Improving Skin Cancer (Melanoma) Detection: New Method

By
Mohamed Khaled Abu Mahmoud

Thesis Submitted as a requirement for the degree of
Doctor of Philosophy

School of Electrical, Mechanical and Mechatronic Systems
Faculty of Engineering and Information Technology

University of Technology, Sydney (UTS)
November, 2014
Abstract

Melanoma, the deadliest form of skin cancer, must be diagnosed early for effective treatment. Rough pigment network and qualities are important signs for melanoma diagnosis using pathologist images. The main focus of this thesis is to improve skin cancer (Melanoma) detection through introducing novel image processing approach for a computer-aided system based on pigment network and elements detection on pathology images. It is important to propose an automated system for differentiating between melanocytic nevi and malignant melanoma. This thesis describes a novel image processing approach for computer-aided pigment network and elements detection on dermoscopy / pathology images. The proposed methods provide meaningful ideas of structures, and extract features for melanoma detection. Additionally, the thesis presents efforts towards prevention of melanoma, by developing a smart system to locate pigment networks.

The thesis aims to cover a complete theoretical model for simulating the processes that takes place when a human interprets an image generated by the eye, through designing a reliable system, that can provide a screening method that “filters” lesions and melanoma in a general practice. The proposed system is to be used with a standard PC with input from a high quality digital camera, dermoscopy / microscopy slides or any other suitable hardware sources. This system analyses the structure of a mole / skin defects, detects cancer, identifies features, makes a decision and provides the result.

The result of the proposed system shows that the Skin Cancer (Melanoma) Detection strategy which uses SVM performs reasonably satisfactorily (accuracy 77.44%, sensitivity 83.60 %, and specify 70.67%). Furthermore, the SVM based wavelet Gabor (SVM-WLG) performs better than the SVM (81.61%, 88.48%, and 74.51 % accuracy, sensitivity, and specify respectively). However, the Swarm-based SVM (SSVM) performs better than the other two algorithms, with average for accuracy, sensitivity, specificity of 87.13%, 94.1% and 80.22%, respectively.
Certificate of Authorship / Originality

I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

Mohamed Khaled Abu Mahmoud

November, 2014
To the soul of my father and my mother
For encouraging me and pounding me with my education
Acknowledgments

Firstly, I would like to express my sincere gratitude to my principal supervisor, Assoc. Prof. Adel Al-Jumaily, who provided such expert guidance and advice throughout this PhD candidature. He possesses an amazing amount of expertise and an ability to critically appraise work, that ensures the end result is worthy and importantly of value to public health.

I would also like to sincerely thank and acknowledge the pathologist Dr. Sarbar Napaki from Southern Pathology laboratory for providing us with pathologist data samples and for updating our medical expertise with the intention of improving our results. Also I would like to extend my thanks to Dr. Ryad Ahmed (for reviewing Chapter 2; Human Skin Biology and Cancer and Related Work in this thesis) and Dr. Rami Khushaba, Dr. Jebrin Sharawneh and Miss. Hayat Al-Dmour who have supported me whenever requested.

I am truly blessed to work in research for an organization dedicated to cancer detection and due to this I would like to express my sincere gratitude to University of Technology for the great experience and knowledge it gave me, my colleagues at the University of Technology, Sydney, Faculty of Engineering and Information Technology, School of Electrical, Mechanical and Mechatronic Systems who always encouraged and supported me, providing that little extra push to enable me to complete this thesis.

I am very lucky to have a wonderful supportive family. My two sons, my three daughters, my three sons in law and my grandkids have always encouraged me in my striving to complete this piece of work. Finally, to my wife, my partner in life for the past 43 years, this would not have been possible without your love and support.
Table of Contents

