High-Sensitivity PET using Optimised Continuous Cylindrical Shell Nanocomposite and Transparent Ceramic Scintillators

Keenan Wilson

School of Electrical and Data Engineering
University of Technology Sydney

A thesis presented for the degree of Doctor of Philosophy

November 25, 2020

Certificate of Authorship / Originality

I, Keenan Wilson declare that this thesis, is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the School of Electrical and Data Engineering at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis. This document has not been submitted for qualifications at any other academic institution.

This research is supported by the Australian Government Research Training Program.

© Copyright 2020 Keenan Wilson

Abstract

Positron emission tomography (PET) systems typically employ 2D or 3D arrays of discrete monocrystalline rectangular prismatic scintillators, arranged in a ring around the imaging object. As PET systems have evolved towards higher spatial resolution and sensitivity, the number of crystals has increased while the dimensions of the crystals have decreased, leading to ever-increasing costs and complexity - particularly in total-body PET. At the same time, the need for optical isolation between crystals limits packing efficiency and hence achievable sensitivity. The chief alternative to discrete-crystal PET - monolithic scintillators with external photodetector arrays - introduces its own challenges, since producing large, high quality scintillator crystals is expensive and technically challenging.

Two new classes of scintillator have recently emerged as alternatives to monocrystalline scintillators for gamma detection - nanocomposites, which combine scintillating nanoparticles with an organic polymer binder - and transparent ceramics. Both are cheaper and easier to manufacture than monocrystalline scintillators, and can be more easily formed into complex shapes - however, they are also less transparent and, in the case of nanocomposites, less dense. Neither has previously been employed in PET systems to any significant degree.

In this work, a new PET system design is proposed which exploits the properties of these new scintillators. Instead of discrete crystals or flat monolithic slabs, the scintillator is formed into a continuous cylindrical shell, tiled on the inner and outer surfaces with silicon photomultiplier photodetectors. The design aims to achieve high sensitivity and competitive spatial resolution compared to similar discrete-crystal PET systems.

Five nanocomposite and four transparent ceramic scintillators are evaluated, and an optimisation method developed to maximise the probability of locating inA technique for localising the endpoints of the lines of response in a monolithic cylindrical shell is developed and evaluated for the best materials of both types. A coincidence detection method based on deconvolution and spatio-temporal partitioning of photon clusters is developed and evaluated. Finally, a simulated PET scan of several point sources inside the optimised scanner is performed, and images reconstructed using analytic and iterative algorithms; spatial resolution and sensitivity are evaluated.

The promising results obtained in this work establish the feasibility of the proposed design and confirm that the design objectives can be achieved. The design offers a markedly different design envelope to conventional PET, and suggests a new pathway to lower-cost total-body PET.

Dedication

For my wife, Yukti.

Acknowledgments

First and foremost I wish to thank my supervisor, Dr. Daniel Franklin at The University of Technology Sydney. It goes without saying that without your guidance and drive this project would not have been possible. I truly appreciate the sheer amount of time, effort and caffeine you have contributed. I want to also thank my co-supervisor, A/Prof Mehran Abolhasan for keeping me on the right track over the years. Special thank you to Dr. Mitra Safavi-Naeini at ANSTO for her many insights and contributions to our work. Thank you to A/Prof Justin Lipman and Dr. Negin Shariati for accommodating me in their lab; it was such a great place to work and I really enjoyed my time there. I want to also show my gratitude to UTS for not only their financial support, but for the structural support within the university, which has carried me to this point. Thank you to Dr. Matt Gaston and ARCLab; without these resources, this work would literally not have been possible. I also greatly appreciated receiving financial support from ANSTO and AINSE for conference funding. My time at UTS would not have been the same without Roumani Alabd. Thank you, not only for your contribution to this work, but also for your friendship. All the best for your own PhD!

