
Table Of Contents

CHAPTER 1: BACKGROUND & BASIC SCIENCE

INTRODUCTION:	1-1
1.1 THE SKIN:	1-1
1.1.1 EPIDERMIS:.....	1-1
1.1.2 MELANOCYTES:.....	1-2
1.1.3 DERMIS:	1-4
1.1.4 PAPILLARY DERMIS:.....	1-4
1.1.5 RETICULAR DERMIS:.....	1-4
1.1.6 COLLAGEN:.....	1-5
1.1.7 VASCULAR SUPPLY AND ARRANGEMENT:.....	1-5
1.1.8 EPIDERMAL APPENDAGES:.....	1-6
1.1.9 NERVES:.....	1-6
1.2 ACQUIRED MELANOCYTIC NAEVI:	1-7
INTRODUCTION:.....	1-7
1.2.1 LENTIGO SIMPLEX:	1-7
1.2.2 JUNCTIONAL NAEVUS:	1-8
1.2.3 COMPOUND NAEVUS:	1-9
1.2.4 INTRADERMAL NAEVUS:.....	1-10
1.2.5 DYSPLASTIC NAEVI:.....	1-10
1.2.6 OTHER NAEVI:	1-11
1.2.7 BLUE NAEVUS:	1-11
1.2.8 SPITZ NAEVUS:.....	1-12
1.2.9 CONGENITAL NAEVI:.....	1-13
<i>Table 1.1: Summary of features of benign naevi</i>	<i>1-14</i>
1.3 NON-MELANOCYTIC PIGMENTED LESIONS.....	1-17
1.3.1. PIGMENTED BASAL CELL CARCINOMA	1-17
1.3.2 SOLAR LENTIGO & BASAL CELL PAPILLOMA.....	1-18
1.4 MALIGNANT MELANOMA.....	1-19
INTRODUCTION:.....	1-19
1.4.1 EPIDEMIOLOGY:	1-19
1.4.1.1 <i>Incidence & Mortality:</i>	<i>1-19</i>
1.4.1.2 <i>Age, Sex & Anatomical Location:</i>	<i>1-20</i>

1.4.1.3 Risk Factors:	1-20
1.4.2 MACROSCOPIC & MICROSCOPIC APPEARANCE OF MALIGNANT MELANOMA:	1-21
1.4.2.1 Clinical (Macroscopic) Appearance:	1-22
1.4.2.2 Microscopic Appearance:	1-22
1.4.2.3 Carcinogenesis and the Horizontal & Vertical Growth Phases	1-24
1.4.3 CLINICAL SUBTYPES OF MELANOMA:	1-27
1.4.3.1 Superficial Spreading Melanoma (SSM):	1-27
1.4.3.2 Nodular Melanoma (NM):	1-27
1.4.3.3 Lentigo Maligna & Lentigo Maligna Melanoma (LMM):	1-28
1.4.3.4 Acral Lentiginous Melanoma (ALM):	1-29
1.4.3.5 Rare Cutaneous Melanomas:	1-29
1.4.4 SPREAD AND STAGING:	1-30
1.4.5 MICROSCOPIC STAGING - TUMOUR THICKNESS:	1-30
1.4.6 PROGNOSIS:	1-31
1.4.7 TREATMENT & SURVIVAL TRENDS:	1-34
DISCUSSION:	1-34

CHAPTER 2: DIAGNOSIS OF CUTANEOUS MALIGNANT MELANOMA

INTRODUCTION:	2-1
2.1 DIAGNOSTIC ACCURACY, SPECIFICITY & SENSITIVITY:	2-1
2.2 CLINICAL DIAGNOSIS:	2-2
2.2.1 HISTORY:	2-2
2.2.2 EXAMINATION:	2-3
2.2.3 ACCURACY	2-4
2.2.4 SCREENING AND PUBLIC EDUCATION:	2-5
2.3 SKIN SURFACE MICROSCOPY:	2-6
2.3.1 MORPHOLOGICAL FEATURES	2-8
2.3.1.1 Colour & Pigmentation	2-8
2.3.1.2 Structural & Morphological Features	2-9
2.3.2 DIAGNOSTIC ACCURACY OF SKIN SURFACE MICROSCOPY	2-12
2.4 NEWER TECHNIQUES FOR ASSESSING PIGMENTED SKIN LESIONS	2-13
2.4.1 HIGH FREQUENCY ULTRASOUND	2-13
2.4.2 OPTICAL COHERENCE TOMOGRAPHY	2-14
2.4.2 MAGNETIC RESONANCE IMAGING	2-14

