### Breast Cancer Risk Assessment using Mammographic Image Texture Analysis



A thesis submitted for the degree of Doctor of Philosophy

By

Xi-Zhao Li

School of Computer Science, Engineering and Mathematics Faculty of Science and Engineering Flinders University

/ P W F N 🕮 F4S,

# Contents

Li	st of ]	Figures			V
Li	st of '	Tables			xi
Li	st of A	Abbrevi	ations	XX	ciii
Su	mma	ary		X	XV
Pu	ıblica	tions ar	ising from the Study	XX	vii
De	eclara	tion		XX	kix
Ac	knov	vledgem	ents	XX	cxi
1	Intr	oductio	n		1
	1.1	Breast	Cancer Incidence		1
	1.2	Breast	Cancer Screening		2
		1.2.1	Screen-film Mammography versus Digital Mammography		3
		1.2.2	Other Modalities		4
	1.3	Breast	Cancer Risk Assessment		4
		1.3.1	Identified Risk Factors for Breast Cancer Risk Assessment		4
		1.3.2	Benefits of Breast Cancer Risk Assessment		8
	1.4	Motiva	tion and Objectives of the Thesis	•	9
	1.5	Overvi	ew of the Data Sets		10
	1.6	Overvi	ew of the Thesis	•	11
2	Tecl	nnical B	ackground and Literature Review		13
	2.1	Textur	e Analysis	•	13
	2.2	Texton	S	•	16
	2.3	Metho	ds for Extracting Local Texture Feature Vectors	•	19
		2.3.1	Standard Filter Banks	•	19
		2.3.2	$N \times N$ Neighborhoods	•	21
		233	Gabor Filters		21

	2.4	Cluste	ring Methods	24
		2.4.1	<i>K</i> -means	24
		2.4.2	Fuzzy C-means	25
	2.5	Classi	fiers	26
		2.5.1	Ensemble k-nearest Neighbor Classifier	26
		2.5.2	Fisher Classifier	29
		2.5.3	Support Vector Machine (SVM)	30
	2.6	Valida	tion	32
	2.7	Accur	acy and ROC Analysis	33
	2.8	Featur	e Selection	38
		2.8.1	Exhaustive Search Feature Selection	39
		2.8.2	Sequential Feature Selection	39
	2.9	Comp	uter-aided Breast Cancer Risk Assessment	40
		2.9.1	Motivation for and Role of Computer-aided Risk Assess-	
			ment	40
		2.9.2	Steps for Conducting Computer-aided Risk Assessment	41
		2.9.3	History of Computer-aided Risk Assessment	41
		2.9.4	Context of the Thesis	44
3	Loca	al Norn	nalization: A Preliminary Study	47
	3.1	Classi	fying ROIs as Cancer or Non-cancer	48
		3.1.1	Data	48
		3.1.2	Experimental Details	48
		3.1.3	Results	51
		3.1.4	Discussion and Conclusion	52
	3.2	Local	Mean and Variance Normalization	52
	3.3	Applic	cation of the Local Normalization to Classify ROIs as Cancer	
		or Nor	n-cancer	54
4	Vari	ations	of Texton Implementation for Risk Assessment	57
	4.1	Data S	Set	58
	4.2	Applic	cation of the Local Normalization to BI-RADS Classification	59
		4.2.1	Experimental Details of Three Algorithms	61
			4.2.1.1 Algorithm with and without normalization	61
			4.2.1.2 Petroudi's algorithm	64
		4.2.2	BI-RADS Classification Results for Three Algorithms	64
		4.2.3	Discussion and Conclusion of Three Algorithms	65
	4.3	Comp	arison of Candidate Methods for Texton Generation	68
		4.3.1	Experimental Details of Three Candidate Methods	68
			4.3.1.1 MR8 filtering	68

		4.3.1.2 $N \times N$ neighborhoods	68
		4.3.1.3 Gabor filtering	68
		4.3.2 Discussion and Conclusion of Three Candidate Methods	70
	4.4	Comparison of Two Clustering Methods	70
5	Text	ture and Region Dependent Risk Assessment	73
	5.1	Data Set	74
	5.2	Delineating Local Regions	75
	5.3	Texture Features and Classification	75
		5.3.1 Texton Features	75
		5.3.2 Oriented Structure Features	78
		5.3.3 Risk Classification	80
	5.4	Results	83
	5.5	Conclusion and Discussion	84
6	Hig	her-order Textons	87
	6.1	Introduction	87
	6.2	Higher-order Textons	89
	6.3	Implementations of Higher-order Textons	92
		6.3.1 Data Set	92
		6.3.2 Textons based on $N \times N$ Neighborhoods	92
		6.3.3 Textons Based on Gabor Filters	93
		6.3.4 Results	94
		6.3.5 Conclusion and Discussion	98
	6.4	Label-Independent Higher-order Texton Generation using $N \times N$ Neigh-	
		borhoods	99
7	Text	ture versus Density 1	05
	7.1	Risk Classification with Texture Features	06
	7.2	Risk Classification with a Density Feature	06
	7.3	Risk Classification with Combined Texture and Density Features 1	08
		7.3.1 The Augmented Feature Set Method	08
		7.3.2 The Reselected Feature Set Method	09
		7.3.3 The Recalculated Feature Set Method	09
	7.4	Results for Sequential Feature Selection	09
	7.5	Results for Exhaustive Search Feature Selection	10
	7.6	Conclusion and Discussion	11
8	Tem	nporal Risk Assessment 1	15
	8.1	Data Set	16