On a personal note, I would like to thank my family (Wilsons and Srivastavas) for their love, guidance and especially patience. I especially want to thank my wife, Yukti for her love, never ending support and belief in me.

Keenan Wilson Sydney, Australia, 2020.

Contents

1	Intr	oduct	ion	1
	1.1	Resea	rch Objectives and Overview	5
		1.1.1	Additional Research Contributions	9
2	$\operatorname{Lit}_{\epsilon}$	erature	e Review	10
	2.1	Positr	on Imaging	10
		2.1.1	Types of Detected Events	12
		2.1.2	Photon Interactions with Matter	14
	2.2	PET I	Radiotracers	15
		2.2.1	Metabolism	16
		2.2.2	Blood Flow and Regional Perfusion	17
		2.2.3	Tumour Proliferation	18
		2.2.4	Positron Energy	18
	2.3	PET I	Detectors	19
		2.3.1	Detector Properties	19
		2.3.2	Semiconductor Detectors	21
		2.3.3	Scintillation Detectors	21
		2.3.4	Photomultiplier Tube	23
		2.3.5	Avalanche Photodiode	25
		2.3.6	Silicon Photomultiplier	27
		2.3.7	Detector Designs	28
		2.3.8	Alternative Detector Configurations	33
		2.3.9	Time-of-Flight PET	34
	2.4	Scintil	llation Materials	35
		2.4.1	Scintillator Properties	35

	2.4.2	Nanocomposite Scintillators	39
	2.4.3	Transparent Ceramic Scintillators	43
2.5	Image	${\bf Reconstruction} \ . \ . \ . \ . \ . \ . \ . \ . \ . \ $	45
	2.5.1	Data Storage	45
	2.5.2	Filtered Backprojection	47
	2.5.3	Backproject Then Filter	49
	2.5.4	Types of Filters	49
	2.5.5	3D Image Reconstruction	51
	2.5.6	Iterative Image Reconstruction	53
	2.5.7	The System Matrix	54
	2.5.8	Iterative Algorithms	56
	2.5.9	Image Reconstruction Software	58
2.6	Conclu	asion	59
N /	1941. 9	None and the second of the sec	
		•	60
Det			
2.1	Introd	nation	$\epsilon 0$
3.1		uction	60
3.1	Mater	ials and Methods	63
	Mater 3.2.1	ials and Methods	63 63
	Mater 3.2.1 3.2.2	ials and Methods	63 63 65
	Mater 3.2.1 3.2.2 3.2.3	ials and Methods	63 63 65 65
	Mater 3.2.1 3.2.2 3.2.3 3.2.4	ials and Methods	63 63 65 65 66
	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5	ials and Methods	63 65 65 66 67
	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5 3.2.6	ials and Methods	63 65 65 66 67 68
3.2	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5 3.2.6 3.2.7	Performance Metric and Optimisation Algorithm Simulation Parameters Detector Geometry GATE Parameters Nanocomposite Loading Scintillation Event Position Determination Materials	63 63 65 65 66 67 68 73
	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5 3.2.6 3.2.7	Performance Metric and Optimisation Algorithm Simulation Parameters Detector Geometry GATE Parameters Nanocomposite Loading Scintillation Event Position Determination Materials s and Discussion	63 65 65 66 67 68
3.2	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5 3.2.6 3.2.7	Performance Metric and Optimisation Algorithm Simulation Parameters Detector Geometry GATE Parameters Nanocomposite Loading Scintillation Event Position Determination Materials	63 63 65 65 66 67 68 73
3.2	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5 3.2.6 3.2.7 Result	Performance Metric and Optimisation Algorithm Simulation Parameters Detector Geometry GATE Parameters Nanocomposite Loading Scintillation Event Position Determination Materials s and Discussion	63 63 65 65 66 67 68 73 74
3.2	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5 3.2.6 3.2.7 Result 3.3.1	Performance Metric and Optimisation Algorithm Simulation Parameters Detector Geometry GATE Parameters Nanocomposite Loading Scintillation Event Position Determination Materials s and Discussion Calculation of the Optimal Scintillator Thickness	63 63 65 65 66 67 68 73 74 74
3.2	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5 3.2.6 3.2.7 Result 3.3.1 3.3.2 3.3.3	Performance Metric and Optimisation Algorithm Simulation Parameters Detector Geometry GATE Parameters Nanocomposite Loading Scintillation Event Position Determination Materials s and Discussion Calculation of the Optimal Scintillator Thickness Analysis of Photoelectric vs Compton Interactions	63 63 65 65 66 67 68 73 74 75 82
3.3	Mater 3.2.1 3.2.2 3.2.3 3.2.4 3.2.5 3.2.6 3.2.7 Result 3.3.1 3.3.2 3.3.3 Conclusion	Performance Metric and Optimisation Algorithm Simulation Parameters Detector Geometry GATE Parameters Nanocomposite Loading Scintillation Event Position Determination Materials s and Discussion Calculation of the Optimal Scintillator Thickness Analysis of Photoelectric vs Compton Interactions Spatial error	63 63 65 65 66 67 68 73 74 75 82 91
	2.6 Mor	2.4.3 2.5 Image 2.5.1 2.5.2 2.5.3 2.5.4 2.5.5 2.5.6 2.5.7 2.5.8 2.5.9 2.6 Concludation	2.4.3 Transparent Ceramic Scintillators 2.5 Image Reconstruction 2.5.1 Data Storage 2.5.2 Filtered Backprojection 2.5.3 Backproject Then Filter 2.5.4 Types of Filters 2.5.5 3D Image Reconstruction 2.5.6 Iterative Image Reconstruction 2.5.7 The System Matrix 2.5.8 Iterative Algorithms 2.5.9 Image Reconstruction Software 2.6 Conclusion Monolithic Nanocomposite and Transparent Ceramic Scintillation Detectors for use in Positron Emission Tomography

