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ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
ΣΤΗΝ ΙΑΤΡΙΚΗ ΦΥΣΙΚΗ**

**ΒΕΛΤΙΣΤΟΠΟΙΗΣΗ ΜΕΓΕΘΥΝΤΙΚΩΝ ΛΗΨΕΩΝ ΣΤΗ
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ΠΡΟΣΟΜΟΙΩΣΗΣ MONTE CARLO**

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ΔΙΔΑΚΤΟΡΙΚΗ ΔΙΑΤΡΙΒΗ

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**OPTIMIZATION OF MAGNIFICATION
MAMMOGRAPHY USING MONTE CARLO
SIMULATION TECHNIQUES**

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ΠΕΡΙΛΗΨΗ.....	1
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CHAPTER A

INTRODUCTION – THEORETICAL PART

A.1. INTRODUCTION

A.1.1. THE PROBLEM.....	16
A.1.2. THESIS ORIGINALITY.....	18
A.1.3. PUBLICATIONS.....	19
A.1.4. THESIS LAYOUT.....	20

A.2. MAMMOGRAPHY

A.2.1. INTRODUCTION TO MAMMOGRAPHIC PRACTICE AND MAGNIFICATION VIEWS.....	23
A.2.2. BENEFITS AND RISKS.....	24

A.3. RADIATION DOSIMETRY

A.3.1. PROTECTION AGAINST IONIZING RADIATION.....	27
A.3.2. QUANTITIES AND UNITS.....	28
A.3.2.1. EXPOSURE.....	28
A.3.2.2. KINETIC ENERGY RELEASED PER UNIT MASS.....	28
A.3.2.3. AVERAGE GLANDULAR DOSE.....	29
A.3.2.4. DOSE.....	29
A.3.2.5. PERCENTAGE DEPTH DOSE.....	29

A.4. IMAGE QUALITY

A.4.1. IMAGE QUALITY CHARACTERISTICS.....	32
A.4.1.1. CONTRAST TO NOISE RATIO.....	32
A.4.1.2. SPATIAL RESOLUTION.....	32

A.5. MONTE CARLO SIMULATION

A.5.1. INTRODUCTION TO MONTE CARLO METHODS.....	34
A.5.2. RANDOM NUMBERS THEORY.....	38
A.5.3. SAMPLING TECHNIQUES.....	39
A.5.3.1. INVERSION METHOD.....	39
A.5.3.2. REJECTION METHOD.....	40

CHAPTER B**MATERIALS & METHODS**

B.1. GEOMETRY	42
B.2. THE MONTE CARLO SIMULATION MODELS	
B.2.1. DOSIS.....	47
B.2.2. MASTOS.....	49
B.3. MAMMOGRAPHIC SPECTRA	51
B.4. BREAST PHANTOMS	
B.4.1. DOSIMETRIC STUDIES.....	53
B.4.2. CNR STUDIES.....	54
B.4.3. SPATIAL RESOLUTION STUDIES.....	56
B.5. CALCULATIONS	
B.5.1. AIR KERMA TO AVERAGE GLANDULAR DOSE CONVERSION FACTORS.....	58
B.5.2. CONTRAST TO NOISE RATIO AND PERFORMANCE INDEX PI_v	60
B.5.3. THE EDGE METHOD FOR THE CALCULATION OF SPATIAL RESOLUTION.....	62
B.6. VALIDATION	
B.6.1. VALIDATION OF THE MONTE CARLO SIMULATION MODELS.....	65
B.6.2. VALIDATION OF THE CALCULATIONS.....	66

CHAPTER C**RESULTS & DISCUSSION**

C.1. DOSIMETRIC STUDIES	
C.1.1. EFFECT OF MAGNIFICATION ON AVERAGE GLANDULAR DOSE.....	73
C.1.2. EFFECT OF TUBE VOLTAGE ON AVERAGE GLANDULAR DOSE.....	74
C.1.3. EFFECT OF MAGNIFICATION ON PERCENTAGE DEPTH DOSE.....	75
C.1.4. EFFECT OF MAGNIFICATION DEGREE, ANODE/FILTER COMBINATION, TUBE VOLTAGE AND GLANDULARITY ON g FACTOR.....	76

C.2. CONTRAST TO NOISE RATIO STUDIES

C.2.1. EFFECT OF MAGNIFICATION ON CONTRAST TO NOISE RATIO.....	81
C.2.2. OVERALL PERFORMANCE OF ANODE/FILTER MATERIAL COMBINATIONS IN MAGNIFICATION MAMMOGRAPHY.....	86
C.2.3. EFFECT OF BREAST COMPOSITION ON CONTRAST TO NOISE RATIO.....	90

C.3. SPATIAL RESOLUTION STUDIES

C.3.1. EFFECT OF FOCAL SPOT SIZE AND DEGREE OF MAGNIFICATION ON SPATIAL RESOLUTION.....	91
C.3.2. EFFECT OF INTENSITY DISTRIBUTION AND DEGREE OF MAGNIFICATION ON SPATIAL RESOLUTION.....	94
C.3.2. EFFECT OF THE DETECTOR BLURRING ON SPATIAL RESOLUTION.....	99

CHAPTER D**CONCLUSIONS & FUTURE WORK**

D.1. CONCLUSIONS.....	101
D.2. FUTURE WORK.....	103

REFERENCES.....	104
-----------------	-----

APPENDIX I

ABBREVIATIONS.....	111
--------------------	-----

APPENDIX II

LIST OF FIGURES.....	112
----------------------	-----

APPENDIX III

LIST OF TABLES.....	115
---------------------	-----

SUMMARY.....	116
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“To those who gave everything for a dream...”

ΠΕΡΙΛΗΨΗ

1) ΕΙΣΑΓΩΓΗ-ΘΕΩΡΙΑ

ΤΟ ΠΡΟΒΛΗΜΑ

Ο καρκίνος του μαστού είναι η πιο συχνή μορφή καρκίνου παγκοσμίως και η δεύτερη μετά τον καρκίνο του πνεύμονα αιτία θανάτου, για τις γυναίκες. Εμφάνιση στους άνδρες είναι επίσης δυνατή, ωστόσο, η πιθανότητα είναι αρκετά μικρή. Η επιτυχής θεραπεία του καρκίνου του μαστού συνδέεται άμεσα με την έγκαιρη διάγνωσή του και τις τελευταίες δεκαετίες γίνεται μεγάλη προσπάθεια προς αυτή την κατεύθυνση. Η προληπτική μαστογραφία, η οποία γίνεται σε κάθε γυναίκα ετήσια μετά την ηλικία των 40 ετών, θεωρείται επί του παρόντος η τεχνική με τη μεγαλύτερη ευαισθησία, όσο αφορά τη διάγνωση. Ωστόσο, γίνεται μεγάλη συζήτηση σχετικά με τα οφέλη και τους κινδύνους της συγκεκριμένης τεχνικής, καθώς πραγματοποιείται σε μη-συμπτωματικές γυναίκες και επιπρόσθετα, η μαστογραφία χρησιμοποιεί ιοντίζουσα ακτινοβολία η οποία μπορεί να προκαλέσει καρκίνο. Για το λόγο αυτό, γίνεται προσπάθεια βελτιστοποίησης της τεχνικής που αποβλέπει στη βέλτιστη εικόνα με τη λιγότερη δυνατή δόση στο μαστό (που μεταφράζεται στη μικρότερη δυνατή πιθανότητα καρκινογένεσης λόγω ιοντίζουσας ακτινοβολίας).

Σε περιπτώσεις που παρατηρείται κάποια ανωμαλία σε συγκεκριμένη περιοχή του μαστού σε μία προληπτική μαστογραφία, γίνεται μία συμπληρωματική εξέταση με σκοπό να μεγεθυνθεί η περιοχή αυτή. Η γεωμετρία της συγκεκριμένης εξέτασης είναι διαφορετική από την αντίστοιχη των προληπτικών μαστογραφιών και η τεχνική ονομάζεται μεγεθυντικές λήψεις μαστογραφίας ή μεγεθυντική μαστογραφία. Έτσι, η μεγέθυνση είναι τεχνική εφαρμοζόμενη σε συμπτωματικές γυναίκες και επηρεάζει σημαντικά τη δόση που εναποτίθεται στο ακτινοβολούμενο τμήμα του μαστού, καθώς επίσης και την ποιότητα της παραγόμενης εικόνας.

Το πλεονέκτημα της μεγεθυντικής μαστογραφίας σε σύγκριση με τη συμβατική σχετίζεται με τον αυξημένο λόγο σήματος προς θόρυβο. Επιπλέον, το κενό που δημιουργείται μεταξύ του μαστού και του ανιχνευτή μειώνει τη σκεδαζόμενη

ακτινοβολία στο επίπεδο του ανιχνευτή, κάνοντας μη απαραίτητη τη χρήση του αντιδιαχυτικού διαφράγματος.

Από την άλλη μεριά, η μεγεθυντική μαστογραφία παρουσιάζει και κάποια μειονεκτήματα. Η δόση που εναποτίθεται στο μαστό είναι μεγαλύτερη λόγω της μειωμένης απόστασης εστίας-δέρματος, καθώς επίσης και του μικρότερου ακτινοβολούμενου όγκου (θεωρώντας ότι τα μεγέθη πεδίου και ανιχνευτή παραμένουν ίδια). Επιπλέον, για να μειωθεί η γεωμετρική ασάφεια που προκαλείται από τη μείωση της απόστασης εστίας-μαστού, απαιτείται χρήση μικρότερης εστίας. Αυτό συνεπάγεται μείωση του ρεύματος της λυχνίας ώστε να προστατευτεί η εστία από καταστροφή λόγω αυξημένου θερμικού φορτίου. Σαν αποτέλεσμα έχουμε αύξηση του χρόνου έκθεσης των ασθενών και της πιθανότητας εμφάνισης ασάφειας κίνησης στην παραγόμενη εικόνα (ανατομική ασάφεια λόγω κίνησης).

Διάφορα μεγέθη έχουν προταθεί μέχρι τώρα αποσκοπώντας στην ποσοτικοποίηση της δόσης που εναποτίθεται στο μαστό και της ποιότητας της μαστογραφικής εικόνας. Σχετικά με τη δόση, η επιφανειακή δόση εισόδου, η δόση στο μέσο του μαστού και η συνολική μεταδιδόμενη ενέργεια είναι τέτοια μεγέθη που σχετίζονται με τον ενδεχόμενο κίνδυνο σε μία μαστογραφία. Ωστόσο, κανένα από αυτά δεν είναι αρκετά ικανοποιητικό. Ο Karlsson et al (1976) πρότεινε ότι είναι ο μαζικός αδένας του μαστού που έχει τη μεγαλύτερη πιθανότητα καρκινογένεσης. Η μέση δόση στο μαζικό αδένα (AGD) είναι το μέγεθος που συστήνεται στις μέρες μας από τα περισσότερα εθνικά πρωτόκολλα ως το πιο άμεσα σχετιζόμενο με την πιθανότητα καρκινογένεσης στο μαστό, σε αντίθεση με τη δόση στο λιπώδη και το συνδετικό ιστό ή το δέρμα. Επίσης, η κατανομή της απορροφώμενης δόσης μέσα στους ιστούς του μαστού είναι η επιπλέον πληροφορία που πρέπει να έχει κάποιος, εκτός από τις απόλυτες τιμές δόσης, έτσι ώστε να μπορεί να φτάσει σε ασφαλή συμπεράσματα. Η κατανομή αυτή περιγράφεται από τις καμπύλες εκατοστιαίας δόσης βάθους (PDD).

Σχετικά με την ποιότητα εικόνας, ο λόγος της αντίθεσης προς το θόρυβο (CNR) και η χωρική διακριτική ικανότητα (SR) είναι τα πιο συνηθισμένα μεγέθη που λαμβάνονται υπόψη. Ειδικότερα, η διακριτική ικανότητα συνδέεται άμεσα με το μέγεθος της εστίας και την κατανομή της εκπεμπόμενης ακτινοβολίας των ακτίνων-χ. Η κατανομή της εκπεμπόμενης ακτινοβολίας είναι μία κρίσιμη παράμετρος όσο αφορά την

ποιότητα εικόνας στη συμβατική καθώς και στη μεγεθυντική μαστογραφία, και στις μέρες μας γίνεται μεγάλη προσπάθεια για την εύρεση μιας κατάλληλης κατανομής, αποσκοπώντας στην βελτιστοποίηση της τεχνικής. Η απλή κανονική κατανομή, η ομοιόμορφη και η διπλή κανονική (κανονική κατανομή δύο κορυφών) αποτελούν τις πιο αντιπροσωπευτικές στις μαστογραφικές λυχνίες και επηρεάζουν άμεσα τη διακριτική ικανότητα τόσο σε γεωμετρία επαφής όσο και υπό μεγέθυνση. Επίσης, έρευνες έχουν δείξει ότι η απλή κανονική κατανομή μετατρέπεται σε διπλή κανονική κατανομή καθώς καταστρέφεται η εστία λόγω της εκτενούς χρήσης της, κάτι που έχει μείζουσα επίδραση στη διακριτική ικανότητα.

Όλα τα προαναφερθέντα μεγέθη τα οποία χρησιμοποιούνται στη μαστογραφία επηρεάζονται άμεσα όταν πραγματοποιείται μεγέθυνση. Ο καθορισμός της επίδρασης της μεγέθυνσης στα μεγέθη αυτά, ωστόσο, δεν είναι τόσο εύκολος στην πράξη, και ειδικά για τη μέση δόση στο μαζικό αδένα δεν είναι καν εφικτό να μετρηθεί, καθώς δεν είναι δυνατό να ανιχνευθεί ο μαζικός αδένας μέσα στο μαστό και να τοποθετηθούν εκεί ανιχνευτές ώστε να μετρηθεί η αντίστοιχη δόση. Ο κίνδυνος καρκινογένεσης που σχετίζεται με τη μαστογραφία είναι άλλος ένας ανασταλτικός παράγοντας ο οποίος περιορίζει τη μελέτη της επίδρασης της μεγέθυνσης. Σαν λύση σε αυτούς τους περιορισμούς έχουν προταθεί διάφορες υπολογιστικές τεχνικές, οι περισσότερες από τις οποίες βασίζονται στην προσομοίωση Monte Carlo. Οι Monte Carlo μέθοδοι έχουν χρησιμοποιηθεί σε διάφορες μελέτες που αφορούν υπολογισμούς δόσης καθώς επίσης και την ποιότητα εικόνας στη μαστογραφία. Ωστόσο, υπάρχουν ακόμα ανοιχτά ζητήματα στις μεγεθυντικές λήψεις, καθώς δεν έχει αναφερθεί ως τώρα καμία συνολική μελέτη που να αποσκοπεί στη βελτιστοποίηση της τεχνικής. Στη συγκεκριμένη διδακτορική διατριβή, χρησιμοποιήθηκαν δύο μοντέλα προσομοίωσης Monte Carlo με σκοπό τη μελέτη της επίδρασης της μεγέθυνσης σε διάφορα χαρακτηριστικά δόσης και ποιότητας εικόνας, με σκοπό να βρεθούν οι βέλτιστες παράμετροι έκθεσης που οδηγούν στην καλύτερη ποιότητα εικόνας με τη λιγότερη δυνατή δόση.

ΠΡΩΤΟΤΥΠΙΑ ΔΙΑΤΡΙΒΗΣ

Η πρωτοτυπία της συγκεκριμένης διατριβής έγκειται σε:

- Την επέκταση των ήδη υπάρχοντων μοντέλων προσομοίωσης Monte Carlo DOSIS και MASTOS ώστε να συμπεριλάβουν γεωμετρίες μεγέθυνσης και διάφορες περιεκτικότητες μαστού σε μαζικό αδένα και λίπος.
- Τη μελέτη της επίδρασης της μεγέθυνσης στη μέση δόση στο μαζικό αδένα και ο υπολογισμός επιπρόσθετων παραγόντων μετατροπής από AIR KERMA σε μέση δόση στο μαζικό αδένα, που διορθώνουν για το βαθμό μεγέθυνσης και το χρησιμοποιούμενο φάσμα (συνδυασμός υλικών ανόδου/φίλτρου και τάση λυχνίας), κάνοντας τον υπολογισμό της μέσης δόσης στο μαζικό αδένα πιο ακριβή.
- Τη χρήση μεγάλου εύρους μαστογραφικών φασμάτων σαν είσοδο στις μελέτες προσομοίωσης που πραγματοποιήθηκαν, συμπεριλαμβάνοντας από τα πιο πρόσφατα εισηχθέντα (Rh-Rh) ως τα παλιότερα (W-Mo). Μελετήθηκε η επίδραση της μεγέθυνσης σε αυτά τα φάσματα τόσο ως προς τη δόση όσο και ως προς την ποιότητα εικόνας, με σκοπό να εξαχθούν συμπεράσματα για την καταλληλότητα του κάθε φάσματος για την τεχνική της μεγέθυνσης.
- Τη μελέτη της επίδρασης του μεγέθους της εστίας και της κατανομής εκπεμπόμενης ακτινοβολίας ακτίνων-χ στη χωρική διακριτική ικανότητα, κάτω από συνθήκες μεγέθυνσης στη μαστογραφία, χρησιμοποιώντας τη μέθοδο αιχμής. Στη μελέτη αυτή συμπεριλήφθησαν μεγέθη εστίας μέχρι και 0.04 mm. Εξήχθησαν συμπεράσματα σχετικά με την καταλληλότητα κάθε μεγέθους εστίας και κατανομής εκπεμπόμενης ακτινοβολίας, σύμφωνα και με τους υπάρχοντες διεθνείς περιορισμούς που αφορούν τη διακριτική ικανότητα.
- Τη συνολική μελέτη της τεχνικής της μεγέθυνσης σε σχέση με τη δόση και την ποιότητα εικόνας με σκοπό τη βελτιστοποίησή της.

II) ΜΕΘΟΔΟΙ

Η συγκεκριμένη διατριβή χωρίζεται σε 3 μέρη: στη δοσιμετρική μελέτη καθώς επίσης σε 2 μελέτες που αφορούν την ποιότητα εικόνας, μία για το λόγο αντίθεσης προς θόρυβο και μία για τη χωρική διακριτική ικανότητα. Οι μελέτες αυτές παρατίθενται παρακάτω σε περίληψη.

ΓΕΩΜΕΤΡΙΑ

Όπως αναφέρθηκε και νωρίτερα, η τεχνική της μεγέθυνσης είναι μία συμπληρωματική εξέταση του μαστού, η οποία πραγματοποιείται όταν έχει ήδη ανιχνευθεί μία ύποπτη ανωμαλία. Σκοπός της εξέτασης αυτής είναι να μεγεθυνθεί η συγκεκριμένη περιοχή του μαστού. Ο απαιτούμενος βαθμός μεγέθυνσης πετυχαίνεται διαμέσου απλών γεωμετρικών αλλαγών σε σχέση με τη γεωμετρία επαφής, θεωρώντας συνήθως μερική ακτινοβολήση του μαστού (Εικόνα 3).

Το αντιδιαχυτικό διάφραγμα απομακρύνεται καθώς το κενό που δημιουργείται ανάμεσα στο μαστό και τον ανιχνευτή προσφέρει ήδη περιορισμό της σκεδαζόμενης ακτινοβολίας που ανιχνεύεται. Ο ακτινοβολούμενος όγκος του μαστού είναι μικρότερος σε αυτή την περίπτωση καθώς το μέγεθος του πεδίου και του ανιχνευτή παραμένουν ίδια. Ωστόσο, σε μερικές περιπτώσεις χρησιμοποιούνται μεγαλύτερα πεδία και ανιχνευτές και ακτινοβολείται ολόκληρος ο μαστός. Η διατριβή αυτή ασχολείται μόνο με την πρώτη περίπτωση. Στις προσομοιώσεις που πραγματοποιήθηκαν χρησιμοποιήθηκαν βαθμοί μεγέθυνσης μεταξύ 1.0 (γεωμετρία επαφής) και 2.0.

