ΠΑΝΕΠΙΣΤΗΜΙΟ ΠΑΤΡΩΝ

ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ ΤΜΗΜΑ ΦΥΣΙΚΗΣ

ΔΙΑΤΜΗΜΑΤΙΚΟ ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΣΠΟΥΔΩΝ ΣΤΗΝ ΙΑΤΡΙΚΗ ΦΥΣΙΚΗ

ΠΡΟΣΟΜΟΙΩΣΗ ΣΧΗΜΑΤΙΣΜΟΥ ΕΙΚΟΝΑΣ ΣΥΣΤΗΜΑΤΩΝ ΠΥΡΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ ΜΕ ΜΕΘΟΔΟΥΣ MONTE CARLO

ΓΕΩΡΓΙΟΣ Ε. ΚΑΡΠΕΤΑΣ

ΔΙΔΑΚΤΟΡΙΚΗ ΔΙΑΤΡΙΒΗ

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SIMULATION OF IMAGE FORMATION IN NUCLEAR MEDICINE IMAGING SYSTEMS USING MONTE CARLO METHODS

GEORGIOS E. KARPETAS

DOCTORATE THESIS

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My young son asks me...

My young son asks me: Must I learn mathematics?
What is the use, I feel like saying. Those two pieces of bread are more than one's about all you'll end up with.

My young son asks me: Must I learn French?
What is the use, I feel like saying. This State's is collapsing.
And if you just rub your belly with your hand and groan, you'll be understood with little trouble.

My young son asks me: Must I learn history?
What is the use, I feel like saying. Learn to stick your head in the earth, and maybe you'll still survive.

Yes, learn mathematics, I tell him.
Learn your French, learn your history!

Bertolt Brecht

This work is dedicated to my little three children,
Maria, Eleni and the unborn one who is on the way!
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ΠΕΡΙΛΗΨΗ

Σκοπός: Ο γενικός σκοπός της παρούσας μελέτης ήταν να προτείνει μια νέα μέθοδο για την πλήρη περιγραφή των χαρακτηριστικών ποιότητας εικόνας και την βελτιστοποίηση της Τομογραφίας Εκπομπής Ποζιτρονίων (PET) αναπτύσσοντας ένα μοντέλο Monte Carlo.

Υλικά και Μέθοδοι: Η μέθοδος αναπτύχθηκε χρησιμοποιώντας τον κώδικα Monte Carlo (GEANT4 Application For Tomographic Emissions) του GEANT4 με το πακέτο λογισμικού GATE που αναπτύχθηκε από την Open-GATE collaboration. Για την ανακατασκευή των εικόνων χρησιμοποιήθηκε το λογισμικό STIR και για τη λήψη των δεδομένων της ανακατασκευής, από το GATE, χρησιμοποιήθηκε μια συστοιχία από 12 επεξεργαστές Dual Core Intel (R) Xeon (TM) 3.00GHz (Supermicro SuperServer 6015B-UR/NTR, Αγγλία). Ο σαρωτής PET που προσομοιώθηκε σε αυτή τη μελέτη ήταν ο General Electric Discovery-ST (HPIA). Το μοντέλο GATE πιστοποιήθηκε μέσω της σύγκρισης των αποτελεσμάτων που ελήφθησαν με δημοσιευμένα αποτελέσματα (Bettinardi et al 2004, Mawlawi et al 2004) τα οποία ακολουθούν τη νεότερη παραδοσιακή προσέγγιση της NEMA NU-2 2001. Οι εικόνες ανακατασκευάστηκαν με τρεις μεθόδους, αρχικά με τη 2D φιλτραρισμένη οπισθοπροβολή (FBP2D), στη συνέχεια με τη μέθοδο της 3D φιλτραρισμένης οπισθοπροβολής (FPB3DRP), των Kinahan και Rogers, και τέλος με χρήση επαναληπτικών αλγορίθμων (MLE-OSMAPOS). Αρχικά έγινε προσδιορισμός της Συνάρτησης Μεταφοράς Διαμόρφωσης (MTF) για την αξιολόγηση της ποιότητας εικόνας συστημάτων PET. Η αξιολόγηση έγινε μέσω της προσομοίωσης μιας νέας επίπεδης πηγής Λεπτού Χρωματογραφικού Φιλμ (Thin Layer Chromatography-TLC) το οποίο αποτελείται από ένα στρώμα Διοξειδίου του Πυριτίου και υποστρώματα φύλλου Αλουμινίου, εμβαπτισμένο σε 18F-FDG με ενεργότητα
44.4MBq.

Η αξιολόγηση της MTF έγινε μέσω των ανακατασκευασμένων εικόνων της επίπεδης πηγής κάνοντας χρήση του λογισμικού STIR. Η αξιολόγηση της MTF πραγματοποιήθηκε επίσης:

α) σε τρεις διαστάσεις (3D), τοποθετώντας την επίπεδη πηγή σε οριζόντια και σε κάθετη κατεύθυνση (διαστάσεις πηγής οριζόντια και κάθετα 5x10 εκατοστά),
β) με σάρωση πηγής μεγαλύτερου πλάτους, ανακατασκευάζοντας την εγκάρσια τομή της (διαστάσεις 18x10cm) και
g) από ανακατασκευασμένες εικόνες σημειακής πηγής.

Να τονίσουμε εδώ ότι η παρούσα μελέτη είχε ως στόχο να συγκρίνει την προτεινόμενη μέθοδο (αξιολόγηση της MTF μέσω επίπεδης πηγής) με την πιο παραδοσιακή τεχνική που βασίζεται σε σημειακές πηγές. Στη συνέχεια έγινε προσδιορισμός της Ανιχνευτικής Κβαντικής Αποδοτικότητας (DQE) για την εκτίμηση της συνολικής απόδοσης του συστήματος PET, μέσω υπολογισμού της Συνάρτησης Μεταφοράς Διαμόρφωσης και του Κανονικοποιημένου Φάσματος Ισχύος Θορύβου (NNPS). Οι καμπύλες της MTF υπολογίστηκαν από την ανακατασκευή των εγκάρσιων τομών της επίπεδης πηγής (1 MBq), ενώ το NNPS υπολογίστηκε από τις αντίστοιχες στεφανιαίες τομές. Οι εικόνες ανακατασκευάστηκαν εφαρμόζοντας επαναληπτικούς αλγόριθμους (MLE-OSMAPOSL), χρησιμοποιώντας διάφορα υποσύνολα των προβολών (subsets) (3 έως 21) και επαναλήψεων (iterations) (1 έως 20). Επιπλέον, η αξιολόγηση της DQE έγινε μέσω διερεύνησης της επίδρασης διαφόρων κρυστάλλων κρυστάλλων σπινθηρίστων στην διακριτική ικανότητα (MTF) και του θόρυβου (NNPS) των ανακατασκευασμένων εικόνων του PET. Σε αυτή την περίπτωση, ο αλγόριθμος ανακατασκευής της εικόνας MLE-OSMAPOSL, υλοποιήθηκε χρησιμοποιώντας 15 subsets και 3
iterations.

Αποτελέσματα και Συζήτηση: Τα αποτελέσματα της πιστοποίησης μέσω σύγκρισης με δημοσιευμένα αποτελέσματα είναι τα ακόλουθα: Η Διακριτική Ικανότητα (Spatial Resolution, SR) στο Πλήρες Εύρος στο Ήμιση του Μέγιστου (Full Width at Half Maximum - FWHM) βρέθηκε να έχει απόκλιση μικρότερη από 3,29% σε λειτουργία 2D και μικρότερη από 2,51% σε λειτουργία 3D, σε σχέση με δημοσιευμένα πειραματικά αποτελέσματα (Mawlawi et al 2004), αντιστοίχως. Οι τιμές 2D, για την Ευαισθησία (Sensitivity), το Ποσοστό Σκέδασης (Scatter Fraction-SF) και την Απόδοση του Ρυθμού Μέτρησης (Count-Rate), τα οποία ελήφθησαν ακολουθώντας το πρωτόκολλο της NEMA NU 2-2001, βρέθηκαν να διαφέρουν λιγότερο από 0,46%, 4,59% και 7,86%, αντίστοιχα με τα δημοσιευμένα πειραματικά αποτελέσματα (Mawlawi et al 2004). Ακολούθως, οι αντίστοιχες τιμές σε λειτουργία 3D βρέθηκαν να διαφέρουν λιγότερο από 1,62%, 2,85% και 9,13%, αντίστοιχα, με τα δημοσιευμένα πειραματικά αποτελέσματα (Mawlawi et al 2004). Η ευαισθησία επιτέλους εκτιμήθηκε χωρίς την παρουσία υλικού εξασθένησης, προσομοιώνοντας απευθείας μια ιδανική πηγή. Οι διαφορές που προέκυψαν μεταξύ της ιδανικής πηγής και της μεθοδολογίας κατά NEMA-NU-2 2001 κυμάνονται από 0,04% έως 0,82% (ακτινική θέση R = 0cm) σε λειτουργία 2D και από 0,52% έως 0,67% σε λειτουργία 3D (ακτινικές θέσεις R = 10cm). Συνεπώς κάνοντας χρήση αυτής της μεθόδου, η ευαισθησία μπορεί να προσδιοριστεί με πιο απλοποιημένη και γρήγορη διαδικασία. Οι τιμές του Ρυθμού Μέτρησης Ισοδύναμου Θορύβου (Noise Equivalent Count Rate-NECR) που προέκυψαν ήταν 94.31kcps σε 2D και 66.9kcps σε 3D στα 70 και 15kBq/mL αντίστοιχα, σε σύγκριση με τα δημοσιευμένα αποτελέσματα τα οποία ήταν 94.08kcps σε 2D και 70.88kcps σε 3D στα 54.6kBq/mL και 14kBq/mL.
αντίστοιχα. Οι τιμές για την ποιότητα εικόνας βρέθηκαν σε εξαιρετική συμφωνία με τα δημοσιευμένα αποτελέσματα. Αφού ολοκληρώθηκε η πιστοποίηση του μοντέλου έγινε υπολογισμός της MTF. Οι τιμές MTF που προέκυψαν από την ανακατασκευή με τον αλγόριθμο FBP2D βρέθηκαν σε εξαιρετική συμφωνία με αυτές που προέκυψαν από την ανακατασκευή με τον αλγόριθμο FBP3DRP, ενώ οι αντίστοιχες τιμές μέσω του αλγόριθμου MLE-OSMAPOSL ήταν σε όλο το φάσμα των χωρικών συχνοτήτων υψηλότερες σε σχέση με τους αλγόριθμους οπισθοπροβολής (FBP). Η προσομοίωση της μεγάλης επίπεδης πηγής με αλγόριθμους οπισθοπροβολής έδειξε ότι οι τιμές της MTF ελαττώνονται κατά κύριο λόγο τον οπτικό πεδίο (Field Of View-FOV). Η MTF, της κάθετης τομής, διέφερε ελάχιστα σε σχέση με την οριζόντια. Η σύγκριση της επίπεδης πηγής με τη σημειακή πηγή έδειξε ότι η πρώτη έναν είναι λιγότερη ευαίσθητη στο θόρυβο (SD = 0,0031 και 0,0203, αντίστοιχα). Η αξιολόγηση της DQE μέσω επαναληπτικών αλγοριθμών MLE-OSMAPOSL έδειξε ότι η απόδοση του συστήματος βελτιώνεται όσο αυξάνεται ο αριθμός των επαναλήψεων μέχρι μια μέγιστη τιμή (12 iterations) και παρέμενε αναλλοίωτη από εκεί και έπειτα. Επιπλέον, η μεταβολή του αριθμού των subsets δεν είχε επίδραση στην MTF, για ίσο αριθμό επαναλήψεων. Αντίστοιχα τα επίπεδα θορύβου (NNPS) μειώθηκαν με την αύξηση του αριθμού των iterations και των subsets. Με βάση τα προηγούμενα οι τιμές της DQE επηρεάστηκαν τόσο από την MTF όσο και από το NNPS και βρέθηκαν να αυξάνουν με την αντίστοιχη αύξηση του αριθμού των iterations και των subsets. Τέλος, ο ανιχνευτής PET στον οποίο τοποθετήθηκαν κρύσταλλοι LuAP, παρέχει τις βέλτιστες τιμές MTF σε οπισθοπροβολή 2D και 3D ενώ η αντίστοιχη διαμόρφωση με κρύσταλλους BGO παρείχε τις βέλτιστες τιμές MTF μετά την ανακατασκευή με MLE-OSMAPOSL.
Αντίστοιχα, ο ανιχνευτής με κρυστάλλους BGO είχε τα χαμηλότερα επίπεδα θορύβου και τις υψηλότερες τιμές DQE μετά από την εφαρμογή όλων των αλγόριθμων ανακατασκευής.

**Συμπερασματικά:** Η παρούσα μελέτη έδειξε ότι η συνολική απόδοση συστημάτων PET μπορεί να χαρακτηριστεί πλήρως, να βελτιωθεί περαιτέρω και να γίνει πιο απλή με τη διερεύνηση των διαφόρων στοιχείων της αλυσίδας απεικόνισης μέσω μεθόδου Monte Carlo.

Η μέθοδος αξιολόγησης ανιχνευτών PET, βασιζόμενη σε επίπεδη πηγή TLC, απαιτεί υλικά που είναι συνηθισμένα στο κλινικό περιβάλλον, μπορεί να εφαρμοστεί πειραματικά και να χρησιμοποιηθεί στην κλινική πράξη. Σε αυτή τη μελέτη χρησιμοποιήθηκε για την εκτίμηση και βελτιστοποίηση της ποιότητας εικόνας, αλλά μπορεί να είναι επίσης χρήσιμη στον τομέα της έρευνας για περαιτέρω ανάπτυξη συστημάτων PET και SPECT, μέσω προσομοιώσεων με το πακέτο λογισμικού GATE.

Οι ανακατασκευασμένες εικόνες από το λογισμικό STIR μπορούν επίσης να χρησιμοποιηθούν για την εκτίμηση της κατανομής του ραδιοφαρμάκου, καθώς και την απευθείας λήψη της δοσιμετρικής κατανομής, με αντίστοιχο όφελος στους πυρηνικούς γιατρούς.
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ΕΙΣΑΓΩΓΗ

Α.1. Το πρόβλημα

Η Τομογραφία Εκπομπής Ποζιτρονίων (PET) είναι πλέον καθιερωμένη μέθοδος λειτουργικής απεικόνισης της κατανομής ραδιοφαρμάκου «in vivo». Οι ανακατασκευασμένες εικόνες, που παράγει το PET, χρησιμοποιούνται από πολλούς ιατρούς διαφόρων ειδικευμάτων. Οι εικόνες αυτές παράγονται χρησιμοποιώντας την ακόλουθη αρχιτεκτονική: Στην 2D λειτουργία (2D mode) ενός PET, γίνεται χρήση των κατευθυντήρων (ή διαφραγμάτων) (septa) που συνήθως αποτελούνται από βολφράμιο, ώστε να μειώνουν τα σκεδαζόμενα φωτόνια μεταξύ των εικόνων των τομών που λαμβάνονται. Αντίθετα στη λειτουργία 3D (3D mode), όταν δηλαδή τα διαφραγμάτια απομακρύνονται, το σύστημα καταγράφει επιπλέον τα φωτόνια που ακολουθούν πλάγιες διαδρομές έως ότου ανιχνευτούν από τους κρυστάλλους. Οι παράλληλες διαδρομές των φωτονίων εξαύλωσης ανιχνεύονται από συστοιχίες κρυστάλλων σπινθηριστών και το φως που παράγεται εντοπίζεται από τις αντίστοιχες ομάδες των Φωτοπολλαπλασιαστών (PMT) ή από Φωτοδιόδους Πυριτίου, τύπου Χιονοστιβάδας (Silicon Avalanche PhotoDiode – Si APD) (Humm et al 2003). Η απεικονιστική απόδοση συστημάτων PET / CT επηρεάζεται από διάφορους παράγοντες όπως έλλειψη συγγραμμικότητας φωτονίων, πλάγια διείσδυση στους κρυστάλλους του ανιχνευτή, το μέγεθος του ανιχνευτή και τον χρόνο απόκρισής του, τη διαδρομή που διαγράφουν τα ποζιτρόνια, τις σκεδάσεις που υφίστανται, καθώς και την κίνηση του εξεταζόμενου ασθενή. Όλα αυτά μειώνουν την απόδοση των συστημάτων PET (Bushberg et al 2002, Mawlawi et al 2004, Schmidtlein et al 2006). Οι παραπάνω παράμετροι μπορούν να
προσομοιωθούν άριστα με μεθόδους Monte Carlo, έτσι ώστε να συμβάλουν στην
μελλοντική κατασκευή τομογράφων υψηλής ποιότητας με αισθητά βελτιωμένη
ποιότητα εικόνας. Παράλληλα οι προσομοιώσεις μπορούν να χρησιμοποιηθούν
στην απεικόνιση της πυρηνικής ιατρικής για το σχεδιασμό αποδοτικότερων

