) and top-down (right) distribution of $10^4$ points generated with uniform angular distributions on an arbitrary sphere.

This dependence on a function of $\theta$ explains why points are distributed in the manner seen in Figure C.1. The solid angle, and so the surface area subtended by these angles, is

$$\Omega = \phi (1 - \cos \theta) .$$  \hspace{1cm} (C.5)

From Equation C.5, $\phi$ may be randomised between 0 and $2\pi$ but it is now clear that the term $(1 - \cos \theta)$ should be randomised rather than $\theta$ itself. Therefore, if $x$ is a randomly generated term, $\theta$ can be calculated from

$$\theta = \cos^{-1} (1 - x)$$ \hspace{1cm} (C.6)

for a hemispherical distribution or, to allow the full range of $\theta$,

$$\theta = \cos^{-1} (1 - 2x) .$$ \hspace{1cm} (C.7)

With this mapping system in place, the new distribution produced on the surface of an arbitrary sphere is shown in Figure C.2. It can be seen that this produces the required result - points uniformly distributed by area.
FIGURE C.2: Side-on (left) and top-down (right) distribution of $10^4$ points generated with uniform area distribution (Equation C.7) on an arbitrary sphere.

C.3 Tabulation of modelled energy transitions

In this section, values used throughout the Monte Carlo simulation described in Chapter 5 are tabulated. The materials currently defined in the model are W, Cs, I, and Al. The K-shells and L-subshells are considered independently, M-shell interactions do not take individual M-subshells into account.

Appendix C.3.1 tabulates binding energy, fluorescence yield and jump factor for each shell. Appendix C.3.2 lists all considered fluorescence transitions, transition rates for each and the energy of fluorescence photons produced. Appendix C.3.3 provides transition rates for all considered non-radiative transitions.
C.3.1 Shell data

<table>
<thead>
<tr>
<th>Element</th>
<th>Shell</th>
<th>Binding energy (keV)</th>
<th>Fluorescence yield</th>
<th>Jump factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>W</td>
<td>K</td>
<td>69.525</td>
<td>0.958</td>
<td>5.099</td>
</tr>
<tr>
<td></td>
<td>L₁</td>
<td>12.100</td>
<td>0.147</td>
<td>1.155</td>
</tr>
<tr>
<td></td>
<td>L₂</td>
<td>11.540</td>
<td>0.270</td>
<td>1.410</td>
</tr>
<tr>
<td></td>
<td>L₃</td>
<td>10.207</td>
<td>0.255</td>
<td>2.613</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>1.80</td>
<td>0.020</td>
<td>‡</td>
</tr>
<tr>
<td>Cs</td>
<td>K</td>
<td>35.985</td>
<td>0.898</td>
<td>5.949</td>
</tr>
<tr>
<td></td>
<td>L₁</td>
<td>5.714</td>
<td>0.049</td>
<td>1.150</td>
</tr>
<tr>
<td></td>
<td>L₂</td>
<td>5.359</td>
<td>0.090</td>
<td>1.400</td>
</tr>
<tr>
<td></td>
<td>L₃</td>
<td>5.012</td>
<td>0.091</td>
<td>2.955</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>0.726</td>
<td>0.004</td>
<td>‡</td>
</tr>
<tr>
<td>I</td>
<td>K</td>
<td>33.169</td>
<td>0.884</td>
<td>6.039</td>
</tr>
<tr>
<td></td>
<td>L₁</td>
<td>5.188</td>
<td>0.044</td>
<td>1.149</td>
</tr>
<tr>
<td></td>
<td>L₂</td>
<td>4.852</td>
<td>0.079</td>
<td>1.400</td>
</tr>
<tr>
<td></td>
<td>L₃</td>
<td>4.557</td>
<td>0.079</td>
<td>2.950</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>0.619</td>
<td>0.003</td>
<td>‡</td>
</tr>
<tr>
<td>Al</td>
<td>K</td>
<td>1.56</td>
<td>0.036</td>
<td>10.959</td>
</tr>
<tr>
<td></td>
<td>L₁</td>
<td>0.118</td>
<td>0.000</td>
<td>1.089</td>
</tr>
<tr>
<td></td>
<td>L₂</td>
<td>0.073</td>
<td>0.000</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>L₃</td>
<td>0.072</td>
<td>0.000</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>0.000</td>
<td>0.000</td>
<td>‡</td>
</tr>
</tbody>
</table>