ΟΜΟΙΩΜΑΤΑ ΜΑΣΤΟΥ

Για τη δοσιμετρική μελέτη προσομοιώθηκε ομοίωμα μαστού αποτελούμενο από ομοιογενές μείγμα λιπώδους και μαζικού ιστού χωρισμένο σε voxel του 1 mm^3 . Η περιεκτικότητα σε μαζικό αδένια ήταν δυνατό να μεταβάλλεται από 1% ως 100%, προσομοιώνοντας με αυτό τον τρόπο μαστούς διαφόρων συνθέσεων. Στην κάθε εξωτερική επιφάνεια του ομοιώματος θεωρήθηκαν 5 mm λίπους για την προσομοίωση του δέρματος και του υποδόριου λίπους, καθώς επίσης χρησιμοποιήθηκε πίεστρο μαστού από υλικό Perspex πάχους 3 mm. Για τον υπολογισμό της μέσης δόσης στο μαζικό

αδένα, η εναποτιθέμενη δόση σε κάθε voxel του ομοιώματος μαστού μοιράστηκε στο μαζικό και τον λιπώδη ιστό με χρήση τεχνικών Monte Carlo, σύμφωνα με τις πιθανότητες αλληλεπίδρασης καθώς επίσης και τη σύσταση του μαστού που είχαμε επιλέξει.

Για τη μελέτη του λόγου αντίθεσης προς θόρυβο χρησιμοποιήθηκε και πάλι ομοίωμα από ομοιογενές μείγμα λιπώδους και μαζικού ιστού. Το ομοίωμα ήταν ημικυλινδρικό σε σχήμα με 4 cm ακτίνα και 4 cm πάχος. Συμπεριελάμβανε δύο σετ από 4 σφαιρικές ανομοιογένειες οι οποίες προσομοίωναν μικρού μεγέθους και υψηλής αντίθεσης αλλοιώσεις όπως ασβεστοποιήσεις, με δύο διαφορετικές συνθέσεις: calcium oxalate (CO, $\text{CaC}_2\text{O}_4 \cdot 3(\text{H}_2\text{O})$) (Εικόνα 5, περιοχή 1) και hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) (Εικόνα 5, περιοχή 2). Η ακτίνα τους ποίκιλλε από 100 μm έως 750 μm . Τα δύο σετ ανομοιογενειών τοποθετήθηκαν στο κέντρο του ομοιώματος σχετικά με το ύψος του. Οι ανομοιογένειες της περιοχής 1 τοποθετήθηκαν σε απόσταση 0.7 cm από το θωρακικό τοίχωμα ενώ οι ανομοιογένειες της περιοχής 2 0.4 cm από αυτό.

Τέλος, για τη μελέτη της χωρικής διακριτικής ικανότητας χρησιμοποιήθηκε απότομη αιχμή πάχους 4 cm αποτελούμενη από μόλυβδο, μη διαπερατή από ακτίνες-χ, τοποθετημένη στο κέντρο του πεδίου με την κετρική ακτίνα της δέσμης κάθετη στην αιχμή και την επιφάνεια του ακτινοβολούμενου αντικειμένου.

ΥΠΟΛΟΓΙΣΜΟΙ

1) ΠΑΡΑΓΟΝΤΕΣ ΜΕΤΑΤΡΟΠΗΣ ΑΠΟ AIR KERMA ΣΕ AGD

Διάφοροι συγγραφείς έχουν αναφερθεί στους παράγοντες μετατροπής που χρησιμοποιούνται για τον υπολογισμό της μέσης δόσης στο μαζικό αδένα του μαστού μέσω της μέτρησης του Air KERMA στην επιφάνεια του ακτινοβολούμενου ομοιώματος. Σαν g ορίζεται ο συνολικός παράγοντας μετατροπής, ίσος με το πηλίκο της δόσης D προς το KERMA K :

$$D = g \cdot K \quad (1)$$

Προηγούμενα δημοσιευμένες εργασίες έχουν προτείνει ένα συνδυασμό από 3 ανεξάρτητους παράγοντες για γεωμετρικές επαφής:

$$D = (g_{Mo/Mo} \cdot c \cdot s) \cdot K \quad (2)$$

όπου το $g_{Mo/Mo}$ είναι παράγοντας διόρθωσης για το $Mo/0.030mmMo$ συνδυασμό υλικών στα 28 kVp, c είναι παράγοντας που διορθώνει για περιεκτικότητα σε μαζικό αδένα διαφορετική από 50% και s είναι παράγοντας που διορθώνει για συνδυασμό υλικών ανόδου/φίλτρου διαφορετικό από το Mo/Mo στα 28 kVp μόνο. Στη συγκεκριμένη μελέτη, ο υπολογισμός των παραγόντων μετατροπής προσαρμόστηκε ώστε να συμπεριλάβει βαθμούς μεγέθυνσης, περιεκτικότητες σε μαζικό αδένα, πάχη μαστού, επιπλέον συνδυασμούς υλικών ανόδου/φίλτρου και διάφορες τάσεις λειτουργίας της λυχνίας. Τα παραπάνω μπορούν να συμπτυχθούν στον παρακάτω τύπο:

$$D_M = (g_{Mo/Mo} \cdot m \cdot s \cdot v \cdot c) \cdot K_M \quad (3)$$

Στον παραπάνω τύπο ο παράγοντας m διορθώνει για το βαθμό μεγέθυνσης, ο παράγοντας v διορθώνει για τάσεις λυχνίας μεταξύ 24 kVp και 34 kVp ενώ ο παράγοντας s επεκτάθηκε ώστε να συμπεριλάβει 14 συνδυασμούς υλικών ανόδου/φίλτρου.

2) ΛΟΓΟΣ ΑΝΤΙΘΕΣΗΣ ΠΡΟΣ ΘΟΡΥΒΟ ΚΑΙ ΔΕΙΚΤΗΣ ΑΠΟΔΟΣΗΣ

Από τις παραγόμενες εικόνες, ο λόγος αντίθεσης προς θόρυβο υπολογίστηκε μέσω του τύπου:

$$CNR = \frac{|C_{INS} - C_{BG}|}{\sqrt{N_{INS}^2 + N_{BG}^2}} \quad (4)$$

όπου C_{INS} και C_{BG} είναι οι μέσες τιμές του grey level των ανομοιογενειών και του υποβάθρου, αντίστοιχα ενώ στον παρονομαστή βρίσκονται οι αντίστοιχες τιμές του θορύβου, ο οποίος έχει εκφραστεί μέσω της τυπικής απόκλισης από τη μέση τιμή.

Αποτελέσματα συνολικής απόδοσης ελήφθησαν συνδυάζοντας αποτελέσματα για την ποιότητα εικόνας για διάφορους βαθμούς μεγέθυνσης και φάσματα με τα αντίστοιχα αποτελέσματα για τη δόση. Όπως έχει προταθεί από τον Nishino et al (2005), το $(CNR)^2$ μπορεί να χρησιμοποιηθεί για την περιγραφή της ποιότητας εικόνας αντί για το (CNR) σε μελέτες βελτιστοποίησης, με σκοπό να δοθεί έμφαση στο απεικονιστικό μέρος του δείκτη απόδοσης σε σχέση με τη δόση, δείχνοντας ότι η ακριβής και έγκαιρη διάγνωση αλλοιώσεων είναι πρωτεύουσας σημασίας στη μαστογραφία. Ειδικά όταν εφαρμόζεται

μεγέθυνση, η οποία είναι μία συμπληρωματική διαγνωστική και όχι προληπτική εξέταση, η ανάγκη να δοθεί έμφαση στο απεικονιστικό κομμάτι της διαδικασίας σε σχέση με τη δόση είναι ακόμα πιο επιτακτική. Για το σκοπό αυτό, μεγαλύτερες δυνάμεις του CNR, $(CNR)^v$, όπου $v > 2$, μπορούν να εισαχθούν ώστε να εξαχθεί ένας συνολικός δείκτης απόδοσης ως ο λόγος του επιθυμητού «κέρδους» (αντιστοιχεί στο $(CNR)^v$) ως προς το «κόστος» (αντιστοιχεί στη δόση), όπως φαίνεται από την παρακάτω σχέση:

$$PI_v = \frac{(CNR)^v}{AGD} \quad (5)$$

Ο συγκεκριμένος δείκτης απόδοσης μπορεί να χρησιμοποιηθεί για την αποτίμηση της συνολικής απόδοσης διαφόρων συνδυασμών υλικών ανόδου/φίλτρου υπό διάφορες συνθήκες έκθεσης (βαθμός μεγέθυνσης, τάση λυχνίας). Για μεγαλύτερες τιμές του v , η σχετική ποσοστιαία διαφορά ανάμεσα σε συγκρινόμενα φάσματα, αποδιδόμενες στην απεικονιστική τους ικανότητα, αυξάνεται. Κάτι τέτοιο μπορεί να είναι πολύ χρήσιμο στην προσπάθεια να αποτιμηθεί και να συγκριθεί η συνολική απόδοση διαφόρων παραμέτρων σε διαδικασίες όπου δίνεται μεγαλύτερη σημασία στην ποιότητα εικόνας σε σχέση με τη δόση, όπως είναι οι μεγεθυντικές λήψεις στη μαστογραφία.

3) Η ΜΕΘΟΔΟΣ ΑΙΧΜΗΣ ΓΙΑ ΤΟΝ ΥΠΟΛΟΓΙΣΜΟ ΤΗΣ ΧΩΡΙΚΗΣ ΔΙΑΚΡΙΤΙΚΗΣ ΙΚΑΝΟΤΗΤΑΣ

Για τον υπολογισμό της χωρικής διακριτικής ικανότητας υπολογίστηκε αρχικά μία συνάρτηση διασποράς ορίου για κάθε εικόνα. Για το σκοπό αυτό μία ορθογώνια περιοχή ενδιαφέροντος επελέγει περιλαμβάνοντας 2 mm από κάθε μεριά της αιχμής. Το προφίλ του κάθετα υπολογισμένου μέσου όρου των τιμών του grey level κατά μήκος αυτής της απόστασης αντιστοιχεί στη συνάρτηση διασποράς ορίου. Από μαθηματική διαφοροποίηση της συνάρτησης αυτής προέκυψε η συνάρτηση διασποράς γραμμής (LSF) και με εφαρμογή σε αυτή μετασχηματισμού Fourier καταλήγουμε στη συνάρτηση μεταφοράς διαμόρφωσης (MTF). Η συγκεκριμένη μέθοδος μέτρησης της συνάρτησης μεταφοράς διαμόρφωσης έχει αποκτήσει μεγάλη δημοτικότητα τελευταία λόγω της απλότητάς της και της καταλληλότητάς της, ειδικά στην ψηφιακή απεικόνιση. Οι

προκύπτουσες συναρτήσεις μεταφοράς διαμόρφωσης προσαρμόστηκαν με τμήμα κανονικής καμπύλης και η διακριτική ικανότητα σε lp/mm εξήχθη από αυτές, θεωρώντας ότι αντιστοιχεί στο 5% της συνάρτησης.

III) ΑΠΟΤΕΛΕΣΜΑΤΑ

1) ΔΟΣΙΜΕΤΡΙΚΗ ΜΕΛΕΤΗ

Η συγκεκριμένη μελέτη έδειξε ότι η μέση δόση στο μαζικό αδένα αυξάνεται με το βαθμό μεγέθυνσης, όπως φαίνεται και στο Σχήμα 10. Αυτό συμβαίνει λόγω του νόμου αντιστρόφου τετραγώνου της απόστασης και του γεγονότος ότι ο ακτινοβολούμενος όγκος είναι μικρότερος σε συνθήκες μεγέθυνσης. Μελετήθηκε, επίσης, η επίδραση της τασής λειτουργίας της λυχνίας στη μέση δόση στο μαζικό αδένα υπό συνθήκες μεγέθυνσης και τα αποτελέσματα βρίσκονται στο Σχήμα 11. Θεωρώντας ίδιο αριθμό αρχικών φωτονίων, η δόση αυξάνει με την τάση της λυχνίας καθώς περισσότερα φωτόνια και με μεγαλύτερη ενέργεια φτάνουν στο ομοίωμα και εναποθέτουν την ενέργειά τους μέσα σε αυτό. Τέλος, η επίδραση του βαθμού μεγέθυνσης στην εκατοστιαία δόση βάθους φαίνεται στο Σχήμα 12. Με βάση αυτό, η συγκεκριμένη δόση μειώνεται με τη μεγέθυνση για δύο λόγους: καθώς ο μαστός τοποθετείται πιο κοντά στην εστία έχουμε μικρότερο μέγεθος πεδίου στην επιφάνειά του. Αυτό οδηγεί σε μικρότερη συνεισφορά σκεδαζόμενων φωτονίων σε σημεία του κεντρικού άξονα. Επίσης, η μείωση της απόστασης εστίας-μαστού προκαλεί τη μείωση της εκατοστιαίας δόσης λόγω της μειωμένης επίδρασης του z στον παράγοντα αντιστρόφου τετραγώνου της απόστασης που υπερισχύει στο πρωτογενές κομμάτι της δέσμης.

Επιπλέον, υπολογίστηκαν οι παραγοντες μετατροπής που χρησιμοποιούνται για τον υπολογισμό της μέσης δόσης στο μαζικό αδένα και οι οποίοι παρουσιάζονται στους Πίνακες 3, 4 και 5.

2) ΜΕΛΕΤΗ ΛΟΓΟΥ ΑΝΤΙΘΕΣΗΣ ΠΡΟΣ ΘΟΡΥΒΟ

Στο Σχήμα 13 παρουσιάζεται η επίδραση του βαθμού μεγέθυνσης στο λόγο αντίθεσης προς θόρυβο για τα δύο σετ των τεσσάρων σφαιρικών ανομοιογενειών με αυξανόμενη ακτίνα, που αναφέρθηκαν προηγούμενα. Τα αποτελέσματα δείχνουν ότι οι

ανομοιογένειες που αποτελούνται από ΗΑ διακρίνονται ευκολότερα σε σχέση με αυτές από CO, καθώς οδηγούν σε υψηλότερο λόγο σήματος προς θόρυβο, ο οποίος ποικίλει από 30% (ανομοιογένεια 100 μm) έως 54% (ανομοιογένεια 750 μm). Επιπλέον, αυτή η διαφορά μειώνεται κατά περίπου 66% καθώς ο βαθμός μεγέθυνσης αυξάνεται από 1.0 σε 2.0. Οι μικρής ακτίνας ανομοιογένειες των 100 μm είναι πιο δύσκολο να διακριθούν μέσα στο ομοίωμα σε σχέση με τις υπόλοιπες, ακόμα και σε μεγάλους βαθμούς μεγέθυνσης, καθώς έχουν πολύ μικρό λόγο αντίθεσης προς θόρυβο.

Ο λόγος αντίθεσης προς θόρυβο βρέθηκε ότι αυξάνει με το βαθμό μεγέθυνσης, κάτι που φαίνεται και από το Σχήμα 14. Από αυτό, γίνεται προφανές ότι η βελτίωση του λόγου είναι μεγαλύτερη για μεγεθύνσεις μεταξύ 1.0 και 1.4, από ότι μεταξύ 1.4 και 2.0. Μάλιστα, η βελτίωση αυτή είναι μεγαλύτερη για τις μικρού μεγέθους ανομοιογένειες.

Λαμβάνοντας υπόψη τα αποτελέσματα που αφορούν τη δόση και παρουσιάστηκαν στην προηγούμενη παράγραφο, υπολογίστηκε ο δείκτης απόδοσης PI_v για διάφορες τιμές του v , καθώς επίσης και ο βαθμός μεγέθυνσης στον οποίο εμφανίζεται η μέγιστη τιμή του δείκτη. Τα αποτελέσματα παρουσιάζονται στον Πίνακα 6. Για τους συγκεκριμένους υπολογισμούς χρησιμοποιήθηκαν 13 συνδυασμοί υλικών ανόδου/φίλτρου. Με βάση τα αποτελέσματα, για τιμές του v μέχρι 2.5 ο βαθμός μεγέθυνσης 1.3 οδηγεί στο μεγαλύτερο «κέρδος» με το μικρότερο «κόστος» για τους περισσότερους συνδυασμούς. Για μεγαλύτερες τιμές του δείκτη v ο βαθμός μεγέθυνσης 1.4 είναι αυτός που υπερισχύει.

Διάφοροι συνδυασμοί υλικών ανόδου/φίλτρου σε τάσεις μεταξύ 24 kVp και 32 kVp χρησιμοποιήθηκαν για να εκτιμηθεί η συνολική τους απόδοση στη μεγεθυντική μαστογραφία. Για $v=1.0$ μπορούν να εξαχθούν συμπεράσματα για συνδυασμούς υλικών για τους οποίους έχουμε ίση βαρύτητα ποιότητας εικόνας και δόσης, όπως συμβαίνει στη συμβατική μαστογραφία. Σύμφωνα με τα αποτελέσματα του Πίνακα 7, οι συνδυασμοί Mo/0.030mmMo και W/0.050mmPd+2.00mmAl είναι οι καταλληλότεροι για τάσεις μέχρι 26 kVp. Ωστόσο, για μεγαλύτερες τάσεις εμφανίζονται συνδυασμοί υλικών με παρόμοια απόδοση με αυτή του Mo/0.030mmMo, όπως οι W/0.050mmAl, Rh/0.51mmAl, W/0.030mmRh, Rh/0.029mmRh, Rh/0.030mmRu και Mo/0.029mmRh.

Αντίθετα, για τιμές του δείκτη v μεταξύ 1.25 και 5.00 μπορούν να εξαχθούν συμπεράσματα για την απόδοση υλικών ανόδου/φίλτρου, σε περιπτώσεις που έχουμε αυξημένη βαρύτητα στο απεικονιστικό κομμάτι σε σχέση με τη δόση, όπως συμβαίνει

στη μεγεθυντική μαστογραφία. Σε αυτή την περίπτωση και καθώς ο δείκτης ν αυξάνεται, η σχετική απόδοση διαφόρων συνδυασμών υλικών σε σχέση με την απόδοση του $\text{Mo}/0.030\text{mmMo}$ μειώνεται, λόγω της μεγάλης απεικονιστικής ικανότητας του συγκεκριμένου συνδυασμού.

3) ΜΕΛΕΤΗ ΤΗΣ ΧΩΡΙΚΗΣ ΔΙΑΚΡΙΤΙΚΗΣ ΙΚΑΝΟΤΗΤΑΣ

Κάνοντας χρήση της διαδικασίας που αναφέρθηκε προηγούμενα για τη μέθοδο της αιχμής, υπολογίστηκε η διακριτική ικανότητα για τιμές μεγέθυνσης από 1.0 μέχρι 2.0 και για 10 διαφορετικά μεγέθη εστίας μεταξύ 0.04 mm και 0.30 mm, χρησιμοποιώντας κανονική κατανομή. Στο Σχήμα 17 παρουσιάζεται η επίδραση του βαθμού μεγέθυνσης στη διακριτική ικανότητα για μερικές αντιπροσωπευτικές τιμές μεγέθους εστίας. Σύμφωνα με τις υπολογισμένες τιμές, η αύξηση του βαθμού μεγέθυνσης από 1.0 σε 2.0 προκαλεί υποβάθμιση της διακριτικής ικανότητας που ποικίλλει από 49% για εστία 0.04 mm μέχρι 53% για εστία 0.14 mm, λόγω της γεωμετρικής ασάφειας που δημιουργείται από τη γεωμετρία της μεγέθυνσης. Για μεγαλύτερες εστίες, αυτή η υποβάθμιση είναι ακόμα μεγαλύτερη, ακόμα και για μικρούς βαθμούς μεγέθυνσης.

Σχετικά με το μέγεθος της εστίας, αύξηση του μεγέθους της από 0.04 mm σε 0.30 mm μειώνει τη διακριτική ικανότητα κατά 15%, για γεωμετρία επαφής. Αυτό το ποσοστό είναι μεγαλύτερο υπό μεγέθυνση και αυξάνεται σχεδόν γραμμικά με το βαθμό μεγέθυνσης. Τα αποτελέσματα αυτά φαίνονται στο Σχήμα 18. Εστίες με μέγεθος μεγαλύτερο από 0.14 mm θα μπορούσαν να χρησιμοποιηθούν μόνο για χαμηλούς βαθμούς μεγέθυνσης, μέχρι 1.5, καθώς οδηγούν σε μικρές τιμές διακριτικής ικανότητας, σε σχέση με μικρότερες εστίες. Σε περιπτώσεις όπου εφαρμόζεται μεγαλύτερη μεγέθυνση, μέχρι 1.9, μικρότερες εστίες θα έπρεπε να χρησιμοποιούνται. Μεγέθυνση μεγαλύτερη από 1.9 οδηγεί σε μη αποδεκτές τιμές διακριτικής ικανότητας με βάση τους διεθνείς κανονισμούς (προβλέπουν διακριτική ικανότητα για τη μαστογραφία μεγαλύτερη από 12 lp/mm), ακόμα και για εστίες μεγέθους 0.04 mm. Οι αριθμητικές τιμές της διακριτικής ικανότητας που υπολογίστηκαν στη μελέτη αυτή παρουσιάζονται στον Πίνακα 8.