To the soul of my father and my mother.................................3
For encouraging me and pounding me with my education...3
Acknowledgments........................................................................4
Table of Contents.........................................................................5
Extended Table of Contents .....................................................7
List of Figures.............................................................................12
List of Tables.............................................................................18
CHAPTER 1..................................................................................19
Introduction................................................................................19
CHAPTER 2..................................................................................32
Human Skin Biology and Cancer. .............................................32
CHAPTER 3..................................................................................53
Image Processing and Automatic Skin Cancer Diagnosing ........53
CHAPTER 4..................................................................................92
Pre-processing and Segmentation............................................92
CHAPTER 5..................................................................................122
Image Representation and Analysis ..........................................122
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHAPTER 6</td>
<td>150</td>
</tr>
<tr>
<td>Experimental Results and Discussion</td>
<td>150</td>
</tr>
<tr>
<td>CHAPTER 7</td>
<td>185</td>
</tr>
<tr>
<td>Conclusion and Future Work</td>
<td>185</td>
</tr>
<tr>
<td>Appendices</td>
<td>189</td>
</tr>
<tr>
<td>Bibliography</td>
<td>220</td>
</tr>
</tbody>
</table>
Extended Table of Contents

Table of Contents

To the soul of my father and my mother ........................................... 3
For encouraging me and pounding me with my education ...3
Acknowledgments..................................................................................4
Table of Contents ...............................................................................5
Extended Table of Contents ..............................................................7
List of Figures ..................................................................................12
List of Tables ..................................................................................18

CHAPTER 1 ..................................................................................19

Introduction .................................................................................... 19
  1.1. Research Aims ...........................................................................20
  1.2. Problem Description .................................................................20
  1.3. Objectives ................................................................................21
  1.4. Methodology ............................................................................22
  1.5. Contribution of the Doctoral Research ....................................23
  1.6. Structure and Summary of the Dissertation .........................27
  1.7. Publications Presented During the Doctoral Research ..........29

CHAPTER 2 ..................................................................................32

Human Skin Biology and Cancer. .................................................... 32
  2.1. Human Skin Biology ................................................................32
  2.2. The Cell (Structure and Function) ...........................................32
    2.2.1. Cell structure ...................................................................33
    2.2.2. Cell Cycle and Replication: .............................................33
Table of Contents

2.3. Haematoxylin and Eosin (H & E) ................................................................. 35
2.4. Skin Cell Structure .................................................................................. 35
   2.4.1. Protection .......................................................................................... 36
   2.4.2. Sensation ......................................................................................... 36
   2.4.3. Thermoregulation ........................................................................... 36
2.5. The Layers of the Skin ........................................................................... 37
   2.5.1. Epidermis ........................................................................................ 37
   2.5.2. Dermis ............................................................................................ 37
   2.5.3. Subcutaneous/hypodermis .............................................................. 37
2.6. Melanocyte .............................................................................................. 38
2.7. Physical Properties of Human Skin ......................................................... 38
2.8. Human Skin ............................................................................................. 40
   2.8.1. Types of Skin ................................................................................... 40
   2.8.2. Layers of Human Skin ..................................................................... 40
   2.8.3. Cancer Types .................................................................................. 41
   2.8.4. Types of Skin Cancer ...................................................................... 41
   2.8.5. Health Behavior of Cancer Survivors ........................................... 49

CHAPTER 3 ....................................................................................................... 53

Image Processing and Automatic Skin Cancer Diagnosing
......................................................................................................................... 53

3.1. Introduction ........................................................................................... 53
3.2. Vision System & Structure of the Human Eye ....................................... 53
   3.2.1. Human Visual Perception .............................................................. 53
   3.2.2. The Human Eye ............................................................................. 54
   3.2.3. Structure of the Eye ...................................................................... 54
3.3. Image Processing & Human skin Imaging .......................................... 55
   3.3.1. Applications of Image Processing ................................................ 56
   3.3.2. Digital Image Acquisition ............................................................. 58
   3.3.3. Digital Camera .............................................................................. 59
   3.3.4. Skin Imaging Techniques ............................................................... 60
   3.3.5. Differential Diagnosis of Pigmented Lesions of the Skin .......... 65
   3.3.6. Automatic Skin Cancer Diagnosing ............................................. 72
# Table of Contents

CHAPTER 4 .................................................................................................................. 92

Pre-processing and Segmentation ................................................................. 92

4.1. Introduction ........................................................................................................ 92
  4.1.1. Digital Image Representation ..................................................................... 93
  4.1.2. Image Types ................................................................................................. 93
  4.1.3. General approach of developing a Computer Aided Design (CAD) system ........................................................................................................ 94