Table C.1: Relevant data for the shells and elements considered in the Monte Carlo model. Jump factors and absorption edges for each element were taken from Brunetti et al. [102]. Fluorescence yields used throughout the model have been obtained from Brunetti et al. [102] for K-, L₁-, L₂- and L₃-shells and Öz et al. [103] for M-shells. A ‡ indicates a value not required by the model.
## Fluorescence transitions

<table>
<thead>
<tr>
<th>Initial vacancy</th>
<th>Transition</th>
<th>Final vacancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
<td>$\alpha_1$</td>
<td>L$_3$</td>
</tr>
<tr>
<td></td>
<td>$\alpha_2$</td>
<td>L$_2$</td>
</tr>
<tr>
<td></td>
<td>$\beta_1$</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td>$\beta_3$</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td>$\beta_2$</td>
<td>X</td>
</tr>
<tr>
<td>L$_1$</td>
<td>$\gamma_3$</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>$\beta_3$</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td>$\beta_4$</td>
<td>M</td>
</tr>
<tr>
<td>L$_2$</td>
<td>$\beta_1$</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td>$\gamma_1$</td>
<td>X</td>
</tr>
<tr>
<td>L$_3$</td>
<td>$\ell$</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td>$\alpha_2$</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td>$\alpha_1$</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td>$\beta_2$</td>
<td>X</td>
</tr>
<tr>
<td>M</td>
<td>Weighted average</td>
<td>X</td>
</tr>
</tbody>
</table>

**Table C.2:** Fluorescence transitions considered in simulation model. These are also displayed graphically in Figure 2.4. An X indicates shells with lower binding energies than the M shell.
### C.3.2.1 Tungsten

<table>
<thead>
<tr>
<th>Initial vacancy</th>
<th>Transition</th>
<th>Energy (keV)</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
<td>$\alpha_1$</td>
<td>59.318</td>
<td>0.5024</td>
</tr>
<tr>
<td></td>
<td>$\alpha_2$</td>
<td>57.982</td>
<td>0.2915</td>
</tr>
<tr>
<td></td>
<td>$\beta_1$</td>
<td>67.245</td>
<td>0.1106</td>
</tr>
<tr>
<td></td>
<td>$\beta_2$</td>
<td>69.067</td>
<td>0.0402</td>
</tr>
<tr>
<td>L$_1$</td>
<td>$\gamma_3$</td>
<td>11.675</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>$\beta_3$</td>
<td>9.819</td>
<td>0.5000</td>
</tr>
<tr>
<td></td>
<td>$\beta_4$</td>
<td>9.526</td>
<td>0.3500</td>
</tr>
<tr>
<td>L$_2$</td>
<td>$\beta_1$</td>
<td>9.672</td>
<td>0.8375</td>
</tr>
<tr>
<td></td>
<td>$\gamma_1$</td>
<td>11.286</td>
<td>0.1625</td>
</tr>
<tr>
<td>L$_3$</td>
<td>$\ell$</td>
<td>7.388</td>
<td>0.0365</td>
</tr>
<tr>
<td></td>
<td>$\alpha_2$</td>
<td>8.335</td>
<td>0.0803</td>
</tr>
<tr>
<td></td>
<td>$\alpha_1$</td>
<td>8.398</td>
<td>0.7299</td>
</tr>
<tr>
<td></td>
<td>$\beta_2$</td>
<td>9.962</td>
<td>0.1533</td>
</tr>
<tr>
<td>M</td>
<td>Weighted average</td>
<td>1.908</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table C.3**: Fluorescence transitions for W. Transition rates were normalised for each initial vacancy. Transition rates were derived from relative intensities in Thompson et. al [15] along with transition energies except in the case of L$_1$ and M vacancy transitions which were drawn from Kaye & Laby absorption tables [16].
## C.3.2.2 Caesium