	8.2	Prelimi	nary Experiments	117
		8.2.1	DDSM Textons Applied to BSSA Data	117
		8.2.2	BSSA Textons without BI-RADS Assignments	118
		8.2.3	BSSA Textons with BI-RADS Assignments	119
		8.2.4	Separating Ipsilateral and Contralateral Breasts	121
	8.3	Final E	xperiment on Temporal Risk Assessment	123
		8.3.1	Methods	123
		8.3.2	Results for Sequential Feature Selection	124
		8.3.3	Results for Exhaustive Search Feature Selection	126
		8.3.4	Conclusion and Discussion	127
9	Final	l Remai	rks	133
A	Feat	ure Inde	exing	135
B	Supp	olement	ary Experimental Results	137
	<b>B</b> .1	Suppler	mentary Results for Region Dependent Risk Assessment	137
	B.2	Suppler	mentary Results for Higher-order Textons	140
	B.3	Detaile	d Results for Risk Classification of Texture vs Density - Part I	143
	B.4	Detaile	d Results for Risk Classification of Texture vs Density - Part	
		II		147
	B.5	Detaile	d Results for Temporal Breast Cancer Risk Assessment - Part	
		Ι		152
	B.6	Detaile	d Results for Temporal Breast Cancer Risk Assessment - Part	
		II		158
Bi	Bibliography 165			

# **List of Figures**

2.1	Framework of texton generation, feature extraction and classifica-	
	tion described in five steps: (1) extracting local feature vector, (2)	
	clustering into textons, (3) creating texton map, (4) constructing	
	histogram of textons and (5) classification. Operationally, feature	
	vectors of texture primitives (multi-dimensional feature vectors) are	
	usually filter responses obtained by applying filter bank on a number	
	of images.	18
2.2	Root filter set.	19
2.3	LM filter bank.	20
2.4	S filter bank.	20
2.5	An example of a Gabor filter bank consisting of 10 Gabor filters with	
	$\lambda = 20,  \sigma = 4.2,  \theta = k\pi/10  (k = 1, 2,, 10),  \varphi = 0,  \gamma = 0.4$ and	
	b=4.	22
2.6	Texture structures from a Gabor filter bank. The original image is a	
	cropped screening mammogram. The filter direction map shows the	
	index of maximum orientation as a gray scale image. In this exam-	
	ple, pixels outside the breast region are assigned index 0 and pixels	
	with maximum response less than the preset threshold are assigned	
	index 11. The index images 1 - 10 show pixels with maximum re-	
	sponse at the orientation corresponding to that index	23
2.7	Framework for the process of subspace ensemble application on k-	
	nearest neighbor classifier.	27

2.8	The process of choosing three parameters for the subspace ensemble	
	k-nearest neighbor classifier: (a) the cross validation errors for dif-	
	ferent numbers of nearest neighbors in the k-nearest neighbor classi-	
	fier, $k$ , (b) the cross validation errors for different numbers of predic-	
	tors, $m$ (how many features were used), (c) the cross validation er-	
	rors for different numbers of k-nearest neighbor classifiers, n. From	
	these figures, the number of nearest neighbors $k$ is chosen to be 2,	
	the number of predictors <i>m</i> is chosen to be 4 and the number of weak	
	learners $n$ is chosen to be 69 since reasonable low evaluation errors	
	were obtained at these values.	28
2.9	An example of Fisher classifier used for classifying two groups. The	
	black line is the Fisher orientation vector and the blue line is the	
	discriminant surface of Fisher classifier.	30
2.10	Illustration of four decision fractions defined by a possible decision	
	threshold. The group with solid line represents high risk and the	
	group with dashed line represents low risk. The blue line perpendic-	
	ular to the decision axis is one possible decision threshold. The cyan	
	colour patch indicates the TPF, the blue colour patch indicates the	
	FNF, the red colour patch indicates the TNF and the yellow colour	
	patch indicates the FPF. By moving the decision threshold line along	
	the decision axis, different four decision fractions are defined	35
2.11	Illustration of the process of generating the ROC curve: (a) Shows	
	the four decision fractions for each of five different decision thresh-	
	olds. (b) Shows five points on the ROC curve corresponding to the	
	five decision thresholds in (a). $P_1$ corresponding to $T_1$ , $P_2$ corre-	
	sponding to $T_2$ , $P_3$ corresponding to $T_3$ , $P_4$ corresponding to $T_4$ , $P_5$	
	corresponding to $T_5$ .	36
3.1	An example of choosing cancer and non-cancer ROIs from the MLO	
	view breast images. On the left of the top row is the right MLO view	
	breast, the circled region indicates a malignant mass region located	
	by an experienced radiologist and the square box is the cancer ROI.	
	On the right of the top row is the left MLO view breast from the	
	same woman. The circled region is the corresponding non-cancer	
	region obtained by symmetry and the square box is the non-cancer	
	ROI. The bottom row shows the extracted cancer and non-cancer	
0.0		49
3.2	ROC curves for classifying ROIs as cancer or non-cancer with 40	<b>.</b> .
	textons	51