4.2. Pre-Processing Stage ...................................................................................... 96
  4.2.1. Wiener Filter: ............................................................................................... 98
  4.2.2. Gabor Filter ................................................................................................ 100
  4.2.3 Median filter: ................................................................................................. 102
  4.2.4. Adaptive Median Filter (AMF): ................................................................. 103

4.3. Image preprocessing: enhancement ........................................................... 104
  4.3.1. Image enhancement .................................................................................... 105
  4.3.2. Intensity transformation ............................................................................. 106
  4.3.3. Histogram Processing ................................................................................ 106
  4.3.4. Histogram Equalization ............................................................................ 108
  4.3.5. Special filtering ........................................................................................... 111

4.4. Image Segmentation ...................................................................................... 113
  4.4.1. Edge-based Image Segmentation ................................................................. 114
  4.4.2. Edge Detection Operations ...................................................................... 114
  4.4.3. Thresholding ............................................................................................... 115
  4.4.4. Global Thresholding .................................................................................. 116
  4.4.5. Optimal Global Thresholding ................................................................... 118
  4.4.6. Pixel Classification through Clustering .................................................... 120

CHAPTER 5 ................................................................................................................. 122

Image Representation and Analysis ......................................................... 122

5.1. Introduction .................................................................................................... 122
5.2. Machine Learning ......................................................................................... 122
5.3. Main Concepts ............................................................................................... 123
5.4. Intelligent Image Features Extraction ....................................................... 124
Table of Contents

5.4.1. Texture: ........................................................................................................ 125
5.4.2. Texture features: ......................................................................................... 126
5.4.3. Grey-Level Co-occurrence Matrix and Features .......................................... 127
5.4.4. Gabor filter feature extraction ..................................................................... 128
5.4.5. Wavelet decomposition of an image ............................................................. 129
5.4.6. Discrete Wavelet Transform ....................................................................... 130
5.4.7. Classifier distance metric equation ............................................................ 131
5.5. Feature Extraction and Representation ......................................................... 131
  5.5.1. Methodology used in feature extraction ....................................................... 132
5.6. Classification and Feature selection ............................................................... 133
  5.6.1. Feature Selection (FS) ................................................................................ 133
  5.6.2. Unbalanced data sets ................................................................................. 136
5.7. SVM for Classification and Regression ......................................................... 137
  5.7.1. Linear support vector machine .................................................................... 137
  5.7.2. Nonlinear support vector machine ............................................................. 140
  5.7.3. Support Vector Regression ....................................................................... 143
5.8. Swarm based Support Vector Machine for Melanoma Detection ............... 144
  5.8.1. Development of a Melanoma Detection based on the Swarm based Support Vector machine ............................................................................. 144
  5.8.2. Optimization of SVM parameters using PSO ......................................... 145
  5.8.3. Fitness function for the optimization ....................................................... 147

CHAPTER 6.............................................................................................................. 150

Experimental Results and Discussion .......................................................... 150

6.1. Introduction ..................................................................................................... 150
  6.1.1. Experiment 1 ............................................................................................. 152
  6.1.2. Experiment 2 ............................................................................................. 160
  6.1.3. Experiment 3 ............................................................................................. 166
  6.1.4. Experiment 4 ............................................................................................. 171
  6.1.5. Experiment 5 ............................................................................................. 174
  6.1.6. Experiment 6 ............................................................................................. 176

CHAPTER 7.............................................................................................................. 185
Conclusion and Future Work ........................................... 185

7.1. Conclusion............................................................................ 185
7.2. Future Research................................................................... 187

Appendices .............................................................................. 189

A. Appendix A: Glossary of Pathology Terminology .................. 189
B. Appendix B. Glossary of Pathology Terminology .................... 196
C. Appendix C: Glossary of Machine Learning and Computer Vision Terminology ................................................................. 197
D. Appendix D: Margin between two hyper planes...................... 203
E. Appendix E: Lagrangian dual optimization............................... 204
F. Appendix F: Soft-margin nonlinear support vector machine ........ 206
G. Appendix G: Sequential minimal optimization (SMO) for SVM .... 208
H. Appendix H: Glossary and Abbreviations ............................... 211