	4.1	Introd	luction	93
	4.2	Mater	rials and methods	95
		4.2.1	Materials	95
		4.2.2	Optimisation of scanner geometry	95
		4.2.3	Localisation method	98
		4.2.4	Simulation	100
	4.3	Result	ts	100
		4.3.1	GLuGAG:Ce	101
		4.3.2	LaF ₃ :Ce-PS	105
		4.3.3	Detector Sensitivity and Detection Accuracy	105
	4.4	Discus	ssion	109
	4.5	Concl	usions and future work	111
5	Effic	cient s	patio-temporal deconvolution-based pulse pile-up corr	ec-
	tion	for c	oincidence detection in monolithic-scintillator PET s	ys-
	tem	S		112
	5.1	Introd	luction	112
	5.2	Mater	rials and Methods	114
		5.2.1	Coincidence Detection Technique	114
		5.2.2	Impulse Response Generation	114
		5.2.3	Single, 2-Coincidence and Multiple-Coincidence Detection	115
		5.2.4	Line of Response Position Estimation	118
		5.2.5	Geometry	121
		5.2.6	GATE Simulation Parameters	121
	5.3	Result	ts	122
		5.3.1	Algorithm Detection Efficiency	122
		5.3.2	Detection Efficiency by Interaction Type	123
	5.4	Discus	ssion	123
	5.5	Concl	usion	124
6	Des	ign an	d Simulation of a Brain PET Scanner with a Continuo	ous
	Cyl	indrica	al Shell Monolithic Scintillator	125
	6.1	Introd	luction	125