Αποτελέσματα που σχετίζονται με την επίδραση της κατανομής της εκπεμπόμενης ακτινοβολίας ακτίνων-χ παρουσιάζονται στα σχήματα 22, 23 και 24. Σύμφωνα με αυτά, η

απλή κανονική κατανομή οδηγεί στις υψηλότερες τιμές διακριτικής ικανότητας μεταξύ των τριών κατανομών που μελετήθηκαν, με τη διπλή κανονική κατανομή να δίνει τις χαμηλότερες τιμές, για όλους τους βαθμούς μεγέθυνσης και τα μεγέθη εστίας.

Όπως ήδη συζητήθηκε, η περιοριστική τιμή του μεγέθους της εστίας ώστε να υπάρχει συμβατότητα με το όριο των 12 lp/mm για τη διακριτική ικανότητα, μειώνεται με την αύξηση της μεγέθυνσης. Έτσι, κάθε μέγεθος εστίας θεωρείται κατάλληλο μέχρι ένα συγκεκριμένο βαθμό μεγέθυνσης. Αυτός ο βαθμός είναι μεγαλύτερος για εστίες με απλή κανονική κατανομή.

Λαμβάνοντας υπόψη τα προηγούμενα αποτελέσματα, γίνεται φανερό ότι κάτω από συνθήκες μεγέθυνσης όπου η γεωμετρική ασάφεια αυξάνεται και η ανάγκη για υψηλές τιμές διακριτικής ικανότητας γίνεται ακόμα πιο επιτακτική, μόνο μια απλή κανονική κατανομή, συνδυασμένη με μικρό μέγεθος εστίας, μπορεί να οδηγήσει σε τέτοιες τιμές. Ομοιόμορφες κατανομές μπορούν να χρησιμοποιηθούν μόνο για χαμηλούς βαθμούς μεγέθυνσης. Ειδικά όταν συνδυάζονται με μικρού μεγέθους εστίες, η μεγέθυνση αυτή μπορεί να είναι μέχρι και 1.7. Ωστόσο, μειώνεται καθώς αυξάνεται το μέγεθος της εστίας. Από την άλλη, διπλές κανονικές κατανομές οδηγούν σε χαμηλές τιμές διακριτικής ικανότητας γενικά, κάνοντας τη χρήση τους αποδεκτή μόνο για χαμηλές μεγεθύνσεις, ειδικά όταν συνδυάζονται με εστίες μεγαλύτερες από 0.12 mm. Τέλος, λαμβάνοντας υπόψη την πιθανή μετατροπή της απλής κανονικής κατανομής σε διπλή κανονική κατανομή, καθώς η εστία καταστρέφεται λόγω της συνεχούς χρήσης της, καθώς επίσης και τα παραπάνω αποτελέσματα, προκύπτει ότι είναι απαραίτητη η αντικατάσταση της μαστογραφικής λυχνίας έγκαιρα, ειδικά όταν χρησιμοποιείται και για μεγεθυντικές λήψεις.

IV) ΣΥΜΠΕΡΑΣΜΑΤΑ

Η διατριβή αυτή αποτελεί μια συνολική μελέτη των μεγεθυντικών λήψεων στη μαστογραφία. Η τεχνική αυτή είναι πολύ σημαντική καθώς αποτελεί ένα πολύτιμο όπλο στην προσπάθεια έγκαιρης ανίχνευσης μικροασβεστώσεων και αλλοιώσεων στο μαστό. Στη διατριβή αυτή, δοσιμετρικά μεγέθη καθώς επίσης και μεγέθη που χαρακτηρίζουν την ποιότητα της εικόνας μελετήθηκαν υπό συνθήκες μεγέθυνσης με σκοπό να βρεθούν οι βέλτιστες συνθήκες έκθεσης για τη συγκεκριμένη τεχνική.

Ο λόγος αντίθεσης προς το θόρυβο βρέθηκε να αυξάνει με το βαθμό μεγέθυνσης. Ωστόσο, ο ρυθμός αύξησης μειώνεται σημαντικά μετά τη μεγέθυνση 1.3-1.4, ενώ η δόση συνεχίζει να αυξάνει σχεδόν γραμικά. Εισάγωντας ένα δείκτη συνολικής απόδοσης εξαρτώμενο από την επιθυμητή βαρύτητα στο απεικονιστικό κομμάτι της διαδικασίας σε σχέση με τη δόση, βρέθηκε ότι αυτοί οι βαθμοί μεγέθυνσης είναι οι πιο κατάλληλοι όταν εφαρμόζεται μεγέθυνση. Αυτό είναι πολύ σημαντικό για το προσωπικό που εργάζεται σε μαστογραφικές μονάδες καθώς, η εφαρμογή του κατάλληλου βαθμού μεγέθυνσης κάθε φορά μπορεί να βοηθήσει στη βελτιστοποίηση της τεχνικής.

Στη δοσιμετρική μελέτη, υπολογίστηκαν νέοι παράγοντες μετατροπής από air KERMA σε AGD ώστε να συμπεριλάβουν γεωμετρίες μεγέθυνσης, τάσεις λειτουργίας της λυχνίας καθώς και νέους συνδυασμούς υλικών ανόδου/φίλτρου. Η χρήση αυτών των παραγόντων από τους φυσικούς ιατρικής κατά τους ποιοτικούς ελέγχους μαστογραφικών συστημάτων ή σε διαδικασίες δοσιμέτρησης μπορεί να αυξήσει την ακρίβεια υπολογισμού της AGD μέχρι και 33%. Επιπλέον, λαμβάνοντας υπόψη την πιθανή μετατροπή της απλής κανονικής κατανομής ακτινοβολίας εξερχόμενων φωτονίων σε διπλή κανονική κατανομή καθώς καταστρέφεται η άνοδος λόγω της αυξημένης χρήσης της, όπως επίσης και την υποβαθμισμένη διακριτική ικανότητα στην οποία μας οδηγεί μια διπλή κανονική κατανομή σε σύγκριση με την αντίστοιχη της απλής κανονικής κατανομής, γίνεται αντιληπτή η αναγκαιότητα αντικατάστασης της μαστογραφικής λυχνίας όταν η άνοδος αρχίζει να καταστρέφεται. Αυτό με τη σειρά του ενισχύει την ανάγκη για συχνό ποιοτικό έλεγχο των μαστογραφικών μονάδων από τους φυσικούς ιατρικής, καθώς επίσης και τη μπερρηση της διακριτικής τους ικανότητας.

Όσο αφορά τη βιομηχανία, μαστογραφικές μονάδες οι οποίες θα μπορούσαν να εναλλάσσουν δύο διαφορετικούς συνδυασμούς υλικών ανόδου/φίλτρου, ανάλογα με την επιθυμητή βαρύτητα στο απεικονιστικό κομμάτι της διαδικασίας (γεωμετρία επαφής ή μεγέθυνση) σε σχέση με τη δόση, θα συνεισέφεραν σημαντικά στην προσπάθεια βελτιστοποίησης και των δύο τεχνικών, με βάση τα αποτελέσματα της μελέτης για την απόδοση διαφόρων συνδυασμών υλικών ανόδου/φίλτρου υπό γεωμετρίες επαφής και μεγέθυνσης. Επίσης, η κατασκευή μιας εστίας 0.04 mm σε συνδυασμό με μια απλή κανονική κατανομή μικρης τυπικής απόκλισης θα μας οδηγούσε σε υψηλές τιμές διακριτικής ικανότητας, ακόμα και σε μεγάλους βαθμούς μεγέθυνσης. Ωστόσο, προς

αυτή την κατεύθυνση θα έπρεπε να ληφθούν υπόψη η υπερθέρμανση της ανόδου και η του χρόνου έκθεσης του ασθενούς.

Γενικά, η μαστογραφία αποτελεί ένα σημαντικό εργαλείο στη μαστογραφία. Ωστόσο, απαιτεί σωστή εφαρμογή καθώς μόνο υπό συγκεκριμένες συνθήκες μπορεί να συνεισφέρει στη διάγνωση. Αντιθέτως, μη σωστή εφαρμογή της μπορεί να αυξήσει σημαντικά τη δόση στον ασθενή χωρίς να προσφέρει επιπλέον διαγνωστική πληροφορία.

CHAPTER A

INTRODUCTION – THEORETICAL PART

A.1. INTRODUCTION

A.1.1. THE PROBLEM.....	16
A.1.2. THESIS ORIGINALITY.....	18
A.1.3. PUBLICATIONS.....	19
A.1.4. THESIS LAYOUT.....	20

A.1.1. THE PROBLEM

Breast cancer is the most common form of cancer for women all over the world and second, only to lung cancer, as a death cause among women (NCI 2003). Occurrence to men is also possible; however, the possibility is quite small. The successful treatment of breast cancer is directly related to its early detection and a lot of effort has been made towards this direction the last decades. Screening mammography, performed annually to every woman after the age of 40, is considered currently the technique with the highest sensitivity, as far as the detection is concerned. However, there has been made a long discussion about the benefits and risks of this technique, as it is performed to asymptomatic women and additionally, mammography uses ionizing radiation which can possibly induce cancer. So, an effort to optimize the technique, aiming to get the best possible breast image with the lowest breast dose (translated to lowest radiation induced breast cancer possibility), is being made.

In cases where breast complaints have been noticed by a woman or her physician or an abnormality has been detected at a specific area of the breast in a screening mammogram, a secondary examination is performed aiming to magnify this area. The geometry of this examination is different than the corresponding for the screening mammogram and the technique is called magnification mammography. Therefore, magnification is a technique applied to symptomatic women and affects seriously the dose delivered in the irradiated part of the breast as well as the quality of the derived image.

The advantage of magnification mammography compared to the conventional (contact) one is related to increased Signal to Noise Ratio (SNR), as far as the image quality is concerned (Liu et al 1995, Sickles et al 1977, Doi and Imhof 1977, Dance et al 2000b, Funke et al 1998a, Funke et al 1998b, Spyrou et al 2000, Spyrou et al 2002, Koutaloni et al 2007). Moreover, the air gap between the breast and the image receptor reduces the scattered radiation at the detector plane, making the use of an antiscatter grid unnecessary.

On the other hand, magnification mammography has some disadvantages. The dose deposited to the breast is higher, due to the decreased Focus to Skin Distance (FSD), combined with the decreased irradiated volume of the breast, considering that the field and the film sizes remain the same. Additionally, in order to reduce the unsharpness caused by the smaller FSD, a smaller focal spot is required, which means that the tube current has to be reduced to protect the anode from being destroyed due to the increased thermal loading (Funke et al 1998b, Liu et al

1995). This, results in increased exposure times and possible appearance of motion unsharpness in the image, due to anatomical motion (Hermann et al 2002, Spyrou et al 2002).

Several quantities have been proposed so far in order to quantify the dose delivered in the breast and the quality of the mammographic image. As far as the dose is concerned, Entrance Surface Dose (ESD), mid-breast dose and total energy imparted are such quantities associated to the potential risk of mammography. However, none of these was satisfactory enough. Karlsson et al (1976) suggested that it is the glandular tissue of the breast which has the highest risk of radiation-induced carcinogenesis. Mean Glandular Dose (MGD) or Average Glandular Dose (AGD) is the quantity recommended nowadays by most national protocols as the one related to breast cancer, rather than the dose in the adipose tissue, in the connective tissue or in the skin. Moreover, the distribution of the absorbed dose inside the breast tissues is the additional information that someone must have, except from the absolute dose values, in order to come into safe conclusions. This distribution is described by the Percentage Depth Dose (PDD) curves. Regarding the image quality, contrast to noise ratio (CNR) and spatial resolution are the most common quantities considered by most of the authors. Especially spatial resolution is directly connected to the focal spot size and the x-ray intensity distribution (Law 1993, Matsui and Katsuhiro 1985, Sickles 1980). The x-ray intensity distribution, also called focus intensity distribution, is a crucial parameter regarding the image quality in contact and magnification mammography (Nickoloff et al 1990, Prasad et al 1976). Nowadays, a lot of effort has been placed in finding an optimum intensity distribution, aiming to improve the image quality of the derived image. Single peak Gaussian (referred as Gaussian), uniform and double peak Gaussian (referred as double Gaussian) intensity distributions are the most representative in mammographic tubes (Nickoloff et al 1990) and affect the spatial resolution in contact geometry, as well as under magnification. Moreover, Gaussian intensity distributions seem to turn to double Gaussian as the focal spot is destroyed, due to its extended use and this has a major effect on the spatial resolution (Brubacher and Moores 1973). This makes the knowledge of the relation between each intensity distribution and the spatial resolution, under contact and magnification conditions, even more important.

All the above quantities utilized in mammography are directly affected when magnification is performed. The determination of the influence of magnification on the above quantities, however, is not so easy in practice and as far as the AGD is concerned it is not feasible to

measure it at all, as it is not possible to detect the glandular tissue inside the breast and to place detectors in order to measure the corresponding dose (Beckett and Kotre 2000, Hammerstein et al 1979, Klein et al 1997, Law 2005, McParland 2000, Shrivastava 1991, Scubic and Fatouros 1989, Stanton et al 1984). The carcinogenic risk related to mammography is another inhibitory factor, limiting the study of the effect of magnification. As solution to these limitations, several computational procedures have been proposed. Most of these procedures are based on Monte Carlo simulation. Monte Carlo methods have been utilized in several studies concerning dose deposition as well as image quality in mammography. However, there are still some open issues regarding the magnification views, as there is no overall study reported so far, aiming to optimize the specific technique. In this study, two Monte Carlo simulation models (Spyrou 2001, Delis 2004) are utilized in order to study the influence of magnification on several dose and image quality characteristics aiming to find the optimum exposure parameters which result in the lowest dose and the highest image quality.

A.1.2. THESIS ORIGINALITY

The originality of this thesis consists in:

- The expansion of the already existing Monte Carlo simulation models DOSIS and MASTOS in order to include magnification geometries and various breast compositions.
- The investigation of the influence of magnification on Average Glandular Dose (AGD) and the calculation of additional air KERMA to AGD conversion factors correcting for the degree of magnification and the spectrum utilized (anode/filter combination and tube voltage operated), making the estimation of AGD more accurate.
- The use of a wide range of mammographic spectra as input for the simulation studies performed, including from the most recently introduced ones (Rh-Rh, etc) to the oldest (W-Mo anode). The influence of magnification on these spectra was studied in terms of dose and image quality in order to extract conclusions about the appropriateness of each spectrum for the magnification technique.

- The study of the effect of focal spot size and x-ray intensity distribution on spatial resolution under magnification conditions in mammography, using the edge method. Focal spots up to 0.04 mm were included in this study. Conclusions about the appropriateness of each focus size and intensity distribution, according to the existing spatial resolution limitations, were extracted.
- The complete investigation of the magnification technique in terms of both dose and image quality aiming to optimize it.

A.1.3. PUBLICATIONS

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

Publications in peer reviewed international journals

- **Koutalonis M**, Delis H, Spyrou G, Costaridou L, Tzanakos G and Panayiotakis G, “Monte Carlo generated conversion factors for the estimation of Average Glandular Dose in contact and magnification mammography”, **Phys. Med. Biol.**, 51 (2006), 5539-5548.
- **Koutalonis M**, Delis H, Spyrou G, Costaridou L, Tzanakos G and Panayiotakis G, “Contrast to Noise Ratio in magnification mammography: a Monte Carlo study”, **Phys. Med. Biol.**, 52 (2007), 3185-3199.
- **Koutalonis M**, Delis H, Spyrou G, Costaridou L, Tzanakos G and Panayiotakis G, “Monte Carlo studies on the influence of focal spot size and intensity distribution on spatial resolution in magnification mammography”, **Phys. Med. Biol.**, 53 (2008) 1369-84.
- **Koutalonis M**, Delis H, Spyrou G, Costaridou L, Tzanakos G and Panayiotakis G, “Monte Carlo simulation studies of spatial resolution in magnification mammography using the edge method”, **Nuclear Inst. and Methods in Physics Research A**, Accepted for publication.

Full publications in international conference proceedings

- **M Koutalonis**, H Delis, G Spyrou, L Costaridou, G Tzanakos and G Panayiotakis, “Dosimetry in contact and magnification mammography using Monte Carlo simulation”,

ASM 2006, 15th IASTED International Conference on Applied Simulation and Modelling, June 26-28, Rhodes, Greece (pp 389 – 394).

- **M Koutalonis**, H Delis, G Spyrou, L Costaridou, G Tzanakos and G Panayiotakis, “Investigation of dose deposition in magnification mammography using Monte Carlo simulation”, 2nd IC-EpsMsO International Conference on Experiments/Process/System Modeling/Simulation & Optimization, July 4-7, 2007, Athens, Greece.

Abstract publications in international conference proceedings

- **M Koutalonis**, H Delis, G Spyrou, L Costaridou, G Tzanakos and G Panayiotakis, “Monte Carlo assessment of Average Glandular Dose and Percentage Depth Dose in magnification mammography”, ISRP10, 10th International Symposium on Radiation Physics, September 15-22, 2006, Coimbra, Portugal.
- **M Koutalonis**, H Delis, G Spyrou, L Costaridou, G Tzanakos and G Panayiotakis, “Monte Carlo simulation studies of spatial resolution in magnification mammography using the edge method”, ITBS 2007, 4th International Conference on Imaging Technologies in Biomedical Sciences, September 22-28, 2007, Milos Island, Greece.

Abstract publications in national conference proceedings

- **M. Koutalonis**, H. Delis, G. Spyrou, L. Costaridou, G. Tzanakos and G. Panayiotakis, “Mean glandular dose in magnification mammography, using Monte Carlo simulation” 16th Interuniversity Radiology Conference, 22-24 September 2006, Alexandroupolis, Greece.
- **M. Koutalonis**, H. Delis, G. Spyrou, L. Costaridou, G. Tzanakos and G. Panayiotakis, “CNR studies in magnification mammography with CsI and GdO₂S₂ detectors, using Monte Carlo simulation” 2nd Bioscience conference, 23-24 April 2007, Patras, Greece.

A.1.4. THESIS LAYOUT

The layout of this thesis has been built as following:

Theoretical information will be discussed during the next three chapters. Section A.2 includes an introduction to the mammographic practice with the discussion of some aspects concerning screening and magnification mammography. Section A.3 is an introduction to radiation dosimetry and includes aspects and guidelines concerning radiation protection against ionizing radiation, as well as an overview of the dosimetric quantities utilized in the study. Section A.4 introduces the main parameters concerning image quality and its characteristics

while information concerning the history and the basic parameters of Monte Carlo simulation is presented in Section A.5.

The materials and methods section begins with Section B.1, where the magnification technique is introduced and Section B.2 where the Monte Carlo simulation models utilized in this study are presented. The mammographic spectra utilized in the study are presented in Section B.3, while the breast phantoms are described in Section B.4. The calculation of several dosimetric and image quality characteristics utilized in the study is presented in Section B.5 and finally, the validation of the calculations which has been realized against published data is shown in Section B.6.

Some representative results of the dosimetric studies are presented in Section C.1, whereas Sections C.2 and C.3 include results concerning image quality characteristics, such as contrast to noise ratio and spatial resolution under magnification conditions.

Finally, some conclusions concerning the results produced during the course of this study are being presented in Section D.1, followed by some suggestions that could furthermore contribute in the effort to optimize the specific technique.

