# Contributions to the Early Diagnosis and Modern Management of Breast Cancer

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For the University of Adelaide

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# Summary of the Application for the Award of Doctor of Medicine

I hereby submit a body of original research for consideration of the award of Doctor of Medicine from the University of Adelaide. This is a collection of published original research that has made substantial contributions to the modern diagnosis and management of breast cancer. The publications have been presented in three clusters, each of which represents one facet of the modern approach to the diagnosis and management of breast cancer.

The first section presents my publications on the theme of population based mammographic screening for the early detection of breast cancer. Broadly, the research focus in these publications is on the evaluation of existing methods of assessment of screen-detected breast lesions in order to improve diagnostic accuracy and limit the morbidity associated with mammographic screening. The clinical value of these contributions has been demonstrated independently since this body of work has informed many of the algorithms and protocols used by the South Australian breast cancer screening program. In addition, the protocols have been adopted for use outside of the screening setting into the wider diagnostic arena. The clinical endorsement of my research contributions is a significant acknowledgement of their practical value.

The middle group of publications describe my contributions towards the evolving role of sentinel node biopsy as an alternative to axillary clearance for the staging of breast cancer. This area is of particular cogent to our setting, since a large proportion of screen-detected breast cancers, approximately 80%, are node negative. Thus, avoidance of the morbidity of axillary clearance while still achieving accurate axillary staging is of enormous appeal to our patients.

My pioneering work in devising and evaluating protocols for the pathologic examination of sentinel nodes has informed the recommendations of the NHMRC sponsored SNAC (Sentinel Node versus Axillary Clearance) randomised trial. Consequently, these protocols have been used extensively and even outside of the trial setting, most pathology laboratories utilise similar assessment protocols as was recommended in SNAC. Furthermore, the United Kingdom's recommendations for the pathology examination of sentinel nodes have drawn on our research.

After validating the concept of SNs in breast cancer, many of the clinically important questions emerging in this field have been addressed by our team. For example, my work on intra-operative imprint cytology was a conclusive demonstration of the value and limitations of this technique for one stage axillary surgery. In the light of our findings intra-operative assessment of sentinel nodes has been expanded to many centres and is endorsed by the SNAC trial.

In the third section of this thesis, my contributions to the rapidly evolving field of molecular and genetics of breast cancer are highlighted. Through the Australian HER2 Advisory Board, we have led the evaluation and roll out of alternative platforms for HER2 testing and in developing algorithms for the efficient use of resources. We have devised national testing algorithms in both settings of metastatic and early breast cancer. These algorithms have since been utilised by the international HER2 testing bodies. In a further bold initiative, our group pioneered the move to the national adoption of bright field In situ hybridization as the first line testing platform for all newly diagnosed breast cancers throughout Australia. This ambitious undertaking entailed design and implementation of a nation-wide program of training, certification, quality assurance and evaluation. It has been deployed successfully and under my leadership, our laboratory was one of only four laboratories in Australia to commence this test in October 2006.

Similarly, in the area of the genetics of breast cancer, my interest in this field and membership of the pathology subcommittee of KCONFAB has provided opportunities to contribute to significant new knowledge that illustrate the role of pathology in identification of mutation associated breast cancers. Under my leadership, our multi-centre studies have provided cogent arguments in favour of the inclusion of the histopathologic and immunophenotypic characteristics of breast cancers in the triage of patients for genetic testing. These results were published in pre-eminent pathology journals and have been referred to at major scientific conferences. Plans are afoot for the future extensions of this work.

I am committed to utilising my expertise for the provision of high quality diagnostic services as part of a multi-disciplinary team involved in the treatment of women with breast diseases. I believe an evidence-based approach is central to achieving continuous improvements in these efforts. I am persuaded that there is substantial evidence demonstrating the value of population based mammographic screening in interrupting the natural history of breast cancer and reducing mortality from this disease. I am grateful to have the opportunity to contribute to the provision of this care.