Κατά τη διάρκεια της τελευταίας δεκαετίας, οι μέθοδοι Monte Carlo
χρησιμοποιήθηκαν ευρέως στην Πυρηνική Ιατρική, δηλαδή στους τομογράφους
PET και SPECT, για να μοντελοποιήσουν ολοκληρωμένα συστήματα, καθώς και να
συμβάλουν στην σχεδιασμό και στην υλοποίηση νέων βελτιωμένων συστημάτων
Πυρηνικής Ιατρικής (Jan et al 2004, Kalantari et al 2011). Προς αυτή την
κατεύθυνση έχουν δημοσιευτεί αρκετοί αλγόριθμοι προσομοίωσης όπως οι:
GEANT3 (Brun et al 1987, GEANT 1999), EGS4 (Electron Gamma Shower) (EGS
1983), MCNP (Monte Carlo N-Particle Transport) (MCNP 1987) και GEANT4
(GEANT 1999). Τα πακέτα αυτά διαθέτουν καλά επικυρωμένα φυσικά μοντέλα,
επαρκή εργαλεία γεωμετρικής μοντελοποίησης και αποδοτικά βοηθητικά προγράμματα
οπτικοποίησης (Visualization Utilities). Πολλές ερευνητικές ομάδες και κλινικοί
πυρηνικοί Ιατροί ασχολούνται με την ανάπτυξη και την κατασκευή νέων πακέτων
προσομοίωσης, τα οποία παρέχουν μεγαλύτερη ακρίβεια, ταχύτητα, ευελιξία και
υποστήριξη της εφαρμογής (Santin et al 2007). Επέκταση του πακέτου GEANT4
ήταν το GATE (Geant4 Application for Tomography Emission), το οποίο
δημιουργήθηκε από την Open-GATE collaboration (Strul et al 2003). Οι
μηχανισμοί που διαχειρίζονται το χρόνο, τη γεωμετρία και τις ραδιενεργές πηγές
σχηματίζουν το επίπεδο πυρήνα (core layer) που αποτελείται από κλάσεις της C++. Πάνω από το οποίο επιτρέπει την υλοποίηση των κλάσεων που ορίζει ο χρήστης
στο στρώμα χρήστη και οι οποίες προέρχονται από το στρώμα πυρήνα. Επομένως το GATE συνδυάζει τα πλεονεκτήματα των καλά επικυρωμένων φυσικών μοντέλων του GEANT4, της έξυπνης γεωμετρικής περιγραφής και των ισχυρών εργαλείων οπτικοποίησης με νέα χαρακτηριστικά, ειδικά σχεδιασμένα για τομογραφία εκπομπής συστημάτων PET και SPECT (Agostinelli et al. 2003, Jan et al. 2004).

Μέχρι σήμερα έχουν δημοσιευτεί και υπάρχουν στην βιβλιογραφία διάφορες μελέτες πιστοποίησης εμπορικών μοντέλων ανιχνευτών PET (Lamare et al. 2006, Schmidtlein et al. 2006, Gonias et al. 2007, Guerin et al. 2008). Τα δεδομένα που λαμβάνονται από το GATE με κατάλληλο προγραμματισμό των αρχείων εξόδου μπορούν να μετατραπούν σε ημιτονογράμματα στις τρεις διαστάσεις (3D). Στη συνέχεια, κάνοντας χρήση του εξειδικευμένου λογισμικού ανοιχτού κώδικα STIR (λογισμικό για ανακατασκευή τομογραφικών εικόνων), τα αποτελέσματα του GATE μπορούν να τα μετατραπούν σε τρισδιάστατες εικόνες. Οι τελευταίες εξελίξεις στο λογισμικό του GATE, σε συνδυασμό με την πολύ μεγάλη αύξηση της υπολογιστικής ισχύος των ηλεκτρονικών υπολογιστών, κάνουν τις προσομοιώσεις με GATE, τις πιο γνωστές και προσιτές στην προσομοίωση τομογραφίας εκπομπής ποζιτρονίων, έχοντας τη δυνατότητα να αναπαραστήσουν σύνθετα πραγματικά δεδομένα, μέσα σε εύλογο χρόνο, συμβάλλοντας στην ανάπτυξη, την πιστοποίηση και την υποστήριξη του OpenGATE Collaboration (Santin et al. 2003, Buvat et al. 2004). Λαμβάνοντας υπόψη τα παραπάνω δεδομένα, τα μοντέλα GATE προσφέρουν τη δυνατότητα για πιο ρεαλιστικές δυναμικές κατανομές των διαφόρων ραδιοφαρμάκων εντός του ανθρώπινου σώματος, όπως συμβαίνει στις αναπνευστικές και καρδιακές κινήσεις, τη μετακίνηση των ανιχνευτών, την περιστροφή της κάμερας στο SPECT, Time Of Flight, (TOF), καθώς και την επίδραση του νεκρού χρόνου (Dead Time, DT). Όλα αυτά τα χαρακτηριστικά
βοηθούν στη προσομοίωση καμπυλών χρόνου σε πραγματικό χρόνο και στον έλεγχο της αξιοπιστίας δυναμικών αλγορίθμων ανακατασκευής (Buva et al 2004).


Επιπρόσθετα, τα μοντέλα GATE θα μπορούσαν να χρησιμοποιηθούν ώστε να βελτιώσουν χαρακτηριστικά ή τη συνολική σχεδίαση των συστημάτων PET και SPECT μέσω:

α) προσομοίωσης συστημάτων PET που βασίζονται σε διαφορετικού τύπου ανιχνευτές, όπως π.χ. διακριτοποιημένους ανιχνευτές ημιαγωγού CdZnTe (CZT) (Visvikis et al 2006),

β) προσομοίωσης της χρήσης κρυστάλλων σπινθηριστών δύο στρώσεων (phoswich) (Chung et al 2005),

d) της διερεύνησης της επίδρασης του μεγέθους και του υλικού του κρυστάλλου στη συνολική απόδοση ενός PET (Ghazanfari et al 2012) και

e) της βελτιστοποίησης της ανακατασκευής της εικόνας και των πρωτοκόλλων αποκόντισης, καθώς και της διόρθωσης των σκεδαζόμενων φωτονίων.

Επιπλέον με το GATE είναι πλέον δυνατή η ταυτόχρονη προσομοίωση δυναμικών 4D δεδομένων συστήματος PET-MR χρησιμοποιώντας ανατομικές και δυναμικές πληροφορίες από πραγματικό σύστημα MR (Tsoumpas et al 2011).


Ταυτόχρονα έχουν δημοσιευτεί πολλές μελέτες σχετικά με τα χαρακτηριστικά εικόνας που λαμβάνεται από PET. Για να αξιολογηθούν όμως αυτά τα χαρακτηριστικά έχει παραδοσιακά επικρατήσει ο υπολογισμός της Συνάρτησης Διασποράς Σημείου (Point Spread Function-PSF) που προσδιορίζεται από το προφίλ μιας τομής της τρισδιάστατης ανακατασκευής (Nusynowitz and Benedetto

Η απόκριση του συστήματος στο πλάτος του προσπίπτοντος σήματος, μέσω της αλυσίδας απεικόνισης, μπορεί να περιγραφεί από την MTF, η οποία εκφράζει την απόκριση του συστήματος στο πεδίο των χωρικών συχνοτήτων μέσω μετασχηματισμού Fourier της αντίστοιχης PSF από ανακατασκευασμένες εικόνες.

Είναι ιδιαίτερα σημαντικό να γίνει λεπτομερής και ακριβής υπολογισμός της MTF προκειμένου να ποσοτικοποιηθεί η επίδραση διαφόρων παραμέτρων σάρωσης και ανακατασκευής εικόνας, έτσι ώστε να μπορεί να γίνει σύγκριση μεταξύ διαφορετικών εμπορικών μοντέλων PET και ειδικότερα για την αξιολόγηση της ακρίβειας των μετρήσεων σε αιτικές εικόνες (Flohr et al. 2005).

προσδιορισμό της MTF σε εικόνες τομογραφίας εισήχθη αρχικά από τον Boone (Boone et al 2001) που εφάρμοσε αυτή την μέθοδο για την αξιολόγηση ανιχνευτών CT. Από τους Fountos et al. (Fountos et al 2012) πρόσφατα εισήχθη μια αντίστοιχη μέθοδο για ανιχνευτές SPECT με εμβάπτιση μαστογραφικού φιλμ (Agfa MammoRay HDR Medical X-ray) σε διάλυμα Διθειοθρεϊτόλης (DTT) / Te-99m (III)-DMSA, έτσι ώστε να υπολογίσει την MTF με τη μέθοδο της LSF σε επίπεδη πηγή. Σύμφωνα με την υπάρχουσα βιβλιογραφία, δεν έχει γίνει προς το παρόν υπολογισμό της MTF μέσω της LSF σε επίπεδη πηγή. Επιπλέον η Ανιχνευτική Κβαντική Απόδοση (Detective Quantum Efficiency - DQE) έχει οριστεί ως η απόδοση ενός συστήματος να μεταφέρει το Λόγο Σήματος προς Θόρυβο (Signal To Noise Ratio-SNR) μέσω της απεικονιστικής αλυσίδας (Darambara et al 2006). Με αυτή την έννοια η DQE έχει χρησιμοποιηθεί ως δείκτης ποιότητας που εκφράζει τη πληροφορία που περιέχεται σε ψηφιακές εικόνες, ο οποίος είναι γενικά αποδεκτός ως ο μοναδικός κατάλληλος δείκτης της συνολικής ποιότητας της εικόνας, που είναι κατάλληλος για τη σύγκριση μεταξύ διάφορων απεικονιστικών τεχνολογιών (Darambara et al 2006).

Η DQE συνδυάζει τη διακριτική ικανότητα μέσω της Συνάρτησης Μεταφοράς Διαμόρφωσης και το θόρυβο της εικόνας μέσω του Κανονικοποιημένου Φάσματος Ισχύος Θορύβου (Noise Power Spectrum - NPS), με σκοπό τη μέτρηση του λόγου σήματος προς θόρυβο που μεταφέρεται μέσω του συστήματος απεικόνισης, από την είσοδο στην έξοδο, ως ουσία συνάρτηση των χωρικών συγγενείων. Αύξηση της DQE έχει θετική επίδραση στη διακριτική ικανότητα χαμηλής αντίθεσης (Darambara et al 2006).

Η έννοια της DQE για τομογράφους PET έχει προσεγγιστεί με διάφορες μεθόδους. Για παράδειγμα στην έρευνα των Herbert et al. η DQE συσχετίστηκε με το μέσο
όρο του σήματος ενός φωτοπολλαπλασιαστή πυριτίου (SiPM) ως συνάρτηση της τάσης πόλωσης (Herbert et al. 2006). Σε μια άλλη προσέγγιση έγινε η υπόθεση ότι ο λόγος του Ρυθμού Μέτρησης Ισοδύναμου Θορύβου (Noise Equivalent Counting Rate - NECR) προς τον αριθμό των πραγματικών φωτονίων σύμπτωσης, ισούται με την DQE, ως συνάρτηση της συγκεκριμένης ενεργότητας (kBq/mL) (Watson et al. 2001). Σε άλλες δημοσιευμένες έρευνες έχει υπολογιστεί η Μέση Ανιχνευτική Κβαντική Απόδοση (adQEn), ενός ανιχνευτή PET, με APD, κάνοντας χρήση του φάσματος εκπομπής του κρυστάλλου LSO, της καμπύλης οπτικής ζεύξης (Meltmount, μεταξύ του κρυστάλλου και της APD) και της καμπύλης Κβαντικής Απόδοσης (QE) της APD (Li 2011). Ωστόσο, σε όλες αυτές τις δημοσιευμένες μελέτες η DQE εκτιμήθηκε στη μηδενική χωρική συχνότητα. Έως σήμερα, δεν έχει ποτέ πραγματοποιηθεί συνολική αξιολόγηση της απεικονιστικής απόδοσης συστημάτων PET ως συνάρτηση της DQE.
ΜΕΛΛΟΝΤΙΚΗ ΔΟΥΛΕΙΑ

Ο σκοπός της μελλοντικής εργασίας θα είναι η εξέλιξη του υπάρχοντος μοντέλου προκειμένου να μπορεί να γίνει συνολική εκτίμηση της απόδοσης συστημάτων PET μέσω της MTF, NNPS και DQE σε όλα τα διαθέσιμα εμπορικά συστήματα. Επιπλέον η μέθοδος θα πιστοποιηθεί πειραματικά σε πραγματικό σύστημα PET. Στη συνέχεια θα εξελιχθεί επιπλέον, προκειμένου να περιλαμβάνει ανιχνευτές PET μικρών ζώων (Small Animal Pet Scanners), καθώς και Τομογράφους Μονοφωτονικής Εκπομπής (Single-Photon Emission Computed Tomography-SPECT). Επιπλέον έρευνα στην απεικονιστική αλυσίδα των ανιχνευτών PET θα πραγματοποιηθεί για τη μελέτη κρυστάλλων-σπινθηριστών δύο στρώσεων (phoswich). Τέλος, μέσω του μοντέλου θα μελετηθεί η ανάκτηση της σκέδασης Compton (Compton Scatter Recovery) με ανιχνευτές Cadmium Zinc Telluride (CdZnTe or CZT).
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ABSTRACT

The overall purpose of this study was to propose a novel method for the complete image quality characterization and optimization of Positron Emission Tomography (PET) scanners with Monte-Carlo (MC) methods. A model was developed using the Monte Carlo package of Geant4 Application for Tomographic Emission (GATE) and the software for tomographic image reconstruction (STIR) with cluster computing to obtain reconstructed images. The PET scanner used in this study was the General Electric Discovery-ST (US). The GATE model was validated by comparing results obtained in accordance with the National Electrical Manufacturers Association NEMA-NU-2-2001 protocol (Bettinardi et al 2004, Mawlawi et al 2004). Validation images were reconstructed with the commonly used 2D Filtered Back Projection (FBP2D) and the Kinahan and Rogers FPB3DRP Reprojection Algorithms. Image quality, in terms of the Modulation Transfer Function (MTF), was initially assessed with a novel plane source consisting of a Thin Layer Chromatography (TLC) plate, simulated by a layer of Silica gel on Aluminium foil substrates immersed in Fluorodeoxyglucose (18F-FDG) bath solution (44.4MBq). MTF was assessed from the evaluated STIR digital reconstructed images of the plane source. MTF was also assessed a) in three dimensions, in lines passing through the central axis of the PET scanner, by placing the plane source only horizontally and vertically (5x10cm), b) by scanning 18cm of the transaxial Field Of View (FOV) through the simulation of a horizontal large plane source (18x10cm) and c) by evaluating reconstructed point source images. Furthermore, the study aimed to compare the proposed method with the more traditional technique based on a line source. The complete image quality characterization was assessed in terms of the Detective Quantum Efficiency (DQE) by estimating the MTF and the Normalized Noise Power Spectrum (NNPS) of the 18F-FDG TLC plane source (1 MBq). MTFs curves were estimated from transverse reconstructed images of the plane source, whereas the NNPS data were estimated from the corresponding coronal images. Images were reconstructed by the Maximum Likelihood Estimation (MLE)-OSMAPOSL reprojection algorithm by using various subsets (3 to 21) and iterations (1 to 20). Additionally, the influence of different scintillating crystals on PET scanner’s image quality, in terms of the MTF, the NNPS and the DQE, was also investigated. In this case, OSMAPOSL image
reconstruction was assessed by using 15 subsets and 3 iterations. The simulated spatial resolution in terms of Full Width at Half Maximum (FWHM) agreed with published data of Mawlawi et al. (2004), within less than 3.29% in 2D and less than 2.51% in 3D with published data of others, respectively. The 2D values for the sensitivity, the scatter fraction and the count-rate were found to agree within less than 0.46%, 4.59% and 7.86%, respectively with corresponding published values. Accordingly, the corresponding 3D values were found to agree to less than 1.62%, 2.85% and 9.13%, respectively with Mawlawi et al. (2004) published values. Sensitivity, which was also estimated in the absence of attenuation material by simulating an ideal source, showed differences between the extrapolated and the ideal source values (with and without attenuation) ranging in 2D from 0.04% to 0.82% (radial location R=0cm) in 2D and from 0.52% to 0.67% in 3D mode (radial locations R=10cm). By using this model, sensitivity can be obtained in a more simplified procedure. The simulated noise equivalent count rate was found to be 94.31kcps in 2D and 66.9kcps in 3D at 70 and 15kBq/mL respectively, compared to 94.08kcps in 2D and 70.88kcps in 3D at 54.6kBq/mL and 14kBq/mL respectively, from the published by others values. The simulated image quality was found in excellent agreement with these published values. The MTFs obtained using the FBP2D were in close agreement to those obtained by the FBP3DRP, whereas the MTFs of the OSMAPOSL show, in all cases, that higher frequencies are preserved than in the case of the FBP. FBP reconstructed images obtained from the large horizontal plane source showed that the MTF was found to degrade gradually as we move towards the edge of the FOV. The MTFs of the FBP images along the vertical direction were slightly lower than the corresponding horizontal ones. In addition, the plane source method is less prone to noise than the conventional line source method (sd=0.0031 and 0.0203, respectively). In the case of DQE investigation, MTF values assessed from the evaluated STIR digital reconstructed images, of the TLC based plane source, were found to improve as the number of iterations increased up to 12 and remain almost constant thereafter. Furthermore, variation in the number of subsets didn’t show any effect on the MTF, for equal number of iterations. The noise levels, in terms of the NNPS, in the reconstructed PET image, were found to decrease with the corresponding increase of both the number of iterations and subsets. DQE values were influenced by both MTF and NNPS and were found to increase with the corresponding increase in both number of iterations and subsets.
Finally, the PET scanner configuration, incorporating LuAP crystals, provided the optimum MTF values in both 2D and 3DFBP whereas the corresponding configuration with BGO crystals was found with the higher MTF values after OSMAPOSL. The scanner incorporating BGO crystals were also found with the lowest noise levels and the highest DQE values after all image reconstruction algorithms. In conclusion, our study showed that the imaging performance of PET scanners can be fully characterized, further improved and simplified by investigation of the imaging chain components through MC methods. The simulated PET evaluation method, based on a TLC plane source, requires materials commonly found in a clinical environment and can be experimentally implemented and used in clinical practice. In this study it was used for the image quality assessment and optimization, but it can be also useful in research for the further development of PET and SPECT (Single Photon Emission Tomography) scanners though GATE simulations. Reconstructed images by STIR can be also used to obtain radiopharmaceutical distribution of images and direct dose maps, quite useful to nuclear medicine practitioners.
CHAPTER A