CHAPTER A**INTRODUCTION – THEORETICAL PART****A.2. MAMMOGRAPHY**

A.1.1. INTRODUCTION TO MAMMOGRAPHIC PRACTICE AND MAGNIFICATION VIEWS.....	23
A.1.2. BENEFITS AND RISKS.....	24

A.2.1. INTRODUCTION TO MAMMOGRAPHIC PRACTICE AND MAGNIFICATION VIEWS

Early breast cancer detection is associated with screening mammography that is performed to asymptomatic women and can image breast cancer findings up to two years before becoming palpable to the patient or her physician. If during screening mammography a suspicious abnormality is detected and more specific images of the breast are required, diagnostic mammography is mandatory. The most common example of such specific views, associated with diagnostic mammography is the magnification views (magnification mammography). The desired level of magnification is achieved through simple geometric changes of the common mammographic setup.

A mammographic unit consists of a rectangular box that houses the tube in which x-rays are produced. The unit (Figure 1) is dedicated equipment as it is used exclusively for breast examinations, with special accessories that allow only the breast to be exposed to the x-rays.

Figure 1: A modern mammographic unit

During mammography, a specially qualified technologist positions the patient in order to place the breast on a special platform and compress it with a paddle (often made of clear Plexiglas or other plastic). Breast compression is necessary in order to:

- Even out the breast thickness so that all of the breast tissue can be visualized
- Reduce breast tissue thickness so that small abnormalities will not be obscured by overlying breast parenchyma
- Decrease the delivered x-ray dose since a thinner amount of breast tissue is being imaged
- Immobilize the breast in order to eliminate blurring of the image caused by motion
- Reduce x-ray scatter to increase sharpness and contrast of the image

During the mammographic examination, the technologist has to stand behind a lead glass shield in order to be protected while realizing the exposure.

A.2.2. BENEFITS AND RISKS

During previous sections the profitable role of mammography has been mentioned as well as the contribution to early diagnosis and therefore to the cure possibility of breast cancer. But mammography, just like every other radiation based technique, is not free of any cost and danger. Following, the main benefits and risks are summarized for the mammographic practice.

Benefits

- Imaging of the breast improves a physician's ability to detect small tumors. When cancers are small, the woman has more treatment options and a cure is more likely.
- The use of screening mammography increases the early detection of small abnormal tissue growths confined to the milk ducts in the breast, called ductal carcinoma in situ (DCIS). These tumors cannot harm patients if they are removed at this early stage and mammography is the only proven method to reliably detect these tumors.

Risks

- The effective radiation dose from a mammogram is about 0.3 mSv, which is about the same as the average person receives from background radiation in one month. Although the magnitude may not seem important, the fact that mammography is a non symptomatic technique makes the dose limitation task obligatory. International guidelines require that each mammographic unit should be checked by a medical physicist each year to ensure that the unit operates correctly.

- False Positive Mammograms. Five to ten percent of mammogram results are abnormal and require more testing (additional mammograms, fine needle aspiration, ultrasound or biopsy) and most of the follow-up tests confirm that no cancer was present. It is estimated that a woman who has yearly mammograms between ages 40 and 49 would have about a 30% chance of having a false-positive mammogram at some point in that decade and about a 7 to 8 percent chance of having a breast biopsy within the 10-year period. The same estimate of false-positive mammograms is about 25% for women over the age of 50.

Moreover, there are some more specific advantages and disadvantages of diagnostic mammography (magnification) against screening one, as also previously mentioned. The main advantages are related to increased contrast and reduced image noise as far as the image quality is concerned. Moreover, the air gap between the breast and the image receptor reduces the scattered radiation at the detector plane, making the use of an antiscatter grid unnecessary. On the other hand, the dose deposited in the irradiated part of the breast is higher due to the decreased focus to breast distance. Furthermore, the demand for smaller focal spot leads to the necessity of lower tube current values, in order to protect the anode from increased thermal loading. This results to increased exposure times that could be the cause for motion unsharpness in the generated image.

Mammography aims towards the optimization of the technique and the implementation of the ALARA principle (As Low As Reasonably Achievable). To this direction several studies have been published concerning combined studies for both image quality and radiation dose in mammography, investigating possible ways of minimizing the risk of the procedure, while keeping the image quality in acceptable and diagnostic level.

CHAPTER A

INTRODUCTION – THEORETICAL PART

A.3. RADIATION DOSIMETRY

A.3.1. PROTECTION AGAINST IONIZING RADIATION.....	27
A.3.2. QUANTITIES AND UNITS.....	28
A.3.2.1. EXPOSURE.....	28
A.3.2.2. KINETIC ENERGY RELEASED PER UNIT MASS.....	28
A.3.2.3. AVERAGE GLANDULAR DOSE.....	29
A.3.2.4. DOSE.....	29
A.3.2.5. PERCENTAGE DEPTH DOSE.....	29

A.3.1. PROTECTION AGAINST IONIZING RADIATION

The use of radiological investigations is an accepted part of medical practice, justified in terms of clear clinical benefits to the patient which should far outweigh the small radiation risks. There is no doubt that if the three basic principles of radiation protection are kept in mind, every single radiation practice can be considered safe. These basic principles, as described by the International Council of Radiation Protection, are:

1. **The justification of practice:** No practice involving exposure to radiation should be adopted unless it produces sufficient benefit to the exposed individual or to society to offset the radiation detriment it causes.
2. **The optimization of protection (the ALARA principle):** In relation to any particular source within a practice, the magnitude of individual doses, the number of people exposed and the likelihood of incurring exposures where these are not certain to be received should all be kept *as low as reasonably achievable*, economic and social factors being taken into account. This procedure should be constrained by restrictions on the doses or the risk to individuals in the case of potential exposures, so as to limit the inequity likely to result from the inherent economic and social judgments. This is popularly referred as the ALARA principle.
3. **Individual dose and risk limits:** The exposure of individuals resulting from the combination of all the relevant practices should be subject to dose limits, or to some control of risk in the case of potential exposures. These are aimed at ensuring that no individual is exposed to radiation risks that are judged to be unacceptable from these practices in any normal circumstances. Not all sources are susceptible of control by action at the source and it is necessary to specify the sources to be included as relevant before selecting a dose limit.

For the case of mammography, where the benefit of the woman is obvious and the amount of radiation is very small, protection and dosimetry of the patient could be considered as an issue of decreased interest. Especially in magnification mammography, which is a secondary examination applied to symptomatic women, this consideration is even more realistic.

A.3.2. QUANTITIES AND UNITS

In this paragraph, the dosimetric quantities utilized in the study are introduced together with their units.

A.3.2.1. EXPOSURE

Exposure was the first dosimetric quantity introduced and is characteristic of a photon radiation field based upon the ionization of air produced by the field. The definition of exposure given by ICRU 1980 is:

$$X=dQ/dm \quad (A.1)$$

where dQ is the absolute value of the total charge of the ions of one sign produced in air when all the electrons liberated by photons in air of mass dm are completely stopped in air. The traditional unit of exposure is the roentgen (R) and corresponds to $2.58 \cdot 10^{-4}$ C/kg. The exposure may be related to the energy deposited in the mass of air since on the average $W=34$ eV is required to produce an ion pair contributing $q_e=1.6 \cdot 10^{-19}$ C of charge. A simple calculation shows that an energy deposition of approximately $5.4 \cdot 10^7$ MeV g^{-1} in air produces an exposure of 1 R.

Although exposure is still widely applied in clinical practice, it suffers from two fundamental drawbacks. The first is that it is only defined for photons interacting in air, and the second is that the quantity is defined only for energies up to 3 MeV, as for higher energies the range of the electrons slowing down becomes extremely large.

A.3.2.2. KINETIC ENERGY RELEASED PER UNIT MASS

Kinetic Energy Released per unit Mass (KERMA) is a non-stochastic quantity applicable to indirectly ionizing radiations, such as photons and neutrons. It quantifies the average amount of energy transferred from the indirectly ionizing radiation to directly ionizing radiation (charged particles-electrons) without concern to what happens after this transfer, and is defined as the energy transferred per unit mass:

$$K = \frac{dE_{tr}}{dm} \quad (A.2)$$

The unit of KERMA is joule per kilogram (Jkg⁻¹) and the special name for this unit is gray (Gy), where 1 Gy=1 Jkg⁻¹.

A.3.2.3. AVERAGE GLANDULAR DOSE

Average Glandular Dose (AGD) is defined as the dose deposited only in the mammary gland of the breast. As there is a significant risk of radiation induced carcinogenesis associated with x-ray mammography, the determination of AGD forms an important part of the quality control of mammographic imaging systems. Because of the difficulty of estimating AGD directly, the entrance air kerma at the upper surface of the breast is determined and the AGD is calculated by multiplying by appropriate conversion factors.

A.3.2.4. DOSE

The primary result of the interaction of a radiation field with matter is the transfer of energy which may then generally result in ionization or excitation of the medium. Dose is defined as the energy of ionization and excitation absorbed per unit mass. If the object of interest is divided into subregions, then the energy absorbed per unit mass can be calculated for each subregion. The values for the different subregions may in fact differ, so that dose may be considered as a distribution. If the dimensions of the subregions are small on the scale of the object, then they may be approximated as point objects and the dose can then be defined at a point.

The absorbed dose is defined as the absorbed energy dE per unit mass dm :

$$D = dE/dm = dE/\rho dV \quad (A.3)$$

The unit of dose is the gray (Gy) which, as derived by the definitions, corresponds to 1 joule of energy deposited in 1 kilogram of water. The older unit of dose is the rad, which corresponds to 1cGy (10^{-2} Gy).

Since the maximum dose for the diagnostic energy range is deposited near the surface of the patient, a very commonly used dose value is the Entrance Surface Dose (ESD) referring to the dose deposited to the upper layer of the patient's skin.

A.3.2.5. PERCENTAGE DEPTH DOSE

Dose distributions inside a phantom or a patient are usually normalized to $D_{\max} = 100\%$ at the depth of dose maximum $z_{\max}$ and then referred to as the percentage depth dose distributions. The percentage depth dose is thus defined as:

$$PDD = 100 D_Q / D_P \quad (A.4)$$

where D_Q is the dose at a point Q and D_P is the dose at a point P at $Z_{\max}$.

CHAPTER A

INTRODUCTION – THEORETICAL PART

A.4. IMAGE QUALITY

A.4.1. IMAGE QUALITY CHARACTERISTICS.....	32
A.4.1.1. CONTRAST TO NOISE RATIO.....	32
A.4.1.2. SPATIAL RESOLUTION.....	32

A.4.1. IMAGE QUALITY CHARACTERISTICS

As also discussed in Section A.3, during the mammographic procedure the image quality has to be kept in acceptable and diagnostic levels, taking also into account the ALARA principle regarding the radiation dose. In this direction, several quantities have been utilized in order to quantify the quality of the mammographic image. The most important of them are presented in this section.

A.4.1.1. CONTRAST TO NOISE RATIO

Several studies have referred to the use of Contrast to Noise Ratio (CNR) as an image quality descriptor. CNR is calculated from the produced radiation image from the formula proposed by Tapiovaara and Wagner (1993):

$$CNR = \frac{|C_{INS} - C_{BG}|}{\sqrt{N_{INS}^2 + N_{BG}^2}} \quad (A.5)$$

where C_{INS} and C_{BG} are the mean greylevel values of the inhomogeneity and its background and N_{INS} and N_{BG} are the noise in the inhomogeneity and its background, correspondingly. Moreover, as suggested by Nishino et al (2005), $(CNR)^2$ can also be used as image quality descriptor when evaluating the figure of merit in mammography, in order to emphasize the importance of the imaging part with respect to the dose, showing that the precise and early detection of abnormalities is the primary aim in mammography. Especially when magnification is performed, which is a secondary diagnostic and not a screening examination, the need of emphasizing the imaging part of the procedure with respect to the dose is even more imperative.

A.4.1.2. SPATIAL RESOLUTION

Spatial resolution is another quantity often utilized for image quality studies in mammography. It can be measured using bar patterns or the edge method through the Modulation Transfer Function (MTF) in line pairs per mm (lp/mm) and it shows the ability of a system to sharply and clearly define the extent or shape of features within the image. It describes how close two features can be within an image and still be resolved as unique. The International Atomic Energy Agency (IAEA) (2002), followed by most of the European countries, designates that it should not be less than 12 lp/mm in mammography, although other values have also been reported so far, such as 14 lp/mm.

CHAPTER A

INTRODUCTION – THEORETICAL PART

A.5. MONTE CARLO SIMULATION

A.5.1. INTRODUCTION TO MONTE CARLO METHODS.....	34
A.5.2. RANDOM NUMBERS THEORY.....	38
A.5.3. SAMPLING TECHNIQUES.....	39
A.5.3.1. INVERSION METHOD.....	39
A.5.3.2. REJECTION METHOD.....	40

A.5.1. INTRODUCTION TO MONTE CARLO METHODS

Numerical methods that are known as Monte Carlo methods can be described as statistical simulation methods, where statistical simulation is defined in quite general terms to be any method that utilizes sequences of random numbers to perform the simulation. Monte Carlo methods have been used for centuries, but only in the past several decades has the technique gained the status of a full-fledged numerical method, capable of addressing the most complex applications. The name “Monte Carlo” was coined by Metropolis (inspired by Ulam’s interest in poker) during the Manhattan Project of World War II, because of the similarity of statistical simulation to games of chance, and because the capital of Monaco was a center for gambling and similar pursuits. Monte Carlo is now used routinely in many diverse fields, from the simulation of complex physical phenomena such as radiation transport in the earth’s atmosphere and the simulation of the esoteric subnuclear processes in high energy physics experiments, to the simulation of games of chance. The analogy of Monte Carlo methods to games of chance is a good one, but the “game” is a physical system, and the outcome of the game is not a pot of money or stack of chips (unless simulated) but rather a solution to some problem. The “winner” is a scientist, who judges the value of his results on their intrinsic worth, rather than the extrinsic worth of his holdings.

Statistical simulation methods may be contrasted to conventional numerical discretization methods, which typically are applied to ordinary or partial differential equations that describe some underlying physical or mathematical system. In many applications of Monte Carlo, the physical process is simulated directly and there is no need to even write down the differential equations that describe the behavior of the system. The only requirement is that the physical (or mathematical) system be described by probability density functions (pdfs). Once the pdfs are known, the Monte Carlo simulation can proceed by random sampling from the pdfs. Many simulations are then performed (multiple “trials” or “histories”) and the desired result is taken as an average over the number of observations (which may be a single observation or perhaps millions of observations). In many practical applications, one can predict the statistical error (the “variance”) in this average result and hence, an estimate of the number of Monte Carlo trials that are needed to achieve a given error.

Figure 2 illustrates the idea of Monte Carlo or statistical simulation as applied to an arbitrary physical system. Assuming that the evolution of the physical system can be described

by pdfs, then the Monte Carlo simulation can proceed by sampling from these pdfs, which necessitates a fast and effective way to generate random numbers uniformly distributed on the interval $[0, 1]$. The outcomes of these random samplings or trials must be accumulated or tallied in an appropriate manner to produce the desired result, but the essential characteristic of Monte Carlo is the use of random sampling techniques (and perhaps other algebra to manipulate the outcomes) to arrive at a solution of the physical problem. In contrast, a conventional numerical solution approach would start with the mathematical model of the physical system, discretizing the differential equations and then solving a set of algebraic equations for the unknown state of the system.

Figure 2: Monte Carlo simulation of a physical system

It should be kept in mind though that this general description of Monte Carlo methods may not directly apply to some applications. It is natural to think that Monte Carlo methods are used to simulate random or stochastic processes, since these can be described by pdfs. However, this coupling is actually too restrictive because many Monte Carlo applications have no apparent stochastic content, such as the evaluation of a definite integral or the inversion of a system of linear equations. However, in these cases and others, one can pose the desired solution in terms of pdfs and while this transformation may seem artificial, this step allows the system to be treated as a stochastic process for the purpose of simulation and hence Monte Carlo methods can be applied to simulate the system. Therefore, we take a broad view of the definition of Monte

Carlo methods and include in the Monte Carlo rubric all methods that involve statistical simulation of some underlying system, whether or not the system represents a real physical process.

Some of the applications of Monte Carlo simulation are in the following fields: nuclear reactor design, quantum chromodynamics, radiation cancer therapy, traffic flow, econometrics, VLSI design and medical imaging.

The major components of a Monte Carlo algorithm are the following:

- Probability Density Functions (PDFs). The physical (or mathematical) system must be described by a set of PDFs.
- Random number generator. A source of random numbers uniformly distributed on the unit interval must be available.
- Sampling rule. A prescription for sampling from the specified PDFs, assuming the availability of random numbers on the unit interval, must be given.
- Scoring (or tallying). The outcomes must be accumulated into overall tallies or scores for the quantities of interest.
- Error estimation. An estimate of the statistical error (variance) as a function of the number of trials and other quantities must be determined.
- Variance reduction techniques. Methods for reducing the variance in the estimated solution to reduce the computational time for Monte Carlo simulation.

In the following Table 1, some of the Monte Carlo codes that have been implemented are presented together with their applications (Andreo 1991).

Monte Carlo Code	Description	Applications
Ho-Chunk 2004	Calculates scattering and polarization in stellar geometries	Computing optical/near-IR images where most of the emitted radiation comes from the central star
MCML 1992	A steady-state Monte Carlo simulation program for multi-layered turbid media with an infinitely narrow photon beam as light source	A very flexible method for simulating light propagation in tissue
MCNP 1994	Describes particle transport	Criticality safety, oil-well logging, nuclear energy, nuclear safeguards, fusion research, medical technology (mammography)
FOTELP 2003	Photon, electron and positron transport	Dosimetry, radiation shielding, radiotherapy, detector and counter efficiency evaluation
BEAM 1995	Simulate the radiation beams from radiotherapy units including high-energy electron and photon beams, ^{60}Co beams and ortho-voltage units	Radiotherapy
EGS 1994	General purpose package for the Monte Carlo simulation of the coupled transport of electrons and photons in an arbitrary geometry for particles with energies from a few keV up to several TeV	Clinical radiation dosimetry (mammography)
CASINO 1995	A single scattering Monte Carlo Simulation of electron trajectory in sOlid specially designed for low-beam interaction	Electron beam interactions

Table 1: Some of the most famous Monte Carlo simulation codes and their applications

A.5.2. RANDOM NUMBERS THEORY

For the implementation of a Monte Carlo simulation process, the first and major part is an infinity sequence of random numbers. A random number is a particular value of a continuous variable uniformly distributed on the unit interval which, together with others of its kind, satisfies certain conditions. A high quality random number sequence is a long stream of numbers with the characteristic that the occurrence of each number in the sequence is unpredictable. Although databases of real random numbers can be found their use is limited due to the large size, which makes the simulation process very slow. Thus, mathematical algorithms for the generation of “pseudorandom numbers” have been introduced. The outputs of pseudorandom number generators are not random; they only approximate some of the properties of random numbers. Careful mathematical analysis is required to ensure that the generated numbers are sufficiently “random”.

By far the most popular random number generators in use today are special cases of the following scheme, introduced by D.H. Lehmer (1951). For the implementation of this scheme, four “magic numbers” are selected:

m, the modulus;

a, the multiplier;

c, the increment;

X_0 the starting value;

Given a modulus m, a multiplier a and a starting value – “seed” X_0 - the desired sequence of random numbers X_n is then obtained by setting:

$$X_{n+1} = (aX_n + c) \bmod m$$

This is called a linear congruential sequence.

Before a random number generator can be regarded as acceptable, its output must pass certain standard randomness tests (Frequency Test, Serial Test, Gap Test, Poker Test, Serial Correlation Test etc), which check very carefully the statistical properties of uniformity and independence. The length of the period of a random number generator must be long enough to avoid repetitions in the sequence of numbers used during the simulation process, as otherwise correlations can be produced. There are simulations however, where the set of independent numbers needed might exceed the repetition period of the generator being used. When the generator is “well behaved”, even if the sequence of numbers is used more than once, the

probability of having more than one particle history starting in the same position of the sequence of random numbers is practically negligible. This means that when the end of the sequence is reached it will be started again during some of the sampling procedures used along the simulation (Andreo 1991).

A.5.3. SAMPLING TECHNIQUES

The selection of a random value of a specific quantity, from a continuous probability density function $f(x)$ is realized in Monte Carlo simulation through sampling methods, which are namely: the inversion method and the rejection method. In the codes utilized in the present study both methods were used.