Bibliography ............................................................................. 220
List of Figures

Figure 2.1 shows, Cells structure; source: www.getting-in.com ................................................................. 33
Figure 2.2 The eukaryotic cell cycle, G Phases: growing, S phase: synthesis/ DNA replication, G2 Phase: Growing and preparing for Mitosis, M mitosis ......................................................... 34
Figure 2.3 The cell cycle; G0 terminally differentiated cell G1 gap phase 1 G2 gap phase 2 M mitotic phase S synthesis phase ............................................................................................... 35
Figure 2.4 H&E-stained section of skin. High magnification (40xs) view. Haematoxylin stains the nuclei of cells blue to bluish-purple, and eosin stains other cellular elements in the tissues from pink to red [43]. ........................................................................................................... 35
Figure 2.5 Displayed Cross Section & the main layers of Human Skin ..................................................... 37
Source: nurrashidah2204.blogspot.com ...................................................................................................... 37
Figure 2.6. Skin Color Distribution around the World .................................................................................. 38
Source: www.gbhealthwatch.com ................................................................................................................. 38
Figure 2.7. a) Cross section of human skin, b) Structure of Epidermis ........................................................... 39
Figure 2.8. The Layers of Skin - the Epidermis and Dermis (At the top, the close up shows a squamous cell, basal cell, and melanocyte). ............................................................................. 42
Figure 2.9- a) Basal Cell Carcinoma (BCC), b) Squamous Cell Carcinoma (SCC) ........................................... 42
Figure 2.10 – Melanoma .............................................................................................................................. 43
Figure 2.11: Malignant Melanoma, World Age-Standardised Incidence Rates, World Regions, 2008 Estimates ........................................................................................................................... 44
Figure 2.12. Lentigomaligna Melanoma ........................................................................................................ 45
Source: melanomaknowmore.com .................................................................................................................. 45
Figure 2.13. Superficial Spreading Melanoma ............................................................................................ 46
Source: melanomaknowmore.com .................................................................................................................. 46
Figure 2.14. Nodular Melanoma .................................................................................................................. 46
Source: melanomaknowmore.com .................................................................................................................. 46
Figure 2.15. Stages of Cancer Development and Metastasis ........................................................................ 47
Figure 2.16: Five-year relative survival from selected cancers by remoteness area, Australia. 2006-2010 ........................................................................................................................................... 49
Figure 3.1 - Show the function of the eye ...................................................................................................... 55
Figure 3.2 - Distance of vision ...................................................................................................................... 55
Figure 3.3 - Structure of the Eye

Source: hyperphysics.phy-astr.gsu.edu/hbase/vision/accom.html

Figure 3.4 - Focal length defined

When parallel rays of light strike a lens focused at infinity, they converge to a point called the focal point. The focal length of the lens is then defined as the distance from the middle of the lens to its focal point.

Figure 3.5 - Displayed similarities of overall design in the principal features of an optical microscope, a transmission electron microscope and a scanning electron microscope.

Source: www.nslc.wustl.edu

Figure 3.6 - Principle of CSLM. Note the same optical path is used for the detector and the source. Optics are used to direct the light towards the detector.

Figure 3.7 - Two-step procedure for the classification of pigmented skin lesions. Adapted from Argenziano.[122]

Figure 3.8 - Algorithm for the determination of melanocytic versus non melanocytic lesions according to the proposition of the Board of the Consensus Netmeeting. Adapted from Argenziano.[122]

Figure 3.9 - A, Macroscopic picture of a superficial spreading malignant melanoma (Breslow thickness 0.52 mm; Clark level II). B, Dermoscopy of A shows (atypical) pigment network and branched streaks and can therefore be considered a melanocytic lesion.

Figure 3.10 - A, Macroscopic picture of a blue nevus. B, Dermoscopy of A shows steel-blue areas (no pigment network, no aggregated globules, and no branched streaks).