<table>
<thead>
<tr>
<th>Initial vacancy</th>
<th>Transition</th>
<th>Energy (keV)</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
<td>α₁</td>
<td>30.973</td>
<td>0.5240</td>
</tr>
<tr>
<td></td>
<td>α₂</td>
<td>30.625</td>
<td>0.2830</td>
</tr>
<tr>
<td></td>
<td>β₁</td>
<td>34.987</td>
<td>0.1020</td>
</tr>
<tr>
<td></td>
<td>β₂</td>
<td>34.920</td>
<td>0.0520</td>
</tr>
<tr>
<td>L₁</td>
<td>γ₃</td>
<td>5.567</td>
<td>0.4220</td>
</tr>
<tr>
<td></td>
<td>β₃</td>
<td>4.717</td>
<td>0.4720</td>
</tr>
<tr>
<td></td>
<td>β₄</td>
<td>4.652</td>
<td>0.1060</td>
</tr>
<tr>
<td>L₂</td>
<td>β₁</td>
<td>4.620</td>
<td>0.8310</td>
</tr>
<tr>
<td></td>
<td>γ₁</td>
<td>5.280</td>
<td>0.1690</td>
</tr>
<tr>
<td>L₃</td>
<td>ℓ</td>
<td>3.795</td>
<td>0.0270</td>
</tr>
<tr>
<td></td>
<td>α₂</td>
<td>4.272</td>
<td>0.1170</td>
</tr>
<tr>
<td></td>
<td>α₁</td>
<td>4.286</td>
<td>0.6230</td>
</tr>
<tr>
<td></td>
<td>β₂</td>
<td>4.936</td>
<td>0.2330</td>
</tr>
<tr>
<td>M</td>
<td>Weighted average</td>
<td>0.843</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table C.4**: Fluorescence transitions for Cs. Transition rates were normalised for each initial vacancy. Transition rates are derived from relative intensities in Thompson et. al [15] along with transition energies except in the case of L₁ and M vacancy transitions which were drawn from Kaye & Laby absorption tables [16].
Appendix C. Verification and validation of Monte Carlo model

C.3.2.3 Iodine

<table>
<thead>
<tr>
<th>Initial vacancy</th>
<th>Transition</th>
<th>Energy (keV)</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
<td>$\alpha_1$</td>
<td>26.612</td>
<td>0.5260</td>
</tr>
<tr>
<td></td>
<td>$\alpha_2$</td>
<td>28.318</td>
<td>0.2830</td>
</tr>
<tr>
<td></td>
<td>$\beta_1$</td>
<td>32.295</td>
<td>0.1010</td>
</tr>
<tr>
<td></td>
<td>$\beta_3$</td>
<td>32.240</td>
<td>0.0520</td>
</tr>
<tr>
<td></td>
<td>$\beta_2$</td>
<td>33.054</td>
<td>0.0380</td>
</tr>
<tr>
<td>L$_1$</td>
<td>$\gamma_3$</td>
<td>5.072</td>
<td>0.414</td>
</tr>
<tr>
<td></td>
<td>$\beta_3$</td>
<td>4.313</td>
<td>0.4830</td>
</tr>
<tr>
<td></td>
<td>$\beta_4$</td>
<td>4.257</td>
<td>0.1030</td>
</tr>
<tr>
<td>L$_2$</td>
<td>$\beta_1$</td>
<td>4.221</td>
<td>0.8650</td>
</tr>
<tr>
<td></td>
<td>$\gamma_1$</td>
<td>4.801</td>
<td>0.1350</td>
</tr>
<tr>
<td>L$_3$</td>
<td>$\ell$</td>
<td>3.485</td>
<td>0.0320</td>
</tr>
<tr>
<td></td>
<td>$\alpha_2$</td>
<td>3.938</td>
<td>0.1100</td>
</tr>
<tr>
<td></td>
<td>$\alpha_1$</td>
<td>3.926</td>
<td>0.7480</td>
</tr>
<tr>
<td></td>
<td>$\beta_2$</td>
<td>4.509</td>
<td>0.1100</td>
</tr>
<tr>
<td>M</td>
<td>Weighted average</td>
<td>0.737</td>
<td>1</td>
</tr>
</tbody>
</table>

