



The RACS SNACTrial

***Sentinel Lymph Node Biopsy
Versus
Axillary Clearance
in Operable Breast Cancer***

Dr Neil R Wetzig May 2005

The RACS SNAC Trial

PARTICIPANTS

RACS Section of Breast Surgery

- **32 Centres Australia & New Zealand**

**A Multicentre Randomised
Controlled Trial**

NHMRC Clinical Trials Centre

- *Sydney, NSW*














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PARTICIPANTS

- Royal Adelaide Hospital (SA)
- Westmead Hospital (NSW)
- Royal Melbourne Hospital (Vic)
- North Shore Hospital (NZ)
- Nambour Hospital (Qld)
- Waikato Hospital (NZ)
- Princess Alexandra Hospital (Qld)
- Mater Hospitals (Qld)
- Wesley Hospital (Qld)
- St Andrews Hospital (SA)
- Sir Charles Gardiner Hospital (WA)
- Coff Harbour Based Hospital
- Baringa Private Hospital (NSW)
- Concord Hospital (NSW)
- Palmerston North Hospital (NZ)
- Strathfield Private Hospital (NSW)
- Royal Women's Hospital (Vic)
- Western Breast Clinic (SA)
- St Vincent's Hospital (NSW)
- Queen Elizabeth Hospital (SA)
- St Vincent's Mater Hospital (NSW)
- Middlemore Hospital (NZ)
- Nepean Hospital (NSW)
- Royal Prince Alfred Hospital (NSW)
- Lismore Base Hospital
- St Vincent's Private Lismore
- Geelong Hospital
- Gold Coast Hospital
- St John of God Hospital Murdoch
- St Vincent's Hospital
- Auckland Hospital

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Management Committee

Study Chair:		<i>A/Prof Grantley Gill</i>
Deputy Study Chair:		<i>Dr Neil Wetzig</i>
CTC: Study Coordinator:		<i>Burcu Cakir</i>
Data Manager		<i>Xanthi Coskinas</i>
		<i>Mr John Collins</i>
Surgeons:		<i>Prof David Gillett</i>
		<i>Dr James Kollias</i>
		<i>Dr Owen Ung</i>
Pathologist:		<i>Dr Michael Bilous</i>
Nuclear Medicine:		<i>A/Prof Roger Uren</i>
Consumer Representatives:		<i>Avis MacAphée (BCNA)</i>
		<i>Leonie Young (ANZ BCTG)</i>
Trial Statistician:		<i>Mr Val Gebski</i>
Clinical Epidemiologist:		<i>Dr Martin Stockler</i>
Clinical Trialist:		<i>Prof John Simes</i>

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AIMS & OBJECTIVES

To determine whether breast cancer outcomes following sentinel node biopsy are equivalent to those following axillary clearance with reduced morbidity

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Inclusion Criteria:

- All women with operable invasive breast cancer < 3cm in diameter (in whom axillary staging is required as part of their treatment)
- Patient Consent

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SCHEMA

ELIGIBILITY:

- Invasive Cancer
- Primary Tumour <3cm
- Clinically Negative Axilla
- Unifocal cancer

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Sentinel Node
Biopsy
(SNB)

SNB
Successful

SNB-

No further
axillary surgery

SNB+

Delayed axillary
surgery

SNB
Unsuccessful

Immediate axillary
clearance

Axillary
Clearance
(AC)

SNB

Immediate axillary
clearance

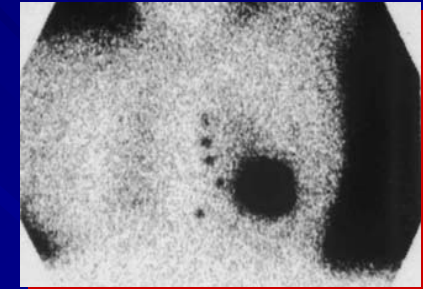


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LYMPHATIC MAPPING - Technique