A.5.3.1. INVERSION METHOD

The reduction of the sampling process (i.e. choose x^* from $f(x)$) to the generation of uniformly distributed random numbers is described by the fundamental inversion theorem:

Let X be a random variable with PDF $f(x)$, cumulative distribution function $F(x)$, and let r^* denote a uniformly distributed random number drawn from the unit interval. Then the probability of choosing x^* as defined by

$$r^* = F(x^*) = \int_{-\infty}^{x^*} f(x)dx$$

is $f(x^*)$.

The algorithm of the inversion technique can be described with the following steps:

Let $f: f(x)$ a PDF, $x \in [a, b]$

- Check if $f(x)$ is normalized:

$$\int_a^b f(x)dx = 1$$

- Calculate the Cumulative Distribution Function:

$$F(x) = \int_a^x f(t)dt$$

- Generate random numbers R
- Let $F(x)=R$ and solve for x : $x = F^{-1}(R)$

It is obvious that in order for the inversion method to be applied the inverse function of $F(x)$ has to be calculated.

A.5.3.2. REJECTION METHOD

When inversion method cannot be implemented, rejection method is a simple alternative solution. However, depending of the shape of the modeled probability density function, this method may be time consuming.

The algorithm of the rejection technique can be described with the following steps:

Let f : $f(x)$ a PDF, $x \in [a, b]$

- Find the maximum of $f(x)$ and name it f_0 .
- Set g : $g(x) = f(x)/f_0$
- Generate a random number $R_1 \in [0, 1)$
- Generate a random value of $x \in [a, b)$, say $x^* = a + (b-a)R_1$
- Generate a random number $R_2 \in [0, 1)$
- Compare R_2 with $g(x^*)$:
- If $g(x^*) < R_2$ then

Reject x^* and return to the third step

Else

Accept x^* and return to the third step if the number of photons has not finished.

Although the rejection method is easier to implement, it carries one major disadvantage with respect to the inversion method. This is not being equally productive to the inversion method, which generates one result for each one random number generated. Depending on the distribution of the function to be sampled, the rejection method could reject several results, before accepting one.

CHAPTER B

MATERIALS & METHODS

B.1. GEOMETRY

B.1 GEOMETRY

As also discussed earlier, the magnification technique is a secondary examination of the breast applied when a suspicious abnormality has already been detected. The aim of this examination is to magnify the suspicious area of the breast. The desired magnification degree in magnification mammography is achieved through simple geometric changes with respect to contact mammography, considering partial breast irradiation, as presented in Figure 3.

Figure 3: Contact (a) and magnification (b) geometry in mammography. In magnification geometry the antiscatter grid is removed and the breast is placed closer to the focal spot.

The antiscatter grid is removed since the air gap between the breast and the image receptor offers inherent limitation of scattered radiation. The irradiated volume of the breast is smaller in this case, since the image receptor and the field sizes do not change. However, in some cases larger image receptors and field sizes are used and the whole breast is irradiated. This thesis deals only with the first case. In the simulation studies performed, the Focus to Breast Holder Distance (FBHD) was altered from 56 cm to about

24 cm resulting in magnification degrees from 1.0 (considered as contact geometry) to 2.0, for a 4 cm breast phantom, according to the formula:

$$M = \frac{FDD}{FBHD} \quad (B.1)$$

where FDD is the Focus to Detector Distance, which was set to 60 cm.

For the dosimetric studies, the focal spot dimensions were 0.01 mm x 0.01 mm, in order to be compatible with the systems available in clinical practice. The same focal spot size was also selected for the calculation of CNR, while the Field Of View (FOV) was considered to be 1.60 cm x 2.08 cm at the image receptor plane, for a focus-to-image receptor distance of 60 cm. The specific FOV was selected in order to irradiate only the appropriate part of the phantom and therefore to reduce the executional time of the simulations.

Concerning the intensity distribution of the outcoming x-ray photons, taken into account in the spatial resolution studies, and according to the MASTOS simulation model (Spyrou et al 2002), the projections of the x-ray emission points on the horizontal plane are generated by Monte Carlo methods in such a way as to obey one of the following three distributions: uniform, Gaussian and double Gaussian. These intensity distributions are considered the most common for mammographic x-ray tubes and most of the efforts of the x-ray tube manufacturers aiming to improve the image quality by altering the intensity distribution are revolving around them (Nickoloff et al 1990). The details of the Gaussian and double Gaussian distributions concerning their mean values (μ) and standard deviations (σ), as well as their Full Width at Half of the Maximum (FWHM) are presented in Table 2. As mean values μ , the centers of the Gaussian peaks were selected and as far as the Gaussian distribution is concerned, the focus size was considered to be equal to 5σ (mean value ± 2.5 standard deviations). This value corresponds to about 98.8% of the area under the Gaussian and is in agreement with the NEMA standards (NEMA 1974, Nickoloff et al 1990). This arbitrary size determines the focal spot, as considered in this study, and can be different from the nominal size given by the x-ray tube manufacturer. This means that two mammographic tubes with the same nominal focus size can result in different values of spatial resolution if their intensity distributions

are different. Double Gaussian represents the twin peaked distribution or may also represent a gradually deterioration of anode (due to thermal effects) which leads to image deterioration. In the case of the double Gaussian distribution, in order to study the effect of the distance separating the two Gaussian peaks this distance was altered and the spatial resolution was calculated for each case. For the rest of the study, the focus size in the case of a double Gaussian distribution was considered to be 10σ . This value was selected as it produces a well defined double Gaussian distribution and it can be considered as the resulting condition of a single Gaussian focal spot (defined as 5σ), when it is destroyed.

Table 2: The Gaussian and double Gaussian distribution details utilized in the simulations performed.

Gaussian Distribution $f(x) = \frac{1}{\sqrt{2\pi} \cdot \sigma} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$	Focal Spot Size (mm)		
	0.04	0.12	0.30
μ	0.020	0.060	0.150
σ	0.008	0.024	0.060
FWHM	0.019	0.057	0.141
Double Gaussian Distribution			
$f(x) = \frac{1}{\sqrt{2\pi} \cdot \sigma} (e^{-\frac{(x-\mu_1)^2}{2\sigma^2}} + e^{-\frac{(x-\mu_2)^2}{2\sigma^2}})$			
μ_1	-0.010	-0.030	-0.075
μ_2	0.010	0.030	0.075
σ	0.004	0.012	0.030
$FWHM = (2\sqrt{2\ln 2}) \cdot \sigma$	0.009	0.028	0.071

Taking into account that the focal spot sizes reported in this study are a function of the standard deviation (5σ), all the corresponding results about spatial resolution can be reduced to 1σ , dividing each focus size by 5. In this way, one can derive the

corresponding results for any focal spot intensity distribution, given the fact that it can be considered as Gaussian and its standard deviation is known.

For the specific simulations, a specific part of the test-object was irradiated, corresponding to a (FOV) of 0.300 cm x 0.301 cm at the collimator plane.

CHAPTER B

MATERIALS & METHODS

B.2. THE MONTE CARLO SIMULATION MODELS

B.2.1. DOSIS.....	47
B.2.2. MASTOS.....	49

B.2.1. DOSIS

The irradiation of the mathematical breast phantom, used in the dosimetric studies, was simulated using a set of earlier developed and validated Monte Carlo software, DOSIS, for deriving the dose delivered to the breast during the mammographic process (Delis *et al* 2005a). This software was differentiated from its initial version in order to include magnification geometries, calculation of the AGD as well as breast phantoms of various compositions (percentage of glandular-adipose tissue).

The flow chart of the proposed simulation model is presented in Figure 4. The “history” of each Monte Carlo photon initiates with the assignment of the initial energy, which is defined depending on the selected geometry and field size. When a photon reaches the phantom it can follow a sequence of possible interactions for this energy range (photoelectric absorption, coherent and incoherent scattering). The type of the interaction (based on the atomic cross sections), the energy deposited (photoelectric, Compton) and the scattering angles (Compton, Rayleigh) have been sampled and included in the model. The air KERMA is calculated exactly before the entrance of each photon in the phantom and the AGD at the end of the photon history in the phantom.

The initialization of the photon history starts with its entrance inside the phantom. On the basis of the total cross-sections the free path length of the photon is defined. At the end of this free path the photon is forced to undergo an interaction, based on the sampling of the cross sections and therefore the interaction probability according to the energy that it initially had. The possible interactions for the mammographic energy range are the photoelectric effect, the coherent scatter (Compton) and the incoherent scatter (Rayleigh), with the photoelectric being by far the most dominant effect. The cross sections that were used for the simulation process come from the database of the National Institute of Standards and Technology and from Hubbel *et al* (1975). The history of the photon continues until one of the following happens:

- Photoelectric effect inside the phantom; the photon deposits the total of its energy at the point of the interaction causing radiation dose.
- Escape of the photon towards the detector; the photon is recorded on a 2D matrix, representing an ideal x-ray detector, and contributes to the image formation.

- Escape the phantom towards another direction causing scattered radiation.

More details about the interactions and the specific Monte Carlo simulation model can be found in the doctorate thesis of Dr Delis (Delis 2004).

Figure 4: The flow chart of the used simulation model.

Concerning the dosimetric studies, in order to minimize the statistical fluctuation of the results, the number of x-ray photons was 10^8 , resulting in execution (computational) time of 16 minutes for each simulation, utilizing a Pentium 4 processor, at 3.0 GHz.

B.2.1. MASTOS

DOSIS simulation model concerns only photons absorbed inside the phantom causing radiation dose. The part concerning image formation is a subject developed in the second Monte Carlo simulation model, MASTOS. This model is dedicated for deriving the produced image during mammographic conditions. The flow chart and the history of each x-ray photon is the same as in the previous case, as far as the interactions inside the phantom are concerned. In order to illustrate the results in a pictorial form, the exposure map under the phantom is converted to an 8-bit grey scale representation, with the exposure considered in each study corresponding to the grey level of 125. This output signal (subject contrast) exiting the phantom or the exit spectrum per pixel can be utilized as the input to a conventional screen-film or a digital detector, and the detected image can be generated, taking into account the effect of the actual response curve of the detector, as well as its energy response. These effects were not considered in the study of contrast to noise ratio (CNR), since the primary aim was the investigation and quantification of the differences in the imaging ability of each spectrum, rather than the generation of the real mammographic image itself.

In order to have comparative results, the number of the initial Monte Carlo photons was selected in order to produce the same exposure at the detector plane. This normalizing exposure was selected to be the 2 mR and 5 mR for the CNR and the spatial resolution studies correspondingly, in order to balance between acceptable statistical fluctuation and reasonable computational time for each simulation experiment. These exposures correspond to about 12 and 30 hours for each simulation, utilizing a Pentium 4 processor, at 3.0 GHz.

CHAPTER B

MATERIALS & METHODS

B.3. MAMMOGRAPHIC SPECTRA

B.2. MAMMOGRAPHIC SPECTRA

The mammographic spectra utilized in the present study were derived using a previously developed and validated program (Delis et al 2006). Various anode/filter combinations were considered and operated at tube voltages between 24 kVp and 34 kVp. Materials such as W, Rh and Mo were used as anodes, combined with Al or k-edge (Mo, Rh, Ru, Nb or Pd) filters. Inherent filtration of 1 mm beryllium (Be) window was also considered, while a correction was made for the anode self-absorption.

CHAPTER B

MATERIALS & METHODS

B.4. BREAST PHANTOMS

B.4.1. DOSIMETRIC STUDIES.....	53
B.4.2. CNR STUDIES.....	54
B.4.3. SPATIAL RESOLUTION STUDIES.....	56

B.4.1. DOSIMETRIC STUDIES

In order to assure compatibility with similar published studies (Dance 1990, Dance et al 2000a, Zoetelief and Jansen 1995), the breast phantom was simulated by a homogeneous mixture of adipose and glandular tissue divided into voxels of 1 mm^3 . The percentage of glandularity could be altered from 1% to 100% in order to simulate breasts of various compositions. A 5 mm thick skin layer of adipose tissue was assumed at the upper and lower surface of the phantom and a 3 mm thick perspex compression plate was also used. The energy absorbed in the skin layers was not included in the calculation of AGD, as the carcinogenic risk for the skin is considered minimal in mammography (Liu et al 1995).

In order to calculate the AGD, the deposited energy in each voxel of the breast phantom was shared to the glandular and adipose tissues utilizing Monte Carlo simulation, according to their interaction probabilities. In the present study, AGD is defined as the dose delivered only to the irradiated portion of the phantom, rather than the whole, as previously proposed (Liu et al 1995). This was considered appropriate, since AGD is otherwise significantly underestimated, due to the large amount of non-irradiated phantom.

B.4.2. CNR STUDIES

The irradiated breast phantom was simulated by a homogeneous mixture of glandular and adipose tissue, being again compatible with phantoms utilized in previously published studies concerning Monte Carlo simulation in mammography (Dance et al 2000, Koutaloni et al 2006). The percentage of glandularity could be altered from 1% to 100% in order to simulate breasts of various compositions. The phantom was semicylindrical in shape with 4 cm radius and 4 cm thickness. It included two sets of four spherical inhomogeneities which simulated small sized high contrast lesions such as calcifications (Cs), with two different compositions: calcium oxalate (CO, $\text{CaC}_2\text{O}_4 \cdot 3(\text{H}_2\text{O})$) (Figure 5, Area 1) and hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) (Figure 5, Area 2). Their radii varied from 100 μm to 750 μm . Both sets of inhomogeneities were placed at the centre of the phantom, as far as its height is concerned. Inhomogeneities of Area 1 were placed 0.7 cm from the “chest wall” while inhomogeneities of Area 2 were placed 0.4 cm from it.

Figure 5: The irradiated part of the phantom used in the simulations performed. Area 1 corresponds to inhomogeneities composed of calcium oxalate (CO, $\text{CaC}_2\text{O}_4 \cdot 3(\text{H}_2\text{O})$) while Area 2 corresponds to inhomogeneities composed of hydroxy apatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$). The background consists of water.

Two representative Monte Carlo generated images of the selected FOV of the breast phantom described above are presented in Figure 6, corresponding to magnification degrees 1.0 and 1.6.

Figure 6: Two Monte Carlo generated images of the selected FOV corresponding to magnification degrees 1.0 (a) and 1.6 (b). The spectrum utilized for these simulations was the Mo\0.030mmMo at 28 kVp.

B.4.3. SPATIAL RESOLUTION STUDIES

A 4 cm thick sharp edge consisted of lead, non-transparent to x-rays, positioned at the center of the field with its central ray vertical to the transition edge and the surface of the test-object, was utilized as an edge-test-object and was imaged under various conditions. Although the International Electrotechnical Commission (IEC) recommends using a 4 mm thick test-object, consisted of 1 mm of tungsten and 3 mm of lead (IEC 2003), several authors have utilized test-objects similar to the one utilized (Carton et al 2005) as the main characteristic of the object is that it must be completely opaque to x-rays. Using a test-object consisted only of lead affects only the low spatial frequencies of the Modulation Transfer Function (MTF) by up to 1.3%, and not the higher spatial frequencies considered in the present study (Carton et al 2005). Moreover, the use of a 4 cm phantom is not practical in experimental studies, since it would introduce alignment difficulties, which obviously do not exist in the case of Monte Carlo simulations.

CHAPTER B

MATERIALS & METHODS

B.5. CALCULATIONS

B.5.1. AIR KERMA TO AVERAGE GLANDULAR DOSE CONVERSION FACTORS...	58
B.5.2. CONTRAST TO NOISE RATIO AND PERFORMANCE INDEX PI_v	60
B.5.3. THE EDGE METHOD FOR THE CALCULATION OF SPATIAL RESOLUTION..	62

B.5.1. AIR KERMA TO AVERAGE GLANDULAR DOSE CONVERSION FACTORS

Several authors have referred to conversion factors in order to calculate the AGD (D) in the breast by measuring the incident air KERMA (K) on the surface of the irradiated phantom (Dance 1990, Dance et al 2000a, Zoetelief and Jansen 1995, Boone 1999). As g is defined the overall conversion factor, equal to the quotient of AGD to air KERMA:

$$D = g \cdot K \quad (\text{B.2})$$

Published studies (Dance 1990, Dance et al 2000a) have proposed a combination of three independent conversion factors for contact mammography, as described in the equation:

$$D = (g_{\text{Mo/Mo}} \cdot c \cdot s) \cdot K \quad (\text{B.3})$$

where $g_{\text{Mo/Mo}}$ is the conversion factor of incident air KERMA to AGD for Mo/0.030mmMo at 28 kVp, c is a factor that corrects for glandularity different from 50% and s corrects for four anode/filter material combinations, other than the Mo/Mo one at 28 kVp only.

For the needs of the present study, the calculation of correction factors has been adapted to account for various degrees of magnification, glandularities, thicknesses, additional anode/filter material combinations and tube voltages. The AGD (D_M) for a degree of magnification M is associated with the air KERMA (K_M) for the same degree of magnification, with the following expression:

$$D_M = (g_{\text{Mo/Mo}} \cdot m \cdot s \cdot v \cdot c) \cdot K_M \quad (\text{B.4})$$

The $g_{\text{Mo/Mo}}$ is the proposed conversion factor for Mo/0.030mmMo at 28 kVp (Dance 1990, Dance et al 2000a), and was utilized as a “golden standard normalization index” for the rest of this study.

The m factor corrects for magnification. Degrees of magnification from 1.0 to 2.1 were considered, with a step of 0.1. For each magnification degree, the overall g factor from formula (B.2) was calculated keeping all the other parameters constant and was normalized with respect to the overall g factor for magnification 1.0, in order to correct for the magnification considered each time. The calculations were made using the Mo/0.030mmMo combination at 28 kVp.

The s factor corrects for 14 anode/filter combinations, other than Mo/0.030mmMo, and is independent of the magnification applied and the breast

thickness (Dance et al 2000a). The overall g factor was calculated again from formula (B.2) for each anode/filter combination and fixed tube voltage of 28 kVp, and divided by the overall g factor for Mo/0.030mmMo at 28 kVp. 14 anode/filter combinations were considered for the calculation of s factor, while the magnification degree chosen for the calculations was 1.6.

The v factor corrects for any different applied tube voltage between 24-34 kVp, with respect to 28 kVp. This is also independent of the magnification and the breast thickness, and was calculated by dividing the overall g factor from formula (B.2) for any tube voltage of each different anode/filter combination used, by the overall g factor for 28 kVp for the same material combination. The magnification degree considered was 1.6.

Finally, c factor corrects for any glandularity other than 50% and for any breast thickness between 2 cm and 10 cm, as proposed by Dance (2000a). Glandularities from 1% to 100% were simulated with a step of 25% for breast thicknesses from 2-10 cm. The overall g factor from formula (B.2) was calculated for each glandularity and was normalized with respect to the overall g factor for 50% glandularity. c factors for the intermediate values can be obtained by interpolation. The spectrum utilized for the specific calculations was the Mo/0.030mmMo at 28 kVp and the magnification degree applied was 1.6.

B.5.2. CONTRAST TO NOISE RATIO AND PERFORMANCE INDEX PI_v

On the produced radiation image, CNR was extracted from the formula proposed by Tapiovaara and Wagner (1993):

$$CNR = \frac{|C_{INS} - C_{BG}|}{\sqrt{N_{INS}^2 + N_{BG}^2}} \quad (B.5)$$

where C_{INS} is the mean grey level value of the simulating insert, and C_{BG} is the mean grey level value of the background, N_{INS} is the noise measured in the simulating insert and N_{BG} is the noise measured in the background. As noise, the standard deviation of the grey level value of the selected Region Of Interest (ROI) was considered. For the measurements of the C_{BG} and the N_{BG} , the irradiated part of the phantom around the inhomogeneities was utilized (Koutalonis et al 2007, Kotre et al 2002, Muntz and Logan 1979, Sorenson and Floch 1985). Finally, Scatter to Primary Ratio (SPR) was derived as the ratio of the scattered to the primary photons on the detector plane (Boone and Cooper 2000a, Boone et al 2000b, Dance and Day 1983).

The Monte Carlo generated images were visualized and analyzed using a software (Medical Image Visualization) developed for medical image processing and analysis applications (Sakellaropoulos et al 1999).