TABLE C.5: Fluorescence transitions for I. Transition rates were normalised for each initial vacancy. Transition rates were derived from relative intensities in Thompson et. al [15] along with transition energies except in the case of L$_1$ and M vacancy transitions which were drawn from Kaye & Laby absorption tables [16].

C.3.2.4 aluminium

<table>
<thead>
<tr>
<th>Initial vacancy</th>
<th>Transition</th>
<th>Energy (keV)</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
<td>$\alpha_1$</td>
<td>1.487</td>
<td>0.6633</td>
</tr>
<tr>
<td></td>
<td>$\alpha_2$</td>
<td>1.486</td>
<td>0.3330</td>
</tr>
<tr>
<td></td>
<td>$\beta_1$</td>
<td>1.558</td>
<td>0.0009</td>
</tr>
<tr>
<td></td>
<td>$\beta_3$</td>
<td>0.000</td>
<td>0.0000</td>
</tr>
<tr>
<td></td>
<td>$\beta_2$</td>
<td>1.588</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

TABLE C.6: Fluorescence transitions for Al. Transition energies and rates were drawn from Brunetti et al. [102]. Transitions in L-shells not considered for Al due to the low energy of fluorescence photons produced.
## C.3.3 Non-radiative transitions

<table>
<thead>
<tr>
<th>Initial vacancy</th>
<th>Transition</th>
<th>Transition Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W</td>
<td>Cs</td>
</tr>
<tr>
<td>K</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KL₁L₁</td>
<td>0.100</td>
<td>0.080</td>
</tr>
<tr>
<td>KL₁L₂</td>
<td>0.148</td>
<td>0.098</td>
</tr>
<tr>
<td>KL₁L₃</td>
<td>0.102</td>
<td>0.115</td>
</tr>
<tr>
<td>KL₂L₂</td>
<td>0.010</td>
<td>0.012</td>
</tr>
<tr>
<td>KL₂L₃</td>
<td>0.188</td>
<td>0.245</td>
</tr>
<tr>
<td>KL₃L₃</td>
<td>0.086</td>
<td>0.123</td>
</tr>
<tr>
<td>KL₁X</td>
<td>0.123</td>
<td>0.092</td>
</tr>
<tr>
<td>KL₂X</td>
<td>0.089</td>
<td>0.082</td>
</tr>
<tr>
<td>KL₃X</td>
<td>0.120</td>
<td>0.136</td>
</tr>
<tr>
<td>KXX</td>
<td>0.034</td>
<td>0.017</td>
</tr>
<tr>
<td>L₁</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L₁L₂X</td>
<td>0.200</td>
<td>0.120</td>
</tr>
<tr>
<td>L₁L₃X</td>
<td>0.382</td>
<td>0.294</td>
</tr>
<tr>
<td>L₁XX</td>
<td>0.472</td>
<td>0.586</td>
</tr>
<tr>
<td>L₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L₂L₃X</td>
<td>0.182</td>
<td>0.169</td>
</tr>
<tr>
<td>L₂XX</td>
<td>0.818</td>
<td>0.831</td>
</tr>
<tr>
<td>L₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L₃XX</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>M</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MXX</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Table C.7: Non-radiative transitions considered in the simulation model. Naming convention is to give the initial vacancy and the two final vacancies e.g. a transition designated $KL₁L₂$ indicates that an initial $K$-shell vacancy is filled by an electron from the $L₁$-shell while an electron from the $L₂$ shell is ejected from the atom. An X indicates shells with lower binding energies than the $L₃$ shell. Auger transitions to L-shells have not been individually considered as these will be from higher energy shells (designated X) that have not been included in the model. LMX transitions have also been disregarded in the model as the likelihood of these occurring is relatively small and secondary effects due to M-shell vacancies will have a minimal effect. Probabilities of non-radiative transitions collated from a range of sources [18, 104–106] and normalised for each initial shell vacancy. Values used for Al are arbitrary as these transitions will have no further effect on modelled results.
C.4 Compton scattering validation

The effects of inner-shell Compton interactions have been neglected in this model. The proportion of the Klein-Nishina Compton cross section which is due to the K-shell Compton cross section varies from 1 (low Z, high photon energy) to 0 (high Z, low photon energy) [21].