3.3 On the left is the original mammogram. The bars show the horizontal and vertical extent of a cancer location. The middle panel shows the texton map of the original mammogram (left panel) obtained by replacing each pixel by the texton label. The result shown is for a final texton dictionary of size 16 learnt from aggregated cancer and non-cancer ROIs. The right panel shows the texton map of the contralateral non-cancer breast mammogram. 52 3.4 An example of a flattened image. On the left is the original mammogram X shown in Figure 3.1 (MLO view) and Figure 3.3 (CC view). The bars show the horizontal and vertical extent of a cancer location. The middle panel is the local mean subtracted image  $D_r$  (Equation 3.1). In this panel, the background has been set to the minimum value of the image to facilitate the display. The right panel is the local standard deviation image  $S_r$ . Due to the nonlinearity of the imaging process, the brightest region in X appear as a relatively 53 3.5 Mammograms normalized using  $N_r$  (Equation 3.2). Each panel shows the normalized image  $N_r$  obtained from the image X in Figure 3.4 for values of r = 1, 10, 22 respectively (left to right). The insets in the lower right of each panel show the region of the known malignant mass (cancer ROI) indicated by the bars in Figure 3.4. The left panel shows essentially no structure for r = 1, but structure emerges with increasing r. In each panel, the background has been set to the minimum image value to facilitate display. . . . . . . . . . . . . . 54 3.6 ROC curves for the application of local normalization to classify cancer and non-cancer ROIs with 40 textons. 55 4.1 Examples of CC view mammogram images from four BI-RADS density classes; (a) BI-RADS I, (b) BI-RADS II, (c) BI-RADS III, 58 4.2 Image preprocessing steps: (a) original breast image with initial breast boundary, (b) the image in (a) after applying the final image template, (c) the image in (a) after normalization, (d) the image in (c) after applying the final image template. The apparent increase in brightness of the breast in (b) is a display artifact. The brightest pixels in (a) comprise anomalies near the edge of the image outside the breast and within the LCC label. These are removed in applying the final template and the intensities within the breast region are 60

4.3	Examples of CC view BI-RADS images (the first row), normalized	
	image patches (the second row), detailed texture features in tex-	
	ton map patches (the third row) and texton histograms (the fourth	
	row) of the algorithm with normalization. Each column corresponds	
	to one of the BI-RADS pattern classes (I - IV from left to right).	
	Patches in the second and third rows were chosen from the same	
	positions in the original BI-RADS images.	62
4.4	Examples of MLO view BI-RADS images (the first row), normal-	
	ized image patches (the second row), detailed texture features in tex-	
	ton map patches (the third row) and texton histograms (the fourth	
	row) of the algorithm with normalization. Each column corresponds	
	to one of the BI-RADS pattern classes (I - IV from left to right).	
	Patches in the second and third rows were chosen from the same	
	positions in the original BI-RADS images.	63
5.1	An example of delineating local regions with three landmark points;	
	the star on the left is the nipple and the two circles on the right are	
	the two extreme points described in the text.	76
5.2	An example of oriented tissue structures in an image patch of Fig-	
	ure 2.6: (a) oriented tissue structures in the normalized image patch,	
	scale bar represents 5mm, (b) connected components after thresh-	
	olding the responses of oriented Gabor filters. Features are extracted	
	from individual Gabor filter responses (after thresholding) but in this	
	figure, for illustration only, the connected components from all the	
	responses are shown together with gray levels indicating the various	
	orientations.	79
5.3	Example of Gabor filters in two consecutive orientations $(\frac{9}{10}\pi$ and	
	$\pi$ ) of showing only positive intensity parts: (1) From left to right,	
	the first picture is the Gabor filter at orientation $\frac{9}{10}\pi$ . (2) The second	
	picture is the Gabor filter at orientation $\pi$ . (3) The last picture is the	
	aggregation of the above two Gabor filters	79
5.4	Features for oriented tissue structure texture. Feature $f_1$ (not indi-	
	cated) is the distance between the nipple and the component which	
	together with feature $f_2$ gives the location of the component relative	
	to the nipple. Feature $f_3$ is the angle between the major axis of the	
	elliptical approximation of the component and the line connecting	
	the centroid of the component to the nipple. Feature $f_4$ is the area of	
	the component (not indicated)	80

