

SURGICAL MANAGEMENT OF AND NEOADJUVANT CHEMOTHERAPY IN BREAST

ADVANCES AND CONTRA

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- Background

DE- ESCALATION BREAST

- Sentinel node biopsy after neoadjuvant chemotherapy
 - ✓ Trials ✓ Feasibility? ✓ Accuracy?
 - ✓ Ways of Improving Accuracy in cN+
- Recommendations for Implementation
- Future Directions
 - Radical Mastectomy

Sim



- Evolved in the last 20 years.

DE-ESCALATION OF AXILLARY

- Sentinel lymph node biopsy (SNB) investigated in the 1990s

NSABP B-32 STUDY

- Randomized >5000 patients
- No significant difference in overall survival



control

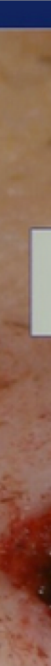
SLN biopsy plus ANC
or SLN biopsy alone

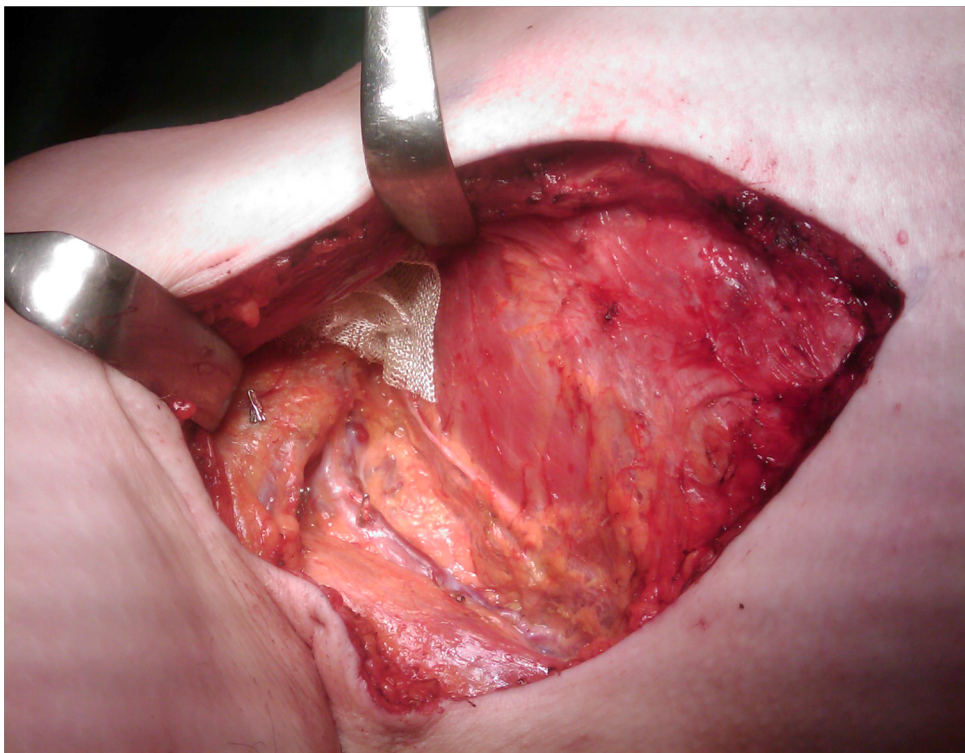
- Reduction in upper limb morbidity at 3 years
- Mean f/u 95.6 months
 - ✓ Shoulder *abduction* deficits
 - ✓ An
 - ✓ Se