INTRODUCTION

A.1. The problem

Positron Emission Tomography (PET) scanners have been an essential, functional, imaging modality for various medical disciplines in which the in vivo radiotracer distribution is reconstructed to form a representing image. The PET images are obtained by using the following architecture: Collimators for the scatter reduction usually consisted of retractable tungsten septa (2D mode) between image slices. When these septa are retracted (3D mode) the system allows oblique lines of response to gamma rays. The collimated gamma rays are detected by a scintillating crystal array in the scanning device, creating a burst of light which is detected by Photomultiplier Tubes (PMT) or Silicon Avalanche Photodiodes (Si APD) (Humm et al 2003).

The imaging performance of PET/CT scanners is affected by factors including photon noncollinearity, oblique detector penetration, detector size and response, positron range, photon scatter, and patient motion all of which contribute to the decreased PET system performance (Bushberg et al 2002, Mawlawi et al 2004, Schmidtlein et al 2006). These parameters could be accurately modelled by Monte Carlo simulation packages so that in the future high quality scanners for improved images could be developed. Simulations can be used in nuclear medicine imaging for designing imaging protocols and for better interpreting SPECT and PET scans (Santin et al 2003, Santin et al 2007). Over the last decade, Monte Carlo methods were extensively used in nuclear medicine, i.e. in PET and in SPECT, to model the performance of complete imaging systems and assist in the design of new emission tomography developments (Jan et al 2004, Kalantari et al 2011). Simulation codes such as GEANT3 (GEANT 1999) (Brun et al 1987), EGS4 (Electron Gamma Shower) (EGS 1983), MCNP (Monte Carlo N-Particle Transport) (MCNP 1987) and Geant4 (GEANT 1999) were published, modeling high energy physics with well validated physics models, geometry modeling tools, and applying better visualization utilities. Research groups and clinical nuclear medicine users
share the need for developing new simulation tools easy to use and with better precision, speed, flexibility and better support of the implemented software (Santin et al 2007). An open-source extension of the GEANT4 Monte Carlo toolkit was the GATE (GEANT4 Application for Tomograpic Emission) package that was developed by the Open-GATE collaboration (Strul et al 2003). GEANT4, as the core of the GATE toolkit, is an international open-source project and has the advantage of being able to incorporate new developments in PET and SPECT scanners by all users (Agostinelli et al 2003, Jan et al 2004).

Several validation studies of GATE models for commercial PET scanners have been reported in the literature (Lamare et al 2006, Schmidtlein et al 2006, Gonias et al 2007, Guerin et al 2008). The GATE projection data can be converted to three dimensional (3D) sinograms which can then be reconstructed by the Software for Tomographic Image Reconstruction (STIR) open source software package in order to obtain 3D PET images (Schmidtlein et al 2006, Thielemans et al 2006, Nehmeh et al 2009).

The latest developments in GATE simulations, together with the increased power of computers, make GATE Monte Carlo simulations a popular accessible tool in emission tomography, which can generate realistic complex data for various applications at a reasonable time, contributing in development, validation and support, of the OpenGATE (Santin et al 2003, Buvat et al 2004). In this context, GATE model offers the opportunity for more realistic dynamic biodistribution of the tracers, such as respiratory and cardiac motions, displacement of the scanner, such as the rotation of the camera heads in SPECT, tracer kinetics, Time-Of-Flight (TOF) PET, radioactive decay, and dead time effects. These features enable us to simulate time curves under realistic acquisition conditions and to test dynamic reconstruction algorithms (Buvat et al 2004). GATE also provides the opportunity for PET dosimetry, such as the study of biodistribution of radiotracers using imaging to predict the dose distribution of a therapeutic agent, or modeling the radiotracer heterogeneity in with tumors with PET imaging (Ljungberg et al 2003, Buvat et al 2004, Visvikis et al 2006, Ferrer et al 2007, Taschereau et al 2007, Thiam et al 2008, Maigne et al 2011, Stute et al 2012). For instance, dosimetry of Zevalin® (Ibritumomab Tiuxetan) labeled with Yttrium-90, using GATE SPECT imaging can be performed as Zevalin® labeled with Indium-111 (Visvikis et al 2006). GATE
simulations can be developed further, in order to obtain directly dose maps from the activity biodistribution used as input in Monte Carlo simulations (Buvat et al 2004).

Furthermore, GATE could be used for the improvement of PET or SPET scanner instrumentation by: a) the simulation of PET cameras using pixellated Cadmium Zinc Telluride, (CdZnTe-CZT) detectors (Visvikis et al 2006), b) the use of dual layer phoswich detectors (Chung et al 2005), c) the design of realistic phantoms with compressed voxels for high-resolution phantom simulations (Pretorius et al 1997, Zubal et al 2004, Taschereau and Chatziioannou 2008), d) the examination of the impact of the crystal material and size on the PET performance (Ghazanfari et al 2012) and e) the optimization of image reconstruction, scatter correction and imaging protocols. Furthermore, with GATE are now possible simultaneous simulations of dynamic 4D PET-MR data using anatomic and dynamic information from real MR acquisitions (Tsoumpas et al 2011).

Various Gate studies have been published on implementing STIR reconstruction simulation for large commercial PET scanners (GEANT 1999, NEMA 2001, Schmidtlein et al 2006, Weber et al 2006, Delso et al 2009, Polycarpou et al 2011, Thielemans et al 2012). From this point on image quality was assessed by evaluating reconstructed images obtained from the STIR software. However quality control in PET scanners is in some cases complex and time is an inhibitory factor. For example sensitivity estimation demands a complex and time worthy procedure (Karakatsanis et al 2006). Furthermore the Compton scatter rejection leads to a sensitivity decrease, affecting the acquisition time.

Several studies have been carried out concerning PET image quality. To evaluate PET scanners performance, the PSF in a slice profile has been traditionally employed (Nusynowitz and Benedetto 1975, Vayrynen et al 1980, Fountos et al 2012). However, in the majority of them spatial resolution was assessed from point sources in terms of the Point Spread Function (PSF) and the corresponding Full Width At Half Maximum (FWHM) (Jakoby et al 2006, Lartizien et al 2007, NEMA 2007, Lodge et al 2009, Bettinardi et al 2011). The FWHM of this function, which is used to measure the spatial resolution, lacks the possibility for complete system characterization and needs to be improved, since different PSF shapes may show equal FWHM values (Starck et al 2005, NEMA 2007, Ryu et al 2012).

The response of the system to the incident signal amplitudes passing through the imaging chain can be described by the MTF, which expresses system’s response
in the spatial frequency domain by taking the Fourier transform of the corresponding PSF from a reconstructed cross sectional image. Precise and accurate determinations of MTF is important for comparing the effects of different scan and reconstruction parameters, for comparison between different PET scanners and especially for evaluating the accuracy of size and density measurements of fine details in medical images (Flohr et al 2005).

Only in a few studies spatial resolution was assessed in terms of the MTF calculated from PSF data (Defrise et al 1994, Stickel et al 2005). The same method was employed in studies concerning combined micro PET/CT scanners, in which MTF was estimated in the CT detector of the combined system (Goertzen et al 2003, Liang et al 2007). MTF can be also assessed from a line source through the estimation of the Line Spread Function (LSF). The use of the LSF method for determining the MTF in tomographic imagers was initially introduced by Boone (Boone et al 2001) who applied this method for CT scanners evaluation. Fountos et al. (Fountos et al 2012) recently introduced a similar method for SPECT scanners by immersing an Agfa MammoRay HDR Medical X-ray film in a solution of Dithiothreitol (DTT)/Tc-99m(III)-DMSA to obtain the MTF through the LSF method. According to our knowledge, PET image quality metrics have not been previously studied in terms of MTF by estimating the LSF of a plane source.

Furthermore, the Detective Quantum Efficiency (DQE) has been defined as the efficiency of a system to transfer the Signal to Noise Ratio (SNR) through the imaging chain (Darambara et al 2006). In this sense DQE has been also used as a figure of merit expressing image information content, which is generally accepted as the most appropriate single objective indicator of overall image quality, suitable for comparison between various imaging detector technologies (Darambara et al 2006). DQE combines spatial resolution through the Modulation Transfer Function (MTF) and image noise through the Normalized Noise Power Spectrum (NNPS), to provide a measure of the signal to noise ratio transfer through the imaging system, from its input to its output, as a function of spatial frequency. An increase in the DQE has positive impact on the low contrast discrimination (Darambara et al 2006). The concept of DQE, for PET scanners, has been previously approached by various methods. For instance, in the work of Herbert et al. DQE was related to the average signal level of a Silicon Photomultiplier (SiPM) as a function of voltage bias (Herbert et al 2006). In another approach it was assumed that the ratio of the Noise
Equivalent Count Rate (NECR) to the true coincidences equals DQE as a function of specific activity (kBq/mL) (Watson et al 2001). Others have computed the ‘average Detection Quantum Efficiency’ (DQE), of a PET detector, based on an Avalanche Photodiode (APD) array based PET detector, by using the emission spectrum of an LSO crystal, the Meltmount optical coupling transmission curve (between the crystal and the APD) and the APDs Quantum Efficiency (QE) curve (Li 2011). However in all these studies DQE was estimated at zero spatial frequency (i.e. in space domain). To our knowledge the overall imaging quality performance of PET scanners has never been previously assessed in terms of the spatial frequency dependent DQE.

A.2. Thesis originality

The originality of this thesis consists in the proposal of a comprehensive method for assessment of the imaging performance of Positron Emission Tomography (PET) scanners. The principal idea is structured around the LSF concept, on the basis of reconstructed cross sectional images of a Thin Layer Chromatography (TLC) flood source. In the present work the method was evaluated by simulations. This was achieved by developing a Monte Carlo model employing the Gate (GEANT4 Application for Tomographic Emission) software. Reconstructed images were obtained using the Software for Tomographic Image Reconstruction (STIR), with cluster computing, to this aim:

1. Initially the GATE model was validated by comparing results obtained in accordance with the National Electrical Manufacturers Association NEMA-NU-2-2001 protocol (Bettinardi et al 2004, Mawlawi et al 2004).
2. During this procedure, sensitivity, complexity and time issues were addressed by simulating an ideal source, without the presence of attenuation material, as an alternative PET sensitivity measurement, thus simplifying the whole procedure.
3. The influence of Compton scatter recovery in PET sensitivity was also investigated by increasing the energy window. A more accurate insight in the emission tomography imaging chain was provided, aiming to be easily reproduced in clinical practice and to obtain specific PET images from a known
radiopharmaceutical distribution in simplified phantoms or in more complex human structures.

- After the software validation, a plane source phantom was proposed in order to predict the Modulation Transfer Function (MTF) through the Line Spread Function (LSF) by simulating a thin layer chromatography (TLC) plate. To this aim, the GATE Monte Carlo package was used in combination with the STIR image reconstruction software in order to simulate:

1. A novel highly uniform plane source implemented by a layer of silica gel on Al foil substrates, immersed in a 18F-FDG bath solution, based on a thin layer chromatography (TLC) plate, to obtain reconstructed plane source images and
2. A conventional 18F-FDG line source, to obtain the Point Spread Function (PSF) of line source reconstructed images, for comparison purposes.

The use of the LSF for determining the MTF in tomographic imagers was initially introduced by Boone who applied this method for CT scanners evaluation (Boone 2001). This method is robust to aliasing when used for MTF calculation, and is more resilient to noise due to greater data averaging when compared to the conventional point source method (Boone 2001). Fountos et al (2012) recently introduced a similar method for SPECT scanners by immersing an Agfa MammoRay HDR Medical X-ray film in a solution of Dithiothreitol (DTT)/Tc-99m(III)-DMSA to obtain the MTF through the plane source method. Building on the work of Fountos, this study introduces a plane source phantom to estimate the MTF through the LSF by simulating a Thin Layer Chromatography (TLC) plate, which can be implemented by a layer of Silica gel on Al foil substrates, immersed in an 18F-FDG bath solution. The idea of simulating TLC films as a plane source in PET imaging was first introduced by Heckathome et al (2008). For comparison purposes, the MTF was also estimated by simulating a conventional 18F-FDG line source. Image quality was assessed by evaluating reconstructed images obtained from the STIR software. Images were reconstructed by the commonly used 2D Filtered Back Projection (FBP2D), the Kinahan and Rogers FPB3DRP and the Maximum Likelihood
Estimation (MLE)-OSMAPOSL reprojection algorithms. The MTF was also assessed, in lines passing through the central axis of the PET scanner, by placing the plane source horizontally and vertically, and allowing for estimation from the center to the edges of the FOV. The simulation of this plane source phantom on the GE Discovery ST PET scanner provides an accurate model that is useful to characterize the performance of nuclear medicine imaging systems.

- The final step for the complete characterization of the imaging performance of PET scanners was the estimation of the spatial frequency dependent Detective Quantum Efficiency (DQE). DQE was assessed in terms of the Modulation Transfer Function (MTF) and the Normalized Noise Power Spectrum (NNPS). MTFs curves were estimated from transverse reconstructed images of the plane source, whereas the NNPS data were estimated from the corresponding coronal images. The concept of DQE was investigated by:

1. The influence of different number of iterations and subsets in the iterative image reconstruction on the GE Discovery ST.
2. The effect of crystal material on PET scanner performance. Scintillating crystals are crucial for the efficiency of the scanner to detect annihilated photons, the subsequent light production and propagation, in order to obtain the final PET image. To this aim, the influence of the replacement of the Bismuth Germinate Oxide (BGO) crystals with various crystal materials on the image quality of the GE Discovery ST scanner was also investigated.

The simulation of this plane source phantom on the GE Discovery ST PET scanner provides an accurate model that is useful to fully characterize the performance of nuclear medicine imaging systems. The model could be useful in implementing experimental methods for systems evaluation in clinical practice as well as in research for further improvement of the image quality performance in Positron Emission Tomography (PET) scanners.
A.3. Publications

This work resulted in publications in international journals, and parts of it have been presented in national and international conferences.

Publications in peer reviewed scientific journals


Publications in international scientific conference proceedings with referees


Conference on Mathematical Modeling in Physical Sciences  September 1-5,  2013 Prague, Czech Republic.

Publications in national scientific conference proceedings with referees
1. Γεώργιος Καρπέτας, Χρήστος Μιχαήλ, Γεώργιος Φούντος, Ιωάννης Κανδαράκης, Γεώργιος Πανακιντάκης, Προσομοίωση των απεικονιστικών χαρακτηριστικών του GE Discovery ST PET μέσω μεθόδων Monte Carlo, 11ο Πανελλήνιο Συνέδριο Πυρηνικής Ιατρικής, 30 Μαρτίου - 1 Απριλίου 2012, Αθήνα, Ελλάδα.