Overall performance results were obtained by combining the image characteristics resulted during this part of the study for different degrees of magnification, tube voltages and anode/filter material combinations with the corresponding AGD results taken from the dosimetric studies (Koutalonis et al 2006). As previously suggested by Nishino et al (2005), $(CNR)^2$ can be used as image quality descriptor when evaluating the figure of merit, in order to emphasize the importance of the imaging part of the performance index derived with respect to the dose, showing that the precise and early detection of abnormalities is the primary aim in mammography. Especially when magnification is performed, which is a secondary diagnostic and not a screening examination, the need of emphasizing the imaging part of the procedure with respect to the dose is even more imperative. For this reason, higher powers of CNR, $((CNR)^v)$, can be introduced in order to derive an overall performance index as the ratio of the desirable “benefit” (which corresponds to the $(CNR)^v$) over the “cost” (which corresponds to the AGD), as described in Equation (B.6):

$$PI_v = \frac{(CNR)^v}{AGD} \quad (B.6)$$

where, v values from 1 to 5, in steps of 0.25, were considered in the study. The specific performance index can be utilized in order to evaluate the overall performance of various anode/filter combinations under different exposure (degree of magnification, tube voltage) parameters. As higher values of v are used in formula (B.6), the relative percentage differences among the various spectra compared, attributed to their imaging ability, are increased. So, using higher powers of CNR in formula (B.6) results in escalated percentage difference between the performance indices of two spectra compared, a difference which is due to their imaging ability. This could be very helpful in the effort to evaluate and compare the overall performance of design parameters in procedures where higher importance is given to the image quality with respect to the dose, such as in magnification views in mammography.

In order for the results to be comparative, the CNR values calculated in the present study were normalized to their maximum CNR value (CNR of Mo/0.030mmMo at 24 kVp), while the results concerning the AGD were normalized to their minimum AGD value (AGD of W/0.050mmPd+2.00mmAl at 32 kVp). Because of the specific normalization of the CNR and AGD values, the above index should ideally have a value of unity for the “ideal spectrum” (resulting in maximum CNR and minimum AGD), which is an ideal case just to represent a point of reference.

B.5.3. THE EDGE METHOD FOR THE CALCULATION OF SPATIAL RESOLUTION

For the calculation of spatial resolution an Edge Spread Function (ESF) was derived from each image. To derive this ESF, a rectangular ROI was selected including 2 mm at each side of the edge transition. The profile of the perpendicularly calculated average greylevel values along these distances corresponds to the ESF. The specific size of the ROI was selected, despite IEC recommendation (IEC 2003) as a result of the small FOV selected, as mentioned above.

Figure 7: Example of the procedure followed for the calculation of the spatial resolution from the derived Monte Carlo image (focal spot size 0.04 mm, magnification 1.8): (a) The derived image and the ROI selected, (b) the derived ESF, (c) the LSF and (d) the MTF and the Gaussian fitting curve. The horizontal dotted line at (d) shows the 5% value of the MTF at which the spatial resolution was measured in lp/mm.

However, the validation concerning the selection of the FOV (see next paragraph) included utilizing each time a larger ROI together with a larger FOV and the results showed that the ROI size has also a minor effect in the calculation of spatial resolution. The same results concerning the ROI dimensions were also extracted by Carton et al (2005). The ESFs were numerically differentiated to obtain the Line Spread Function (LSF), from which the Modulation Transfer Function (MTF) was calculated by a Fourier transform. The difficulty to precisely determine the tail portion of LSF using this approach, does not influence the results of this study, as this only affects the low frequencies of the MTF (Fujita et al 1992). This method of measuring the MTF has gained popularity recently, due to its simplicity and appropriateness especially for digital imaging (Samei et al 1998, Cunningham and Fenster 1987). The corresponding MTFs were fitted as part of Gaussian curves, resulting in a coincidence between the fitted and the calculated points of about 99% on average. However, a Sigmoidal fitting would also be acceptable. The spatial resolution in lp/mm can be extracted from the MTF and corresponds to the spatial frequency where MTF reaches a specific threshold. This threshold varies among the different authors between 2% and 5%, most of whom stretch it as far as possible (Koutalonis et al 2008a, 2008b, Illers et al 2005, Neitzel et al 2004, Bosmans et al 2005). For the purposes of this study it was considered 5%. The above procedure is presented schematically in Figure 7.

The Monte Carlo generated images were produced given a pixel size of 20 μm in order to have a relatively high Nyquist frequency of 25 cycles/mm, which is enough for the calculation of the spatial resolution in the specific study. The Monte Carlo generated images were processed using a software (Medical Image Visualization) developed for medical image processing and analysis applications (Sakellaropoulos et al 1999).

CHAPTER B

MATERIALS & METHODS

B.6. VALIDATION

B.6.1. VALIDATION OF THE MONTE CARLO SIMULATION MODELS.....	65
B.6.2. VALIDATION OF THE CALCULATIONS.....	66

B.6.1. VALIDATION OF THE MONTE CARLO SIMULATION MODELS

When proposing a simulation model, it is essential to assure that this model behaves like the original modeled system. To assure the accuracy of the proposed model it was necessary to estimate the validity of the produced results. To this direction, both simulation models were validated against published data as well as experimentally. The Monte Carlo simulation results were found to differ by about 4% from published data and by about 5% from experimental results. These differences are considered satisfactory and can be granted to a number of parameters. The changes in the spectral distributions and the differences between phantom materials used for the validation are only two of the major components severely affecting the produced results of the validation. More details about the specific validations can be found in the doctorate thesis of Dr Delis and Dr Spyrou.

B.6.2. VALIDATION OF THE CALCULATIONS

Although the Monte Carlo simulation models were already validated, some extra validation was made to some of the results of this study. Moreover, some simulations were made to justify and validate some approximations, which are introduced in the following paragraphs:

A) Validation of the AGD calculation

In addition to the already published validation results of both the Monte Carlo simulation model DOSIS and the mammographic spectra utilized in this study (Spyrou et al 1998, Delis et al 2005a, Delis et al 2004), the results concerning the AGD were compared with those of Boone (1999), as an additional validation. Boone presented AGD values in unit mrad/R, which were converted into unit $\text{mGy} \cdot \text{mGy}^{-1}$ for the needs of this comparison. A 100% glandular breast of 4 cm thickness was utilized, while the skin thickness was set to 4 mm of adipose tissue. For consistency of the validation results, the utilized spectra were the same as those utilized by Boone (Boone et al (1997), Boone and Seibert (1997) and Boone and Chavez (1996)), for deriving the original results. The anode/filter material combinations used were the Mo/0.030mmMo, Mo/0.025mmRh, Rh/0.025mmRh and W/0.050mmRh for several values of tube voltage ranging from 20 kVp to 40 kVp.

The AGD results from our study were found to differ from those of Boone (1999), on average, by 3.13%. This small variation can be attributed to differences in the Monte Carlo simulation code, the utilized interaction coefficients and the breast phantom composition.

Moreover, by comparing the g value calculated in this study for the Mo/0.030mmMo combination at 28 kVp for contact geometry with the one calculated by Dance (1990) or Dance et al (2000a) we find an average difference of about 6%, which can be considered inside the acceptable levels, as also suggested by Dance (2000a). This variation can be attributed mainly to different utilized Monte Carlo simulation codes, mammographic spectra and interaction cross-sections.

B) Validation of the independence of the proposed formula factors

The validity of the independence of the factors proposed in formula (B.4) was performed by comparing the Monte Carlo directly calculated overall g factor, from

the formula (B.2) for specific exposure parameters concerning the anode/filter combination, tube voltage, degree of magnification, glandularity and breast thickness, with the product of the conversion factors in formula (B.4) corresponding to these specific parameters. This validation was carried out for a random sample of 130 combinations, considering various degrees of magnification, glandularities and breast thicknesses, rather than in the total of 83160 possible combinations, that can be derived from the 11 tube voltages, 12 degrees of magnification, 14 anode/filter material combinations, 5 glandularities and 9 breast thicknesses. The results from the two calculations were found to differ on average by 0.14%, which is attributed to statistical fluctuations.

C) Validation for the FOV selected in the CNR studies

For the calculations concerning this study not the entire phantom was irradiated, as also mentioned earlier. A specific FOV of 1.60 cm x 2.08 cm at the image receptor plane, containing the inserted inhomogeneities and their surroundings was selected, in order to reduce the executional time of the simulations. In order to validate the accuracy of this approximation, even in low degrees of magnification where the presence of scattered radiation is higher, Monte Carlo simulation experiments were executed for various exposure conditions (degree of magnification, breast glandularity, spectrum), irradiating the whole phantom described above, corresponding to FOV of 8 cm x 4 cm at the image receptor plane. CNR was calculated for these conditions and compared to the corresponding CNR for the irradiation with the FOV considered in the study. Results demonstrate that the average variation between the two irradiation conditions is 3.94% showing that this approximation has only minor effect on the results as in magnification conditions the extended air gap between the breast and the image receptor reduces further the scattered radiation.

D) Validation for the FOV selected in the spatial resolution studies

For the specific simulations, a specific part of the test-object was irradiated, corresponding to a FOV of 0.300 cm x 0.301 cm at the collimator plane, although a larger FOV could be selected in real practice. This FOV was chosen in order to reduce the executional time of the simulations performed and since the FOV does not significantly affect the spatial resolution (Carton et al 2005). In order to further

validate the accuracy of this approximation, Monte Carlo simulations were executed using several FOVs up to 0.600 cm x 0.601 cm, keeping the same irradiation conditions. The spatial resolution was calculated and compared to the corresponding spatial resolution for the irradiation with the FOV considered in the study. Results demonstrate that the maximum variation between the irradiation with various FOVs is up to 2.8% (corresponding to up to 0.4 lp/mm), showing that this approximation has only a minor effect on the results.

E) Validation for the exposure selected in the spatial resolution studies

In order to minimize the statistical fluctuation of the results and to better approximate the real mammographic process, an Automatic Exposure Control (AEC) system was simulated and the number of x-ray photons in the studies was normalized to produce 5 mR exposure at the detector plane. The same exposure has also been utilized in studies in real practice (Carton et al 2005), resulting in low statistical fluctuations in the produced image. In order to study the influence of this statistical fluctuation on the calculated spatial resolution, the noise in the produced Monte Carlo images was quantified. The standard deviation of the grey level values was utilized for this reason. In Figure 8 (a) the standard deviation is plotted as a function of the exposure, for various values of exposure between 0.1 mR and 15 mR, while in Figure 8 (b) the calculated spatial resolution is plotted as a function of the standard deviation for each exposure. According to these two figures, the effect of noise on the spatial resolution for exposure higher than 5 mR is small and the spatial resolution for exposures between 5 mR and 15 mR alters by up to 4% (corresponding to up to 0.5 lp/mm), showing that Monte Carlo noise does not affect substantially the results.

(a)

(b)

Figure 8: (a) The standard deviation (in greylevel values) as a function of the exposure and (b) the spatial resolution as a function of the standard deviation for a 0.10 mm focal spot and 1.9 magnification.

F) Effect of detector blurring on spatial resolution

Although the primary aim of the study was to evaluate the system performance regarding the spatial resolution, it was considered necessary to partially explore the effect of the detector. Towards this direction, the performance of the detecting system and the degradation of the spatial resolution caused by the intrinsic characteristics of the detector were studied via an analytical model. The x-ray photons exiting the phantom do not necessarily interact at the point of intersection with the detector, and furthermore the generated image formation particles (either electrons or optical photons) may spread inside the detector and be recorded at a distance from the interaction site. This causes a blurring of the initial image that can be studied by means of the Point Spread Function (PSF) and the subsequent FWHM of the detector.

Two detectors for mammographic purposes were considered, one with FWHM of 100 μm and one with 150 μm (Kiss et al 2002, Liaparinos et al 2006, 2007). As this FWHM is directly related to the standard deviation of the Gaussian shaped PSF, it was utilized to generate the pixel based PSF. A mask of adequate dimensions was generated, representing the effect of the PSF and adjusted to the pixel size utilized ($20 \times 20 \mu\text{m}^2$). Then, the convolution between the initially Monte Carlo generated images was produced, acting as a smoothening filter of the image (Olivo et al 2000). The initial and the convolved image were then compared with respect to the corresponding spatial resolution, and the degree of degradation caused by the detector blurring was estimated.

Using the PSF mask presented above, the spatial resolution was calculated taking into account the detector blurring, for most of the cases considered in the study. The spatial resolution degradation due to the detector blurring was found to be up to about 3%. For example, the spatial resolution of 22.0 lp/mm was degraded to 21.7 lp/mm and the 11.1 lp/mm was degraded to 10.7 lp/mm when the detector blurring was also considered. An indicative result is shown in Figure 9, where the spatial resolution is presented with respect to the degree of magnification for the two cases and for a 0.10 mm focus. From this figure, one can conclude that although the effect of the detector blurring has an effect on the spatial resolution as far as the numerical values are concerned, it does not qualitatively affect the relative results presented in this study, where the primary aim is to study the system spatial resolution.

Figure 9: The spatial resolution as a function of the degree of magnification, with and without considering the effect of the detector blurring (0.10 mm focal spot size and Gaussian intensity distribution).

CHAPTER C

RESULTS & DISCUSSION

C.1. DOSIMETRIC STUDIES

C.1.1. EFFECT OF MAGNIFICATION ON AVERAGE GLANDULAR DOSE.....	73
C.1.2. EFFECT OF TUBE VOLTAGE ON AVERAGE GLANDULAR DOSE.....	74
C.1.3. EFFECT OF MAGNIFICATION ON PERCENTAGE DEPTH DOSE.....	75
C.1.4. EFFECT OF MAGNIFICATION DEGREE, ANODE/FILTER COMBINATION, TUBE VOLTAGE AND GLANDULARITY ON g FACTOR.....	76

C.1.1. EFFECT OF MAGNIFICATION ON AVERAGE GLANDULAR DOSE

In Figure 10, the influence of magnification on AGD is presented, for the Mo/0.030mmMo at 28 kVp. The results demonstrated in this figure are through direct calculation of AGD using Monte Carlo simulation. According to the assumption made about the definition of the irradiated volume and because of the effect of the inverse square law, the AGD increases with increasing magnification.

Figure 10: The influence of magnification factor on AGD for the Mo/0.030mmMo combination at 28 kVp and for 4 cm breast phantom.

C.1.2. EFFECT OF TUBE VOLTAGE ON AVERAGE GLANDULAR DOSE

The effect of tube voltage on AGD for the Mo/0.030mmMo combination and for magnification degree 1.6 is presented in Figure 11. For the same number of photons used, AGD increases with tube voltage because more photons and with higher energies reach the phantom and deposit their energy in it. In Figure 11, a comparison between magnification degrees 1.0 and 1.6, as well as a comparison of the results obtained from direct calculation of AGD from the Monte Carlo simulation and the indirect calculation of AGD through the Monte Carlo calculated conversion factors for magnification degree 1.0 is demonstrated. The average difference between results from direct and indirect calculation of AGD is 0.57%, validating again the independence of the conversion factors.

Figure 11: The influence of tube voltage on AGD for the Mo/0.030mmMo combination and for magnification factors 1.6 and 1.0. Results from the use of conversion factors are also presented, for magnification factor 1.0.

C.1.3. EFFECT OF MAGNIFICATION ON PERCENTAGE DEPTH DOSE

Figure 12 shows the effect of the degree of magnification on PDD. PDD is decreased with magnification due to two main reasons. As the breast is placed closer to the focal spot a smaller field size appears on the surface of the breast. This results in lower contribution of scattered photons to points on the central axis. Moreover, the decrease of the focus-to-breast distance causes the decrease of PDD because of the decreasing effect of z on the inverse square factor which governs the primary component of the photon beam (Koutaloni et al 2006).

Figure 12: The effect of the degree of magnification on PDD for three degrees of magnification

C.1.4. EFFECT OF MAGNIFICATION DEGREE, ANODE/FILTER COMBINATION, TUBE VOLTAGE AND GLANDULARITY ON g FACTOR

Monte Carlo calculations of air KERMA and AGD were utilized in order to derive the $g_{Mo/Mo}$ value that is 0.216, calculated for contact geometry and breast thickness of 4 cm. This value is considered a constant and is used in subsequent calculations of AGD, based on formula (B.4), regardless of the breast thickness, as there has been made a correction for the thickness in the calculation of c factor.

Results concerning m correction factor are presented in Table 3. Although, as presented in Figure 10, AGD increases with the magnification degree, the m correction factor decreases with the magnification, as presented in Table 3. The reason for this is that m factor is the quotient of the AGD and air KERMA measured on the surface of the phantom. However, air KERMA increases according to the inverse square law, while AGD increases less rapidly. So, the m correction factor decreases with magnification. Moreover, m factor varies from 1.000 to 0.885 for magnification degrees between 1.0 and 2.1, showing that the error that can be introduced if the conversion factor for contact mammography is considered for this magnification, can be up to 12%, underlining the necessity of utilizing a proper m factor.

The combined effect of s and v factors, for 14 anode/filter combinations and 11 values of tube voltage, is presented in Table 4, offering a more practical alternative for direct correction, depending on the selected spectrum. The effect of the filter material's k-absorption edge can be noticed in this table. For example, considering Mo as anode material and for a fixed value of tube voltage, Rh as filter material has 25% and 16% larger conversion factors than Nb and Mo, correspondingly, resulting in this way in higher AGD. In the same table, the impact of anode material's k-emission edge can also be obtained, where W/Rh combination has larger s conversion factor than Mo/Rh and Rh/Rh.

Moreover, the effect of tube voltage on the combined s and v factor is obvious in Table 4. The increase of tube voltage from 24 kVp to 34 kVp leads to about 25% larger combined conversion factor for all combinations, which is translated into a corresponding increase in AGD, for a fixed value of air KERMA. The introduction of v factor correcting for any tube voltage different from the 28 kVp for any anode/filter material combination is as important as the introduction of m factor correcting for the

degree of magnification. Without correcting for the tube voltage, neglecting the v factor, the error which enters into the calculation of AGD can be up to 19% for some

Table 3: The m correction factor for magnification degrees from 1.0 to 2.1, corresponding to focus to skin distance from 56 cm to 24 cm.

Magnification Degree	m Correction Factor
1.0	1.000
1.1	0.988
1.2	0.977
1.3	0.965
1.4	0.954
1.5	0.944
1.6	0.933
1.7	0.923
1.8	0.913
1.9	0.903
2.0	0.894
2.1	0.885

tube voltages applied on anode/filter combinations. So, the total error of non-using both of the factors can lead to a significant underestimation or overestimation of AGD.

Finally, the effect of glandularity on AGD is presented in Table 5. Decrease of the glandularity of the breast results in higher AGD because of the increased penetrating ability of the photon beam in thick breasts, which correspond to low glandularity.

$g_{Mo/Mo}$ and c factor values of this thesis are in good agreement with those calculated by Dance et al (2000), having an average difference of about 6% and 2% correspondingly. Higher differences that appear in the values referring to glandularity 1% are due to bad statistics concerning the composition of the simulated phantom.

Differences in the values of the s factor calculated are on average about 17%. This variation can be attributed mainly to the different utilized mammographic spectra.

Table 4: The combined s and v correction factor for the various anode/filter combinations and for tube voltage between 24-34 kVp.