	6.2	Mater	ials and Methods	. 127
		6.2.1	Simulation Parameters	. 127
		6.2.2	Image Reconstruction	. 127
		6.2.3	Image Correction	. 129
	6.3	Result	S	. 134
		6.3.1	Image Reconstruction	. 134
		6.3.2	Spatial Resolution Measurements	. 134
	6.4	Discus	ssion	. 142
	6.5	Conclu	usion	. 145
7	Con	clusio	n	146
	7.1	Summ	ary	. 147
	7.2	Recon	nmendations & Future Work	. 150
	7.3	Conclu	uding Remarks	. 152
\mathbf{A}	Cod	le Doc	umentation	173
	A.1	Nanoc	composite & Transparent Ceramic Optimal Thickness Code	. 173
		A.1.1	Code Availability	. 173
		A.1.2	Software Requirements	. 173
		A.1.3	GATE Code - How to Run	. 173
		A.1.4	MATLAB Code - How to Run	. 175
	A.2	Contin	nuous Cylindrical Shell PET Code	. 176
		A.2.1	Code Availability	. 176
		A.2.2	Software Requirements	. 176
		A.2.3	GATE Code - How to Run	. 177
		A.2.4	MATLAB Code - How to Run	. 179
		A 2.5	STIR Code - How to Run	185

List of Figures

2.1	Positron annihilation	11
2.2	Types of detected events: true, random, scatter and multiple	13
2.3	Compton angular probability distribution	15
2.4	Scintillation energy states	23
2.5	Operation of a photomultiplier tube (PMT)	24
2.6	Operation of a avalanche photodiode (APD) $\ \ldots \ \ldots \ \ldots$	26
2.7	Scintillation detector designs featuring depth encoding	31
2.8	Time-of-flight PET	35
2.9	Scintillator pulse shape.	37
2.10	Calculated optical and gamma photon attenuation lengths in nanocom-	
	posite materials	42
2.11	Construction of a sinogram from projection data	46
2.12	Filter functions used for 2D Filtered Back-Projection	50
2.13	Iterative image reconstruction: the system matrix	55
2.14	Iterative reconstruction algorithm flow diagram	57
3.1	Simulated photoelectric interaction captured in GATE	66
3.2	Nanocomposite scintillator loading factor determination	69
3.3	Position of interaction estimation: scintillation photon maps	70
3.3	Position of interaction estimation (continued): analytic model fitting.	71
3.4	Geometry of the photon distribution parametric model	72
3.5	Percentage of events detected as a function of scintillator thicknesses:	
	nanocomposite materials - $\mathrm{Gd_2O_3}$ PVT & LaBr ₃ :Ce PS	76
3.5	Percentage of events detected as a function of scintillator thicknesses	
	(continued): nanocomposite materials - LaF_3 :Ce OA & LaF_3 :Ce PS	77

3.5	Percentage of events detected as a function of scintillator thicknesses
	(continued): nanocomposite materials - YAG:Ce PS
3.6	Percentage of events detected as a function of scintillator thicknesses:
	transparent ceramic materials - GAGG:Ce & GLuGAG:Ce 79
3.6	Percentage of events detected as a function of scintillator thicknesses
	(continued): transparent ceramic materials - GYGAG:Ce & LuAG:Pr 80
3.7	Estimated position of interaction error ($\Delta X \& \Delta Y$) as a function of
	scintillator depth (LaF ₃ :Ce-PS)
3.7	Estimated position of interaction error (ΔZ & total error) as a func-
	tion of scintillator depth (LaF ₃ :Ce-PS)(continued)
3.8	Estimated position of interaction error ($\Delta X \& \Delta Y$) as a function of
	scintillator depth (GLuGAG:Ce)
3.8	Estimated position of interaction error (ΔZ & total error) as a func-
	tion of scintillator depth (GLuGAG:Ce)(continued)
4.1	Geometry of the simulated cylindrical shell scanner
4.2	GLuGAG:Ce: endpoint errors (R and Z) vs depth of penetration 102
4.2	GLuGAG:Ce: endpoint errors (θ and total error) vs depth of pene-
	tration
4.2	GLuGAG:Ce: LOR error vs depth of interaction
4.3	LaF_3 :Ce-PS: endpoint errors (R and Z) vs depth of penetration 106
4.3	LaF ₃ :Ce-PS: endpoint errors (θ and total error) vs depth of penetration. 107
4.3	GLuGAG:Ce: LOR error vs depth of interaction
5.1	Generated impulse responses for five discrete radial bins
5.2	Coincidence detection: spatial event sorting
5.3	Coincidence detection by pulse deconvolution
5.4	Line of response generation
6.1	Random, normalisation and attenuation corrections in projection and
	image space
6.2	2D analytic image reconstruction of three 3 MBq $^{18}\mathrm{F}$ sources encap-
	sulated in cylindrical water phantoms, using STIR's FBP2D algorithm.135