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CHAPTER B

MATERIALS AND METHODS

B.1. Validation of the Monte Carlo model

B.1.1. Geometry of the modeled PET scanner

The scanner modeled in this study was the Discovery ST (US) PET/CT scanner an integrated second generation PET/CT system. The system incorporates bismuth germinate oxide (BGO) crystals of 6.3x6.3x30mm in the axial, transaxial and radial directions, respectively (Fig. 1). The crystals are assembled into 6x6 blocks. Each block is coupled to a Photomultiplier Tube (PMT) consisting of four square channels, and assembled in modules of 8 blocks (2x4) each. The detector ring is finally comprised of 35 modules, i.e. 280 crystal blocks, or 24 rings of 420 crystals (in a total of 10080 BGO crystals). Ring dimensions are 88.6cm in diameter with a 15.7cm axial and 70cm transaxial field of view (FOV). The scanner was designed to acquire images in both 2D and 3D modes. In 2D mode, collimation between image slices was achieved with retractable tungsten septa (54mm length and 0.8mm thick) which reduce scatter by restricting gamma rays entering the BGO crystals to only those traveling nearly perpendicularly to the axial direction. Thus, every image plane counts events from ±5 crystal rings in a high sensitivity mode. In 3D mode, the septa were absent and the system allowed oblique lines of response with all the 24 rings. The energy window width in both cases was set from 375 to 650keV with a coincidence timing window of 11.7ns.
B.1.2. Physics processes

The production of secondary electrons (X-rays and \( \delta \)-rays) in GATE can be settled by thresholds similar with Geant4 (Santin et al 2003). Furthermore GATE uses the standard and low-energy Geant-4 packages in order to simulate electromagnetic processes (Santin et al 2003). In this study, the standard energy package was used to model the photoelectric and Compton interactions and the low-energy package to simulate the Rayleigh interactions. The following energy and range cuts, for photons and electrons, were used (Jan et al 2004): electron range =30cm, \( \delta \)-ray =1GeV and X-ray =1GeV.

B.1.3. Signal processing (or Digitizer chain)

GATE simulation is extended beyond physics processes, upon the scanner’s detectors and the signal processing chain. In order to accomplish this, a series of signal processors were used referring as the Gate Digitizer object or Digitizer. The Digitizer was composed of different modules that may be inserted into the linear signal processing chain to process photon interactions that produce single events from which the coincidence events are formed. Every Digitizer’s signal processed mimics a separate segment of the simulated PET scanner’s signal processing chain (Schmidtlein et al 2006). Then the particles interact within an individual crystal and an Adder module sums the deposited energy to yield a pulse. Following this, a Readout module regroups pulses for every block of crystals in order to create a final

Figure 1. Geometry of the modeled PET scanner.
pulse per photon detected. Afterwards, a Gaussian energy blur, with an average energy resolution for each crystal of the detector block of 17% referenced at 511keV, is attributed by a Crystal Blurring module applying a Quantum Detection Efficiency (QDE) of 0.94 at 511keV (Boone 2000, Michail et al 2010). Next, a 300ns dead time value is applied on the single events in the BGO crystal (Van Eijk 2002, Valais et al 2008) by a paralysable Deadtime module. Then, at the same level, an Energy Window discriminator between 375 and 650keV is applied via the Thresholder and Upholder modules, both incorporated within the energy window (Karpetas et al 2013). The chain describing single events as above can result in the creation of nine types of files, in order to be used for various applications which require the specific file types. These file types contain the detected single events and can be enabled or disabled, when needed. For each single event they contain data about the energy deposited in the crystal and the coordinates of detection within the modeled scanner geometry. These file types are:

1) the American Standard Code for Information Interchange (ASCII),
2) the root file containing four histograms and four tree files (gate, coincidence, hits and singles),
3) the online plotter which allows online display of several variables,
4) the interfile projection set designed to mimic an acquisition protocol for multiple headed gamma cameras,
5) the sinogram output file which is the 2D array of data containing projections,
6) the ECAT7 binary format which uses data blocks for the header information,
7) the List Mode Format (LMF),
8) the imageCT output which is a binary matrix of float numbers that stores the simulated CT image and
9) the raw output file which is stored in binary format and provides access to raw images (OpenGATE Collaboration).

In this study the root output file (Brun et al 1997) was selected, in order to obtain the validation results in the sense of spatial resolution, sensitivity and noise equivalent count rate (NECR) according to the NEMA protocol (NEMA 2001). The sinogram output file (.ima), obtained from the ECAT system, is a raw data file (unsigned short integer), used by STIR as input file for the reconstruction of the simulated flood source image (OpenGATE Collaboration). All evaluations of this study were performed on the central slice of the reconstructed images. Once these
files were created, a second processing stage was inserted, aiming to search the
*Singles’* list for coincidences within a given time, which is called “the coincidence
time window”. The module which is responsible for the aforementioned process is
the *Coincidence Sorter* defined in the digitizer chain terminology, leading to the
creation of a *Coincidence file*. In this study on the GE DST PET/CT scanner, the
coincidence time window was set to 11.7ns. All simulations were obtained using a
computer cluster with 12 dual core Intel(R) Xeon(TM) CPU 3.00GHz processors
(Supermicro SuperServer 6015B-UR/NTR, UK).

**B.1.4. Coincidence processing**
The event identification (ID) number, which uniquely identifies the annihilation
event from where each single is coming and the number of Compton interactions
that have occurred during the tracking of each photon are also stored in the Singles
list (*OpenGATE Collaboration*). The event ID number and the number of the
Compton interactions were used in the classification of random, trues and scattered
coincidences (*OpenGATE Collaboration*).

**B.1.5. Evaluation protocols NEMA NU 2-2001 (N-01) measurements**
All simulations performed in this work, were obtained following the NEMA 2001
protocol under both 2D and 3D modes (NEMA 2001) as stated below.

**B.1.5.1. Spatial resolution**
Spatial Resolution (SP) of the GE Discovery ST (DST) was simulated by using six
point sources of $^{18}$F- FDG with concentration >80MBq/mL, positioned at six points.
These six points were two groups of three, one group at the center of the field of
view and the second group shifted by one fourth of the FOV, at positions: $x=0$cm,
y=1cm; $x=0$cm, $y=10$cm; and $x=10$cm, $y=0$cm in the FOV of the scanner,
according to NEMA NU 2-2001 protocol (NEMA 2001, Bettinardi *et al* 2004). The
positron sources were inside glass capillaries with ID of 1mm. Both 2D and 3D
mode data were acquired. Following the above, in both 2D and 3D modes, the
images were reconstructed using STIR with the 3D filtered back projection
(FBP3DRP) algorithm using Colsher filter with additional apodizing window 0.5
(Labbe *et al* 2004, Thielemans *et al* 2012). Spatial resolution was determined by
measuring both the Full Width at Half Maximum (FWHM) and the Full Width at
Tenth Maximum (FWTM) of the point spread functions PSFs in all three orthogonal directions, according to the NEMA 2001 protocol (NEMA 2001).

B.1.5.2. Sensitivity

The sensitivity of a scanner represents its ability to detect annihilation of radiation. In the NU 2-2001 standard, the absolute sensitivity of a scanner is expressed as the rate of detected coincidence events in counts per second (cps) for a given source activity, in MBq. Since the emitted positrons annihilate with electrons to create pair(s) of $\gamma$-rays, a significant amount of material (for example Aluminum) must surround the source to ensure annihilation. The positron annihilation distance for $^{18}$F is less than 0.5mm while few positrons annihilate at distances of more than 1mm. The surrounding material also attenuates the created $\gamma$-rays, prohibiting a simulation without interfering attenuation. To achieve an attenuation-free value of the sensitivity, successive simulations were made with a uniform line source surrounded by known absorbers. The sensitivity without absorbers can be obtained by linear extrapolation to the successive sensitivity values, obtained from each absorber in Figures 5 and 6 (Mawlawi et al 2004). The sensitivity of the scanner was modeled by simulating a 70cm long plastic tube with 5 Aluminum sleeves, filled with a known amount of radioactivity and defined in the center of the transverse FOV. A $^{18}$F source was used with activity of 9.25MBq (Fig. 2) (Mawlawi et al 2004). This radioactivity is sufficiently low so that count losses due to deadtime and randoms coincidences are negligible. The central Polyethylene tube has an internal diameter of 1mm and an external diameter of 3mm (Mawlawi et al 2004). Data were acquired in 2D and 3D modes. Afterwards, the source and sleeves were placed at 10cm off the central axis and acquisition was repeated.
Sensitivity was also obtained with a broadened energy window 200-650keV in order to investigate the impact of Compton Scatter Recovery (Comanor et al 1996). For comparison purposes an ideal source with no attenuation was also modeled with source activity of 9.25MBq and external diameter of 3mm, in order to validate the accuracy of the NEMA sensitivity extrapolation method.

**B.1.5.3. Scatter fraction and count rates**

A cylindrical polyethylene phantom of 70cm length and 20cm diameter with an internal 3.1cm circular opening, parallel to its central axis was modeled (Fig. 3) (NEMA 2001). The hole was located at a radius of 4.5cm off the central axis of the phantom. A Teflon line source with solution of water and $^{18}$F with activity of 100kBq/mL and 35kBq/mL for the 2D and 3D respectively, with internal diameter of 2.3mm was defined in the hole.

**Figure 2.** Sensitivity phantom.

**Figure 3.** Left: NEMA phantom. Right: acquisition starts.
The simulation was performed for both 2D and 3D modes. The phantom was simulated at the center of the FOV. Data acquisition was recorded without delayed-event randoms data. The simulated phantom was scanned over a period of 12h and imaged repeatedly in 2D and 3D modes for each activity point. A total of 24 2D and 24 3D data acquisition frames were recorded and each frame was recorded for 15min with no delay between consecutive acquisitions. The raw data with no corrections applied were then reconstructed into sinograms. The average system Scatter Fraction (SF), as well as the scatter fraction for each slice across the axial FOV were then calculated and plotted according to the NU 2-2001 protocol (NEMA 2001):

\[ SF = \frac{S}{S + T} \]  

(1)

where \( S \) and \( T \) are the number of true and scattered coincidences.

The counting rate performance of the scanner was evaluated using all data acquisition time points. The total system counting rate (trues, random and scatter event rates) as well as the Noise Equivalent Counting Rates (NECR) were then calculated:

\[ NECR = \frac{T^2}{(T + S + kR)} \]  

(2)

where \( R \) is the number of random coincidences. A \( k \) value of 1 during the direct measurements of NECR rates was used denoting a noiseless random correction (NEMA 2001). Peak values and corresponding activity concentration, for these rates, were also determined according to the NEMA NU 2-2001 protocol (NEMA 2001).

**B.1.5.4. Image quality**

Image quality, in both 2D and 3D modes, was evaluated by simulating the NEMA/IEC torso phantom. The phantom contains six co-axial isocentric spheres (Fig. 4) (NEMA 2001). A cylindrical insert of 5cm diameter was positioned in the centre of the phantom (Fig. 4). The cylinder was simulated as a cold insert with a density of 0.30g/mL, to simulate the lungs. Four of the spheres with diameters 1.0, 1.3, 1.7 and 2.2cm were used to simulate hot lesions, while the other two (2.8 and...
3.7cm) were used to simulate cold lesions. The background of the phantom was filled with 6kBq/mL of $^{18}$F-FDG whereas the hot spheres were filled with an activity four times greater than the background activity (i.e. 24kBq/mL).

![NEMA/IEC torso phantom](image)

**Figure 4.** NEMA/IEC torso phantom.

The obtained images were acquired using STIR, after reconstruction of the arc corrected sinogram data with the Kinahan and Rogers (1989) FPB3DRP (3D Reprojection) (Kinahan et al 1989, Labbe et al 2004, Thielemans et al 2012) using by default a Colsher filter with additional apodizing window with a cutoff frequency at 0.5 cycles (Thielemans et al 2012). FPB3DRP reprojection method was used to account for the problem of axial shift variance or truncation of the projection data. A first estimate of the image was reconstructed using a sufficient data set with all projections (usually the set of transaxial or direct projections) fully measured. By calculating line integrals through this first image, along the missing detection channels, the truncated parts of the projections can be recovered at all remaining angles. This was obtained by forward-projecting from a first image estimate what would have been detected by an axially longer scanner. Having artificially restored the axial shift invariance of the data, the image was then reconstructed by Filtered Backprojection (FBP) of the 2D projections using the Colsher filter (Labbe et al 2004). The Amide's Medical Imaging Data Examiner (AMIDE) viewer was used to read the STIR image data (Thielemans et al 2012).
Attenuation correction was performed according to the method described by Zaidi and Hasegawa (2003) (Zaidi and Hasegawa 2003) with perfect scatter rejection. Attenuation correction was performed by applying the Attenuation Correction Factors (ACF) of the created attenuation map on the reconstructed image (Zaidi and Hasegawa 2003).

The sinograms of the projections were defined by 47 segments, bin size 0.3195cm, 221 arc-corrected and 249 non arc-corrected bins, span 3 and mashing 1. The hot and cold sphere contrast for each sphere size was then calculated according to the NEMA NU 2-2001 protocol. From these images the hot and cold sphere percentage contrast was calculated as:

\[
Q_{h,j} = \frac{(C_{h,j} / C_{b,j}) - 1}{(A_{h} / A_{b}) - 1} \cdot 100\% \\
\text{and} \quad Q_{c,j} = (C_{c,j} / C_{b,j} - 1) \cdot 100\%
\]

where \(Q_{h,j}\) and \(Q_{c,j}\) are the hot and cold sphere percentage contrast, \(C_{h,j}\) and \(C_{c,j}\) are the count densities of the hot and cold spheres, \(C_{b,j}\) is the count density of the background for sphere \(j\), \(A_{h}\) is the activity concentration in the hot sphere and \(A_{b}\) is the background concentration activity (NEMA 2001).

The percent background variability \(N\) for sphere \(j\) is calculated as:

\[
N_{j} = \frac{SD_{j}}{C_{b,j}} \cdot 100
\]

where \(SD_{j}\) is the standard deviation of the background for sphere \(j\), calculated as:

\[
SD_{j} = \sqrt{\sum_{k=1}^{K} \frac{(C_{b,j,k} - C_{b,j})^2}{(K - 1), K = 60}}
\]

Finally, in the image quality estimation, the residual error due to scatter and attenuation corrections \((\Delta C_{\text{lung},i})\) in percentage units for each slice \(i\), shall be calculated as follows:

\[
\Delta C_{\text{lung},i} = C_{\text{lung},i} / C_{b,i} \cdot 100\%
\]
where $C_{\text{lung},i}$ is the count density in the lung insert.

## B.2. Simulation of the MTF test object

### B.2.1. Plane source phantom simulation

The plane source, that is introduced in this study, following the works of Boone (2001) for CT and Fountos et al. (2012) for SPECT systems, is based on the excellent binding of 18F-FDG with TLC plates. The plate was implemented as a layer of Silica gel on Al foil substrates (Al density $2.7 \text{ g/cm}^3$). The dimensions of the TLC plate were $5 \times 10 \text{ cm}^2$ and it was immersed in 18F-FDG bath solution (44.4 MBq) (see Fig. 5). The MTF test object (plane source, i.e. the radioactive plate) was simulated within a phantom, consisting of two semi-cylindrical Polyethylene blocks with 20 cm diameter and 70 cm length, as shown in Fig. 5 in the horizontal and vertical direction for both 2D and 3D data acquisitions. From the three colored cross sectional lines, shown in Fig. 5, the LSFs can be obtained for the MTF estimation in three planes, in lines passing though the central axis. The plane source was also simulated with dimensions $18 \times 10 \text{ cm}^2$ in order to investigate the effect of the field size on the MTF of the transaxial FOV, as shown in Fig. 6.

![Figure 5](image.png)  
**Figure 5.** Simulation of the plane source (colored red) for the MTF measurement. Left) The source is placed horizontal, transverse (green) and saggital (blue) lines for
the MTF calculation. Right) The source is placed vertical, transverse (green) and coronal (yellow) lines for the MTF calculation.

![Figure 6](image)

**Figure 6.** Large plane source phantom simulation for the MTF measurement covering 18 cm of the transaxial FOV placed horizontal.

Plane source images were acquired from STIR, after reconstruction of the arc-corrected sinogram data with the commonly used 2D Filtered Back Projection (FBP2D) (Ramp filter with additional apodizing window 0.5) the Kinahan and Rogers FPB3DRP and for comparison purposes with the Maximum Likelihood Estimation Ordered Subsets version of Green's MAP one step late (MLE)-OSMAPOSL reprojection algorithms (Kinahan and Rogers 1989, Labbe *et al* 2004, Thielemans *et al* 2006, Thielemans *et al* 2012). The sinogram was defined by 47 segments, bin size 0.3195 cm, 221 arc-corrected and 249 non arc-corrected bins, span 3 and mashing 1.