Figure 3.11 - A, Macroscopic picture of a seborrheic keratosis. B, Dermoscopy of A shows comedolike openings (a), multiple milia-like cysts (b), and fissures (c).

Figure 3.12 - A, Macroscopic picture of a seborrheic keratosis. B, Dermoscopy of A shows comedolike openings and multiple milia-like cysts.

Figure 3.13 - A, Macroscopic picture of a basal cell carcinoma. B, Dermoscopy of A shows maple lifelike areas, ovoid nests, and arborized telangiectasia.

Figure 3.14 - A, Macroscopic picture of a basal cell carcinoma. B, Dermoscopy of A shows multiple spoke wheel areas.

Figure 3.15 - A, Macroscopic picture of an angioma. B, Dermoscopy of A shows red lagoons.

Figure 3.16 - Asymmetry Border Color Diameter Evolution (ABCD-E) rule for Diagnosis of Melanoma.

Source: www.webmd.com

Figure 3.17 - Normal moles and Melanomas [Benign and Malignant].

Source: www.skinbychar.com

Figure 3.18 - Showed: a) Melanoma in skin biopsy with H&E Stain (“This case may represent superficial spreading melanoma.”), b) Lymph node with almost complete replacement by metastatic melanoma. The brown pigment is focal deposition of melanin.
Figure 3.19. Diagnosis of Melanoma using Three-point Checklist...............................72

Figure 3.20 - Example of pigmented skin lesion. Left: Traditional imaging technique. Right: Dermoscopy imaging technique.................................................................73

Figure 3.21. (a) Macroscopic Image of a Lesion (b) Dermatoscopic Image of the same Lesion. Source: www.jle.com.............................................................................................74

Figure 3.22- Show the results of skin lesion boundary tracing algorithm, my data experiment shown [a] Image center of mass, [b] Image process.........................................................75

Figure 3.23- From left to right: the original image (source image from: http://ijplugins.sourceforge.net/plugins/clustering/), clustered image using 2 clusters (poor), clustered image using 3 clusters (close but one key cluster is missing), clustered image using 4 clusters (optimal), and clustered image using 10 clusters (artifacts are noticeable).........................................................77

Figure 3.24- Structure of fuzzy image processing ........................................................................78

Figure 3.25- Steps of fuzzy image processing................................................................78

Figure 3.26. Manual Segmentation by trained pathologists using the ‘Aperio Image Scope’ software [156]........................................................................................................82

Figure 3.27 Showed the Radial growth phase melanoma..................................................83

Figure 3.28 showed the Vertical growth phase melanoma..................................................84

Figure 3.29 Microscopic satellites, (a). Shows neoplastic group is discontinuous (arrow) from the overlying vertical growth phase component. Shows the melanocytes must have a malignant cytomorphology (b) ........................................................................................................85

Figure 3.30 Regression: Regression of over 75% of the tumor volume of a melanoma is considered a bad prognostic sign.................................................................86

Figure 3.31: a) An image of a lesion under clinical view (naked eye). b) Shows the same lesion under a dermoscopy with oil immersion.................................................86

Figure 3.32: a) Colors allow the physician, to some extent, to draw conclusions about the localization of pigmented cells within the skin. Black and brown indicate pigmentation in the epidermis, while grey and blue correspond to pigmented cells within the superficial and deep dermis, respectively [185].........................................................................87

Figure 3.33: Figures (a, b, c, d, and e) show analogue dermoscopy. All of them, except (a), are attachable to digital cameras to function as digital dermoscopy. Figures (f, g, and h) show DinoLite, Handy scope, and Dermoscopy which are modern digital dermoscopy....88

Figure 3.34. The Solar Scan instrument: (a) global appearance, (b) camera, (c) user interface [192]. Source: www.medgadget.com ............................................................................90

Figure 4.1 Showed: Four stages CAD system for skin lesions.......................................96

Figure 4.2 true color Pathological Digital Image.................................................................96

Figure 4.4, calculating the median value of a pixel neighborhood..................................102

Figure 4.5. The basic structure of the MACWM filter .......................................................104

Figure 4.6. Shows the output image of Adaptive median Filtering.................................104

Figure 4.7 Showed: (a) grayscale image, (b) Histogram out............................................107