6.3	3D analytic image reconstruction of three 3 MBq ¹⁸ F sources en-
	capsulated in cylindrical water phantoms, using STIR's FBP3DRP
	algorithm
6.4	3D iterative image reconstruction of three 3 MBq $^{18}\mathrm{F}$ sources en
	capsulated in cylindrical water phantoms, using STIR's OSMAPOSL
	algorithm
6.5	Intensity profile of the FBP2D-reconstructed image along the X axis. 138
6.6	Intensity profile of the FBP2D-reconstructed image along the Y and
	Z axes
6.7	Intensity profile of the FBP3DRP-reconstructed image along the X
	axis
6.8	Intensity profile of the FBP3DRP-reconstructed image along the Y
	and Z axes
6.9	Intensity profile of the OSEM-reconstructed image along the X axis 142
6.10	Intensity profile of the OSEM-reconstructed image along the Y and
	7. 2005

List of Tables

2.1	PET radioisotopes	16
2.2	A comparison of typical photodetector properties	29
2.3	Single crystal scintillation materials	36
2.4	Physical and optical properties of nanocomposite scintillators	40
2.5	Physical and optical properties of transparent ceramic scintillators	44
3.1	Summary of nanocomposite loading factors (by % volume) used in GATE simulations	69
3.2	Summary of optimal scintillator thickness and detection probability	
	for nanocomposite and transparent ceramic materials	78
3.3	Distribution of photoelectric and Compton-scattered interactions for	
	a 1 cm thick scintillator slab	83
3.4	Distribution of photoelectric and Compton-scattered interactions for	
	a 2 cm thick scintillator slab	83
3.5	Distribution of photoelectric and Compton-scattered interactions for	
	a scintillator slab equal to the HVL	84
3.6	Distribution of photoelectric and Compton-scattered interactions for	
	a scintillator slab equal to the optimal thickness	84
3.7	Mean and median errors in the estimation of the point of interaction	
	within scintillators of 1 cm thickness	85
3.8	Mean and median errors in the estimation of the point of interaction	
	within scintillators of 2 cm thickness	90
3.9	Mean and median errors in the estimation of the point of interaction	
	within scintillators of thickness equal to the HVL	90

3.10	Mean and median errors in the estimation of the point of interaction
	within scintillators with thickness equal to the optimum 91
4.1	Properties of scintillator materials used in the cylindrical shell PET
	scanner
4.2	Scanner dimensions and expected detection efficiency 96
4.3	GLuGAG:Ce error statistics summary
4.4	LaF ₃ :Ce-PS error statistics summary
4.5	Fractions of decays yielding usable LORs and accuracy of detected
	endpoints
5.1	True, random and missed detections as a percentage of the total num-
	ber of decays
5.2	Detection type and probability of occurrence
6.1	STIR parameters
6.2	Full width at half maximum (FWHM) of the intensity profiles at zero
	degrees in the transverse plane (x -axis of the system)
6.3	Full width at half maximum (FWHM) of the intensity profiles at 90
	degrees in the transverse plane (y-axis of the system)
6.4	Full width at half maximum (FWHM) of the intensity profiles at 90
	degrees in the coronal plane (z-axis of the system). $\dots \dots \dots$