5.5	Example histograms of angle features for connected components. Top row (a), (b), (c) and (d) are four example histograms of feature $f_3$ . Bottom row (e), (f), (g) and (h) are four example histograms of the orientation of the connected component relative to the horizontal axis.	81
6.1	Examples of texton maps: (a) the locally normalized image, (b) the first-order texton map, (c) the second-order texton map, (d) the third-order texton map. The first-order texton map for $X^1$ is the second-order texton map of $X^0$ and so on. The insets show texture patterns in a patch of size 250 × 220 from the same location	90
6.2	First-, second- and third-order feature spaces for the toy example in section 6.2: (a) the feature space for both $X^0$ and $Y^0$ , (b) the feature space for both $X^1$ and $Y^1$ , (c) the feature space for $X^2$ and (d) the feature space for $Y^2$ . <i>A</i> , <i>B</i> , <i>C</i> , <i>D</i> and <i>m</i> are constants that depend	
6.3	only on the length of the strings and not the patterns of $1s$ and $0s$ Examples of texton maps for label-independent higher-order texton generation: (a) the locally normalized image, (b) the first-order texton map, (c) the second-order texton map, (d) the third-order texton map. The inset shows texture patterns in a patch of size $250 \times 220$ from the same location.	91 101
7.1	Schematic of the physical layout of a mammographic X-ray ma- chine.	107
7.2	Radial projection of the scattering filter used in the density feature calculation.	108
8.1	Temporal AUC scores for risk classification with label-independent higher-order textons and sequential backward feature selection. The three dark green bars are the AUC scores for the classification of ipsilateral high risk vs low risk in the current year, previous two years and previous four years; the three yellow bars are the AUC scores for the classification of contralateral high risk vs low risk in the current year, previous two years and previous four years. The	
8.2	error bars show one SD	125
	higher-order textons and exhaustive search feature selection. Details of the representation are as in Figure 8.1.	127

8.3	Temporal AUC scores for risk classification with label-independent	
	higher-order textons learnt from the current year period and sequen-	
	tial backward feature selection. Details of the representation are as	
	in Figure 8.1	129
8.4	Temporal AUC scores for risk classification with label-independent	
	higher-order textons learnt from the current year period and exhaus-	
	tive search feature selection. Details of the representation are as in	
	Figure 8.1	130

# **List of Tables**

Surrogates of risk used in the literature on computer-aided breast cancer risk assessment and in this thesis. "*" denotes surrogates for	40
	42
AUC scores for classifying ROIs as cancer or non-cancer described in Section 3.1.2.	51
AUC scores for the application of local normalization to classify	
cancer and non-cancer ROIs	22
Classification performance tables and confusion matrices for CC view testing mammograms: (a) the algorithm with normalization.	
(b) Petroudi's algorithm. (c) the algorithm without normalization.	65
Classification performance tables and confusion matrices for MLO view testing mammograms: (a) the algorithm with normalization	
(b) Petroudi's algorithm (c) the algorithm without normalization	66
Classification performance tables and confusion matrices for com-	00
bined CC and MI O view testing mammograms: (a) the algorithm	
with normalization (b) Petroudi's algorithm (c) the algorithm with-	
out normalization	66
Classification performance tables and confusion matrices for the can-	00
didate methods for the generation of textons: (a) MR8 filtering, (b)	
$N \times N$ neighborhood method, (c) Gabor filter texton method, (d) Ga-	
bor oriented feature method, (e) Gabor oriented texton method	69
BI-RADS classification performance table and confusion matrix for	
testing images using fuzzy C-means clustering instead of K-means	
clustering (Table 4.1 (a)).	71
Risk classification performance for different size $N \times N$ local neigh-	
borhoods for six different regions of the breast from $\Omega_1$ to $\Omega_6$ ; (a)	
total accuracies of ensemble k-nearest neighbor classifier, (b) total	
accuracies of SVM classifier, (c) testing AUC scores from the Fisher	
classifier.	77
	Surrogates of risk used in the literature on computer-aided breast cancer risk assessment and in this thesis. "**" denotes surrogates for risk used in this thesis

5.2	Classification performance for texton features with different clas-	
	sifiers; ensemble <i>k</i> -nearest neighbor classifier, SVM classifier and	
	Fisher classifier.	81
5.3	Classification performance for oriented tissue structure features with	
	different classifiers; ensemble k-nearest neighbor classifier, SVM	
	classifier and Fisher classifier.	82
6.1	Risk classification performance for $N \times N$ neighborhood experiments	
	with different sizes of $N \times N$ neighborhoods: (a) total accuracies of	
	ensemble $k$ -nearest neighbor classifier, (b) total accuracies for the	
	SVM classifier, (c) testing AUC scores for the Fisher classifier	94
6.2	Classification performance for higher-order textons using the 3 $\times$	
	3 method with different classifiers: ensemble k-nearest neighbor	
	classier, SVM classifier and Fisher classifier. The rank for (a) and	
	(b) is based on the total accuracy. The rank for (c) is based on the	
	testing AUC score.	96
6.3	Classification performance for higher-order textons using the Gabor	
	filter method with different classifiers: ensemble k-nearest neighbor	
	classifier, SVM classifier and Fisher classifier. The rank for (a) and	
	(b) is based on the total accuracy. The rank for (c) is based on the	
	testing AUC score.	97
6.4	5-fold cross validation results for the $N \times N$ method with $N = 3$	
	for all texton orders. "texton order" refers to the texton order or	
	combination of texton orders, "mean" is the mean of the AUC scores	
	from the cross validation, "std" is the standard deviation of the AUC	
	scores from the cross validation, and <i>p</i> -value is the probability that	
	the mean is different from the mean of the first-order texton (on its	
	own) by chance alone.	97
6.5	5-fold cross validation results for the Gabor filter method. The rows	
	have the same meaning as in Table 6.4.	98
6.6	Classification AUC scores for second-order textons calculated from	
	several relabeled first-order texton maps. The second row shows the	
	AUC scores of the original first-order texton maps. The third row	
	shows the AUC scores when relabeling texton 7 and 8 by 21 and	
	22. The fourth row shows the AUC scores when relabeling texton	
	7 and 8 by 25 and 29. The fifth row shows the AUC scores when	
	relabeling texton 7 and 8 by 25 and 32.	100