Combination\kVp	24	25	26	27	28	29	30	31	32	33	34
Mo/0.51mmAl	1.055	1.107	1.152	1.194	1.232	1.263	1.294	1.321	1.348	1.372	1.395
Mo/0.030mmMo	0.887	0.921	0.951	0.979	1.000	1.030	1.050	1.071	1.091	1.110	1.127
Mo/0.030mmNb	0.774	0.810	0.843	0.873	0.898	0.930	0.956	0.980	1.004	1.026	1.047
Mo/0.029mmRh	1.068	1.113	1.146	1.174	1.199	1.220	1.239	1.255	1.272	1.286	1.301
Rh/0.51mmAl	1.033	1.103	1.165	1.224	1.276	1.325	1.370	1.412	1.451	1.488	1.522
Rh/0.030mmNb	0.699	0.728	0.757	0.785	0.813	0.842	0.871	0.898	0.926	0.955	0.983
Rh/0.029mmRh	1.050	1.109	1.159	1.204	1.241	1.278	1.308	1.339	1.367	1.395	1.419
Rh/0.030mmRu	1.010	1.058	1.102	1.140	1.175	1.209	1.237	1.267	1.295	1.322	1.345
W/0.50mmAl	1.095	1.116	1.178	1.238	1.296	1.349	1.403	1.455	1.505	1.554	1.602
W/0.030mmMo	0.825	0.853	0.878	0.906	0.931	0.961	0.990	1.020	1.053	1.086	1.119
W/0.050mmNb	0.832	0.855	0.879	0.905	0.930	0.958	0.987	1.020	1.053	1.089	1.127
W/0.050mmPd+2.00mmAl	1.774	1.863	1.909	1.941	1.969	1.992	2.016	2.042	2.069	2.102	2.134
W/0.030mmRh	1.086	1.137	1.180	1.216	1.248	1.280	1.310	1.340	1.369	1.398	1.428
W/0.050mmZr	0.711	0.735	0.760	0.786	0.813	0.842	0.873	0.905	0.939	0.976	1.014

Table 5: The c factor correcting for glandularities from 1% to 100% and breast thicknesses from 2 cm to 10 cm.

c Correction Factor					
Glandularity %					
Thickness (cm)	1	25	50	75	100
2	2.768	2.094	1.895	1.744	1.627
4	1.548	1.137	1.000	0.900	0.814
6	1.009	0.732	0.639	0.570	0.512
8	0.728	0.526	0.458	0.407	0.366
10	0.594	0.407	0.353	0.314	0.282

CHAPTER C

RESULTS & DISCUSSION

C.2. CONTRAST TO NOISE RATIO STUDIES

C.2.1. EFFECT OF MAGNIFICATION ON CONTRAST TO NOISE RATIO.....	81
C.2.2. OVERALL PERFORMANCE OF ANODE/FILTER MATERIAL COMBINATIONS IN MAGNIFICATION MAMMOGRAPHY.....	86
C.2.3. EFFECT OF BREAST COMPOSITION ON CONTRAST TO NOISE RATIO.....	90

C.2.1. EFFECT OF MAGNIFICATION ON CONTRAST TO NOISE RATIO

Figure 13 presents the effect of the degree of magnification on CNR for the two sets of four spherical inhomogeneities with increasing radius, one composed of calcium oxalate (CO) and the other composed of hydroxyapatite (HA), for magnification degrees from 1.0 to 2.0. The anode/filter material combination chosen for the specific calculations was the Mo/0.030mmMo at 28 kVp which is considered as the “golden standard” in mammography. Results demonstrate that inhomogeneities consisted of HA are discriminated more easily compared to those of CO, as they result in higher CNR, which was found to vary from 30% (100 μ m inhomogeneity) to 54% (750 μ m inhomogeneity). Moreover, this difference is reduced by about 66% as the degree of magnification increases from 1.0 to 2.0. Small radius inhomogeneities of 100 μ m are more difficult to be distinguished in the phantom than the rest of the inhomogeneity sizes considered, even in high degrees of magnification, as they have a very low CNR.

According to the results, CNR was found to increase with the degree of magnification. This is more obvious in Figure 14, where the CNR improvement factor representing the CNR under magnification normalized with respect to the contact CNR is shown, for the four sizes of HA inhomogeneity. Results are similar for both compositions of inhomogeneities considered in the study, showing that for all sizes considered, the improvement of CNR is higher in the range of magnification 1.0 to 1.4, than that from 1.4 to 2.0. This improvement varies from 75% for the 750 μ m inhomogeneity to 167% for the 100 μ m one, for magnification from 1.0 to 1.4, while for magnification from 1.4 to 2.0 the further improvement ranges from 26% to 37%, respectively. This improvement is higher for the small sized inhomogeneities. Therefore, further decrease of the FBD (from 1.4 to 2.0 magnification) induces smaller improvement on the CNR because of the lower reduction rate of the scattered radiation after magnification 1.4. This can also be noticed in Figure 15, where the effect of magnification on normalized SPR with respect to contact geometry is presented. Scattered radiation (and therefore SPR) is reduced with high rate between magnifications 1.0 to 1.4, resulting after this point to almost a plateau. At degree of magnification 1.4, the normalized SPR has been reduced by 86% from its maximum value, while at magnification 2.0 it has been reduced by 96%.

Taking into account the dosimetric results concerning normalized AGD with respect to their minimum value (corresponding to degree of magnification 1.0)

Figure 13: The influence of degree of magnification on CNR for inhomogeneities of two compositions (CO and HA) and four sizes (spherical with radii from 100 μm to 750 μm). The Mo/0.030mmMo combination at 28 kVp was utilized for the specific calculations.

(Koutalonis et al 2006), the PIV from equation (6) was calculated for various values of v , and the degree of magnification where the maximum PIV appears for each v , is presented in Table 6. Thirteen anode/filter material combinations were utilized for the specific calculations, operated at 28 kVp which is considered a common tube voltage applied in clinical practice. In this table, for values of v up to 2.50, magnification degree 1.3 results in the higher “benefit” with the lower “cost” for most of the combinations. CNR increases with magnification in the way presented in Figures 13 and 14, while according to the dosimetric study (Koutalonis et al (2006)), AGD increases with magnification almost linearly. So, the reduction of the CNR increase rate for magnification degree above 1.3 is the critical factor that determines this good performance at the specific magnification. If a higher importance is to be given in the imaging part of the PIV, demoting even more the role of dose in the examination, higher powers of CNR can be considered. Increasing the value of v , between 2.75 and 5.00 or even more, results in best performance under magnification 1.4 for most of the anode/filter combinations.

Figure 14: The CNR improvement factor representing the normalization of CNR with respect to that for degree of magnification 1.0, for the four sizes of inhomogeneities consisted of HA.

Figure 15: The effect of degree of magnification on SPR. SPR values are normalized with respect to the SPR for magnification 1.0. The calculations were performed using the Mo/0.030mmMo combination at 28 kVp with a 4 cm phantom consisting of equally weighted glandular and adipose tissues.

Table 6: The degree of magnification where the maximum value of Performance Index $PI_v = \frac{(CNR)^v}{AGD}$ appears, for various values of v and for the anode/filter combinations studied (accuracy for the degree of magnification in steps of 0.05).

v	Degree of Magnification at which the PI_v maximum occurs												
	Anode/filter Combination												
	Mo/0.030 mmMo	Mo/0.51 mmAl	Mo/0.030 mmNb	Mo/0.029 mmRh	Rh/0.51 mmAl	Rh/0.030 mmNb	Rh/0.030 mmRu	Rh/0.029 mmRh	W/0.50 mmAl	W/0.030 mmMo	W/0.050 mmNb	W/0.030 mmRh	W/0.050 mmPd/2.00 mmAl
1.00	1.00	1.20	1.20	1.10	1.30	1.10	1.10	1.20	1.20	1.10	1.10	1.00	1.10
1.25	1.30	1.30	1.25	1.10	1.30	1.10	1.10	1.20	1.20	1.10	1.15	1.05	1.10
1.50	1.30	1.30	1.30	1.20	1.30	1.10	1.10	1.20	1.30	1.10	1.20	1.10	1.10
1.75	1.30	1.30	1.30	1.20	1.30	1.15	1.20	1.20	1.30	1.10	1.20	1.15	1.15
2.00	1.30	1.30	1.30	1.20	1.30	1.20	1.20	1.25	1.30	1.15	1.20	1.20	1.20
2.25	1.30	1.30	1.30	1.20	1.30	1.20	1.20	1.30	1.30	1.20	1.20	1.20	1.25
2.50	1.30	1.30	1.30	1.20	1.35	1.20	1.20	1.30	1.30	1.20	1.20	1.20	1.30
2.75	1.30	1.30	1.30	1.20	1.40	1.20	1.25	1.30	1.30	1.20	1.25	1.25	1.30
3.00	1.35	1.30	1.30	1.30	1.40	1.20	1.30	1.30	1.30	1.20	1.30	1.30	1.30
3.25	1.35	1.35	1.30	1.30	1.40	1.20	1.30	1.30	1.30	1.20	1.30	1.30	1.30
3.50	1.40	1.40	1.30	1.30	1.40	1.20	1.30	1.30	1.30	1.20	1.30	1.30	1.30
3.75	1.40	1.40	1.35	1.30	1.40	1.20	1.30	1.30	1.35	1.25	1.30	1.30	1.30
4.00	1.40	1.40	1.30	1.30	1.40	1.20	1.30	1.30	1.40	1.30	1.30	1.35	1.30
4.25	1.40	1.40	1.30	1.30	1.40	1.20	1.30	1.30	1.40	1.30	1.30	1.40	1.30
4.50	1.40	1.40	1.30	1.30	1.40	1.20	1.35	1.30	1.40	1.30	1.30	1.40	1.30
4.75	1.40	1.40	1.30	1.35	1.45	1.20	1.40	1.35	1.40	1.30	1.30	1.40	1.30
5.00	1.40	1.45	1.30	1.40	1.45	1.20	1.40	1.40	1.40	1.30	1.30	1.40	1.30

C.2.2. OVERALL PERFORMANCE OF ANODE/FILTER MATERIAL COMBINATIONS IN MAGNIFICATION MAMMOGRAPHY

Various combinations of anode/filter materials, operated at tube voltages in the range between 24 kVp and 32 kVp were used to evaluate their overall performance in magnification mammography. A very commonly used degree of magnification in clinical practice, 1.6, was utilized for both the calculation of CNR and AGD and results are presented in Table 7. In this table, the PIV maximum and the tube voltage at which it appears for various values of parameter v are presented. Relative data concerning analytically the PIV of all anode/filter combinations at tube voltages from 24 kVp to 32 kVp are available on request to the authors, but are not presented in the text due to the huge space needed.

For $v=1.0$, conclusions about the performance of anode/filter combinations for which we have equal weighting of image quality and radiation dose, can be obtained. According to Table 7 and our data, Mo/0.030mmMo and W/0.050mmPd+2.00mmAl combinations are the most appropriate for low tube voltages up to 26 kVp. However, as the tube voltage is increased up to 32 kVp, anode/filter material combinations with similar overall performance with Mo/0.030mmMo appear, as for this value of v they have comparable PI_{1s} . W/0.050mmAl, Rh/0.51mmAl, W/0.030mmRh, Rh/0.029mmRh, Rh/0.030mmRu and Mo/0.029mmRh are such combinations. These results are in agreement with previously published studies (Dance et al 2000, Delis et al 2005b, Delis et al 2006, Thilander-Klang et al 1997, Wu et al 1991, 1994, Desponds et al 1991), concerning the performance of anode/filter combinations in contact mammography.

In the range between $v=1.25$ and $v=5.00$, information about the overall performance of anode/filter combinations for which we have increased weighting for the image quality can be derived. The performance of the material combinations in this range depends on the desirable “benefit” for the image quality in each examination. For low values of parameter v ($v \leq 2$) in this range ($1.25 \leq v \leq 5$) and low tube voltages up to 26 kVp, only W/0.050mmPd+2.00mmAl can compete with Mo/0.030mmMo, as it results in similar PIV. For higher tube voltages, up to 32 kVp, various combinations, different than the Mo/0.030mmMo, can be utilized, as they result in similar PIV. W/0.050mmAl, Rh/0.51mmAl, Rh/0.029mmRh, Mo/0.029mmRh and Rh/0.030mmRu are such combinations with PIV comparable to that of Mo/0.030mmMo.

Table 7: The maximum Performance Index value of the anode/filter material combinations studied for various values of the power of CNR, v. In parenthesis the respective tube voltage in kVp. Calculations were performed for 1.6 degree of magnification.

v	PI, maximum and tube voltage at which it appears												
	Anode/Filter Combination												
	Mo/0.030 mmMo	Mo/0.51 mmAl	Mo/0.030 mmNb	Mo/0.029 mmRh	Rh/0.51 mmAl	Rh/0.030 mmNb	Rh/0.030 mmRu	Rh/0.029 mmRh	W/0.50 mmAl	W/0.030 mmMo	W/0.050 mmNb	W/0.030 mmRh	W/0.050 mmPd/2.00 mmAl
1.00	0.463 (26)	0.433 (31)	0.400 (32)	0.434 (30)	0.443 (32)	0.358 (30)	0.437 (31)	0.445 (32)	0.439 (31)	0.364 (25)	0.353 (24)	0.437 (32)	0.511 (25)
1.25	0.456 (26)	0.389 (26)	0.372 (32)	0.393 (30)	0.381 (32)	0.324 (30)	0.390 (31)	0.393 (32)	0.380 (29)	0.346 (25)	0.345 (24)	0.386 (27)	0.446 (25)
1.50	0.449 (26)	0.357 (26)	0.345 (32)	0.359 (30)	0.340 (26)	0.302 (26)	0.348 (31)	0.354 (26)	0.330 (29)	0.329 (25)	0.337 (24)	0.347 (27)	0.389 (25)
1.75	0.444 (24)	0.327 (26)	0.327 (26)	0.330 (26)	0.306 (25)	0.285 (26)	0.312 (27)	0.321 (26)	0.308 (24)	0.317 (24)	0.329 (24)	0.317 (24)	0.339 (25)
2.00	0.444 (24)	0.300 (26)	0.312 (26)	0.304 (26)	0.277 (25)	0.271 (25)	0.283 (27)	0.291 (26)	0.283 (24)	0.304 (24)	0.321 (24)	0.291 (24)	0.296 (25)
2.25	0.444 (24)	0.278 (24)	0.299 (25)	0.280 (26)	0.251 (25)	0.258 (25)	0.257 (27)	0.265 (24)	0.259 (24)	0.291 (24)	0.313 (24)	0.267 (24)	0.258 (25)
2.50	0.444 (24)	0.259 (24)	0.289 (24)	0.259 (25)	0.228 (25)	0.248 (24)	0.234 (25)	0.244 (24)	0.238 (24)	0.279 (24)	0.306 (24)	0.246 (24)	0.227 (24)
2.75	0.444 (24)	0.241 (24)	0.280 (24)	0.239 (25)	0.207 (25)	0.239 (24)	0.214 (25)	0.224 (24)	0.218 (24)	0.267 (24)	0.299 (24)	0.226 (24)	0.189 (24)
3.00	0.444 (24)	0.224 (24)	0.271 (24)	0.220 (25)	0.188 (25)	0.229 (24)	0.197 (24)	0.205 (24)	0.200 (24)	0.256 (24)	0.292 (24)	0.207 (24)	0.175 (24)
3.25	0.444 (24)	0.208 (24)	0.262 (24)	0.204 (25)	0.172 (24)	0.220 (24)	0.181 (24)	0.188 (24)	0.184 (24)	0.246 (24)	0.285 (24)	0.191 (24)	0.154 (24)
3.50	0.444 (24)	0.194 (24)	0.254 (24)	0.189 (25)	0.157 (24)	0.212 (24)	0.167 (24)	0.173 (24)	0.168 (24)	0.235 (24)	0.278 (24)	0.175 (24)	0.135 (24)
3.75	0.444 (24)	0.180 (24)	0.246 (24)	0.175 (25)	0.144 (24)	0.204 (24)	0.153 (24)	0.159 (24)	0.154 (24)	0.225 (24)	0.272 (24)	0.161 (24)	0.119 (24)
4.00	0.444 (24)	0.168 (24)	0.238 (24)	0.162 (25)	0.131 (24)	0.196 (24)	0.141 (24)	0.146 (24)	0.142 (24)	0.216 (24)	0.265 (24)	0.148 (24)	0.104 (24)
4.25	0.444 (24)	0.156 (24)	0.230 (24)	0.149 (24)	0.120 (24)	0.188 (24)	0.130 (24)	0.134 (24)	0.130 (24)	0.207 (24)	0.259 (24)	0.136 (24)	0.092 (24)
4.50	0.444 (24)	0.145 (24)	0.222 (24)	0.138 (24)	0.110 (24)	0.181 (24)	0.119 (24)	0.123 (24)	0.119 (24)	0.198 (24)	0.253 (24)	0.125 (24)	0.081 (24)
4.75	0.444 (24)	0.135 (24)	0.216 (24)	0.129 (24)	0.100 (24)	0.174 (24)	0.110 (24)	0.113 (24)	0.109 (24)	0.190 (24)	0.247 (24)	0.115 (24)	0.071 (24)
5.00	0.444 (24)	0.126 (24)	0.209 (24)	0.119 (24)	0.092 (24)	0.167 (24)	0.101 (24)	0.103 (24)	0.100 (24)	0.182 (24)	0.241 (24)	0.105 (24)	0.062 (24)

However, it is easily noticeable from Table 7, that as higher values of parameter v are considered, the relative performance of the anode/filter combinations with respect to the performance of Mo/0.030mmMo is reduced due to the high imaging ability of the specific combination. This is even more evident for values of $v > 2.75$. At these values and for the whole range of tube voltages considered, between 24 kVp and 32 kVp, the Mo/0.030mmMo is the dominant combination, having much higher PIV compared to all the other combinations. The reason for this is that although the specific material combination results to comparable AGD with the other combinations considered, it has the higher CNR. So, upgrading the weighting of the imaging part of the PIV, by increasing the value of v , makes the Mo/0.030mmMo combination having the best overall performance. W/0.050mmPd+2.00mmAl is a combination which results to the lowest AGD and although it has comparable CNR with the other combinations it can compete with the Mo/0.030mmMo only for low values of v , due to this reason. Finally, for all the anode/filter material combinations studied, increasing the value of v results in the reduction of the maximum PIV, which appears each time at lower tube voltage.

C.2.3. EFFECT OF BREAST COMPOSITION ON CONTRAST TO NOISE RATIO

Various breast compositions were simulated, in order to study their effect on CNR. Figure 16 presents the influence of breast glandularity on CNR. The calculations were performed using the most commonly utilized anode/filter combination at 28 kVp, the Mo/0.030mmMo, at 1.6 degree of magnification, while two sizes of inhomogeneity were considered, consisted of HA, with radii 750 μm and 250 μm . CNR was found to decrease for both sizes of inhomogeneities with the percentage of breast glandularity, bearing out that inhomogeneities lying in glandular tissue are more difficult to distinguish, compared to those lying in adipose tissue, even under magnification conditions. The CNR between a 10% and a 90% glandular breast can be reduced up to 21 % under magnification for a 750 μm inhomogeneity and up to 48% for a 250 μm inhomogeneity, according to our results. This difference is reasonable as large sized calcifications are easier to discriminate even in a high glandular breast and the increase of the breast glandularity does not affect significantly the CNR. On the other hand, for small sized calcifications, where the discrimination is already difficult, increase of breast glandularity has a more important effect on the CNR.

Figure 16: The influence of percentage of glandularity in the breast on the CNR, for two sizes of inhomogeneities consisted of HA. The calculations were performed using the Mo/0.030mmMo combination at 28 kVp, degree of magnification 1.6 and breast thickness 4 cm.

CHAPTER C

RESULTS & DISCUSSION

C.3. SPATIAL RESOLUTION STUDIES

C.3.1. EFFECT OF FOCAL SPOT SIZE AND DEGREE OF MAGNIFICATION ON SPATIAL RESOLUTION.....	91
C.3.2. EFFECT OF INTENSITY DISTRIBUTION AND DEGREE OF MAGNIFICATION ON SPATIAL RESOLUTION.....	94
C.3.2. EFFECT OF THE DETECTOR BLURRING ON SPATIAL RESOLUTION.....	99

In the following paragraphs, the effect of focal spot size (0.04 mm to 0.30 mm) and intensity distribution (Gaussian, double Gaussian and uniform) on spatial resolution, under magnification conditions, is investigated. Moreover, conclusions about focal spot sizes and intensity distributions that can be used at each degree of magnification, according to the existing spatial resolution requirements, are extracted.

C.3.1. EFFECT OF FOCAL SPOT SIZE AND DEGREE OF MAGNIFICATION ON SPATIAL RESOLUTION

Using the aforementioned procedure about the edge method, the spatial resolution was calculated for degrees of magnification from 1.0 to 2.0 with a step of 0.1 and for ten focal spot sizes between 0.04 mm and 0.30 mm utilizing a Gaussian intensity distribution. Figure 17 shows the effect of the degree of magnification on spatial resolution for some representative values of focal spot size. According to the calculated values, the increase of the magnification from 1.0 to 2.0 induces degradation on spatial resolution which varies from 49% for the 0.04 mm focal spot to 53.2% for the 0.14 mm one, due to the geometrical unsharpness caused by the air gap between the breast and the image receptor. For focus sizes larger than 0.14 mm this degradation is high, even for low degrees of magnification and the resulted resolution is very poor. For this reason, the spatial resolution corresponding to magnification degrees higher than 1.6 were not calculated for these sizes of focal spot.