Figure 4.8. Showed: intensity image using........................................................................109
List of Figures

Figure 4.9. Sobel Edge Detection Image ................................................................. 114
Figure 4.10. Binary Output Image Otsu’s Method[ .................................................. 114
Figure 4.11. selected thresholds in valleys between peaks .................................... 116
Figure 4.12. obtaining the best possible separation measure for two classes ....... 116
Figure 4.13. selecting a threshold by visually analyzing a bimodal histogram ...... 116
(Principle of histogram peak separation) ............................................................ 116
Figure 5.1. displayed the main categories: texture elements, regularity, randomness, directionality and regularity ................................................................. 126
Figure 5.2. showed, (a) images (5x 5) matrix with 3 grey levels 0, 1, and 2. (b) The co-occurrence matrix for d= (1, 1) ................................................................. 127
Figure 5.3. displayed the response from convolving image sample with filter ....... 129
Figure 5.4. (a) Wavelet decomposition of an image (b) Block diagram of the decomposition of an image ................................................................. 130
Figure 5.5. displayed a block diagram of the discrete wavelet transforms (DWT – Gabor approach) ................................................................. 130
Figure 5.6. the three principal approaches of feature Mammographic e selection. The shades show the components used by the three approaches: filters, wrappers and embedded methods ................................................................. 133
Figure 5.7: Two-out-of-many separating lines; (a) with smaller margin and (b) with larger margin ................................................................. 138
Figure 5.8: Margin m between two supporting hyperplanes. ................................ 139
Figure 5.9: Illustration of mapping using a transform Ψ: R2 → R3 ..................... 140
Figure 5.10: Introducing slack variable ξ in soft-margin SVM ......................... 142
Figure 5.11: Loss Functions ............................................................................... 144
Figure 5.12: Melanoma detection using swarm based support vector machine .... 145
Figure 5.13: The pseudo of the PSO for the SVM parameter optimization .......... 146
Figure 5.14: The particles of the PSO .................................................................. 147
Figure 6.2 Skin Cancer Image, (a) Original RGB true colour image ............... 153
Figure 6.3. The basic structure of the MACWM filter ........................................ 154
Figure 6.4. A snake with traditional potential forces cannot move into the concave boundary region ................................................................. 156
Figure 6.5 A snake with GVF external forces moves into the concave boundary region. 157
Figure 6.6. Skin Cancer greyscale image showing: (a) Wiener2 filter has removed the spots effectively (b) noisy image filtered by the median filter ................................................................. 157
(a) Without filtering, (b) with filtering ................................................................. 158
Figure 6.7 Skin Cancer Image Histogram .......................................................... 158
Figure 6.8 Skin Cancer greyscale image showing: (a) Sobel segmented image .... 159
(b) Gradient vector flow (GVF) segmented image ............................................. 159
List of Figures

Root mean square error.......................................................................................................................... 160

Figure 6.9. Result of segmentation by threshold with GHE (bottom right) and LHE (bottom left), Top: shows histogram Local and Global results ........................................... 162

Figure 6.10. Segmentation by Thresholding (ROI) ................................................................. 162

Figure 6.11. Segmentation by SRM.................................................................................... 163

Figure 6.12. Display of the image and its transform (wavelet coefficients) ..................... 164

Figure. 6.13: A single curvelet with width $2 - 1$ and length $2 - 12$ ........................................ 164

Figure 6.14. Display of the image and its transform (wavelet coefficients) ................. 164

Figure. 6.15. Curvelet demising image that contains oriented texture and cartoon edges (a) Original (b) Noisy, and (c) Curvelet................................................................. 166

Figure. 6.16. The results showed, original image, image after median filter, gray scale image,................................................................................................................................. 172

Figure. 6.17. - A Wavelet Packet decomposition tree ......................................................... 178

Figure. 6.18 shows the melanoma detection employing SVM (SVMR, SVMP, and SVML); the input is pathology images and the output is melanoma (-1) or benign (+1). 181

Figure A1, showed a physician’s hands are seen performing a needle biopsy to determine nature of lump either fluid-filled cyst or solid tumour ........................................... 189