A Compton scattered photon may only cause a K-shell vacancy if the energy lost is equal to or greater than the binding energy for that shell. If it is assumed that all photons losing sufficient energy will cause a K-shell vacancy (which the literature would suggest is a reasonable estimate for low Z and an overestimate for high Z [21]) the expected contribution of this effect to the total number of K-shell vacancies can be seen in Figure C.3.

For a typical energy of 141 keV, vacancies were underestimated by the simulation <5%, with the effect becoming more significant at higher energies. Fluorescence from W will have the largest effect on imaging quality, as the majority of Cs or I fluorescence will be reabsorbed by the scintillator at a distance less than the spatial resolution (>99% within 0.5 mm from Equation 2.2).

K-shell vacancies in Al are not shown in Figure C.3; for Al, Compton scattering is the dominant effect, four orders of magnitude more likely to occur than the photoelectric effect at 141 keV. The model therefore greatly underestimated fluorescence from Al. Al fluorescence produces very low energy photons, these photons are likely to be absorbed due to interaction prior to reaching the detector and would be expected to produce a low number of counts on the detector.

Within the scintillator, the exclusion of inner-shell interactions caused an overestimation of deposited energy, as losses due to binding energy were not taken into account. At 200 keV this overestimation will be ~2%.

Due to these considerations, inner-shell Compton scattering was not considered to have a large impact on the results of the model.
FIGURE C.3: Number of expected K-shell vacancies due to Compton scattering as a percentage of the number of currently modelled K-shell vacancies.
Appendix D

Curve fitting and statistical tests

This appendix describes the statistical procedures used throughout this work. Statistical analysis was performed either through Origin software [190] or through IDL [69].

D.1 Curve fitting

Throughout this work, curve fitting has been performed using the Levenberg Marquardt algorithm, a variation on the least squares fitting algorithm. The Levenberg Marquardt algorithm differs from traditional least squares fitting due to a damping factor $\mu$, discussed in more detail below. This is a robust fitting algorithm [191] however care must be taken that the initial parameters do not lead to a local minimum. This can be checked by running a number of fits with greatly varying initial parameters.

The algorithm aims to minimise

$$X^2 = \sum [y_i - f(x_i, \theta)],$$

where $x_i$ and $y_i$ are paired experimental data points and $f$ is the function to be fitted with parameters $\theta$. Each fitting parameter is varied by a small amount $\delta$, which is adjusted until the gradient of $X^2$ with respect to $\delta$ is zero (i.e. a minimum has been reached).
In traditional least squares fitting, $\delta$ will be varied by a fixed amount for each iteration step. When using the Levenberg Marquardt algorithm, $\delta$ will be different for each iteration based on the value of the damping factor $\mu$. For each iteration $\mu$ is varied, if $X^2$ varies rapidly a small $\mu$ can be used and, conversely, a large $\mu$ is applied when there is only slight variation in $X^2$ [192]. This allows the Levenberg Marquardt algorithm to efficiently converge on appropriate values for $\theta$ in a small number of steps.

### D.2 Goodness-of-fit statistics

Throughout this work, the $R^2$ (coefficient of determination) statistic has been used as a measure of the quality of the fit to experimental data. As with all goodness-of-fit statistics, the $R^2$ value of a fit cannot determine whether a fit is correct or not but provides an indication of its accuracy.