- 6.7 Classification performance for label-independent higher-order textons using the  $3 \times 3$  method with different classifiers: ensemble knearest neighbor classifier, SVM classifier and Fisher classifier. The rank for (a) and (b) is based on the total accuracy. The rank for (c) 7.1 Classification AUC scores for the label-dependent higher-order texton method for texture alone, density alone and the combination of texture and density according to the augmented method, the reselected method and the recalculated method. Values are the 5-fold cross validation averages  $\pm$  SD. *n* denotes the number of optimal features which were obtained from sequential backward feature selection. The index set for the texture features comprising the optimal set of *n* features is shown underneath. Indices 1 - 20 are first-order textons, 21 - 40 are second-order textons, and 41 - 60 are thirdorder textons. The label d is used to denote the single density fea-7.2 Classification AUC scores for the label-independent higher-order texton method for texture alone, density alone and the combination of texture and density according to the augmented method, the reselected method and the recalculated method. All the values have the same meaning as explained in Table 7.1. 7.3 Classification AUC scores for the label-dependent higher-order texton method for texture alone, density alone and the combination of texture and density according to the augmented method, the reselected method and the recalculated method. Values are the 5-fold cross validation averages  $\pm$  SD. *n* denotes the number of optimal features which were obtained by exhaustive search feature selection. The index set for the texture features comprising the optimal set of *n* features is shown underneath. Indices 1-20 are first-order textons, 21 - 40 are second-order textons, and 41 - 60 are third-order textons. The label d is used to denote the single density feature. . . 112 7.4 Classification AUC scores for the label-independent higher-order texton method for texture alone, density alone and the combination of texture and density according to the augmented method, the reselected method and the recalculated method. All the values have the 8.1 Illustration of the structure of the BSSA data set. *n* is the number of
  - images in each experimental group for every time period. . . . . . 117

8.2	Testing AUC scores for DDSM textons applied to BSSA data using 5-fold cross validation.	119
8.3	Testing AUC scores for BSSA textons without BI-RADS assignments using 5-fold cross validation.	119
8.4	Illustration of 100 current ipsilateral high risk images, 100 current contralateral high risk images and 100 current low risk images from the BSSA data set plus 100 contralateral low risk images from the original mammogram data set obtained from BreastScreen SA used in Section 8.2.3. "Tr" denotes the training group, "V" denotes the	
8.5	validation group and "Te" denotes the testing group	120
8.6	Testing AUC scores for separating ipsilateral and contralateral breasts	121
8.7	without 5-fold cross validation	122
8.8	ing ipsilateral and contralateral breasts using 5-fold cross validation. Testing AUC scores for contralateral high risk vs low risk for sepa- rating ipsilateral and contralateral breasts using 5-fold cross valida-	123
A.1	DDSM data set feature indexing for texture features calculated from higher-order textons generated with the label-dependent and label- independent methods. Table entries are indices to features described	123
A.2	in Chapters 6 and 7	135 135
<b>B</b> .1	Classification performance for the $5 \times 5$ neighborhood method with different classifiers; ensemble <i>k</i> -nearest neighbor classifier, SVM	
B.2	classifier and Fisher classifier	138
B.3	classifier and Fisher classifier. $\dots \dots \dots$	139
	AUC score	141

B.4	Classification performance for higher-order textons using the $7 \times 7$	
	method with different classifiers; ensemble <i>k</i> -nearest neighbor clas-	
	sifier, SVM classifier and Fisher classifier. The rank for (a) and (b) is	
	based on the total accuracy. The rank for (c) is based on the testing	
	AUC score.	142
B.5	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-dependent higher-order textons using 5-fold cross	
	validation and sequential feature selection.	143
B.6	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection.	143
B.7	Detailed risk classification AUC scores for combining 60 texton fea-	
	tures calculated from label-dependent higher-order textons and one	
	density feature through the augmented feature set method using 5-	
	fold cross validation and sequential feature selection.	143
B.8	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-independent higher-order textons and	
	one density feature through the augmented feature set method using	
	5-fold cross validation and sequential feature selection	144
B.9	Detailed risk classification AUC scores for combining 60 texton fea-	
	tures calculated from label-dependent higher-order textons and one	
	density feature through the reselected feature set method using 5-	
	fold cross validation and sequential feature selection	144
<b>B</b> .10	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-independent higher-order textons and	
	one density feature through the reselected feature set method using	
	5-fold cross validation and sequential feature selection	144
B.11	Detailed risk classification AUC scores for combined 60 texton den-	
	sity features calculated from label-dependent higher-order textons	
	through the recalculated feature set method using 5-fold cross vali-	
	dation and sequential feature selection.	145
B.12	Detailed risk classification AUC scores for combined 60 texton den-	
	sity features calculated from label-independent higher-order textons	
	through the recalculated feature set method using 5-fold cross vali-	
	dation and sequential feature selection.	145
B.13	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-dependent higher-order textons using 5-fold cross	
	validation and exhaustive search feature selection	145