Figure 17: The influence of magnification degree on spatial resolution for various values of focal spot size between 0.04 mm and 0.30 mm and Gaussian intensity distribution. The dotted line shows the spatial resolution limit of 12 lp/mm.

As far as the focal spot size is concerned, the increase from 0.04 mm to 0.30 mm reduces the spatial resolution by 15.2% for contact geometry. This percentage is higher under magnification and increases almost linearly with the degree of magnification. These effects are presented in Figure 18, where the spatial resolution is shown as a function of the focal spot size for various degrees of magnification. Focal spots larger than 0.14 mm could be used only when low degrees of magnification, up to 1.5, are performed as they result in relatively low values of spatial resolution, compared to smaller foci. For degrees of magnification up to 1.7, focal spot sizes up to 0.10 mm can be considered appropriate. However, for higher degrees of magnification the focal spot size should ideally be 0.04 mm or even smaller. The construction of such a microfocus would result in increased values of spatial resolution even in high degrees of magnification. Moreover, magnification higher than 1.9 results in unacceptable spatial resolution, even for the smaller of the foci considered in this study. However, if we take into consideration other European or national protocols which consider as acceptable limit for the spatial resolution 13 lp/mm or 14 lp/mm, all the above conclusions are altered proportionately and the maximum degree of magnification that each focal spot size can be utilized reaching the specified limit is reduced. This shows that the strictness of the protocol taken into consideration is the factor which determines the focal spot size that has to be utilized when magnification is performed. The spatial resolution values for the simulations performed in this part of the study are analytically presented in Table 8. As far as the uncertainty of the results is concerned, it was found to vary from 0.2 lp/mm to 0.4 lp/mm with an average value of 0.3 lp/mm.

Figure 18: The effect of focal spot size on spatial resolution for various degrees of magnification, considering Gaussian intensity distribution. The dotted line shows the limit of 12 lp/mm.

Table 8: Spatial resolution values in lp/mm for various focal spot sizes and degrees of magnification, considering Gaussian intensity distribution. The dotted line distinguishes the acceptable spatial resolution values from those that do not reach the limit of 12 lp/mm.

m	Focal Spot Size (mm)									
	0.04	0.06	0.08	0.10	0.12	0.14	0.18	0.22	0.26	0.30
1.0	22,7	22,4	22,1	21,8	21,5	21,2	20,6	20,1	19,7	19,3
1.1	21,1	20,7	20,4	20,0	19,7	19,3	18,8	18,3	17,8	17,4
1.2	19,0	18,6	18,3	17,9	17,6	17,3	16,8	16,3	15,9	15,4
1.3	17,4	17,0	16,6	16,3	15,9	15,6	15,1	14,6	14,3	13,9
1.4	16,2	15,7	15,3	14,9	14,7	14,3	13,9	13,3	12,9	12,5
1.5	15,2	14,8	14,4	14,0	13,7	13,4	12,9	12,4	11,9	11,5
1.6	14,2	13,8	13,5	13,1	12,8	12,5	12,0	11,2		
1.7	13,4	13,1	12,7	12,3	12,0	11,7				
1.8	12,6	12,2	11,6	11,5	11,2	11,0				
1.9	12,0	11,7	11,3	10,9	10,6	10,3				
2.0	11,6	11,2	10,8	10,5	10,2	9,9				

C.3.2. EFFECT OF INTENSITY DISTRIBUTION AND DEGREE OF MAGNIFICATION ON SPATIAL RESOLUTION

In all of the measurements made in this study, the high-frequency end of the MTF is found to be practically affected rather than the low frequencies. This is more obvious in Figure 19 where two MTFs are plotted corresponding to focus size of 0.30 mm and for a Gaussian and a double Gaussian distribution. For spatial frequencies between 0 and 6-7 lp/mm the MTFs do not change significantly, while for frequencies higher than these values there is an important variation in the MTFs.

Figure 19: The effect of focal spot intensity distribution on the whole MTF for a Gaussian and a double Gaussian distribution. The focus size in both cases is 0.30 mm and the degree of magnification is 1.3.

As also mentioned earlier, the limits of the area under the Gaussian distribution (which are defined as 5σ in our study) determine the arbitrary size of the focal spot which is usually different from the nominal size given by the x-ray tube manufacturer. This means that two mammographic tubes with the same nominal focus size can result in different values of spatial resolution if their intensity distributions are different. In order to demonstrate this, a focal spot of 0.10 mm was utilized (under 1.5 magnification), with standard deviation between 0.10 mm and 0.02 mm, thus corresponding to focal spot sizes between 1σ and 5σ , correspondingly. The spatial resolution was calculated each time and the results are presented in Figure 20.

According to this figure, the spatial resolution among mammographic systems with different standard deviations concerning their Gaussian distributions may differ by up to 35%, for the studied values.

Figure 20: The effect of standard deviation σ on spatial resolution for a given nominal focus size of 0.10 mm and a single peak Gaussian distribution.

As far as the double Gaussian distribution is concerned, the effect of the distance separating the two peaks on spatial resolution was studied and the results are presented in Figure 21. The distance between the peaks was expressed in terms of the number of σ with which the focus is defined. As the number of σ is increased the distance between the two peaks is decreased and the spatial resolution is increased. This means that the two peaks tend to become one and the double Gaussian distribution turns to a single Gaussian. For the rest of the study the focal spot size for the case of the double Gaussian distribution is considered 10σ .

Figure 21: The effect of the distance separating the two peaks of a double Gaussian intensity distribution on spatial resolution. The distance is expressed in terms of standard deviation σ .

Results concerning the effect of x-ray intensity distribution on spatial resolution, under magnification conditions are presented in Figures 22, 23 and 24, where the calculated spatial resolution is shown with respect to the degree of magnification. According to the results, Gaussian intensity distribution results in the highest spatial resolution among the three distributions considered in the study, with the double Gaussian giving the lowest values, for all the magnification degrees and focal spot sizes studied. More specifically, the increase of the degree of magnification from 1.0 to 2.0 reduces the spatial resolution by 49% and 52.8%, considering the 0.04 mm and the 0.12 mm focus, correspondingly, and Gaussian intensity distribution. This reduction is even higher for the 0.30 mm focus. The corresponding percentages regarding the uniform intensity distribution are 51.4% and 54.4%, while for the double Gaussian, which results in the lowest values of spatial resolution, it is 54.2% and 55.8%. Moreover, the increase of the focal spot size from 0.04 mm to 0.30 mm reduces the spatial resolution by 15.2%, 20.1% and 24.4% considering Gaussian, uniform and double Gaussian distribution, correspondingly, and degree of magnification 1.0. For higher degrees of magnification this degradation further increases.

Figure 22: The influence of magnification on spatial resolution for the three representative x-ray intensity distributions and for a 0.04 mm focal spot. The dotted line shows the limit of 12 lp/mm.

Figure 23: The influence of magnification on spatial resolution for the three representative x-ray intensity distributions and for a 0.12 mm focal spot. The dotted line shows the limit of 12 lp/mm.

Figure 24: The influence of magnification on spatial resolution for the three representative x-ray intensity distributions and for a 0.30 mm focal spot. The dotted line shows the limit of 12 lp/mm.

As already discussed, the limiting value of the focal spot size that is acceptable, in order to comply with the spatial resolution requirement of 12 lp/mm, decreases for increasing degree of magnification. Thus, any focal spot size can only be considered appropriate for up to a certain degree of magnification. This degree is higher for foci with Gaussian distribution, with indicative values for 0.04 mm, 0.12 mm and 0.30 mm being 1.9, 1.6 and 1.4, while the corresponding values for the uniform and the double Gaussian distribution being 1.7, 1.5, 1.2 and 1.6, 1.5 and 1.2, respectively.

Considering the aforementioned results, it is obvious that under magnification conditions, where the geometric unsharpness rises and the need for high values of spatial resolution becomes even more imperative, only a Gaussian intensity distribution with a small focal spot size would have high values of spatial resolution. Uniform distributions can be utilized mainly for small degrees of magnification. Especially when combined with small foci this magnification can be up to 1.7, however, it is reduced as the focal spot size increases. On the other hand, double Gaussian distributions result in low values of spatial resolution in general, making its use acceptable only for low magnification, especially when combined with focal spots larger than 0.12 mm. If the focus size is smaller than 0.12 mm, double Gaussian could be utilized for degrees of magnification up to 1.6; however, the resulting values of

spatial resolution are quite low compared to the corresponding values from Gaussian and uniform distributions. Taking into account the possible alteration of the Gaussian distribution to double Gaussian as the focal spot is destroyed due to its long use and the above results, it becomes requisite to replace the x-ray tube on time, especially when it is utilized for magnification views.

C.3.2. EFFECT OF THE DETECTOR BLURRING ON SPATIAL RESOLUTUION

Results concerning the effect of the detector blurring on spatial resolution have already been introduced in paragraph B.6.2.

CHAPTER D

CONCLUSIONS AND FUTURE WORK

D.1. CONCLUSIONS.....	101
D.2. FUTURE WORK.....	103

D.1. CONCLUSIONS

Magnification views are very crucial, as they constitute an important tool in the effort to discriminate microcalcifications and breast lesions. In this doctorate thesis dosimetric as well as image quality characteristics were studied under magnification conditions aiming to find the optimum exposure parameters for the specific technique.

CNR was found to increase with the degree of magnification. However, the increase rate decreases significantly after 1.3-1.4 magnification, while the dose continuous to increase almost linearly. Introducing a performance index which depends on the desired weighting of the imaging part of the procedure with respect to the dose, it was found that these degrees of magnification are the most appropriate when the magnification technique is applied. This is very important for the clinical staff working in a mammographic unit as, applying the appropriate degree of magnification each time, could contribute in the optimization of the technique.

In the dosimetric study, new air KERMA to AGD conversion factors adapted for magnification geometries, tube voltages and anode/filter material combinations were calculated. The application of these factors by medical physicists during the quality control of mammographic systems or during dosimetric procedures can improve the estimation of AGD by up to 33%. Moreover, taking into account the possible alteration of a single Gaussian intensity distribution into a double Gaussian intensity distribution as the anode is destroyed due to its extended use, as well as the degraded spatial resolution of a double Gaussian distribution compared to that of a single one, the replacement of the mammographic tube becomes imperative when the anode starts to destroy. This by turn reinforces the need for a frequent quality control of the mammographic unit by medical physicists and the measurement of its spatial resolution.

Finally and concerning the industry, mammographic units which could alternate between two different anode/filter material combinations, depending on the desired weighting of the imaging part of the procedure (contact or magnification views) with respect to the dose, would contribute in the effort to optimize both techniques, based on the results about the performance of several anode/filter material combinations under contact and magnification geometry. Also, the construction of a microfocus of 0.04 mm, combined with a single Gaussian distribution of low standard deviation

would lead to high values of spatial resolution, even under high degrees of magnification. To this direction however, the thermal load of the anode as well as the increased exposure time should be taken into consideration.

In general, magnification constitutes an important tool in mammography. However, it requires careful use as only under specific conditions it can contribute in the diagnosis. On the contrary, non-appropriate use can increase significantly the dose delivered in the patient without offering any additional diagnostic information.

D.2. FUTURE WORK

As a future work the study of new theoretical spectra could be very useful in the optimization task as it could reveal new materials more suitable for the magnification views, than the routinely used Mo/Mo.

Moreover, the development of a complete Monte Carlo tool for mammography which also simulates the performance and the physical characteristics of real detectors (both film-screen and digital detectors) would be very helpful in order to be able to investigate the real conditions of the image formation and replace the ideal detector currently used. To this direction, the data of this doctorate thesis could be used as input.

The case of the full breast irradiation using larger field and image receptor is another topic that should be studied under magnification conditions, considering that this study deals only with the case of the partial irradiation.

A more realistic simulation of the breast is another topic to be studied, regarding the composition of the breast as well as the inhomogeneities considered inside.

Finally, a comparison between electronic magnification (zoom) and real magnification should be made in order to assure the necessity of magnification views in mammography.

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APPENDIX I

ABBREVIATIONS

AEC	Automatic Exposure Control
AGD	Average Glandular Dose
ALARA	As Low As Reasonable Achievable
CDF	Cumulative Density Function
CNR	Contrast to Noise Ratio
ESD	Entrance Surface Dose
ESF	Edge Spread Function
FBD	Focus to Breast Distance
FBHD	Focus to Breast Holder Distance
FDD	Focus to Detector Distance
FOV	Field Of View
FSD	Focus to Skin Distance
FWHM	Full Width at Half of the Maximum
IEC	International Electrotechnical Commission
KERMA	Kinetic Energy Released per unit of MAss
LSF	Line Spread Function
MGD	Mean Glandular Dose
MTF	Modulation Transfer Function
PDD	Percentage Depth Dose
PDF	Probability Density Function
PSF	Point Spread Function
ROI	Region Of Interest
SNR	Signal to Noise Ratio
SPR	Scatter to Primary Ratio

LIST OF FIGURES

Figure 1: A modern mammographic unit.

Figure 2: Monte Carlo simulation of physical system.

Figure 3: Contact (a) and magnification (b) geometry in mammography. In magnification geometry the antiscatter grid is removed and the breast is placed closer to the focal spot.

Figure 4: The flow chart of the utilized simulation model.

Figure 5: The irradiated part of the phantom used in the simulations performed. Area 1 corresponds to inhomogeneities composed of calcium oxalate (CO, $\text{CaC}_2\text{O}_4 \cdot 3(\text{H}_2\text{O})$) while Area 2 corresponds to inhomogeneities composed of hydroxy apatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$). The background consists of water.

Figure 6: Two Monte Carlo generated images of the selected FOV corresponding to magnification degrees 1.0 (a) and 1.6 (b). The spectrum utilized for these simulations was the Mo/0.030mmMo at 28 kVp.

Figure 7: Example of the procedure followed for the calculation of the spatial resolution from the derived Monte Carlo image (focal spot size 0.04 mm, magnification 1.8): (a) The derived image and the ROI selected, (b) the derived ESF, (c) the LSF and (d) the MTF and the Gaussian fitting curve. The horizontal dotted line at (d) shows the 5% value of the MTF at which the spatial resolution was measured in lp/mm.

Figure 8: (a) The standard deviation (in greylevel values) as a function of the exposure and (b) the spatial resolution as a function of the standard deviation for a 0.10 mm focal spot and 1.9 magnification.

Figure 9: The spatial resolution as a function of the degree of magnification, with and without considering the effect of the detector blurring (0.10 mm focal spot size and Gaussian intensity distribution).

Figure 10: The influence of magnification degree on AGD for the Mo/0.030mmMo combination at 28 kVp and for 4 cm breast phantom.

Figure 11: The influence of tube voltage on AGD for the Mo/0.030mmMo combination and for magnification factors 1.6 and 1.0. Results from the use of conversion factors are also presented, for magnification factor 1.0.

Figure 12: The effect of the degree of magnification on PDD for three degrees of magnification.

Figure 13: The influence of degree of magnification on CNR for inhomogeneities of two compositions (CO and HA) and four sizes (spherical with radii from 100 μm to 750 μm). The Mo/0.030mmMo combination at 28 kVp was utilized for the specific calculations.

Figure 14: The CNR improvement factor representing the normalization of CNR with respect to that for degree of magnification 1.0, for the four sizes of inhomogeneities consisted of HA.

Figure 15: The effect of degree of magnification on SPR. SPR values are normalized with respect to the SPR for magnification 1.0. The calculations were performed using the Mo/0.030mmMo combination at 28 kVp with a 4 cm phantom consisting of equally weighted glandular and adipose tissues.

Figure 16: The influence of percentage of glandularity in the breast on the CNR, for two sizes of inhomogeneities consisted of HA. The calculations were performed using the Mo/0.030mmMo combination at 28 kVp, degree of magnification 1.6 and breast thickness 4 cm.

Figure 17: The influence of magnification degree on spatial resolution for various values of focal spot size between 0.04 mm and 0.30 mm and Gaussian intensity distribution. The dotted line shows the spatial resolution limit of 12 lp/mm.

Figure 18: The effect of focal spot size on spatial resolution for various degrees of magnification, considering Gaussian intensity distribution. The dotted line shows the limit of 12 lp/mm.

Figure 19: The effect of focal spot intensity distribution on the whole MTF for a Gaussian and a double Gaussian distribution. The focus size in both cases is 0.30 mm and the degree of magnification is 1.3.

Figure 20: The effect of standard deviation σ on spatial resolution for a given nominal focus size of 0.10 mm and a single peak Gaussian distribution.

Figure 21: The effect of the distance separating the two peaks of a double Gaussian intensity distribution on spatial resolution. The distance is expressed in terms of standard deviation σ .

Figure 22: The influence of magnification on spatial resolution for the three representative x-ray intensity distributions and for a 0.04 mm focal spot. The dotted line shows the limit of 12 lp/mm.

Figure 23: The influence of magnification on spatial resolution for the three representative x-ray intensity distributions and for a 0.12 mm focal spot. The dotted line shows the limit of 12 lp/mm.

Figure 24: The influence of magnification on spatial resolution for the three representative x-ray intensity distributions and for a 0.30 mm focal spot. The dotted line shows the limit of 12 lp/mm.

LIST OF TABLES

Table 1: Some of the most famous Monte Carlo simulation codes and their applications

Table 2: The Gaussian and double Gaussian distribution details utilized in the simulations performed.

Table 3: The m correction factor for magnification degrees from 1.0 to 2.1, corresponding to focus to skin distance from 56 cm to 24 cm.

Table 4: The combined s and v correction factor for the various anode/filter combinations and for tube voltage between 24-34 kVp.

Table 5: The c factor correcting for glandularities from 1% to 100% and breast thicknesses from 2 cm to 10 cm.

Table 6: The degree of magnification where the maximum value of Performance Index

$PI_v = \frac{(CNR)^v}{AGD}$ appears, for various values of v and for the anode/filter combinations

studied (accuracy for the degree of magnification in steps of 0.05).

Table 7: The maximum Performance Index value of the anode/filter material combinations studied for various values of the power of CNR, v. In parenthesis the respective tube voltage in kVp. Calculations were performed for 1.6 degree of magnification.

Table 8: Spatial resolution values in lp/mm for various focal spot sizes and degrees of magnification, considering Gaussian intensity distribution. The dotted line distinguishes the acceptable spatial resolution values from those that do not reach the limit of 12 lp/mm.

SUMMARY

In the framework of this doctorate thesis, two simulation models based on Monte Carlo were expanded in order to include magnification geometries and various breast compositions, and were utilized aiming to study and optimize the magnification views in mammography. With the use of these models, dosimetric as well as image quality characteristics were evaluated and combined in order to come into conclusions.

More specifically, the dose in the glandular tissue of the breast, which is directly associated with the carcinogenic risk during mammography, was found to increase with the degree of magnification, mainly due to the inverse square law. Contrast to Noise Ratio also increases with magnification. However, the increase rate is higher for magnification up to 1.4. With the introduction of a Performance Index, which is a function of the desirable benefit (expressed by the $(CNR)^V$) and the cost (expressed by the dose), several exposure and design parameters (degree of magnification, spectrum) were evaluated under magnification conditions. Degree of magnification 1.3 was found to have the best overall performance for all the anode/filter combinations considered. Several combinations like W/0.050mmAl, Rh/0.51mmAl, W/0.030mmRh, Rh/0.029mmRh, Rh/0.030mmRu and Mo/0.029mmRh can compete with the Mo/0.030mmMo under contact geometry. However, when magnification is performed and especially degree higher than 1.3, Mo/0.030mmMo has the best overall performance between the anode/filter combinations considered.

Moreover, the effect of focal spot size and x-ray intensity distribution on the spatial resolution was studied under magnification, using the edge method. Focal spots larger than 0.12 mm should be utilized only for screening mammography, especially when combined with uniform or double Gaussian intensity distributions. Small focal spots of 0.04 mm or less, combined with Gaussian distribution result in acceptable values of spatial resolution, according to the international regulations, even for high degrees of magnification. Finally, a degradation of the spatial resolution was found with the degree of magnification, which is mainly caused by the geometrical unsharpness.