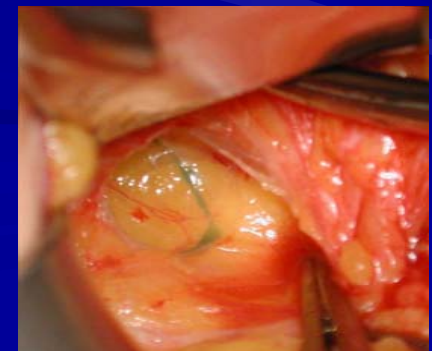
◆ **Combined Method**

- ☞ *Lymphoscintigraphy Preoperatively*
- ☞ *40-80 mbq Tc 99 antimony colloid*
- ☞ *Peritumoral injection with massage*
- ☞ *Patent blue injected in OR*
- ☞ *Gamma Probe*



◆ **Patent Blue Dye alone**

(if nuclear medicine not available)



ACCREDITATION OF CENTRE

- ◆ **Completion of 20 consecutive cases of SNB reviewed by management committee (>90% success)**

- ◆ **SITE VISIT :**
 - ◆ **External review of nuclear medicine facility**
 - ◆ **External review of operative technique**

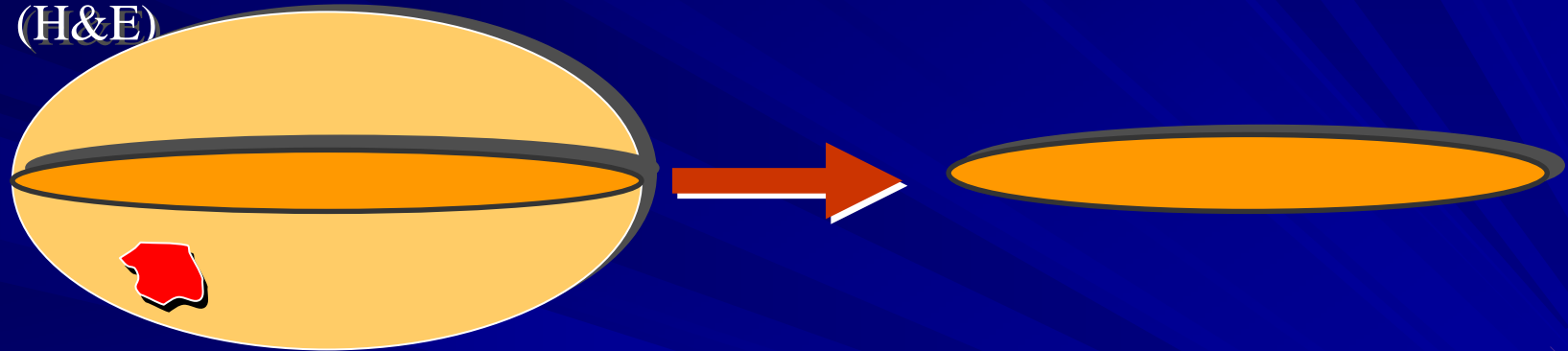
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PATHOLOGICAL ASSESSMENT OF THE SENTINEL NODE