2.4.4 CONFOCAL MICROSCOPY	2-15
2.5 COMPUTER IMAGING, FEATURE EXTRACTION & ARTIFICIAL INTELLIGENCE ..	2-16
2.5.1 IMAGE PROCESSING	2-16
2.5.2 IMAGE ANALYSIS & FEATURE EXTRACTION - PRINCIPLES	2-17
2.5.3 FEATURE ANALYSIS APPLIED TO MELANOMA	2-19
2.5.3.1 <i>Asymmetry</i>	2-19
2.5.3.2 <i>Border</i>	2-20
2.5.3.3 <i>Colour</i>	2-20
2.5.3.4 <i>Diameter</i>	2-21
2.5.4 ARTIFICIAL INTELLIGENCE (AI)	2-21
2.6 SPECTROPHOTOMETRIC INTRACUTANEOUS ANALYSIS	2-22
2.6.1 LIGHT & COLOUR THEORY.....	2-23
2.6.2 THE OPTICS OF HUMAN SKIN	2-26
2.6.2.1 <i>Optical Properties of the Epidermis</i>	2-26
2.6.2.2 <i>Optical Properties of the Dermis</i>	2-27
2.6.3 THEORETICAL BASIS OF SPECTROPHOTOMETRIC INTRACUTANEOUS ANALYSIS.....	2-29
2.6.3.1 <i>A model of the epidermis</i>	2-29
2.6.3.2 <i>A model of the dermis</i>	2-29
2.6.3.3 <i>Pathological conditions - dermal melanin and collagen loss</i>	2-33
2.6.3.4 <i>The SIAscope</i>	2-35
2.7 SUMMARY	2-36

CHAPTER 3: METHODS

INTRODUCTION	3-1
3.1 EXPERIMENTAL DESIGN - DATA COLLECTION.....	3-1
3.1.1 PATIENT SELECTION.....	3-1
3.1.2 35MM PHOTOGRAPHY	3-2
3.1.2.1 <i>Macro Photography</i>	3-3
3.1.2.2 <i>Skin Surface Microscopy Photography</i>	3-4
3.1.3 SIASCOPE	3-4
3.1.4 HISTOPATHOLOGY	3-7
3.2 EXPERIMENTAL DESIGN - DATA ANALYSIS	3-9
3.2.1 NAMING AND DEFINING SIASCOPE FEATURES	3-9
3.2.1.1 <i>Refining the definitions of SIAscope features</i>	3-13

3.2.1.2 <i>The Definition of SIAscopy Features</i>	3-13
<i>Collagen Holes</i>	3-13
<i>Blood Displacement</i>	3-13
<i>Erythematous Blush</i>	3-13
<i>Dermal Melanin</i>	3-14
<i>Dermal Melanin Globules</i>	3-14
<i>Blood or Melanin Globules</i>	3-14
<i>Asymmetry</i>	3-14
3.2.2 FEATURE ANALYSIS: METHODS.....	3-14
3.3 PROBABILITY & DECISION MAKING USING DIAGNOSTIC TESTS -	
SPECIFICITY, SENSITIVITY & RECEIVER OPERATING CHARACTERISTIC CURVES .	3-16
3.3.1 SPECIFICITY AND SENSITIVITY	3-16
3.3.1.1 <i>Multiplication Rule of Probability and Bayes' Theorem</i>	3-17
3.3.1.2 <i>Consideration of Prevalence</i>	3-19
3.3.2 RECEIVER OPERATING CHARACTERISTIC (ROC) CURVES.....	3-19
3.3.2.1 <i>Comparing ROC curves</i>	3-20
3.3.2.3 <i>Tied Data Points</i>	3-21
3.4 LOGISTIC REGRESSION ANALYSIS	3-23
3.4.1 INTRODUCTION & BACKGROUND	3-23
3.4.1.1 <i>Interpreting the Logistic Regression Model: , exp (), the Wald Statistic and the R-Statistic</i>	3-24
3.4.1.2 <i>Creating Probability & Odds Tables</i>	3-26
3.4.2 CONSTRUCTING LOGISTIC REGRESSION MODELS	3-27
3.4.3. MODEL DIAGNOSTICS	3-28
3.4.3.1 <i>Likelihood Function, Deviance & -2 Log Likelihood (-2LL)</i>	3-29
3.4.3.2 <i>Model Chi-Square Statistic</i>	3-29
3.4.3.3 <i>Akaike Information Criterion, Schwartz Criterion</i>	3-29
3.4.3.4 <i>Residuals Analysis</i>	3-30
3.4.3.5 <i>Multicollinearity</i>	3-31
3.4.4 MODEL TESTING	3-31
3.5 OBSERVER AGREEMENT - THE KAPPA STATISTIC	3-32
3.6 CLASSIFICATION & REGRESSION TREE ANALYSES - 'CART' & 'QUEST'	3-34
3.6.1 INTRODUCTION.....	3-34
3.6.2 PROPERTIES AND NATURE OF CLASSIFICATION TREES	3-34