**B.2.2. Line source phantom simulation**

In order to simulate the thin line source, the following procedure was followed: A cylindrical glass capillary with 1 mm internal, 2 mm outside diameter and 4 cm length was modeled (Fountos *et al* 2012). The radioactivity of the line source occupies 3 of the 4 cm due to the combination of surface tension (which is caused by cohesion within the liquid) and adhesive forces between the liquid and glass capillary acting to lift the liquid. Additional length can only be achieved by forcing radioactive solution to the glass capillary (Fig. 7) (Mehta *et al* 2008). The line
source phantom was filled with 18F-FDG (activity 0.37 MBq), shown in Fig. 7 (x and y axes are shown with red and green lines in Fig. 7). For the purposes of the present study and in order to obtain an appropriate simulation that could be reproducible in clinical practice, the capillary tube was simulated into a plastic 76-823 PET/SPECT performance phantom (dimensions: internal diameter 20.3 cm, external 21.59 cm and length 30.5 cm) (Fluke biomedical, Everett, WA), shown in Fig. 7. The phantom was filled with water. Transverse slice image of the line source was acquired from STIR after reconstruction of the sinogram data with the 2D FBP (FBP2D), 3D FBP (FPB3DRP) and with the Maximum Likelihood Estimation (MLE)-OSMAPOSL reprojection algorithms (Thielemans et al 2006, Thielemans et al 2012).

Figure 7. Line source phantom simulation for the measurement of the MTF through PSF. The glass capillary is 4cm in total. The radioactivity of the point source occupies 3cm and the other 1cm is the empty space of the glass capillary.

B.2.3. MTF

The MTF is the equivalent of LSF and PSF in the spatial frequency domain. However the MTF has some advantages originating from its ability to express the filtering properties of an imaging system in the spatial frequency domain:

(i) In this domain structures (e.g. like malignant lesions), in PET images, can be decomposed into sine waves and provide useful information concerning signal
amplitude, frequency, and phase.

(ii) In the spatial frequency domain computations are easier than in the spatial domain since multiplication is used instead of convolution.

Since the imaging performance of a PET scanner depends on size of the structures being imaged, a single analysis in the spatial frequency domain can be used to predict the system performance for all possible structures. In this sense MTF can be a useful tool that can quantify directly the attenuation of the signal passing through the imaging chain of an imaging system, as a function of the spatial frequency (i.e. the filtering properties of a system) and can also be used to characterize high contrast image resolution. In addition the MTF of a complete imaging chain can be expressed as the simple product of the MTFs of the various stages in the imaging chain (i.e. photon absorption and light emission in scintillator, light to electron conversion in photomultipliers etc) and hence stages can be separately analyzed and their effect on system performance can be found (Cunningham 2000). Thus, additionally to the commonly used FWHM from slice profiles of point source images, image quality was further assessed in terms of the spatial frequency dependent MTF obtained by using the plane source method. MTF was also obtained in lines passing through the central axis of the PET scanner, by placing the source horizontally and vertically, instead of placing a line source in three directions (Fountos et al 2012). By placing the plane source horizontally, transverse and sagittal images of the source can be obtained. In these images the source appears as a line. From these lines the LSF can be calculated. By changing the orientation of the plane source from horizontal to vertical, a coronal slice image of the plane source can be obtained. In this image the source will appear as a line (Fig. 5). In this way the MTF of a PET scanner can be estimated in three dimensions.

**B.2.3.1. Plane source method**

In the plane source method, the thin plane source was simulated at angles ranging from 2° to 8° with respect to the horizontal or vertical axis. This technique was followed in order to avoid aliasing effects, as described in the Fujita technique (Fujita et al 1992). Considering angles greater than 8°, the dimensions of the vertical LSFs will be different from those of the true LSFs by more than 1% and geometrical corrections should then be applied (Boone 2001). The final LSF was
obtained by averaging all line LSF profiles after angle correction. The angle correction was performed following the procedure described in Fountos et al (2012). The line LSF profile can be written as \( LSF(x) = G(i_x, i_y) \), where \( G(i_x, i_y) \) represents the slit region of interest (ROI) image pixel values. \( i_x, i_y \) are the pixel coordinates in the horizontal and vertical axes respectively, ranging as follows \( x_1 \leq i_x \leq x_2, y_1 \leq i_y \leq y_2 \) (Fujita et al 1992). \( x_1, x_2 \) define the range, where each line LSF was calculated and \( y_1, y_2 \) are the corresponding lengths. The average LSF profile was calculated as (Fujita et al 1992):

\[
LSF(\xi) = \frac{\sum_{i_x=x_1}^{x_2} \sum_{i_y=y_1}^{y_2} G(i_x, i_y)}{\sum_{i_x=x_1}^{x_2} \sum_{i_y=y_1}^{y_2} 1}
\]

Where \( \xi = \tan(\theta) \cdot i_x + i_y \) and \( \theta \) is the angle between the line image and the horizontal or vertical axis. Since the plane source could have been positioned either clockwise or counter clockwise, in a slight angle ranging from -8° to -2° and 2° to 8°, a custom made software was used for angle correction (Fountos et al 2012). In this study the MTF of the PET scanner was estimated by averaging line profiles across the whole length of the plane source transverse image. Furthermore the spatial variation of the MTF, from the centre to the edge of the large plane source, was investigated successively in 2 cm spaces, allowing the investigation of the image resolution off centre, in a specific ROI inside the Field Of View (FOV). This is one of the advantages of the present method, as compared to the conventional line source method, since PET scanner’s spatial resolution can be fully investigated from the centre to the edges of the FOV, with a single source. Furthermore the plane source was placed with a slight angle in order to avoid aliasing effects, as described in the Fujita technique (Fujita et al 1992). Fourier transformation and subsequent normalization were then applied on the final LSF to compute the MTF (Boone 2001, Fountos et al 2012). The fitting function providing the optimum correlation coefficient (\( R^2 \)) was selected.

**B.2.3.2. Line source method**

MTF was also obtained through the line source method as described in Fountos et al (2012). The centre of the point image was determined \((x_0, y_0)\) coordinates) and line
profiles passing from this point were obtained, covering various angles ranging from 0° to 180° with a 2° angle step.

The PSF profile can be written as \( \text{PSF}(\xi) = G(x_i, y_i) \), where \( G(x_i, y_i) \) are the image pixels values \( \text{(Fujita et al. 1992)} \). \( x_i, y_i \) are the pixel coordinates in the horizontal and vertical axes respectively, fulfilling the line equation criteria for the following equation:

\[
y = \frac{y_2 - y_1}{x_2 - x_1} (x - x_1) + y_1
\]

where \( x_1 = x_0 + r \cdot \sin \theta \), \( x_2 = x_0 - r \cdot \sin \theta \), \( y_1 = y_0 - r \cdot \cos \theta \), \( y_2 = y_0 + r \cdot \cos \theta \), \( 0^\circ \leq \theta \leq 180^\circ \) and \( r \) is the half length of the line profile. Almost all applications of the PSF, as a generalized descriptor of tomographic systems performance, follow the assumption of rotational symmetry; therefore the PSF profiles in the radial directions can be averaged to produce a 1D PSF profile, which was calculated as \( \text{(Erhardt 1986, Chen and Ning 2004, Zhou and Qi 2009, Fountos et al. 2012)} \):

\[
\text{PSF}(\xi) = \frac{\Sigma_{x_i} \Sigma_{y_i} G(x_i, y_i)}{\Sigma_{x_i} \Sigma_{y_i} 1}
\]

where \( \xi \) is the pixel position in horizontal axis. The MTF was then calculated as described in the plane source method.

\section*{B.3. DQE}

\subsection*{B.3.1. MTF-Plane source phantom simulation}

The MTF test object, for the DQE assessment, was simulated according to the methodology described in section B.2.1 and calculated according to section B.2.3.1. In this case the dimensions of the TLC plate were again 5x10 cm\(^2\) and it was assumed to be immersed in an 18F-FDG bath solution (1 MBq). Plane source images were acquired from STIR, after reconstruction of the arc corrected sinogram data with the Maximum Likelihood Estimation Ordered Subsets version of Green’s MAP one step late (MLE)-OSMAPOS algorithm (Thielemans et al.
In order to study the influence of the number of iterations and subsets of the OSMAPOSL image reconstruction on the DQE various subsets (3 to 21) and iterations (1 to 20) were used. The influence of the different crystal scintillator on PET’s image quality was studied by using 15 subsets and 3 iterations.

**B.3.2. Normalized Noise Power Spectrum (NNPS)**

To estimate noise, NNPS data were obtained at the same activity concentration as that of the MTF from the coronal images, using the following method. A sub-image was first extracted from the coronal plane images. Half overlapping ROIs were then taken from the sub-images. The mean pixel value of each ROI was calculated and subtracted from each ROI. Thus an image corresponding to signal variations remained. The squared modulus of the 2D Fast Fourier Transform (FFT) of each ROI was calculated and added to the NPS ensemble. This was repeated for all the ROIs taken from each image. Finally, the NNPS was calculated by dividing with the square mean value of the sub-image and afterwards the ensemble average was obtained according to (11) (Williams et al 1999, Dobbins et al 2000):

\[
NPS(v, u) = \lim_{X, Y \to \infty} \left\{ \frac{1}{XY} \left[ \int_{-X/2}^{X/2} \int_{-Y/2}^{Y/2} p(x, y) \times e^{-2\pi i(vx + uy)} dx dy \right]^2 \right\}
\]

(11)

where the terms inside the brackets \(< >\) stand for ensemble average, \(p(x, y)\) is the difference between the average image signal and the signal at points \(x, y\) of the spatial coordinates, sampled at regular intervals \((dx, dy)\).

**B.3.3. Detective Quantum Efficiency (DQE)**

DQE has been defined as \(DQE = \frac{SNR_{out}^2}{SNR_{in}^2}\) (Dainty and Shaw 1974, Hendee and Ritenour 2002). According to this, \(SNR_{out}\) and \(SNR_{in}\) are the output and input signal to noise ratios respectively. In the present study \(SNR_{out}\) was expressed in terms of MTF and NNPS and thus it is a function of spatial frequency, while \(SNR_{in}\) was expressed through radiation intensity. High DQE values indicate that identical
image quality can be achieved with less photon; increasing the DQE and leaving radiation exposure constant will improve image quality (Grammaticos and Fountos 2006). DQE=1, corresponds to an ideal detector meaning that all incident radiation energy is absorbed and converted into useful image information. During the past few years, different methods of measuring DQE have been established, thus making difficult, if not impossible, the comparison imaging systems on this basis. The DQE of the PET scanner was calculated from the MTF, NNPS, and incoming $SNR_{in}^2$ as described in previous publications by using equation (12) (Michail et al 2011):

$$DQE(u) = \frac{MTF^2(u)}{SNR^2_{in} \cdot NNPS(u)}$$  \hspace{1cm} (12)

$SNR_{in}^2$ was defined as the activity (in counts/mm$^2$), of the plane source phantom, incident on the detectors. Since the spatial frequency sampling steps of MTF and NNPS are generally not the same, NNPS was linearly interpolated at the frequency sampling points of MTF and then DQE was calculated at these points.

### B.3.4 Effect of crystal material on DQE

The system was also simulated by replacing the BGO crystal arrays with Yttrium Orthoaluminate Perovskite (YAlO$_3$:Ce or YAP) (Van Eijk 2002, Kalivas et al 2006), Lutetium Orthoaluminate Perovskite LuAlO$_3$:Ce or LuAP:Ce, Lutetium Yttrium Orthoaluminate Perovskite ([(LuY)AlO$_3$:Ce or LuYAP:Ce) with 70% Lutetium (Lu) atomic fraction, LuYAP:Ce with 80% Lu atomic fraction (Van Eijk 2002, Valais et al 2008, Valais et al 2010), Lutetium Oxyorthosilicate (Lu$_2$SiO$_5$:Ce or LSO) (Van Eijk 2002, Michail et al 2007, Michail et al 2009, Michail et al 2009), and Gadolinium Oxyorthosilicate (Gd$_2$SiO$_5$:Ce or GSO) (Van Eijk 2002, Valais et al 2007, Valais et al 2007, Valais et al 2008) crystals with dimensions equal to those of BGO (6.3x6.3x30 mm) in the tangential, axial and radial directions, respectively. The calculated Quantum Detection Efficiency (QDE) (Boone 2000, Michail et al 2010) and Mass Attenuation Coefficients (Hubbel and Seltzer 1995) ($\mu / \rho$) of the 3 cm long crystals under investigation are listed in Table 1.
**Table 1.** Scintillating crystals properties.

<table>
<thead>
<tr>
<th>Scintillating crystal</th>
<th>Density (g/cm$^3$)</th>
<th>Mass Attenuation Coefficients ($\mu/\rho$) @ 511 keV</th>
<th>Quantum Detection Efficiency (QDE) @ 511 keV</th>
</tr>
</thead>
<tbody>
<tr>
<td>BGO</td>
<td>7.13$^a$</td>
<td>0.1350</td>
<td>0.94</td>
</tr>
<tr>
<td>Gd$_2$SiO$_5$:Ce</td>
<td>6.71$^a$</td>
<td>0.1048</td>
<td>0.88</td>
</tr>
<tr>
<td>Lu$_2$SiO$_5$:Ce</td>
<td>7.40$^a$</td>
<td>0.1174</td>
<td>0.93</td>
</tr>
<tr>
<td>LuAP:Ce</td>
<td>8.34$^a$</td>
<td>0.1145</td>
<td>0.94</td>
</tr>
<tr>
<td>LuYAP:Ce-70%</td>
<td>7.2$^a$</td>
<td>0.1080</td>
<td>0.90</td>
</tr>
<tr>
<td>LuYAP:Ce-80%</td>
<td>7.2$^a$</td>
<td>0.1103</td>
<td>0.91</td>
</tr>
<tr>
<td>YAlO$_3$:Ce</td>
<td>5.37$^b$</td>
<td>0.0852</td>
<td>0.75</td>
</tr>
</tbody>
</table>

$^a$Reference (Valais et al 2010).

$^b$Reference (Michail et al 2007).
CHAPTER C

RESULTS AND DISCUSSION

C.1. Validation according to NEMA NU 2-2001

C.1.1. Spatial resolution

Table 2 shows a comparison between the spatial resolution obtained from the GATE simulations and the published experimental data (Bettinardi et al 2004, Mawlawi et al 2004). Spatial resolution was assessed in both axial and transverse directions, according to NEMA NU 2-2001 protocol (NEMA 2001). The differences between simulated results and experimental FWHM data (Bettinardi et al 2004, Mawlawi et al 2004) range from 0.16%-3.28% in 2D and from 0.33%-3.29% in 3D modes. The corresponding differences of the FWTM data range from 0.17%-0.86% in 2D and 0.17%-1% in 3D modes. In all cases, 2D FWHM and FWTM were lower than the corresponding 3D values, due to the collimators used in the 2D set-up that determines a narrower FOV, which in turn provides better resolution properties.

Table 2. Simulated and measured spatial resolution.

<table>
<thead>
<tr>
<th>Spatial resolution</th>
<th>y-coordinate (cm)</th>
<th>FWHM (mm)</th>
<th>FWTM (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>2D</td>
<td>Axial</td>
<td>5.01a</td>
<td>6.10a</td>
</tr>
<tr>
<td></td>
<td>Transverse Radial</td>
<td>6.22a</td>
<td>6.75a</td>
</tr>
<tr>
<td></td>
<td>Tangential</td>
<td>6.12a</td>
<td>6.88a</td>
</tr>
<tr>
<td>3D</td>
<td>Axial</td>
<td>5.82a</td>
<td>6.47a</td>
</tr>
<tr>
<td></td>
<td>Transverse Radial</td>
<td>6.25a</td>
<td>6.81a</td>
</tr>
<tr>
<td></td>
<td>Tangential</td>
<td>6.13a</td>
<td>6.89a</td>
</tr>
</tbody>
</table>

a. This work, b. Reference (Mawlawi et al 2004), c. Reference (Bettinardi et al 2004), d. Radial and Tangential average.