SENTINEL NODE BIOPSY

Standard of care for clinically node
negative patients with early breast cancer

KRAG D Lancet Oncol 2010; 11: 927 – 33
Benson JR Lancet Oncol 2010; 11: 908 - 9





- Pro
- Gu
- Pro
- Ass
- Infl

INDICATIONS FOR NEOADJUVANT CH

Established

- Oth

-
- N2 or N3 disease

King T, M

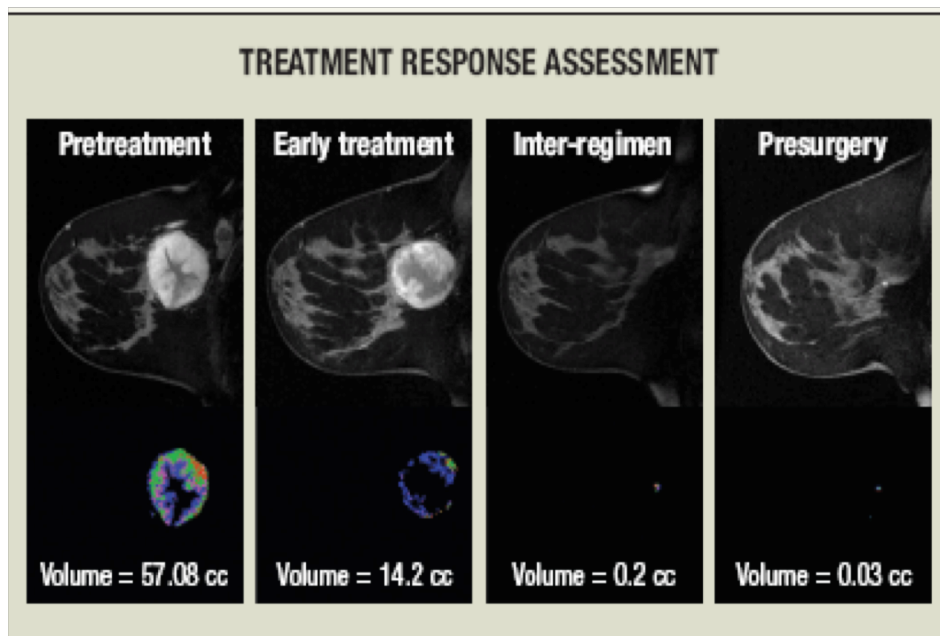
Newer

- Facilitate breast conservation
- **Reducing need for ANC**
- Increases the rate of lumpectomy (10 – 30%)

BENEFITS OF NEOADJUVANT CHE

- Decreases the rate of axillary positivity (40%)
- Achievement of pCR correlates with improved
- Survival outcomes similar to adjuvant chemothe

NEOADJUVANT CHEMOTHERAPY



Incorporat

- **Before** ne

- **After** neo

SNB +/- co

THIS DEBATE IS FAR FROM SETTLED

- SNB post NAC Advantages ✓ Assess ✓
- chemosensitivity of nodal metastases new
- ✓ Downstaging of nodal status avoids ANC ✓
- ✓ Adjust adjuvant chemotherapy if needed rele

THIS DEBATE IS FAR FROM SETTLED

SNB post NAC

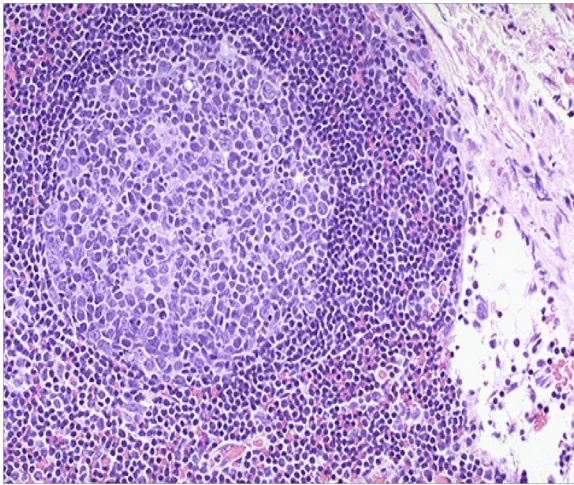
Concerns

- Lower SN identification rate



- Higher false-negative
- Potentially less a

CLINICALLY NODE NEGATIVE cN



- What is the evidence?
- How feasibility and

FEASIBILITY AND ACCURACY OF

	Xing ¹ 2006	Kelly ² 2009	van Deurzen 2009
No. of studies	21	24	27
No. of patients	1273	1799	2148
IR (%)	90	90	91
FNR (%)	12	8	10.5

Identification rate similar with single-agent

False-negative rate similar to upfront

¹Xing Y, Br J Surg, 2006;93:539
²Kelly A, Acad Radiol, 2009;16:551
³Van Deurzen C, Eur J Cancer, 2009;45:3124
⁴Tan V, J Surg Oncol 2011;104:97
⁵Geng C, PLoS One, 2016;11:e0162605