<b>B</b> .14	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and exhaustive search feature selection.	145
B.15	Detailed risk classification AUC scores for combining 60 texton fea-	
	tures calculated from label-dependent higher-order textons and one	
	density feature through the augmented feature set method using 5-	
	fold cross validation and exhaustive search feature selection	146
B.16	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-independent higher-order textons and	
	one density feature through the augmented feature set method using	
	5-fold cross validation and exhaustive search feature selection	146
B.17	Detailed risk classification AUC scores for combining 60 texton fea-	
	tures calculated from label-dependent higher-order textons and one	
	density feature through the reselected feature set method using 5-	
	fold cross validation and exhaustive search feature selection	146
<b>B</b> .18	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-independent higher-order textons and	
	one density feature through the reselected feature set method using	
	5-fold cross validation and exhaustive search feature selection	146
B.19	Detailed risk classification AUC scores for combined 60 texton den-	
	sity features calculated from label-dependent higher-order textons	
	through 5-fold cross validation and exhaustive search feature selec-	
	tion	147
B.20	Detailed risk classification AUC scores for combined 60 texton den-	
	sity features calculated from label-independent higher-order textons	
	through 5-fold cross validation and exhaustive search feature selec-	
	tion	147
B.21	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-dependent higher-order textons using hold-out val-	
	idation and sequential feature selection.	147
B.22	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons using hold-out	
	validation and sequential feature selection.	148
B.23	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-dependent higher-order textons and	
	one density feature through the augmented feature set method using	
	hold-out validation and sequential feature selection.	148

B.24	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-independent higher-order textons and	
	one density feature through the augmented feature set method using	
	hold-out validation and sequential feature selection.	148
B.25	Detailed risk classification AUC scores for combining 60 texton fea-	
	tures calculated from label-dependent higher-order textons and one	
	density feature through the reselected feature set method using hold-	
	out validation and sequential feature selection.	149
B.26	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-independent higher-order textons and	
	one density feature through the reselected feature set method using	
	hold-out validation and sequential feature selection.	149
B.27	Detailed risk classification AUC scores for combined 60 texton den-	
	sity features calculated from label-dependent higher-order textons	
	through the recalculated feature set method using hold-out valida-	
	tion and sequential feature selection.	149
B.28	Detailed risk classification AUC scores for combined 60 texton den-	
	sity features calculated from label-independent higher-order textons	
	through the recalculated feature set method using hold-out valida-	
	tion and sequential feature selection.	150
B.29	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-dependent higher-order textons using hold-out val-	
	idation and exhaustive search feature selection.	150
B.30	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons using hold-out	
	validation and exhaustive search feature selection.	150
<b>B.3</b> 1	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-dependent higher-order textons and	
	one density feature through the augmented feature set method using	
	hold-out validation and exhaustive search feature selection	151
B.32	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-independent higher-order textons and	
	one density feature through the augmented feature set method using	
	hold-out validation and exhaustive search feature selection.	151
B.33	Detailed risk classification AUC scores for combining 60 texton fea-	
	tures calculated from label-dependent higher-order textons and one	
	density feature through the reselected feature set method using hold-	
	out validation and exhaustive search feature selection.	151

B.34	Detailed risk classification AUC scores for combining 60 texton	
	features calculated from label-independent higher-order textons and	
	one density feature through the reselected feature set method using	
	hold-out validation and exhaustive search feature selection	151
B.35	Detailed risk classification AUC scores for combined 60 texton den-	
	sity features calculated from label-dependent higher-order textons	
	through hold-out validation and exhaustive search feature selection.	152
B.36	Detailed risk classification AUC scores for combined 60 texton den-	
	sity features calculated from label-independent higher-order textons	
	through hold-out validation and exhaustive search feature selection.	152
B.37	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection for classifying current ip-	
	silateral high and low risk images.	152
B.38	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection for classifying current	
	contralateral high and low risk images.	153
B.39	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection for classifying previous	
	two year ipsilateral high and low risk images.	153
B.40	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection for classifying previous	
	two year contralateral high and low risk images.	153
<b>B.</b> 41	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection for classifying previous	
	four year ipsilateral high and low risk images	154
B.42	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection for classifying previous	
	four year contralateral high and low risk images.	154
B.43	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous two year ipsi-	
	lateral high and low risk images using 5-fold cross validation and	
	sequential feature selection.	154

B.44 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons generated fr	rom	
current year mammograms for classifying previous two year c	con-	
tralateral high and low risk images using 5-fold cross validation	and	
sequential feature selection.		155
B.45 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons generated from	rom	
current year mammograms for classifying previous four year i	psi-	
lateral high and low risk images using 5-fold cross validation	and	
sequential feature selection		155
B.46 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons generated fr	rom	
current year mammograms for classifying previous four year c	con-	
tralateral high and low risk images using 5-fold cross validation	and	
sequential feature selection		155
B.47 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons using 5-	fold	
cross validation and exhaustive search feature selection for cla	ıssi-	
fying current ipsilateral high and low risk images.		156
B.48 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons using 5-	fold	
cross validation and exhaustive search feature selection for cla	ıssi-	
fying current contralateral high and low risk images		156
B.49 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons using 5-	fold	
cross validation and exhaustive search feature selection for cla	ıssi-	
fying previous two year ipsilateral high and low risk images		156
B.50 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons using 5-	fold	
cross validation and exhaustive search feature selection for cla	ıssi-	
fying previous two year contralateral high and low risk images.		156
B.51 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons using 5-	fold	
cross validation and exhaustive search feature selection for cla	ıssi-	
fying previous four year ipsilateral high and low risk images.		157
B.52 Detailed risk classification AUC scores for 60 texton features	cal-	
culated from label-independent higher-order textons using 5-	fold	
cross validation and exhaustive search feature selection for cla	ıssi-	
fying previous four year contralateral high and low risk images.		157