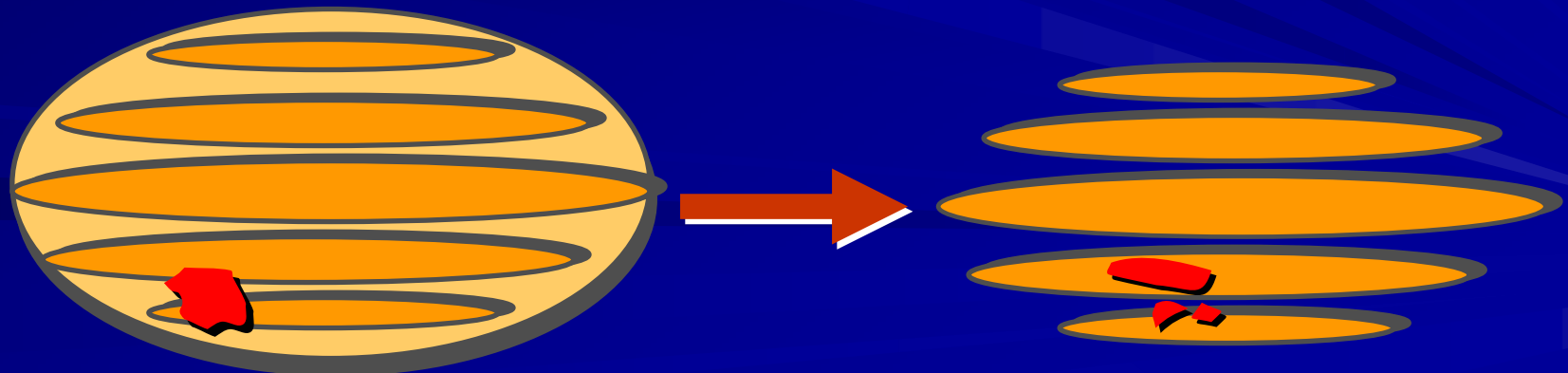
- ◆ ***Sentinel node is sliced into 2mm slices***
- ◆ ***4 step sections from each slice***
- ◆ ***Sections stained for H&E and CAM 5.2***

PATHOLOGICAL ASSESSMENT OF THE SENTINEL NODE

AXILLARY CLEARANCE – single section on each non-sentinel node (H&E)



SENTINEL NODE BIOPSY – multiple sections on SN (H&E and IHC)



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FOLLOW UP & ASSESSMENT

- ◆ ***At 1, 6 and 12 months***
 - ◆ ***Annually thereafter***
-

Endpoints

- ***Disease Status – axillary recurrence and DFS***
- ***Arm volume***
- ***Quality of life (global and arm symptoms)***
 - ***BIBCQ, EORTC, QLQ-C30, QLM-B23***

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MORBIDITY AND QUALITY OF LIFE

Objective Outcomes

- ◆ **Arm swelling and numbness**
 - ◆ **Shoulder movement (goniometer)**
 - ◆ **Seroma rate, infection**
 - ◆ **Hospital stay and number of surgical episodes**
-

Self Assessed

- **Subjective arm symptoms**
- **Quality of Life instruments**
 - **Body Image after Breast Cancer Qu (BIBCQ);**
 - **EORTC Core Quality of Life Qu (QLQ-C30)**
 - **EORTC Breast Module (QLM-B23)**

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Trial Commenced May 2001

- **Stage 1:**
 - 150 Patients to assess Study Procedures
(Optimisation of Outcome Measures) (1 year)

- **Stage 2:**
 - 1100 Patients over 5 year period
(Comparison of treatments)