C.1.2. Sensitivity

Figures 8 and 9 show a comparison of the simulated system’s count rate with experimental data (Mawlawi et al 2004) in both 2D and 3D, at radial locations R=0 and R=10cm. The attenuation coefficient of the aluminum sleeve was found equal to
0.1097/cm in 2D mode and 0.073/cm in 3D mode, by using the exponential law, after extrapolation of the system events counting rate (Fig. 8, 9) (NEMA 2001). The extrapolated values, obtained after linear regression to the data of Figs. 8 and 9, were used to calculate the total counting rate in the absence of any attenuating material (no wall thickness). The difference in linear attenuation coefficient of the Al sleeve between 2D and 3D (0.1097 for 2D and 0.073 cm\(^{-1}\) for 3D), calculated according to the sensitivity measurement of the NEMA protocol, was attributed to the septa, present in 2D (Bailey et al 1991). Accurate determination of the linear attenuation coefficient requires narrow beam geometry conditions (Zaidi and Hasegawa 2003). These conditions are more similar with the 2D geometry rather than the 3D, in which geometry is closer to conditions measuring energy absorption coefficient (0.077 cm\(^{-1}\) at 511keV for Al) (Hubbel and Seltzer 1995). The linear attenuation coefficient of Aluminum (0.22/cm) was calculated from tabulated data on attenuation coefficients (0.08cm\(^2\)/g at 511keV) and density (2.7g/cm\(^3\)), which have been obtained with narrow beam geometry (Hubbel and Seltzer 1995). The ratio of the total counting rate to the administered activity equals the system’s sensitivity, which is shown in Table 3. This table shows a comparison of the simulated system’s sensitivity with experimental data (Mawlawi et al 2004) in both 2D and 3D, at radial locations R=0 and R=10cm. The differences between simulated and experimental (Mawlawi et al 2004) sensitivity values are shown in Table 3 ranging from 0.06% to 1.62% in both 2D and 3D modes. The differences between the extrapolated and the ideal source values (with and without attenuation) range from 0.04% to 0.82% (radial location R=0cm) in 2D and 0.52% to 0.67% (radial locations R=10cm) in 3D mode. Taking this into account, the sensitivity simulations could be obtained only from the ideal source simplifying the NEMA sensitivity method and reducing the simulation time.
Figure 8. 2D System count rate with the phantom positioned at R=0cm and at R=10cm with respect to the centre of the scanner FOV.

Figure 9. 3D System count rate with the phantom positioned at R=0cm and at R=10cm with respect to the centre of the scanner FOV.

Table 3. System sensitivity in 2D and 3D modes.

<table>
<thead>
<tr>
<th>Radial location (cm)</th>
<th>Sensitivity (cps/kBq)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Simulated (GATE)</td>
<td>Experimental</td>
<td>Deviations (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2D</td>
<td>3D</td>
<td>2D</td>
<td>3D</td>
<td>2D</td>
<td>3D</td>
</tr>
<tr>
<td>0</td>
<td>1.94</td>
<td>9.03</td>
<td>1.93</td>
<td>9.17</td>
<td>0.46</td>
<td>1.62</td>
</tr>
<tr>
<td>10</td>
<td>1.99</td>
<td>9.28</td>
<td>1.98</td>
<td>9.42</td>
<td>0.06</td>
<td>1.51</td>
</tr>
</tbody>
</table>

*Reference (Mawlawi 2004).*
Figures 10 and 11 show the 2D and 3D sensitivity profiles across the axial FOV of the scanner, in the centre (0cm) and for radial position 10cm off the central axis. Summation of the true events contained in the 47 planes provides also verification of the system sensitivity, as shown in Table 3. By increasing the energy window and thus allowing more scattered events to contribute as useful signal (besides the 40% of the interactions that fall within the photo peak at 511keV in the 375-650keV energy range) (Van Eijk 2002), sensitivity was further improved by the following ratios: (i) 1.34 at radial location of 0cm, and 1.31 at 10cm, in 2D mode (25.37% increase at 0cm and 23.82% at 10cm), (ii) 1.17 at 0cm, and 1.17 at 10cm, in 3D mode (14.58% increase at 0cm and 14.81% at 10cm).

![Sensitivity Profile](image)

**Figure 10.** Sensitivity across axial FOV of scanner simulated according to NEMA NU01 standard in 2D data acquisition mode.
Figure 11. Sensitivity across axial FOV of scanner simulated according to NEMA NU01 standard in 3D data acquisition mode.

C.1.3. Counting rate performance

Figures 12 and 13 show the counting rate performance of the scanner in 2D and 3D modes compared to published data (Mawlawi et al 2004) for activity concentration of 100 and 35kBq/mL for the 2D and the 3D respectively. The simulated 2D true coincidences were higher than 307.17kcps, whereas the 2D randoms were higher than 1100.23kcps, at 100kBq/mL, respectively. The 2D peak scatter count rates, in 2D, were 82.83kcps at 100kBq/mL. The corresponding simulated 2D peak NECR was 94.31kcps at 70kBq/mL. For the 3D data acquisition mode, the simulated true, random and scatter count rates were greater than 352.21, 1800.34 and 273.07kcps at 35kBq/mL, respectively. The corresponding simulated 3D peak NECR was 66.93kcps at 15kBq/mL. Deviations between simulated model count rate values and measured data (Mawlawi et al 2004) for activity concentration up to 100kBq/mL (35kBq/mL) in 2D (3D) were smaller than 7.76% (9.13%).
Figure 12. Simulated and measured 2D count rate performance (true, scatter and random coincidences, as well as the NECR).

Figure 13. Simulated and measured 3D count rate performance (true, scatter and random coincidences, as well as the NECR).

C.1.4. Scatter fraction

The average scatter fraction estimated by the ratio of the scattered events to the sum of the scattered and true events in 2D and 3D was 20.02% and 43.85%, whereas the measured data were 19.1% and 45.1% respectively (Mawlawi et al 2004).
C.1.5. Image quality

The Image Quality (IQ) results in both 2D and 3D, obtained from the simulated torso image quality phantom are shown in Fig. 14 and summarized in Table 4. Hot and cold sphere contrasts, as well as the background variability in the lung, are higher in 2D than in 3D. The average residual error over the ‘lung’ insert was found 20% in 2D and 15% in 3D.

![Image Quality Torso Phantom](image)

**Figure 14.** Image quality torso phantom in 2D (left) and 3D (right).

<table>
<thead>
<tr>
<th>Sphere diameter (mm)</th>
<th>1</th>
<th>1.3</th>
<th>1.7</th>
<th>2.2</th>
<th>2.8</th>
<th>3.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot sphere contrast (%)</td>
<td>29&lt;sup&gt;a&lt;/sup&gt;</td>
<td>27&lt;sup&gt;b&lt;/sup&gt;</td>
<td>47&lt;sup&gt;a&lt;/sup&gt;</td>
<td>53&lt;sup&gt;b&lt;/sup&gt;</td>
<td>64&lt;sup&gt;a&lt;/sup&gt;</td>
<td>63&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cold sphere contrast (%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>2D</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background variability (%)</td>
<td>7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Average residual error over ‘lung’ insert (%)</td>
<td>20%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sphere diameter (mm)</th>
<th>1</th>
<th>1.3</th>
<th>1.7</th>
<th>2.2</th>
<th>2.8</th>
<th>3.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot sphere contrast (%)</td>
<td>24&lt;sup&gt;a&lt;/sup&gt;</td>
<td>22&lt;sup&gt;b&lt;/sup&gt;</td>
<td>40&lt;sup&gt;a&lt;/sup&gt;</td>
<td>40&lt;sup&gt;b&lt;/sup&gt;</td>
<td>52&lt;sup&gt;a&lt;/sup&gt;</td>
<td>55&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Cold sphere contrast (%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>3D</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background variability (%)</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Average residual (%) over ‘lung’ insert (%)</td>
<td>15%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> This work, <sup>b</sup> Reference (Mawlawi et al 2004).
An application of this GATE model on complex human structures is shown in Fig. 15, where the grey scales have been translated to activity distributions. In order to obtain these slices, a brain phantom (Hoffman) (Hoffman et al. 1990, OpenGATE Collaboration, Users Guide V6.1) was used for simulation. The brain slices were acquired from STIR, after reconstruction of the arc-corrected sinogram data with the commonly used 2D filtered back projection (FBP2D) (Ramp filter with additional apodizing window 0.5) (Brun et al. 1997, Thielemans et al. 2006) the Kinahan and Rogers FPB3DRP (Colsher filter with additional apodizing window 0.5) and with the iterative, Maximum Likelihood Estimation Ordered Subsets version of Green's MAP One Step Late (MLE-OSMAPOSL) reprojection algorithms (Kinahan Rogers 1989, Labbe et al. 2004, Thielemans et al. 2012).

![Figure 15. Hoffman brain phantom in FBP2D (upper left), FBP3DRP (upper right), OSEM with 15 subsets/3 iterations (down left) and 21 subsets/3 iterations (down right).](image)

In this study sensitivity was estimated without the presence of attenuation material by simulating an ideal source in order to validate the accuracy of the NEMA sensitivity extrapolation method. The ideal source simulation results showed excellent agreement with those obtained from the extrapolation method. Taking this agreement into account we suggested that simulations for sensitivity could be
obtained just from an ideal source simplifying the method and reducing simulation time.

The influence of Compton scatter recovery was also investigated showing that sensitivity can be further improved from 14.58% to 25.37% by increasing the energy window.

Image quality was also assessed by simulations of the IQ torso phantom using the STIR reconstruction software. The simulated image quality was also found in excellent agreement with Mawlawi et al (2004) published data.

Furthermore, the STIR reconstructed GATE simulated data were used to obtain PET images from specific radiopharmaceutical distribution using simplified phantoms or more complex human structures. The above results will assist nuclear medicine physicians, as an efficient diagnostic tool.

On a pre-clinical level any potential imaging agent can first be controlled in a fast and straightforward manner. In addition, relevant clinical applications would include:

- a) Novel and worth mentioning imaging protocols for simpler and faster quantitative interpretation of SPECT and PET scans, with better anatomical correlation.
- b) The STIR reconstructed images, could also be used to bridge the gap between imaging and dosimetry, in order to obtain directly dose maps from the activity distribution as input for PET and SPECT Monte Carlo simulations. From the latter, physicians could directly compare the actual dose biodistribution map of a tracer, used for the production of SPET or PET data, with the data estimated from the reconstructed PET or SPET images.

Dosimetry on pre-treatment scans in terms of target and dose-limiting tissue uptake determination for optimal targeted radionuclide treatment conditions and for dose reduction to essential levels, could also be assessed (Grammaticos and Fountos 2006). Considering that the increasing nuclear medicine therapeutic applications, have known drawbacks regarding dosimetric issues even in case of $\gamma$-emitting radionuclides, the clinical benefit by the use of the model we suggest in this study would be quite important for example, the simplified exact determination of tumour-absorbed dose and toxicity limits, when administering peptide receptor radionuclide treatment (PRRT) with 90Y- or lutetium (177Lu)-labeled somatostatin analogues, or 131I-MIBG treatment in patients bearing neuroendocrine tumour (Shapiro et al...
At last, on conventional SPECT images, image interpretation is mostly qualitative, except for certain examinations, like Datscan, for which Regions of Interest (ROI) with corresponding count rates are utilized to produce formula-based values for comparison with reference values. In 18F-FDG-PET, a powerful oncology tool, images are also generally interpreted qualitatively. Both the PET associated semi-quantitative parameter of Standardized Uptake Value (SUV) and the SPECT computed values vary with the use of an average pixel value versus a maximum pixel value for each ROI, besides several other parameters. Uniformity of SPECT computed values and SUV by using the model dose maps would allow for a quantitative SPET and 18F-FDG-PET image evaluation and subsequent feasibility for direct interstudy comparison (Shreve et al 1999, Bombardieri et al 2003, Krenning et al 2003). Overall this model would allow for faster and more precise detection, e.g. of parathyroid adenomas using 99mTc-Sestamibi (double phase or subtraction) scintigraphy, as well as for avoiding potential pitfalls such as focal uptake in brown fat with 18F-FDG-PET and focal uptake in the bowel due to physiological excretion in 67Ga-Citrate or 111In-DTPA-Octreotide used for scintigraphies comparison (Shreve et al 1999, Bombardieri et al 2003, Krenning et al 2003).

C.2. MTF

Figure 16 shows the reconstructed slice profiles of the plane source and the corresponding point profiles of the line source images obtained from the STIR software. The first column shows the FBP2D reconstructed images in both horizontal and vertical directions (tilted by 3°), as well as the point profiles of the line source 2D image in the bottom. The second column shows the FBP3DRP (horizontal, vertical and point) and the third the corresponding OSMAPOSL (horizontal, vertical and point) reconstructed images (21 subsets, 2 iterations), respectively. Finally, the fourth (right) column shows the large (18 cm) plane sources, that was used to examine resolution of the PET scanner in a large part of the field of view, in FBP2D (top), FBP3DRP (middle) and OSMAPOSL (bottom).
Figure 16. Reconstructed line and point images obtained from the STIR software. A) First column shows the FBP2D reconstructed images in both horizontal and vertical directions (tilted by 30°) and the point 2D image in the bottom. B) Second column shows the FBP3DRP, c) third the OSMAPOSL reconstructed images (21 subsets, 2 iterations) respectively, d) fourth (right) column shows the large (18 cm) plane sources in, FBP2D (up), FBP3DRP (middle) and OSMAPOSL (down).

C.2.1. Plane source

Figures 17 and 18 show a comparison between the MTFs obtained with the plane source method, from the horizontal (Fig. 17) and vertical (Fig. 18) plane source reconstructed images, with the FBP2D, the FBP3DRP and the OSMAPOSL (21 subsets, 2 iterations) reconstruction algorithms. MTF of the FBP2D and FBP3DRP are almost identical in the horizontal direction, whereas in the vertical, deviations less than 2.45%, with an average value of 0.92% in the whole spatial frequency range are observed. The MTF of the OSMAPOSL reconstructed image shows that higher frequencies are preserved, compared to the case of the other two methods, in the whole spatial frequency range. This finding justifies the observations depicted in Fig. 16 regarding the resolution uniformity. By inspection of the large (18 cm) plane source images, shown in Fig. 16, which is reconstructed by the 2D and 3D filtered back projection algorithms, it can be observed that resolution is degraded off centre.
Figure 17. Comparison between the MTFs obtained with the plane source method, from the horizontal plane source reconstructed image with the FBP2D, the FBP3DRP and the OSMAPOSL (21 subsets, 2 iterations), respectively. FBP2D, FBP3DRP and OSMAPOSL (21 subsets, 2 iterations) MTF curves, with energy window 200-650 keV, are also provided for comparison.

Figure 18. Comparison between the MTFs obtained with the plane source method, from the vertical plane source reconstructed image with the FBP2D, the FBP3DRP and the OSMAPOSL (21 subsets, 2 iterations), respectively.

Quantification of the above observations are shown in Figs. 19 and 20, which show
the MTFs obtained with the plane source method, from the large plane source reconstructed images, with the FBP2D and the FBP3DRP, respectively. MTFs were obtained every 2 cm from the centre to the edge of the plane source in order to investigate image resolution off centre. Figs. 19 and 20, as well as Table 5 show that the possible spatial frequencies (in cycles/mm) that can be resolved are gradually reduced from the center towards the edge of the field of view, in both FBP2D and FBP3DRP images. This is due to the streak artifacts and the parallax effect that are present in the images (Kontaxakis and Strauss 1998, MacDonald and Dahlbom 1998). With the plane source method spatial resolution was assessed by examining MTF in a large part of the field of view. Fig. 17 shows that when the energy window is broadened from 375-650 to 200-650 keV, allowing more scattered events to contribute as useful signal, the spatial resolution of the FBP2D, FBP3DRP and OSMAPOSL reconstructed images is degraded by a 6.94%, 7.30% and 4.82%, respectively in the whole spatial frequency range.

Figure 19. Comparison between the MTFs obtained with the plane source method, from the large (18 cm) horizontal plane source FBP2D reconstructed image.
Figure 20. Comparison between the MTFs obtained with the plane source method, from the large (18 cm) horizontal plane source FBP3DRP reconstructed image.

Table 5. Image Resolution of the Large Plane Sources at 5% MTF.

<table>
<thead>
<tr>
<th>Radial distance (cm)</th>
<th>FBP 3D (cycles/mm)</th>
<th>FBP 2D (cycles/mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full width (18)</td>
<td>0.0571</td>
<td>0.0519</td>
</tr>
<tr>
<td>0-2</td>
<td>0.0624</td>
<td>0.0623</td>
</tr>
<tr>
<td>2-4</td>
<td>0.0613</td>
<td>0.0612</td>
</tr>
<tr>
<td>4-6</td>
<td>0.0581</td>
<td>0.0567</td>
</tr>
<tr>
<td>6-8</td>
<td>0.0446</td>
<td>0.0435</td>
</tr>
</tbody>
</table>

C.2.2. Line source

Figure 21 shows a comparison between the MTFs obtained with the line source method, from the point source reconstructed images, with the FBP2D, the FBP3DRP and the OSMAPOL (21 subsets, 2 iterations), respectively. MTF values of the FBP3DRP are 14.21% higher than the FBP2D. MTF values of the OSMAPOL reconstructed image are higher than both FBP2D and FBP3DRP by 31.64% and 20.32% respectively.
Figure 21. Comparison between the MTFs obtained through the point sources with the FBP2D, the FBP3DRP and the OSMAPOSL (21 subsets, 2 iterations), respectively.