B.53	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous two year ipsi-	
	lateral high and low risk images using 5-fold cross validation and	
	exhaustive search feature selection.	157
B.54	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous two year con-	
	tralateral high and low risk images using 5-fold cross validation and	
	exhaustive search feature selection.	157
B.55	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous four year ipsi-	
	lateral high and low risk images using 5-fold cross validation and	
	exhaustive search feature selection.	158
B.56	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous four year con-	
	tralateral high and low risk images using 5-fold cross validation and	
	exhaustive search feature selection.	158
B.57	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons using hold-out	
	validation and sequential feature selection for classifying current ip-	
	silateral high and low risk images	159
B.58	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons using hold-out	
	validation and sequential feature selection for classifying current	
	contralateral high and low risk images.	159
B.59	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons using hold-out	
	validation and sequential feature selection for classifying previous	
	two year ipsilateral high and low risk images	159
B.60	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons using hold-out	
	validation and sequential feature selection for classifying previous	
	two year contralateral high and low risk images.	160

<b>B.6</b> 1	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection for classifying previous	
	four year ipsilateral high and low risk images	160
B.62	Detailed risk classification AUC scores for 60 texton features calcu-	
	lated from label-independent higher-order textons using 5-fold cross	
	validation and sequential feature selection for classifying previous	
	four year contralateral high and low risk images.	160
B.63	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous two year ipsilat-	
	eral high and low risk images using hold-out validation and sequen-	
	tial feature selection.	161
B.64	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous two year con-	
	tralateral high and low risk images using hold-out validation and	
	sequential feature selection.	161
B.65	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous four year ipsilat-	
	eral high and low risk images using hold-out validation and sequen-	
	tial feature selection.	161
B.66	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons generated from	
	current year mammograms for classifying previous four year con-	
	tralateral high and low risk images using hold-out validation and	
	sequential feature selection.	162
B.67	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons using hold-out	
	validation and exhaustive search feature selection for classifying	
	current ipsilateral high and low risk images	162
B.68	Detailed risk classification AUC scores for 60 texton features cal-	
	culated from label-independent higher-order textons using hold-out	
	validation and exhaustive search feature selection for classifying	
	current contralateral high and low risk images	162

- B.69 Detailed risk classification AUC scores for 60 texton features calculated from label-independent higher-order textons using hold-out validation and exhaustive search feature selection for classifying previous two year ipsilateral high and low risk images. . . . . . . 163
  B.70 Detailed risk classification AUC scores for 60 texton features cal-
- culated from label-independent higher-order textons using hold-out validation and exhaustive search feature selection for classifying previous two year contralateral high and low risk images. . . . . . 163
- B.71 Detailed risk classification AUC scores for 60 texton features calculated from label-independent higher-order textons using hold-out validation and exhaustive search feature selection for classifying previous four year ipsilateral high and low risk images. . . . . . . 163
- B.72 Detailed risk classification AUC scores for 60 texton features calculated from label-independent higher-order textons using hold-out validation and exhaustive search feature selection for classifying previous four year contralateral high and low risk images. . . . . 163

- B.75 Detailed risk classification AUC scores for 60 texton features calculated from label-independent higher-order textons generated from current year mammograms for classifying previous four year ipsilateral high and low risk images using hold-out validation and exhaustive search feature selection.
  B.76 Detailed risk classification AUC scores for 60 texton features calculated rest classification AUC scores for 60 texton features calculated rest classification AUC scores for 60 texton features calculated rest classification AUC scores for 60 texton features calculated rest classification AUC scores for 60 texton features calculated rest classification AUC scores for 60 texton features calculated rest classification AUC scores for 60 texton features calculated rest classification and classification and

### **List of Abbreviations**

- BSSA BreastScreen South Australia
- CC craniocaudal (top) view of the breast
- DDSM Digital Database of Screening Mammograms
- ER Estrogen-Receptor
- FNF false negative fraction
- FPF false positive fraction
- MLO ---- mediolateral oblique (side) view of the breast
- MR8 Maximum Response 8 filter bank
- ROC the recever operating characteristic
- ROIs regions of interest
- SCC six-category classification
- SD Standard deviation
- TNF true negative fraction
- TPF true positive fraction

### Summary

Breast cancer is one of the most common cancers among women and early detection plays an important role in reducing the mortality and morbidity due to breast cancer. Importantly, early breast cancer detection is facilitated by accurate breast cancer risk assessment. This thesis aims to develop computer methods for analyzing tissue texture in screening mammograms in order to assess the risk of breast cancer.