3.6.2.1 Hierarchical Nature of Classification Trees.....	3-35
3.6.2.2 Advantages and Disadvantages of Classification Trees.....	3-39
3.6.3 GENERATING CLASSIFICATION TREES	3-40
3.6.3.1 Costs and Priors.....	3-40
3.6.3.2 Splitting Methods: CART and QUEST	3-41
3.6.3.3 Stopping Criteria.....	3-42
3.6.3.4 Pruning The Tree - Determining The Right Size.....	3-42
3.6.4 SUMMARY.....	3-44

CHAPTER 4: VALIDATION EXPERIMENTS

4.1 INTRODUCTION	4-1
4.2 TOTAL MELANIN & HAEMOGLOBIN	4-1
4.2.1 METHODS	4-1
4.2.2 RESULTS	4-3
4.2.3 DISCUSSION.....	4-8
4.3 PAPILLARY COLLAGEN	4-11
4.3.1 INTRODUCTION & METHODS	4-11
4.3.2.RESULTS	4-12
4.3.3 DISCUSSION.....	4-13
4.4 DERMAL MELANIN.....	4-14
4.4.1 INTRODUCTION & METHODS	4-14
4.4.2 RESULTS	4-16
4.4.3 DISCUSSION.....	4-18
4.5 SUMMARY	4-18

CHAPTER 5: RESULTS

5.1 INTRODUCTION	5-1
5.2 INTRA- & INTER-OBSERVER AGREEMENT OF SIASCOPY FEATURES	5-2
5.2.1 DISCUSSION.....	5-4
5.3 DEVELOPING PREDICTIVE MODELS USING LOGISTIC REGRESSION	5-7
5.3.1 THE MODEL-BUILDING DATASET	5-7
5.3.2 UNIVARIATE ANALYSIS.....	5-9
5.3.3 CONSTRUCTING THE LOGISTIC REGRESSION MODELS.....	5-11

5.3.4 ADDING CLINICAL DATA.....	5-15
5.3.4 CHOOSING A DIAGNOSTIC CUT-OFF	5-23
5.3.5 DEVISING A SCORING SYSTEM	5-24
5.3.6 SUBGROUP ANALYSIS.....	5-25
5.3.7 TESTING THE MODELS	5-27
5.3.7.1 <i>The Validation Dataset</i>	5-27
5.3.7.2 <i>Results of Model Validation</i>	5-27
5.3.8 COMPARISON WITH SKIN SURFACE MICROSCOPY & REVISED SEVEN POINT CHECKLIST	5-29
5.4 DEVELOPING PREDICTIVE MODELS USING CLASSIFICATION TREES.....	5-32
5.4.1 CART ANALYSIS.....	5-32
5.4.1.1 <i>Validation of the CART models</i>	5-36
5.4.2 QUEST ANALYSIS	5-36
5.4.3 COMPARISON WITH SKIN SURFACE MICROSCOPY	5-38
5.5 SUMMARY	5-39

CHAPTER 6: CONCLUSIONS AND FURTHER WORK

6.1 INTRODUCTION	6-1
6.2 CONCLUSIONS	6-1
6.2.1 SUMMARY	6-1
6.2.2 EVALUATION	6-2
6.2.3 CRITICISMS	6-3
6.3 FURTHER WORK.....	6-3
6.3.1 IDENTIFYING FURTHER SIASCOPY FEATURES	6-3
6.3.2 USING SIASCOPY WITH SKIN SURFACE MICROSCOPY	6-4
6.3.2.1 <i>The Objective Identification of Skin Surface Microscopy Features</i>	6-4
6.3.3 AUTOMATION AND COMPUTERISED IMAGE ANALYSIS	6-5
6.3.4 MONITORING & SCREENING PATIENTS	6-6
6.3.4.1 <i>Monitoring of Patients</i>	6-6
6.3.4.2 <i>Screening Patients</i>	6-6
6.3.5 APPLICATION OF THE SIASCOPE IN OTHER CUTANEOUS DISEASES.....	6-7
6.3.5.1 <i>Basal Cell Carcinoma</i>	6-7
6.3.5.2 <i>Port Wine Stains</i>	6-8

APPENDIX A: SCORING METHODS & QUEST CLASSIFICATION TREE

THE SIASCOPY SCORING METHOD:	A-1
---	------------

THE COMBINED SCORING METHOD: A-1
THE QUEST CLASSIFICATION TREE A-2

APPENDIX B: EXAMPLE SIAGRAPHS