Figure 22 shows a comparison between the two methods (plane and line source) for the assessment of the MTF. Both MTF curves were obtained after FBP 3D image reconstruction. The MTFs are shown along with their standard deviation (sd) values for the whole spatial frequency range. The differences between the two methods, in the MTF calculation, could be attributed to the fact that the points and lines which were employed in this study were assumed to have physical dimensions (Kaftandjian et al 1996).
Chapter C  

Results & Discussion

Figure 22. Comparison between the MTFs obtained through the plane and the line source methods (FBP3DRP) with the corresponding standard deviations values.

The plane source method is less prone to noise due to the benefits of averaging larger amount of data, by using more samples (Fountos et al 2012) (line profiles), providing a mean standard deviation of $\overline{sd} = 0.0031$, in contrary to the line source method, which showed $\overline{sd} = 0.0203$, regarding the MTF calculation of the PET plane source images. This may be the principal benefit of the proposed technique in the context of the spatial resolution assessment of clinical PET images. The limitations of the MTF calculation, through the line source method, arise from the assumption of rotational symmetry, in the spatial resolution, that has been also adopted in previous works (Prevrhal et al 1999). Following this assumption, the PSF profiles could be averaged in radial directions, regarding the fact that the PSF has a complicated, non-separable three dimensional shape, as has been reported for Spiral CTs (Prevrhal et al 1999). Furthermore, PSF and LSF may not fulfill the Shift Invariance condition of linear systems theory and thus it may depend on the position within the image (Williams et al 1999).

Figure 23 shows reconstructed slices of a brain phantom (Hoffman et al 1990, OpenGATE Collaboration). The brain slices were acquired from STIR, after reconstruction of the arc-corrected sinogram data with the FBP2D (Brun and Rademakers 1997, Thielemans et al 2006) the FPB3DRP and with the OSMAPosl (21 subsets/2 iterations) reprojection algorithms (Kinahan and Rogers 1989, Labbe

Figure 23. Hoffman brain phantom after FBP2D (left), FBP3DRP (middle), OSMAPOSL with 21 subsets/2 iterations (right).

The significance of the MTF measurement for the accurate PET image resolution estimation can arise from the following considerations. MTF is the equivalent of the LSF in the spatial frequency domain where signals can be easily decomposed into sine waves. In this way the signal obtained from the plane source can provide useful information concerning the signal amplitude, frequency and phase of object signals passing through the imaging system. In other words, for each spatial frequency (which corresponds to a particular object size in the spatial domain) MTF gives the corresponding amplitude of useful signal, i.e. the contrast level in the final image of the particular object size. Thus a single MTF analysis in the spatial frequency domain can be used to predict the system performance for all possible structure sizes. Analysis of cascaded imaging systems (with multiple signal conversion stages), such as a PET scanner, can be easily done since MTF (in spatial frequency domain) is expressed through a simple product of the individual MTFs of separate stages (instead of using convolution for LSFs in space domain). Thus the effect of weak or strong imaging chain links, on the overall system response, can be more easily investigated.

In the line source based, MTF estimation method, presented here, the possibility for inaccurate estimation of the resolution is reduced, as compared to the NEMA protocol, due to following: 1) irregular (e.g. oblong) PSF shapes, often found in the peripheral areas of the FOV, may over or under estimate axial and transverse image
resolution, when using the NEMA protocol. In contrast in this study, averaged PSF profiles are obtained after integration of line profiles passing through the centre of the point image and covering various angles ranging from $0^0$ to $180^0$ with a $2^0$ angle step. The FWHM as a measure of spatial resolution lacks the possibility for correct and complete system characterization, since different PSF shapes may show equal FWHM values (Starck et al 2005, NEMA 2007).

Furthermore the plane source method proposed in the present work has advantages, over the FWHM method of the NEMA NU 2-2001 protocol: In the NEMA protocol, the point sources are positioned at six points in the FOV of the scanner (i.e. in two groups of three, one at the center of the field of view and the second shifted by one fourth of the FOV, at positions: $x=0$ cm, $y=1$ cm; $x=0$ cm, $y=10$ cm; and $x=10$ cm, $y=0$ cm) in the FOV of the scanner. Taking into account that these point sources are placed at the centre and at a distance (displacement) of 10 cm of the FOV, the available resolution information is restricted only to particular coordinates, excluding intermediate values (between 0 and 10 cm) as well as values beyond 10 cm. Thus, possible non-uniformities within these regions of interest may not be revealed. This is also the case when multiple point sources could be positioned across the FOV, thus increasing the difficulty to assess resolution with custom made phantoms, and hence making the use of commercialized phantoms necessary (Kotasidis et al 2011).

The point sources in glass capillaries free in air could be affected by the range of the positrons emitted by the source due to the finite source size, whereas methods that use cylindrical phantoms as attenuation media do not have this dependence. Measuring spatial resolution from a sharp interface (such as the plane source presented here) that produces a line response function may become increasingly important as the spatial resolution of PET systems improves. Such measurements have been widely investigated in other areas of medical imaging. Examples of similar work can be also found in CT (Boone 2001), and SPECT (Fountos et al 2012) imaging.

With the method presented in this work only one plane source, covering a relatively large portion of the whole FOV, is required to estimate image resolution. Moreover the present method provides the ability to obtain image resolution in three dimensions by placing the source only horizontally and vertically. Also from the images of the plane source, proposed in this work, a significant number of pixels,
over the entire LSF, are averaged to estimate the MTF. This is an advantage over the NEMA NU 2-2001 method, since the point sources appearing in PET images of 128x128, 256x256 or 512x512 typical dimensions, will incorporate only a few pixels, which may be insufficient to correctly characterize image contrast (Greenes and Brinkley 1997, Soret et al 2007). Furthermore, the poor spatial resolution of PET systems is a limiting factor for the accurate quantitative estimation of the PSF of structures more than three times smaller than the FWHM (Partial Volume Effect-PVE) of the reconstructed image resolution (Soret et al 2007). The partial volume effect alternates the pixel values of a structure, by forcing lower activity peripheral tissues, to gain uptake with higher activities from hot lesions spreading to the surrounding (spill-out effect) (Parka et al 2007). Thus, hot lesions will appear with reduced maximum values and the PSF will appear broader, with low-intensity tails. In the latter case, the low intensity values dominating the shape of the PSF necessitate the estimation of the Full Width at Tenth Maximum (FWTM), along with the FWHM, in order to assess the positron range effects on spatial resolution (Levin and Hoffman 1999). The plane source MTF method proposed in this work provides complete image resolution characterization comparing to the single value image quality metrics of FWHM and FWTM.

In conclusion, the broadening of the PSF, along with the finite number of image pixels available within the PSF area may also lead to erroneous estimation of the FWHM taking also into account that the width of a PSF does not track well with the perception of the individual performing the measurement (Smith 1997, Palmer 2005).

Due to aforementioned, MTF could be useful for comparing the effects of different scan and reconstruction parameters (FBP, OSEM etc), for PET scanners quality control and especially for evaluating the accuracy of size and density measurements of fine details in nuclear imaging (Flohr 2005). Also it can be used as a long term quality control method to identify the system’s performance stability. Additionally, this method could be useful for the comparison between different PET scanners in multicenter PET studies and in particular for the accurate image resolution determination of new technology PET scanners incorporating high resolution detectors (Chatziioannou et al 1999, Palmer et al 2005, Parka et al 2007, Ryu et al 2012).

Scatter and streak artifacts could be possible disadvantages of the plane source
method in comparison with the line source one. In this sense the plane source method could be considered as more realistic, with respect to clinical practice, since both scattering and streak artifacts are present in PET in vivo clinical imaging.

One of the challenges of assessing spatial resolution with a clinical PET scanner is that iterative reconstruction algorithms, which are offered in most clinical systems, are non-linear and difficult to evaluate (Liow and Strother 1993, Lodge et al 2009). However since resolution is object-dependent, due to the non linear nature of iterative reconstruction algorithms, the use of a plane source to assess resolution will potentially lead to different resolution results than those obtained by a point source, and in turn both sources (plane and point) will potentially provide different resolution results than a realistic object such as a patient, in different parts of the image (Lodge et al 2009). For this reason, standardized measurement geometries of the method presented here are of practical importance when comparing clinical reconstruction protocols.

The possible challenges for the implementation of the plane source method for routine PET quality control may be related to: a) The total time required for the preparation of the source, b) the total dose that will be received by the personnel and the precautions that should be undertaken on to avoid contamination during the implementation and the quality control procedure, c) the specific radioactivity of the solution that the plane source should be immersed in, d) the uniformity distribution of the Fluorodeoxyglucose (18F-FDG) radiopharmaceutical on the plane source, e) the requirement of a cylindrical PMMA phantom consisting of two D-shaped parts from the positioning in between of the plane source, f) placing and holding of the phantom on the bed as well as, the orientation of the plane source in a slight angle ranging from 3 to 8 degrees in order to avoid aliasing effects, g) the necessity of a software for the MTF determination. This software can be freely distributed on demand by our group.

C.3. Iterative Image Reconstruction

Figure 24 shows transverse and coronal slices (tilted by 3°), from the horizontal plane source reconstructed images with the OSMAPOSL reconstruction algorithm
with subsets ranging from 3 to 21 with various iterations, ranging from 2 to 20 with a step of 2.

<table>
<thead>
<tr>
<th>Iterations</th>
<th>MTF Transverse</th>
<th>NNPS Coronal</th>
<th>MTF Transverse</th>
<th>NNPS Coronal</th>
<th>MTF Transverse</th>
<th>NNPS Coronal</th>
<th>MTF Transverse</th>
<th>NNPS Coronal</th>
<th>MTF Transverse</th>
<th>NNPS Coronal</th>
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</table>

**Figure 24.** Transverse and coronal slices, from the plane source reconstructed images with the OSMAPOSL (3, 5, 7 and 21 subsets, various iterations).

The first column shows the number of iterations, the second one the transverse slices which were used for the MTF calculation, through the LSF method (Fountos *et al* 2012), while the third column shows the coronal slices which were used for the NNPS estimation, respectively. The impact of the progressively increase in the number of iterations is clearly shown in each image, whereas the corresponding increase in the number of subsets does not show any influence on image quality. This claim is quantitatively shown in Figs. 25 and 26 whereas the MTF is clearly influenced by the number of iterations but remains unaltered by the change in the number of subsets for fixed number of iterations.

**C.3.1. MTF**

Figures 25 and 26 show MTF curves obtained from iterative STIR reconstructed LSF images. The curves correspond to transverse reconstructed slices in which the number of subsets was kept fixed and the number of iterations was increased with a step of 2. In every case MTF was found to increase up to 10 iterations and remain almost steady thereafter. However, the range of this increase in the MTF is limited as the number of subsets increases. In Fig.25 (3 subsets) the MTF values at 0.04 cycles/mm ranges from 0.208 (2 iterations) to 0.507 (20 iterations). The MTF value
where this increase stops is 0.492 (12 iterations). In Fig.26 (21 subsets) the MTF values at 0.04 cycles/mm ranges from 0.432 (2 iterations) to 0.495 (20 iterations). The MTF value where the increase stops is 0.489 (12 iterations) (see Table 6).

**Figure 25.** Comparison between the MTFs obtained with the LSF method, from the plane source reconstructed image with the OSMAPOSL (3 subsets, various iterations).

**Figure 26.** Comparison between the MTFs obtained with the LSF method, from the plane source reconstructed image with the OSMAPOSL (21 subsets, various iterations).
Table 6. Influence of the number of subsets and iterations on the MTF.

<table>
<thead>
<tr>
<th>Number of subsets</th>
<th>Number of Iterations</th>
<th>% difference between the minimum and maximum values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>0.208</td>
<td>0.492</td>
</tr>
<tr>
<td>5</td>
<td>0.217</td>
<td>0.504</td>
</tr>
<tr>
<td>7</td>
<td>0.377</td>
<td>0.504</td>
</tr>
<tr>
<td>15</td>
<td>0.432</td>
<td>0.498</td>
</tr>
<tr>
<td>21</td>
<td>0.432</td>
<td>0.489</td>
</tr>
</tbody>
</table>

In Table 7 the influence of the number of subsets on the reconstructed image is shown. In order to obtain these values, the number of iterations was kept constant (10 iterations) and the number of subsets was allowed to vary from 3 to 21. The obtained MTF values show that there is no significant impact on image resolution.

Table 7. Comparison between the MTFs obtained from the plane source reconstructed image with the OSMAPOS (various subsets, 10 iterations), respectively.

<table>
<thead>
<tr>
<th>Spatial frequency (cycles/mm)</th>
<th>Number of iterations: 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td>0.02</td>
<td>1.000</td>
</tr>
<tr>
<td>0.02</td>
<td>0.829</td>
</tr>
<tr>
<td>0.04</td>
<td>0.493</td>
</tr>
<tr>
<td>0.06</td>
<td>0.211</td>
</tr>
<tr>
<td>0.08</td>
<td>0.073</td>
</tr>
</tbody>
</table>

C.3.2. NNPS

Figures 27 and 28 show NNPS results obtained from iterative reconstructed STIR images. The curves, shown in Figs. 27 and 28, correspond to coronal reconstructed slices in which the number of subsets was kept fixed and the number of iterations was increased with a step of 2.
In every case the noise levels of the PET reconstructed images, in terms of the NNPS, were found to decrease as the number of iterations increase. The maximum noise levels for the 3 subsets, 2 iterations iterative reconstructed image (shown in Fig. 27) is 0.931 mm² at 0 cycles/mm, whereas the corresponding maximum NNPS
value of the 21 subsets, 2 iterations image (shown in Fig. 28) is 0.4 mm$^2$ at equal spatial frequency.

Furthermore, noise levels were also found to decrease as the number of subsets increase. This is also shown in Table 8 in which the number of subsets was allowed to vary (3 to 21) and the number of iterations was kept constant (10 iterations). For example NNPS values (mm$^2$) at spatial frequency of 0.01 cycles/mm range from 0.777 (in the 3 subsets, 10 iterations iterative reconstructed image) to 0.357 (in the 21 subsets, 10 iterations iterative reconstructed image).

**Table 8.** Comparison between the NNPS obtained from the plane source reconstructed images with the OSMAPosl (various subsets, 10 iterations).

<table>
<thead>
<tr>
<th>Spatial frequency (cycles/mm)</th>
<th>Number of iterations:10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of subsets 3</td>
</tr>
<tr>
<td>0.00</td>
<td>0.995</td>
</tr>
<tr>
<td>0.02</td>
<td>0.576</td>
</tr>
<tr>
<td>0.04</td>
<td>0.232</td>
</tr>
<tr>
<td>0.06</td>
<td>0.053</td>
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<tr>
<td>0.08</td>
<td>0.017</td>
</tr>
</tbody>
</table>

**C.3.3. DQE**

Figures 29 and 30 show DQE results obtained from iterative reconstructed STIR plane source images. The curves correspond to the combined MTF and NNPS results from both the transverse and the coronal reconstructed slices, in which the number of subsets was kept fixed and the number of iterations was increased with a step of 2. The behavior of the DQE was influenced by both MTF and NNPS. As the number of iterations was increased, higher MTF values were obtained with parallel reduction of image noise, as depicted from the NNPS results. Thus, the impact on the DQE was the improvement of the output signal to noise ratio with the increase of the number of iterations. In particular, the maximum DQE values of Fig. 29 range from 0.006 (in the 3 subsets, 2 iterations iterative reconstructed image) to 0.015 (in the 3 subsets, 20 iterations iterative reconstructed image). The corresponding maximum DQE values of Fig. 30 range from 0.013 (in the 21 subsets, 2 iterations iterative reconstructed image) to 0.021 (in the 21 subsets, 20 iterations iterative
reconstructed image. Furthermore increasing the number of subsets had also a positive contribution on DQE values. For example, DQE values of Table 9 range from 0.005 (in the 3 subsets, 10 iterations iterative reconstructed image) to 0.011 (in the 21 subsets, 10 iterations iterative reconstructed image), at 0.01 cycles/mm.

**Figure 29.** Comparison between the DQEs obtained from the plane source reconstructed images with the OSMAPOSL (3 subsets, various iterations).

**Figure 30.** Comparison between the DQEs obtained from the plane source reconstructed images with the OSMAPOSL (21 subsets, various iterations).
TABLE 9. Comparison between the DQEs obtained from the plane source reconstructed images with the OSMAPOS (21 subsets, various iterations).