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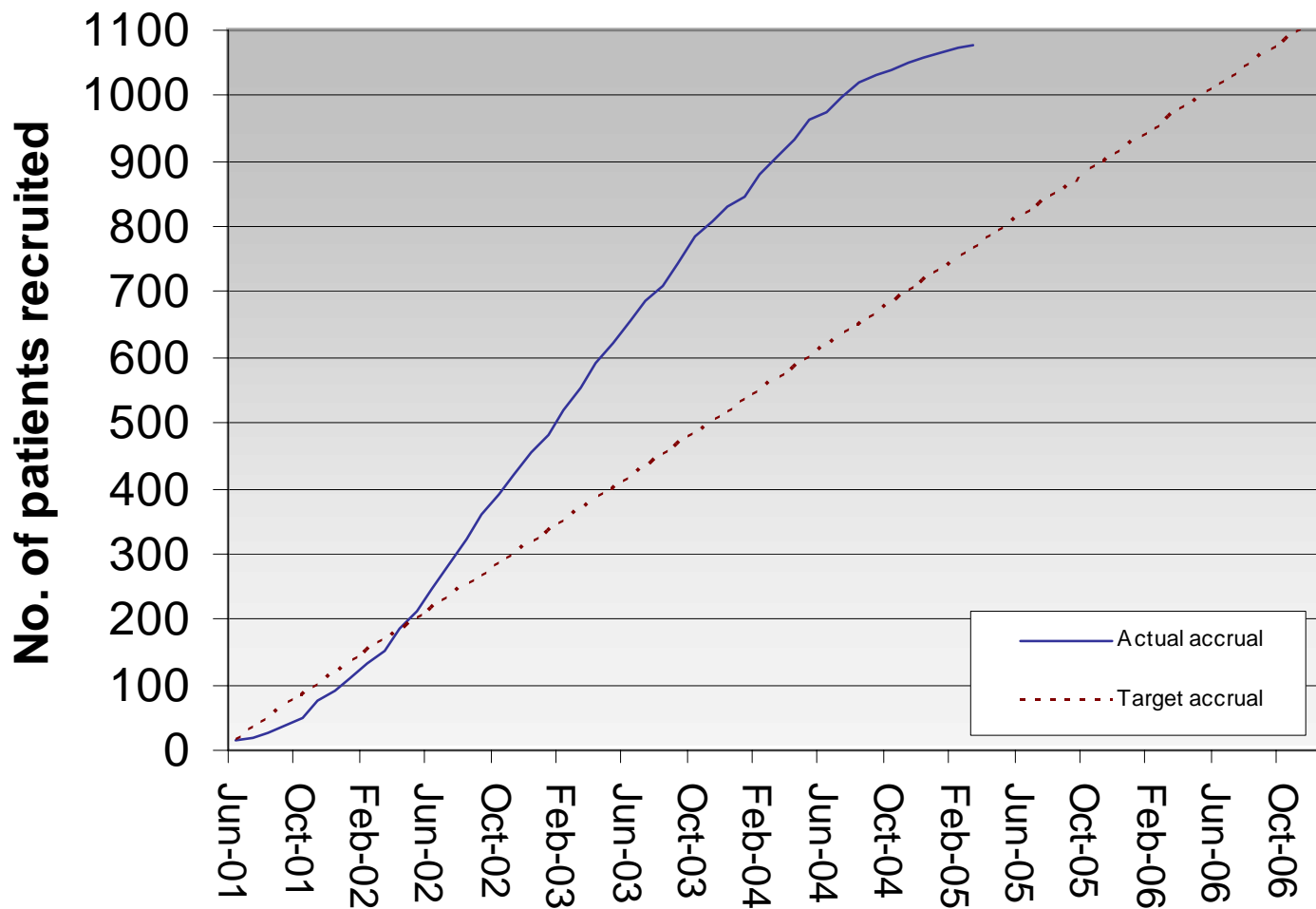
To 18th April 2005:

1080 Patients randomised

**Recruitment Ceased
as of
6th May 2005
Total Accrual 1088**

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SNAC Recruitment



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Recruitment by State

First 150 patients

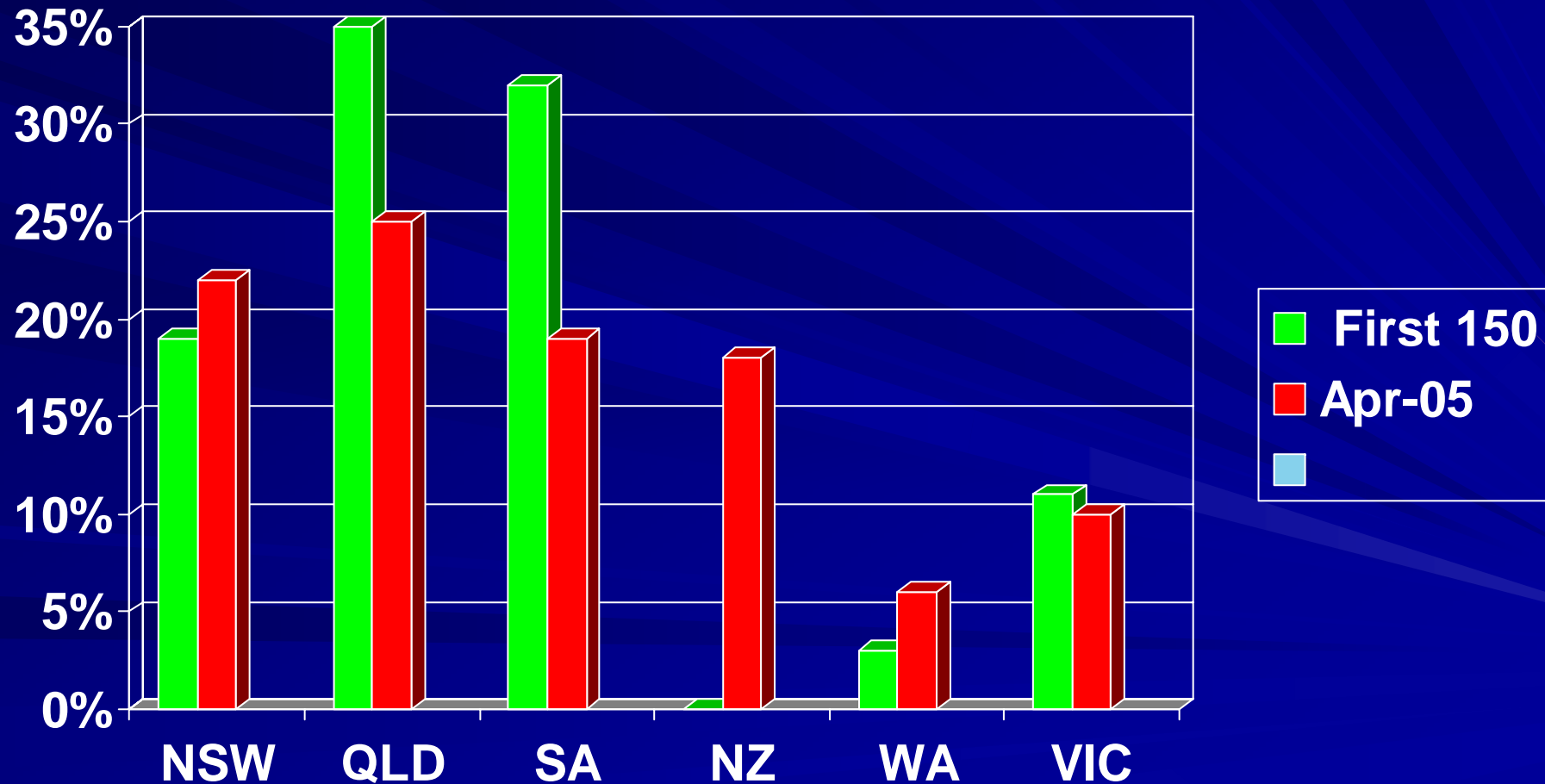
NSW	29	19%
QLD	52	35%
SA	48	32%
VIC	16	11%
WA	5	3%
NZ	0	