[This image was released by the National Cancer Institute, an agency part of the National Institutes of Health, with the ID 1973 (image)] ................................................................. 189

Figure A2, the diagnostics showed: Micrograph of a needle aspiration biopsy specimen of a salivary gland showing adenoid cystic carcinoma. (Source: Pap stain. MeSH D044963). ................................................................................................................ 189

Figure A3, showed a Normal Epidermis and Dermis with Intradermal Nevus 10x-cropped.
(Source, Kilbad). ................................................................................................................................. 190

Figure A4, this image shows a crossection of the vascular tissue in a plant stem. Showed as an example for bright field micrograph. (Source: Wikipedia). ......................................................... 190

Figure A5, Principle of confocal microscopy ............................................................................ 191

Figure A6 showed the nucleolus is contained within the cell nucleus. (Source: Wikimedia Foundation, Inc.) ................................................................................................................ 192

Figure A7 displayed the negative of the logarithm (base 10) of the optical Density (OD), (Source: semrock@idexcorp.com) ............................................................................................. 193

Figure A8, showing a pathologist examines a tissue section for evidence of cancerous cells while a surgeon observes. (Source: wikipedia.org) ......................................................... 193

Figure A9, showed: a) A TEM image of the polio virus is 30 nm in size, b) Layout of Optical components in a basic TEM. (Source: Wikimedia) Appendix B: Optical Density of Transmission Microscopy Images ................................................................. 194

Figure B1. Example optical density image .............................................................................. 196

Figure C1, showed a graph with three connected components. ........................................ 197
**Figure C2**, displayed the machine learning and data mining which used to solve problem in the areas of Classification, Clustering, Regression, Anomaly detection, Association rules, Reinforcement learning, Structured prediction, Feature learning, Online learning, Semi-supervised learning, and Grammar induction. ......................................................... 198

**Figure D1**: Margin $m$ between two supporting hyperplanes..............................................................203
List of Tables

Table 2.1: Breslow's depth ............................................................................................................. 48
Table 2.2: Survival figures from British Association of Dermatologist Guidelines 2002 .. 48
Table 2.3: Observed incidence (2009), and morality (2010) of melanoma of the skin and estimated for 2012 .............................................................................................................. 51
Table 2.4: Observed incidence (2009), and morality (2010) of non-melanoma of the skin and estimated for 2012 ......................................................................................................... 52
Table 6.1 Sensitivity and Specificity comparison ............................................................... 152
Table 6.2 Comparison between proposed operators (Sobel, Roberts, Prewitt, Laplacian, Canny and Otsu) and Gradient vector flow (GVF) segmented images .............................................................................. 160
Table 6.3 BNN Classification Test with Different Wavelet ................................................. 161
Table 6.4. BNN Classification Test for SRM & Thresholding .......................................................... 163
Table 6.6. Displaying the comparison between wavelet and curvelet features results .... 166
Table 6.7. svm classification for all the dataset (including dermoscopy images) with features extracted from wavelets ........................................................................................................... 169
Table 6.8. svm classification excluding dermoscopy images with features extracted from wavelets ............................................................................................................................................. 170
Table 6.9. svm classification for all the dataset (including dermoscopy images) with features extracted from curvelets ............................................................................................................................................. 170
Table 6.10. svm classification excluding dermoscopy images with features extracted from curvelets ............................................................................................................................................. 170
Table 6.11. sensitivity and specificity statistics [310] ............................................................. 171
Table 6.12. Described sensitivity and specificity ........................................................................ 174
Table 6.13. show result after training or the (svm) network. using (sfs) technique .......... 174
Table 6.14. the result after training of the (svm) network with using (sfs) technique ..... 175
Table 6.15. the result after training of the (svm) network without using (sfs) technique. .................................................................................................................................................. 175
Table 6.17 The Result after Training of the (SVM) Network, with using (SFS)Technique. .................................................................................................................................................. 180
Table 6.18 The Result after Training of the (SVM) Network. with using (SVM+WLG+PSO) .................................................................................................................................................. 180
Table 6.19 Described Sensitivity and Specificity [31] ............................................................. 181