According to the literature, the breast density is a strong indicator of breast cancer risk and is independent of non-mammographic risk factors (age, race, family history, etc.). In addition, texture from screening mammograms is also considered to play an important role in predicting breast cancer risk. However, the contribution of texture alone to breast cancer risk is unclear and the role of texture for assessing breast cancer risk over time is also unknown. The focus of this thesis is on studying the role of texture, independent of density, in breast cancer risk assessment.

In this thesis, the emphasis is on characterizing texture through the use of textons. Textons can be described as ubiquitous local texture patterns. The distribution of conventional textons (referred to as first-order textons in this thesis) has been shown to characterize texture in visual images and has been successful in tasks such as separating regions corresponding to grass from regions representing trees or animals. An important contribution of this thesis is the introduction of higher-order textons. The notion of higher-order textons is to extend the power of the first-order textons. Higher-order textons allow quantitative analysis of commonly occurring patterns of patterns, offering a mechanism for understanding more complex texture structure in images. In this thesis, textons and higher-order textons are used to distinguish mammograms from women having a high risk of breast cancer from women having a low risk of breast cancer.

A number of experiments were conducted to determine the best implementation of textons and higher-order textons for breast cancer risk assessment. Results indicate that texture analysis based on higher-order textons predicts risk at least as well as any method currently available for estimating breast cancer risk from mammograms. Risk of breast cancer can be measured using texture at least four years prior to the cancer becoming apparent mammographically.

In addition, a number of discoveries were made in the course of the study. Tex-

ture features from CC view mammograms (top view) perform better than texture features from MLO view mammograms (side view). Better risk assessment is obtained by measuring texture over the full breast than any particular local region of the breast. Texture features calculated from  $3 \times 3$  local neighborhoods perform as good or better than texture features based on larger patches. Texture information relevant to breast cancer risk is more pronounced in the breast in which cancer eventually occurs than in the breast without known cancer of the same woman. These discoveries have potential impact on the fields of image analysis and computer-aided mammography and so form natural seeds for future work.

### **Publications arising from the Study**

### **Referred Conference Paper**

[1] Xi-Zhao Li, Simon Williams, and Murk J. Bottema. Intensity independent texture analysis in screening mammograms. In *11th International Workshop on Breast Imaging, IWDW2012, Philadelphia, PA, USA*, pages 474-481, July 2012.

[2] Xi-Zhao Li, Simon Williams, Gobert Lee, and Min Deng. Computer-aided mammography classification of malignant mass regions and normal regions based on novel texton features. In 12th International Conference on Control, Automation, Robotics and Vision, Guangzhou, China, ICARCV2012, pages 1431-1436, December 2012.

[3] Xi-Zhao Li, Simon Williams, Peter Downey and Murk J. Bottema. Temporal breast cancer risk assessment based on higher-order textons. In *12th International Workshop on Breast Imaging, IWDW2014, Gifu, Japan, pages 565-572, June-July 2014.* 

### **Referred Journal Paper**

[4] Xi-Zhao Li, Simon Williams and Murk J. Bottema. Background intensity independent texture features for assessing breast cancer risk in screening mammograms. *Pattern Recognition Letters*, 34(9):1053-1062, Feb 2013.

[5] Xi-Zhao Li, Simon Williams and Murk J. Bottema. Texture and region dependent breast cancer risk assessment from screening mammograms. *Pattern Recognition Letters*, 36(15):117-124, Jan 2014.

[6] Xi-Zhao Li, Simon Williams and Murk J. Bottema. Constructing and applying higher order textons: Estimating breast cancer risk. *Pattern Recognition*, 47(3):1375-1382, Mar 2014.

#### xxviii

### Declaration

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Xi-Zhao Li, Candidate

Murk J. Bottema, Principal Supervisor Simon Williams, Co-supervisor

### Acknowledgements

I would like to thank my supervisor, A/Prof. Murk J. Bottema for his support and encouragement throughout my PhD study. Importantly, he helped me improve my research skills in medical image analysis, academic writing and mathematical theories for my project. Specifically, I really thank him for giving me the opportunity to study in Flinders University.

I would like to also thank my co-supervisor, Dr. Simon Williams for his guidance and supervision throughout my PhD study. Specifically, he provided me great help in using Lyx for academic writing and opportunity for practicing teaching.

I thank Dr. Gobert Lee for her support in academic fundamental knowledge, suggestions for my research and guidance in using university resources for doing research. Special thanks to Dr. Mariusz Bajger for his technical help; Dr. Ray Booth and A/Prof. Alan Branford for giving me the opportunity of doing some mathematics and statistic related part-time jobs in the school. A special thank to Dr. Shu-Chuan Chu for her support in my study as a friend.

Special thanks to Dr. Adham Atyabi for his help in using the super computer for running my time consuming programs. Particularly, I thank Dr. Adham Atyabi for all his precious suggestions of doing research.

I would also like to thank BreastScreen South Australia (BSSA) for providing mammogram images for my final stage research.

Gratefully, I thank China Scholarship Council (CSC) and Flinders University for all their financial support for my whole study.

Finally, I thank all my family for their great support and love all the way through.

#### xxxii