Total to 8.4.05

NSW	238	22%
QLD	274	25%
SA	204	19%
VIC	94	10%
WA	70	6%
NZ	199	18%

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Recruitment by State



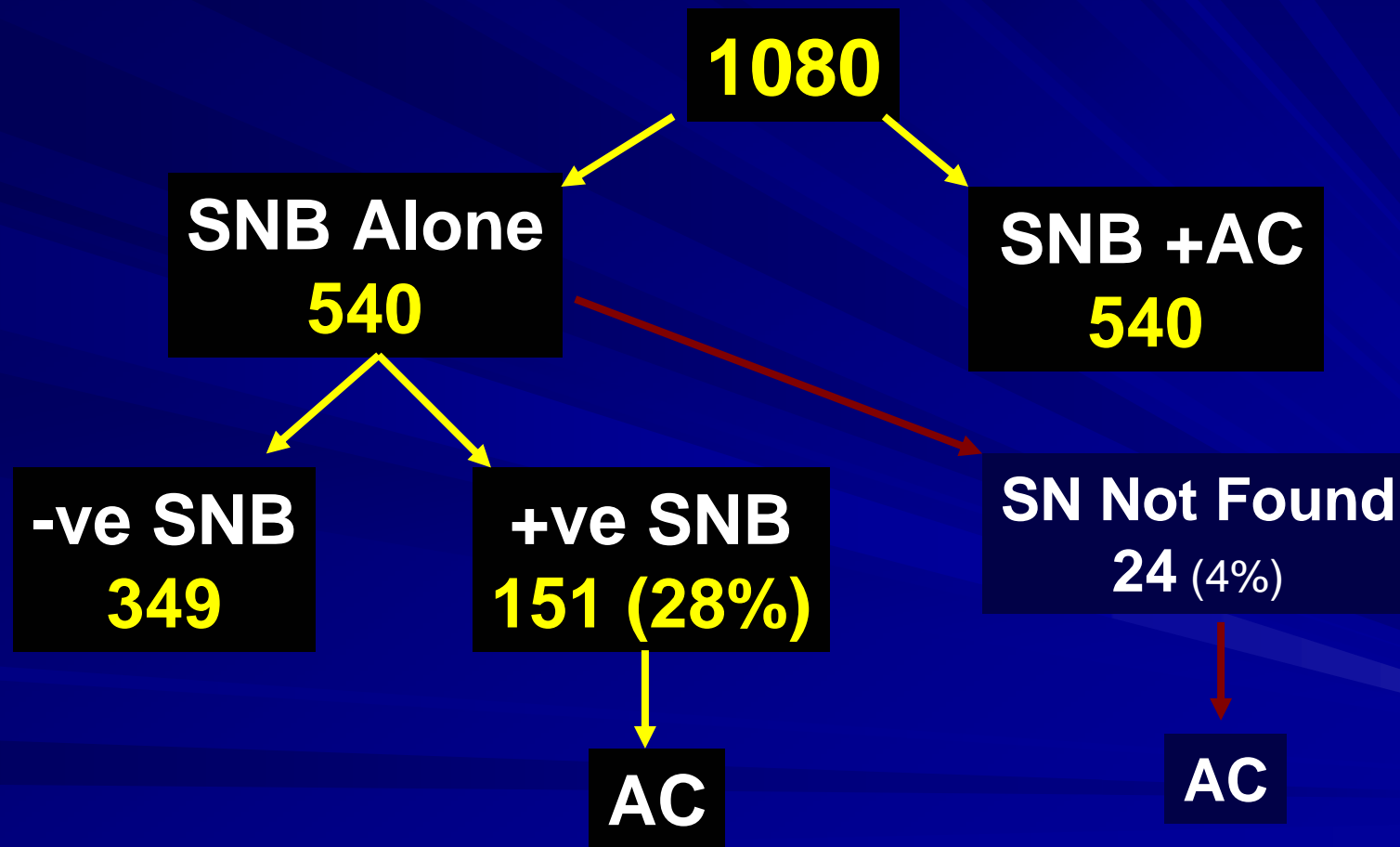
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SUCCESSFUL RECRUITMENT

- ◆ ***A RACS study conducted by surgeons***
- ◆ ***Informed Consent Workshops***
- ◆ ***Regular newsletters for participants***
- ◆ ***Supported by NHMRC, NBCF, DHAC and state cancer councils and other organizations***

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RANDOMISATION



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PROJECT STATISTICS : (N= 1080)

(CRF's)

	Number	Entered	Clean
CRF Retrieval	14894	98%	89%
QOL Retrieval	18695	98%	96%
		% of Patients at each stage of FU	
1 month FU	1070	99%	
6 month FU	1024	95%	
1 year FU	878	81%	
2 year FU	519	48%	
3 year FU	131	12%	

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STUDY VARIABLES

	MEAN \pm SD
◆ <u>Age</u>	58.0yr \pm 10.2
◆ <u>Weight</u>	72.4kg \pm 15.7
◆ <u>Tumour Diameter</u>	16.1mm \pm 9.0

★ *Equally distributed between both arms*

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STUDY VARIABLES★ (N= 974)