The $R^2$ statistic is defined as [193]

$$R^2 = 1 - \frac{\sum (y_i - \hat{y}_i)^2}{\sum (y_i - \bar{y})^2},$$

(D.2)

where $y_i$ is the $i$th experimental value, $\hat{y}_i$ the $i$th fitted value and $\bar{y}$ the mean of the experimental data. A perfect fit to the data would result in $R^2 = 1$ with poorer fits giving $0 < R^2 < 1$.

The coefficient of determination may be used directly when a fit with only one variable is performed. When more than one coefficient is calculated during fitting, it is more appropriate to use the adjusted $R^2$ statistic [193];

$$\text{Adj. } R^2 = 1 - (1 - R^2) \left( \frac{n-1}{n-p} \right).$$

(D.3)

This equation takes into account the number of data points fitted $n$ and the number of parameters in the fitted model $p$; whereas $R^2$ will always equal 1 if $p \geq n$, this is not the case for Adj. $R^2$. For a linear fit where the intercept or gradient is known, $R^2 = \text{Adj. } R^2$. Throughout this thesis, any reference to $R^2$ refers to the adjusted $R^2$ value.
D.3 Interpolation

Interpolation has been used to investigate quantities where directly measured results are not available. In Chapter 8 this allowed for a more accurate determination of FWHM than would be possible with direct measures of pixel values.

Interpolation was performed by fitting (using the Levenberg-Marquardt algorithm) a cubic spline to the data for sets of four points (i.e. $x[i-1], x[i], x[i+1], x[i+2]$) for a point near $x[i]$). This results in a cubic equation describing the curve in this region, and an estimated $y$ value may be then be found for any $x$ within the region.
Appendix E