NODE POSITIVITY DECREASES AFTER NAC IN cN0 PAT

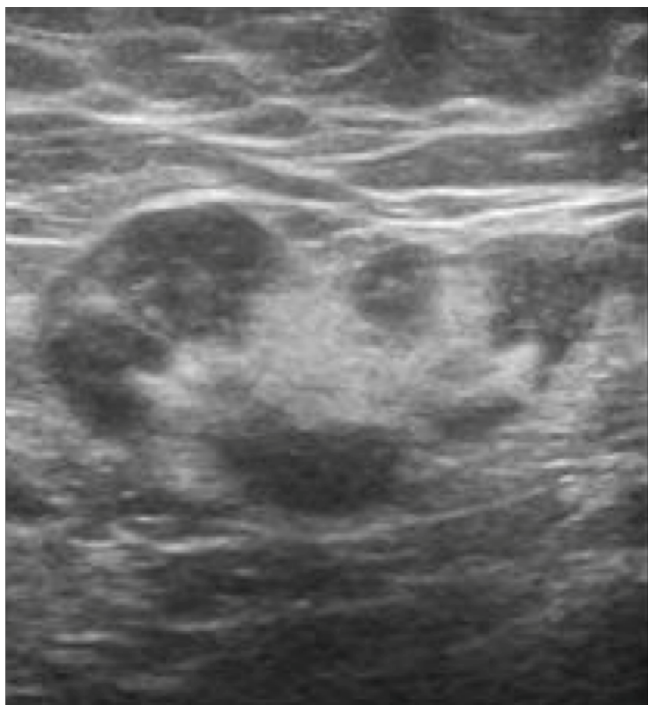
n		
Upfront SNB		
NSABP B-18		1097 48%
	T2	992 37%
	T3	106 51%

RECOMMENDATION FOR PRACTICE

SNB Post NAC Reasonable

- Appears reliable for staging in NAC
- Reduces node positivity and thus avoids ANC
- Avoids additional surgical procedure
- Comparable FNR to upfront surgery
- No increase in axillary LR rates

SNB IN cN+ PATIENTS AFTER NAC



- The Trials
- Feasibility a
- Methods of
- Implementa

TUMOR BIOLOGY - RESPONSE TO NEO

Increasing pCR rates:

- Anthracyclines 10-15%
- Anthracyclines + taxanes 25-30%
- Targeted anti-Her2 therapy:
 - Trastuzumab + chemo 40-50%
 - 2 anti-her2 agents + chemo 50-60%

Pathol
the Ax

Triple Neg



Nodal response rates (cN1 to ypN0):

- Anthracyclines 30%
- Anthracyclines + taxanes 40%
- Anti-Her2 therapy up to 70-75%

SNB FEASIBILITY AND ACCURACY IN

Prospective Multicenter Trials

- ACOSOG Z1071
- FN SNAC
- SENTINA

SNBACCURACY IN cN+ PATIENTS

SNB Accuracy in cN+ Patients: N=1071

	Z1071	FN SN
cTN	cT0 – 4 N1/2	cT0 – 3 N1
SN Identification Rate	92.7%	82.2%
	12.6%	13.4%

METHODS OF DECREASING THE FNR

METHODS OF DECREASING THE FNR

1. Removing more SN
2. Using dual tracer

	Z1071	FN SN
FNR with Single Node	31.5%	18.2%
FNR ≥ 2 SN	12.6%	4.9%
FNR Dual Tracer	10.8%	5.2%

REDUCING FNR IN cN+ PATIENTS

Tee SR BJS 2018; 105: 1541-1552

- Meta-analysis 13 studies
- N = 1921 biopsy proven
- SNB / ANC after NAC

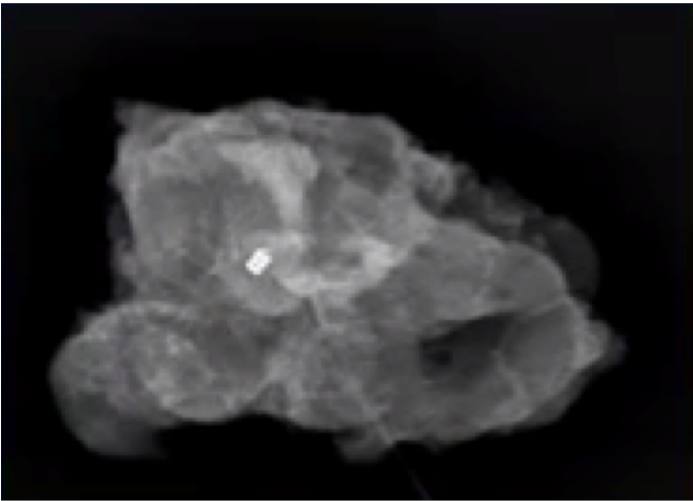
✓ SN Identifi

✓ FNR ≥ 3

✓ FNR with

✓ FNR sing

METHODS OF MARKING POSITIVE



Marking

- Clip
- Tattoo

Localisation

- Iodine

- Other seeds (eg Magseed)
- Ultrasound

TARGETED AXILLARY NODE DIS

Author	N	Technique
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Donker 2015	100	Iodine-125 seed + C
Caudle 2016	85	Iodine-125 seed + S ANC
Siso 2017	35	IOUS clip + SN + ANC
Boughey 2016	107	

