THE TRUE NATURE OF
ATYPICAL BREAST CYTOLOGY

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Declaration

Statement of Originality
The thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to the final version of my thesis being made available worldwide when deposited in the University’s Digital Repository subject to the provisions of the Copyright Act 1968.

Thesis by Publication
I hereby certify that this thesis is in the form of a series of papers. I have included as part of the thesis a written statement from each co-author, endorsed in writing by the Faculty Assistant Dean (Research Training), attesting to my contribution to any jointly authored papers.

Julie Weigner
January 2018
Dedication

To my cherished family; Rudi, Matthew, Kirra, Nick, Margaret and Joseph for lifelong love and support.
Acknowledgements

This project began as a means of self-education to improve my professional knowledge and a desire to assist in adding to the quality of an FNA service in the local community. In the very beginning, little did I realise the full impact of this undertaking. As the project grew and developed, many more people were needed to bring this project to fruition.

Fundamental to this research project were my supervisors, Stephen Braye and Ibrahim Zardawi. Stephen’s extensive and valuable knowledge was freely given and helped steer the project in a forward direction. His encouragement, patience and intuition was always present. This was complemented by Ibrahim whose boundless enthusiasm, moral support and academic input was immeasurable. His strength of conviction and persistence has been paramount to seeing this project to completion. Patrick McElduff came on board as a supervisor after the confirmation process for Master’s degree. Without Patrick’s contribution to the statistical analyses, the project would not be as robust as it currently is. Patrick’s endless patience and creative thinking has led to some interesting paths not perceived by our medically biased minds. I am truly grateful and privileged to have such quality supervisors and I sincerely thank them all.

This project was mostly conducted within the cytology laboratory at Pathology North Hunter. Without the support of Pathology North, I would not have been able to complete this project. In particular, I’d like to thank the cytology staff. The manager, Sharon Ling has provided ongoing moral support and access to laboratory resources. The scientific staff have contributed their value time, skills and expertise, and the technical staff have provided encouragement and logistic support. To work with these people every day is a pleasure.

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experience in the field of breast cancer. I am very fortunate to be part of this medical community.

Throughout this project, I have been indebted to Dr Ricardo Vilain who has inadvertently become a surrogate mentor to me, having walked his own PhD journey recently. All the small things which challenge a mature student returning to study after a significant break were made so much easier with Ric’s help and academic wisdom.

Finally to my family whose faith in me never waned. For the duration of this project, my children Matthew, Kirra and Nick have grown and developed into capable young adults. They have shared this journey with me and now embark on their own study challenges as they forge their own careers. I recognise determination, resilience and hard work traits abound in their attitude and know they will be successful in their future paths. To my parents who value education and who have always supported me in whatever venture I embarked upon. They took on some of the burdens of family life in times when I could not fulfil my family responsibilities and I am so grateful. Although my father is not here to see me complete this project, I know he would have been very proud. Finally, to my husband, Rudi who has underpinned this project from the beginning. He has endured all the low points but still managed to put on a positive slant and keep me afloat in overwhelming times. Without his love and dedication I could not have completed this project.
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2. **The Microscopic Complexities of C3 in Breast Cytology.**

3. **The Conundrum of Papillary Breast Lesions within the C3 Category.**

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6. **The legitimacy of the atypical (C3) breast cytology category.**
   Invited lead article.

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*Julie Weigner*
Conference Proceedings

1. Atypical Breast Cytology
   Oral Presentation
   The Breast and Endocrine Centre Education Meeting
   Gateshead, Newcastle, NSW 2010

2. The True Nature of Atypical Breast Cytology
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3. Atypical Breast Cytology
   Oral presentation
   44th Annual Scientific and Business Meeting, Darwin Oct 2014

4. The Validity of Atypical breast Cytology
   Award winning Poster
   44th Annual Scientific and Business Meeting, Darwin Oct 2014

5. Should Breast Papillary Lesions be Automatically Placed into the Atypical (C3)
   Reporting Category?
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6. Can atypia in breast fine needle aspiration be tamed?
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<td>Atypical ductal hyperplasia</td>
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<tr>
<td>ALH</td>
<td>Atypical lobular hyperplasia</td>
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<tr>
<td>ASC</td>
<td>Australian Society of Cytology</td>
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<tr>
<td>AUC</td>
<td>Area under Curve</td>
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<tr>
<td>BI-RAD</td>
<td>Breast Imaging Reporting &amp; Data System</td>
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<td>BS</td>
<td>BreastScreen</td>
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<td>C1</td>
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<td>Fibrocystic change</td>
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<td>FNA</td>
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<td>Laboratory information system</td>
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<td>Nuclear to cytoplasmic ratio</td>
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<td>NHSBSP</td>
<td>National Health System Breast Screen Program</td>
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<td>PBD</td>
<td>Proliferative benign disease</td>
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<td>PT</td>
<td>Phyllodes tumour</td>
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<tr>
<td>QD</td>
<td>Quik Diff</td>
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<td>Red blood cell</td>
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<td>RCPA</td>
<td>The Royal College of Pathologists of Australasia</td>
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<tr>
<td>ROC</td>
<td>Receiver operating curve</td>
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<td>Terminal ductal lobular unit</td>
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Abstract

Breast cancer is the most prevalent cancer in women in the western world including Australia. Early detection and accurate diagnosis of new breast lesions is essential for appropriate medical management. Fine needle aspiration (FNA) is a cytological investigative tool commonly used to provide the initial pathological diagnosis of breast lesions. An atypical cytology report (C3) is an ambiguous or equivocal result. This uncertainty creates a dilemma and a more invasive investigative procedure such as core biopsy or incisional biopsy may be required, which comes at greater cost and anxiety to the patient.

The aims of this project were to understand the true nature of C3, to determine the underlying causes of C3 and to devise a strategic approach to minimise its use without compromising the other cytological categories. The practical aims were to create a greater understanding of the issue and to produce a collective uniform approach to reporting atypical breast cytology cases thereby refining its use.

The results of a blind rescreen of 256 consecutive C3 cases were statistically analysed. From these results, a cytomorphological approach to assess the risk of malignancy was developed and tested against a validation set of 230 subsequent C3 cases. Various strategies have been developed to reduce the incidence of the C3 category. Extrinsic factors can be easily reduced by greater involvement by cytology staff in the FNA procedure. Intrinsic factors can be understood and considered when allocating cases into C3. Specific diagnoses, such as papillary neoplasm can direct more appropriate definitive management. The cytologists in our institution have gained greater awareness of the atypical category by actively participating in the project and by having access to teaching resources and examples. The benefits manifest as financial, medical and social enhancements. It is hoped that some of these approaches will be taken up by other institutions in Australia and internationally.