	Number	%
● <i>Symptomatic</i>	412	42%
● <i>Screen detected</i>	559	57%
● <i>Palpable</i>	548	56%
● <i>Impalpable</i>	426	44%
<i>Method of Diagnosis</i>		
➤ <i>FNA Cytology</i>	354	36%
➤ <i>Core Biopsy</i>	524	54%
➤ <i>Open Biopsy</i>	92	9.6%



Equally distributed between both arms

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STUDY VARIABLES★ (N= 974)

	Number	%
Tumor Grade		
High	233	25%
Moderate	392	41%
Low	302	32%
Lymphatic Invasion		
No	757	80%
Yes	178	19%
EIC Positive		
No	772	82%
Yes	161	17%

★ Equally distributed between both arms

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STUDY VARIABLES[★] (N=869)

Equally[★]
distributed
between
both arms

Surgery for Primary Tumour

	Number	%
❖ WLE (wide local excision)	622	66%
❖ WLE & Re-excision	138	15%
❖ Mastectomy	47	5%
❖ Completion Mastectomy	62	6%

LYMPHATIC MAPPING & SN DETECTION - Results

	SNB + AC	SNB
• <i>Lymphoscintigraphy Used</i>	90%	90%
• SN Detected Lymphoscintigraphy	86%	84%
• <i>Gamma Probe</i>	90%	90%
• Detected as “Hot” by Gamma Probe	96%	94%
• <i>Blue Dye Used</i>	99%	99%
• Detected by Blue Dye	85%	85%
• <i>Blue Dye only</i>		8.7%

Total Number = 991

SN DETECTION - Results

	SNB + AC	SNB
• <i>SNB Attempted</i>	100%	100%
• SN Identified	99.7%	96%
• <i>SN Removed</i>	99.7%	96%

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SENTINEL LYMPH NODE SITES

<i>Axilla</i>	694	91%
<i>Internal Mammary</i>	46	6%
<i>Intra-mammary</i>	3	2%
<i>Other</i>	5	<1%

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LYMPH NODES

MEAN \pm

❖ *Lymph Nodes in AC specimen 14.6 \pm 7.1*

		Number	%
Number of Positive Nodes in Axillary Clearance	0 -	448	79%
	1 -	50	8.8%
	2 -	28	5.0%
	>3 -	41	6.1%
	N = 567 includes those with positive SN who went on to AC		

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DIAGNOSTIC ACCURACY OF SNB

ALL Patients with SNB + AC

		Nodes in Axilla		
		Positive	Negative	Total
Sentinel Nodes	Positive	49	84	133
	Negative	11	337	348
	Total	60	421	481

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PERFORMANCE STATISTICS :

★ (N= 489)

% of Total Tumour size 19% 54% 20% 7%

Tumour size	All	<1cm	1-2cm	2-3cm	>3cm
◆ Sensitivity	92%	100%	93%	88%	94%
◆ Specificity	100%	100%	100%	100%	100%
◆ False Neg	8%	0%	7%	12%	4%
◆ False Pos	0%	0%	0%	0%	0%
+ve Predictive	100%	100%	100%	100%	100%
-ve Value	96%	100%	97%	92%	90%

★ Control Arm only

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OTHER FACTORS

	SNB + AC	SNB
<i>Operative Duration</i>	1.5 hrs	1.2hrs
<i>Duration Hospital Stay</i>	2.8 days	1.8 days
<i>Duration of Drain</i>	7.1 days	4.2 days
<i>No of Cases per Institut'n</i>	2 (0.2%) - 150 (14.2%)	
<i>No of Cases per Surgeon</i>	1 (0.1%) - 108 (10.2%)	

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CONCLUSIONS

❖ *Rapid recruitment*

Recruitment has now closed

❖ *Accurate performance of SNB across multiple centres*

❖ *Satisfactory compliance with randomised treatments*

❖ *Outcomes for quality of life, arm symptoms and recurrence free survival to be determined*

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FUNDING

Supported by :

- MBF
- DHAC

- WESLEY RESEARCH INSTITUTE
 - ESA INTERNATIONAL
- BREAST CANCER ASSOC of QLD
 - TYCO
 - ASTRA ZENECA

National Breast Cancer Foundation

NHMRC



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