<table>
<thead>
<tr>
<th>Spatial frequency (cycles/mm)</th>
<th>Number of iterations:10</th>
<th>Number of subsets</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>0.00</td>
<td>0.0050</td>
<td>0.0065</td>
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<tr>
<td>0.02</td>
<td>0.0059</td>
<td>0.0090</td>
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<tr>
<td>0.04</td>
<td>0.0050</td>
<td>0.0073</td>
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<tr>
<td>0.06</td>
<td>0.0038</td>
<td>0.0062</td>
</tr>
<tr>
<td>0.08</td>
<td>0.0013</td>
<td>0.0022</td>
</tr>
</tbody>
</table>

The influence of the number of subsets and iterations of the iterative image reconstruction, shown in Figs. 24 to 30, can be also depicted on complex human structures as shown in Fig. 31, where the grey scales have been translated to activity distributions. In order to obtain these slices, a brain phantom (Hoffman) (Hoffman et al 1990, OpenGATE Collaboration) was used for the simulation. The brain slices were acquired from STIR, after reconstruction of the arc-corrected sinogram data with the iterative, MLE-OSMAPOS reprojection algorithms (Thielemans et al 2006).

Figure 31. Hoffman brain phantom in OSEM with 3 and 21 subsets/2, 6, 12 and 21 iterations.
C.4. Effect of the Crystal material

Figure 32 shows transverse and coronal slices (tilted by 3°), from the horizontal plane source reconstructed images with the FBP2D, FBP3DRP and OSMAPOSL reconstruction algorithms. The first column, in Fig. 32, shows the crystal scintillator material, the second the transverse slices of the FBP2D, the third the transverse slices of the FBP3DRP and the fourth the transverse slices of the OSMAPOSL reconstruction algorithms, which were used for the MTF calculation, through the LSF method, respectively (Fountos et al 2012). Accordingly, the second column, in Fig. 32, shows the coronal slices of the FBP2D, the third the coronal slices of the FBP3DRP and the last the coronal slices of the OSMAPOSL reconstruction algorithms, which were used for the NNPS calculation, respectively. The impact on image quality of the detector material is initially depicted by inspection of Fig. 32.

<table>
<thead>
<tr>
<th></th>
<th>FBP2D</th>
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<th>OSMAPOSL</th>
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<tr>
<td>BGO</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>GSO:Ce</td>
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</tr>
<tr>
<td>LSO:Ce</td>
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<tr>
<td>LuAP:Ce</td>
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<tr>
<td>LuYAP:Ce-70</td>
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</tr>
<tr>
<td>LuYAP:Ce-80</td>
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<td>--</td>
</tr>
<tr>
<td>YAP:Ce</td>
<td>--</td>
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</tr>
</tbody>
</table>

Figure 32. Transverse and coronal slices of the plane source reconstructed images with the FBP2D, FBP3DRP and OSMAPOSL reconstruction algorithms.
C.4.1. MTF

Figures 33 to 35 show comparisons between the MTF curves obtained from the horizontal plane source reconstructed images, with the FBP2D, FBP3DRP and OSMAPOSL reconstruction algorithms for the PET scanner configurations incorporating successively BGO, YAP, LuAP, LuYAP-70, LuYAP-80, LSO and GSO crystals. The PET scanner configuration incorporating LuAP crystals provided the optimum MTFs in both 2D and 3D FBP image reconstruction whereas the configuration BGO was found with the higher MTF values after the iterative reconstruction.

Figure 33. Comparison between the MTFs obtained from the plane source reconstructed images with the FBP2D for various crystals.
Figure 34. Comparison between the MTFs obtained from the plane source reconstructed images with the FBP3DRP for various crystals.

Figure 35. Comparison between the MTFs obtained from the plane source reconstructed images with the OSMAPOSL (15 subsets, 3 iterations) for various crystals.

C.4.2. NNPS

Figures 36 to 38 show NNPS results from the coronal reconstructed slices, obtained from the FBP2D, FBP3DRP and OSMAPOSL reconstruction algorithms, for the PET scanner configurations incorporating BGO, YAP, LuAP, LuYAP-70, LuYAP-80, LSO and GSO crystals. The configuration, incorporating BGO crystals, were
found with the lowest noise levels after all image reconstruction algorithms. This finding, along with the data provided in Table 10, confirms also the choice for the commercial use of BGO crystals in clinical PET systems.

Figure 36. Comparison between the NNPS obtained from the plane source reconstructed images with the FBP2D for various crystals.

Figure 37. Comparison between the NNPS obtained from the plane source reconstructed images with the FBP3DRP for various crystals.
Figure 38. Comparison between the NNPS obtained from the plane source reconstructed images with the OSMAPosl (15 subsets, 3 iterations) for various crystals.

C.4.3. DQE

Table 11 shows the calculated true coincidences counted by all the crystal/detector electronics combinations under investigation. Figures 39 to 41 show DQE results obtained from the FBP2D, FBP3DRP and OSMAPosl reconstruction algorithms, for the PET scanner configurations incorporating successively BGO, YAP, LuAP, LuYAP-70, LuYAP-80, LSO and GSO crystals. The curves correspond to the combined MTF and NNPS results from both the transverse and coronal reconstructed slices. The behavior of the DQE was influenced by both MTF and NNPS. DQE values of the PET configuration incorporating BGO crystals were found higher after all image reconstruction algorithms examined in this study. In Figs. 39 to 41 the DQE results provided the overall performance of a PET scanner. However these results cannot be straightforward translated into predictions about the clinical usefulness of images produced by the system for a human observer (Eriksson et al 2010). When the quantum noise is a limiting factor for the observer, the performance is dependent on the task, and hence the relevance of the DQE at different spatial frequencies varies. Due to this, cumulative image quality results, in the sense of Figures of Merits (FOMs), were also obtained by integrating the entire MTF, NNPS and DQE (all spatial frequencies were given equal weight). The single
index values obtained this way is related to the performance of the ideal observer in the task of detecting a point source. However, for any other task, a different weighting of the frequencies must be used and, consequently, the optimal system setting for obtaining the maximal FOM will change (Eriksson et al. 2010). Table 12 shows cumulative image quality results for all the crystals in the spatial frequency range under investigation. As it can be depicted from this Table the Discovery ST PET scanner provided the optimum image quality combined with BGO scintillating crystals. This can be also explained by taking also into consideration the mass attenuation coefficient ($\mu/\rho = 0.1350$) value and the Quantum Detection Efficiency (QDE=0.94) at 511 keV which is the highest among the crystals under investigation.

**Table 11.** Calculated true coincidences counted by all the crystal/detector electronics.

<table>
<thead>
<tr>
<th>Scintillating crystal</th>
<th>True counts/mm$^2$</th>
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<tr>
<td>BGO</td>
<td>108.27</td>
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<td>Gd$_2$SiO$_5$:Ce</td>
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<td>YAlO$_3$:Ce</td>
<td>2.88</td>
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</table>

**Figure 39.** Comparison between the DQEs obtained from the plane source reconstructed images with the FBP2D for various crystals.
Figure 40. Comparison between the DQEs obtained from the plane source reconstructed images with the FBP3DRP for various crystals.

Figure 41. Comparison between the DQEs obtained from the plane source reconstructed images with the OSMAPosl (15 subsets, 3 iterations) for various crystals.
Table 12. Imaging performance comparison between the various scintillating crystals.

<table>
<thead>
<tr>
<th>Scintillating detectors</th>
<th>MTF</th>
<th>NNPS</th>
<th>DQE</th>
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<td>31.12</td>
<td>43.10</td>
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<td>GSO:Ce</td>
<td>26.96</td>
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<td>25.67</td>
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<td>33.15</td>
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<td>36.05</td>
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<td>23.09</td>
<td>35.21</td>
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<tr>
<td>YAP:Ce</td>
<td>6.66</td>
<td>21.43</td>
<td>22.56</td>
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</table>

The influence of the crystal material and the different image reconstruction algorithms can be also depicted on complex human structures as shown in Fig.42, where the grey scales have been translated to activity distributions. In order to obtain these slices, a brain phantom (Hoffman) (Hoffman et al 1990, OpenGATE Collaboration) was used for the simulation. The brain slices were acquired from STIR, after reconstruction of the arc-corrected sinogram data with the commonly used 2D filtered back projection (FBP2D) (Ramp filter with additional apodizing window 0.5) (Thielemans et al 2006) the Kinahan and Rogers FPB3DRP (Colsher filter with additional apodizing window 0.5) and with the iterative, Maximum Likelihood Estimation Ordered Subsets version of Green's MAP One Step Late (MLE-OSMAPOSL) reprojection algorithms (Thielemans et al 2012).
<table>
<thead>
<tr>
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<th>FBP3DRP</th>
<th>OSMAPOSL</th>
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<td><img src="image21.png" alt="Image" /></td>
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**Figure 42.** Hoffman brain phantom in 2D (left), 3D (middle) and OSEM with 15 subsets/3 iterations (right).
CHAPTER D

CONCLUSIONS AND FUTURE WORK

D.1 Conclusions

In this study a novel method for the complete image quality characterization and optimization of Positron Emission Tomography (PET) scanners with Monte-Carlo methods was proposed. The model was developed using the Monte Carlo package of GEANT4 Application for Tomographic Emission (GATE) and the Software for Tomographic Image Reconstruction (STIR) with cluster computing to obtain reconstructed radionuclide medical images.

Validated results of this study showed that:

a) the simulated Spatial Resolution (FWHM), Sensitivity, Scatter Fraction, Count-Rate and simulated Noise Equivalent Count Rate (NECR) in 2D and 3D were in close agreement, with others’ published experimental values,

b) the STIR reconstructed GATE simulated data as the ones used in the present study can be used to obtain realistic PET images, that can be used as a more accurate and simplified diagnostic tool for the improvement of image quality,

c) physicians could directly compare the actual dose biodistribution map of a tracer in PET or SPECT images, reducing the cost and time for consuming new radiopharmaceuticals, as well as improving the possibility for quantitative measurements of SPECT and PET studies.

The Modulation Transfer Function (MTF), that could be useful for the characterization of the Spatial Resolution of a PET system, was determined by the simulation of a novel plane source. This method is based on a thin plane source filled with 18F-FDG. The MTFs obtained for the FBP2D were in close agreement to those corresponding to the FBP3DRP image reconstruction, whereas the MTFs of the OSMAPSOI image reconstruction preserve, in all cases, higher frequencies than those found by FBP. FBP reconstructed images obtained from large horizontal plane
sources showed that MTFs were degraded from the centre of the FOV to the edges. Furthermore, MTF of the FBP reconstructed images in vertical directions were slightly lower than the corresponding horizontal ones. The method is less prone to noise and provides the ability to estimate MTF in three dimensions with a simplified procedure by placing the thin plane source phantom horizontally and vertically.

Furthermore, complete image quality characterisation of a PET scanner was held through the additional estimation of the MTF and the Normalised Noise Power Spectrum (NNPS) in order to assess the Detective Quantum efficiency (DQE) of thin 18F-FDG plane source reconstructed images. The influence of iterative image reconstruction algorithms on the plane source simulated images was investigated by using various subsets (3 to 21) and iterations (1 to 20). Image quality in terms of MTF was found to improve by increasing the number of iterations (up to 12), whereas it remained unaffected by changing the number of subsets for equal number of iterations. The corresponding reconstructed image noise levels, in terms of the NNPS, were found to decrease with both number of iterations and subsets. DQE values, which were influenced by both MTF and NNPS, were found to increase with the increase of both number of subsets and iterations. The influence of the detector material on the image quality of a PET scanner was also investigated. Our study showed that: a) LuAP crystal provided the optimum MTFs in both 2D and 3D FBP image reconstruction whereas BGO was found with the higher MTF values after the iterative reconstruction, b) BGO crystals were also found with the lowest noise levels and the highest DQE values after all image reconstruction algorithms. These finding show that the BGO crystal provided the optimum overall image quality parameters for the specific PET scanner implementation. Furthermore, the STIR reconstructed GATE simulated data were used to obtain PET images from specific radiopharmaceutical distribution using simplified phantoms or more complex antropomorphic structures. The above results will assist nuclear medicine physicians, as an efficient diagnostic tool. The method modelled and simulated in this work can be experimentally implemented and used for the routine PET quality control. In this study the method was used for the image quality assessment and optimisation, but it can be also useful for the further development of PET and SPECT scanners though GATE simulations.
D.2 Future work

The aim of the future work is to extend the current model in order to assess image quality through the estimation of MTF, NNPS and DQE of the flood source in all commercial PET scanners. Also the method will be also verified experimentally in real PET scanners. Furthermore this model will be further developed in order to include both small animal PET scanners, as well as Single-Photon Emission Computed Tomography (SPECT) scanners. Additionaly, further investigation in the imaging chain of PET scanners will be held through the modeling of phoswich detectors. Finally, the model will be also used to study the Compton Scatter Recovery in PET scanners with Cadmium Zinc Telluride (CdZnTe or CZT) detectors.
# APPENDIX: ABBREVIATIONS

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>18F-FDG</td>
<td>Fluorodeoxyglucose</td>
</tr>
<tr>
<td>ACF</td>
<td>Attenuation Correction Factors</td>
</tr>
<tr>
<td>APD</td>
<td>Avalanche Photodiode</td>
</tr>
<tr>
<td>ASCII</td>
<td>American Standard Code for Information Interchange</td>
</tr>
<tr>
<td>BGO</td>
<td>Bismuth Germinate Oxide</td>
</tr>
<tr>
<td>CdZnTe-CZT</td>
<td>Cadmium Zinc Telluride</td>
</tr>
<tr>
<td>DQE</td>
<td>Detective Quantum Efficiency</td>
</tr>
<tr>
<td>EGS</td>
<td>Electron Gamma Shower</td>
</tr>
<tr>
<td>FBP2D</td>
<td>2D Filtered Back Projection</td>
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<tr>
<td>FFT</td>
<td>Fast Fourier Transform</td>
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<tr>
<td>FOMs</td>
<td>Figures of Merits</td>
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<tr>
<td>FOV</td>
<td>Field Of View</td>
</tr>
<tr>
<td>FPB3DRP</td>
<td>3D Filtered Back Projection Reprojection Algorithms</td>
</tr>
<tr>
<td>FWHM</td>
<td>Full Width At Half Maximum</td>
</tr>
<tr>
<td>FWTM</td>
<td>Full Width Tenth Maximum</td>
</tr>
<tr>
<td>GATE</td>
<td>Geant4 Application For Tomographic Emission</td>
</tr>
<tr>
<td>GSO</td>
<td>Gadolinium Oxyorthosilicate</td>
</tr>
<tr>
<td>IQ</td>
<td>Image Quality</td>
</tr>
<tr>
<td>LMF</td>
<td>List Mode Format</td>
</tr>
<tr>
<td>LSF</td>
<td>Line Spread Function</td>
</tr>
<tr>
<td>LSO</td>
<td>Lutetium Oxyorthosilicate</td>
</tr>
<tr>
<td>LuAP</td>
<td>Lutetium Orthoaluminate Perovskite</td>
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<td>LuYAP - 70</td>
<td>Lutetium Yttrium Orthoaluminate Perovskite - 70</td>
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<td>Acronym</td>
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<td>LuYAP – 80</td>
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<td>MC</td>
<td>Monte-Carlo</td>
</tr>
<tr>
<td>MCNP</td>
<td>Monte Carlo N-Particle Transport</td>
</tr>
<tr>
<td>MLE</td>
<td>Maximum Likelihood Estimation</td>
</tr>
<tr>
<td>MTF</td>
<td>Modulation Transfer Function</td>
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<tr>
<td>NECR</td>
<td>Noise Equivalent Counting Rates</td>
</tr>
<tr>
<td>NEMA</td>
<td>National Electrical Manufacturers Association</td>
</tr>
<tr>
<td>NNPS</td>
<td>Normalized Noise Power Spectrum</td>
</tr>
<tr>
<td>PET</td>
<td>Positron Emission Tomography</td>
</tr>
<tr>
<td>PMT</td>
<td>Photomultiplier Tubes</td>
</tr>
<tr>
<td>PSF</td>
<td>Point Spread Function</td>
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<tr>
<td>PVE</td>
<td>Partial Volume Effect</td>
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<td>QDE</td>
<td>Quantum Detection Efficiency</td>
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<td>ROI</td>
<td>Regions Of Interest</td>
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<td>SNR</td>
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<td>software for tomographic image reconstruction</td>
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<td>Thin Layer Chromatography</td>
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<td>Time-Of-Flight</td>
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<td>YAP</td>
<td>Yttrium Orthoaluminate Perovskite</td>
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## INDEX OF TERMS

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