Comparison of gamma camera performance characteristics

In this appendix, Table 8.6 - which compares the performance characteristics of the CGC to a number of gamma camera in development and clinical use - is reproduced at a larger size.
<table>
<thead>
<tr>
<th>Field of view</th>
<th>CGC&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Nuclide Cardio&lt;sup&gt;b&lt;/sup&gt;</th>
<th>LFOV scintillator/PMT detectors</th>
<th>SFOV scintillator/PSPMT detectors</th>
<th>Infinia Hawkeye&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Olcott et al.&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Guardian&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Trolta et al.&lt;sup&gt;a&lt;/sup&gt;</th>
<th>MONICA&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal (mm)</td>
<td>40 × 40</td>
<td>370 × 210 210 Ø</td>
<td>540 × 400</td>
<td>500 × 500</td>
<td>44 × 44</td>
<td>100 × 100</td>
<td>49 × 92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrinsic spatial resolution</td>
<td>0.16</td>
<td>2.8</td>
<td>2.7</td>
<td>3.8</td>
<td>1.8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FWHM (mm)</td>
<td>0.29</td>
<td>5.6</td>
<td>7.6</td>
<td>7.1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>System spatial resolution</td>
<td>2.6</td>
<td>7.1</td>
<td>7.8</td>
<td>7.4</td>
<td>-</td>
<td>2.5</td>
<td>3.3</td>
<td>2.2</td>
<td>-</td>
</tr>
<tr>
<td>FWHM (mm)</td>
<td>3.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Spatial linearity Absolute (mm)</td>
<td>0.12</td>
<td>0.38</td>
<td>0.5</td>
<td>0.5</td>
<td>-</td>
<td>0.4</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diff (mm)</td>
<td>0.09</td>
<td>0.18</td>
<td>0.2</td>
<td>0.1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Intrinsic spatial uniformity</td>
<td>8.5</td>
<td>2.4</td>
<td>2.5</td>
<td>3.0</td>
<td>-</td>
<td>8.8</td>
<td>-</td>
<td>&lt;3</td>
<td>-</td>
</tr>
<tr>
<td>Diff (mm)</td>
<td>1.32</td>
<td>1.9</td>
<td>1.7</td>
<td>2.1</td>
<td>-</td>
<td>4.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Count rate 20% expected value (kBq)</td>
<td>&gt;1.2</td>
<td>200</td>
<td>180</td>
<td>300</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>&gt;275</td>
<td>-</td>
</tr>
<tr>
<td>Capability Maximum counts (kBq)</td>
<td>&gt;1.2</td>
<td>220</td>
<td>250</td>
<td>370</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>&gt;275</td>
<td>-</td>
</tr>
<tr>
<td>Sensitivity Intrinsic (%)</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Extrinsic (cps/MBq)</td>
<td>40</td>
<td>144</td>
<td>122</td>
<td>144</td>
<td>135</td>
<td>204</td>
<td>211</td>
<td>149</td>
<td>-</td>
</tr>
<tr>
<td>Energy resolution FWHM at 141 keV (%)</td>
<td>58</td>
<td>9.7</td>
<td>9.4</td>
<td>9.8</td>
<td>12.1</td>
<td>20</td>
<td>19.1</td>
<td>10.8</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Field of view</th>
<th>CGC&lt;sup&gt;c&lt;/sup&gt;</th>
<th>POCF</th>
<th>Ergo&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Scintillator/photodiode detectors</th>
<th>Scintillator/CCD detectors</th>
<th>Semiconductor detectors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nominal (mm)</td>
<td>40 × 40</td>
<td>40 Ø</td>
<td>396 × 311</td>
<td>24 × 18</td>
<td>100 × 100</td>
<td>32 × 32</td>
</tr>
<tr>
<td>Intrinsic spatial resolution</td>
<td>0.16</td>
<td>2.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FWHM (mm)</td>
<td>0.29</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>System spatial resolution</td>
<td>2.6</td>
<td>3.2</td>
<td>3.0</td>
<td>-</td>
<td>1.2</td>
<td>2.2</td>
</tr>
<tr>
<td>FWHM (mm)</td>
<td>3.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Spatial linearity Absolute (mm)</td>
<td>0.12</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diff (mm)</td>
<td>0.09</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Intrinsic spatial uniformity</td>
<td>8.5</td>
<td>-</td>
<td>&lt;5</td>
<td>-</td>
<td>-</td>
<td>1.6</td>
</tr>
<tr>
<td>Diff (mm)</td>
<td>1.32</td>
<td>-</td>
<td>&lt;3</td>
<td>-</td>
<td>-</td>
<td>1.3</td>
</tr>
<tr>
<td>Count rate 20% expected value (kBq)</td>
<td>&gt;1.2</td>
<td>-</td>
<td>&gt;20000</td>
<td>-</td>
<td>-</td>
<td>&gt;180</td>
</tr>
<tr>
<td>Capability Maximum counts (kBq)</td>
<td>&gt;1.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sensitivity Intrinsic (%)</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Extrinsic (cps/MBq)</td>
<td>40</td>
<td>290</td>
<td>112</td>
<td>-</td>
<td>477</td>
<td>300</td>
</tr>
<tr>
<td>Energy resolution FWHM at 141 keV (%)</td>
<td>58</td>
<td>32</td>
<td>7.4</td>
<td>24</td>
<td>-</td>
<td>8.6</td>
</tr>
</tbody>
</table>

Notes:
- CGC<sup>a</sup>: CsI:Tl scintillator.
- CGC<sup>b</sup>: NaI:Tl scintillator.
- CGC<sup>c</sup>: CsI:Na scintillator.
- CGC<sup>d</sup>: CdZnTe semiconductor.
- CGC<sup>e</sup>: CdTe semiconductor.

Table E.1: Comparison of performance characteristics for a range of gamma cameras [5, 6, 49–55, 61, 129, 157, 162–164]. The derivation of the performance characteristics for the CGC are described in Chapter 8. CGC, CsI:Tl scintillator; NaI:Tl scintillator; CsI:Na scintillator; CdZnTe semiconductor; CdTe semiconductor.
Bibliography


[64] e2v technologies limited. Waterhouse Lane, Chelmsford, Essex, CM1 2QU, UK.


[74] 7compound. Dow Corning Corporation, Midland, Mich. 48640, USA.


Bibliography


[156] *NU1-2007*. National Electrical Manufacturers Association, 1300 North 17th Street, Suite 1752, Rosslyn, Virginia 22209, USA.