ONCOLOGICAL SAFETY

European Inst



- 147 patients cN1/2
- 70 converted to cN
- Median f/u 61 months
- Axillary recurrence

IMPLEMENTING SNB AFTER NA

- Physical Examination
- Axillary Ultrasound
- Core biopsy /FNA

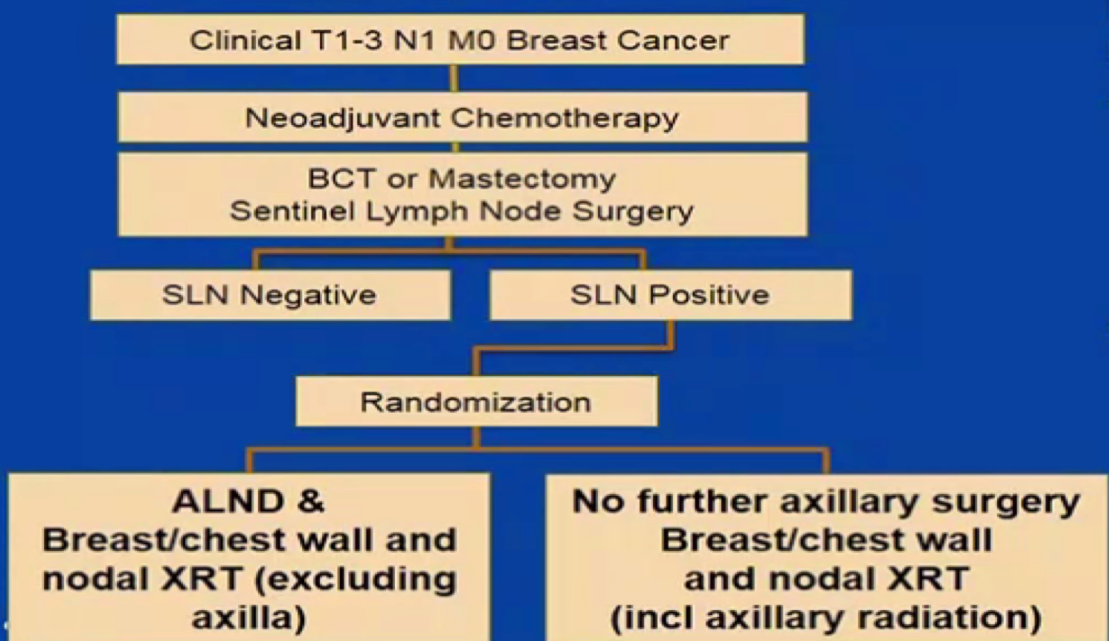
- Neo-Adjuvant Chemotherapy
- Repeat Axillary Ultrasound?
- Sentinel Node Biopsy

IMPLEMENTING SNB AFTER NAC II

- Use dual tracer
- Retrieve more than 2 SN or proceed
- Use TAD if only clip found await pa
- Select favorable tumour biology

FUTURE DIRECTIONS

A011202 - A randomized phase III trial of axillary lymph node dissection to axillary radiation (cT1-3 N1) who have positive sentinel lymph nodes receiving neoadjuvant chemotherapy





SUMMARY

- SNB accurate in cN0 patients
- SNB post NAC in cN+ needs further evaluation
- Need more data on rates of regional recurrence
- ANC remains the standard of care outside clinical trials

How Often Are ≥ 3 SLN

Use of SLNB in cN+ patients as
ALND is appropriate if removal of

Study	n
ACOSOG Z1071	651
SENTINA	592

Tumor size	Tumor size < 2 cm	Tumor size 2-5 cm
T	 T1	 T2
Lymph Nodes N	N0 No lymph node metastasis	N1 Metastasis to ipsilateral, movable, axillary LNs
Metastasis M	M0 No distant metastasis	M1 Distant metastasis

FUTURE DIRECTIONS

SOUND trial (European Institute of Oncology Milan)

SOUND = **S**entinel node versus **O**bservation after A

- Multi-center non-inferiority trial
- Accrual target of **1560** clinically node negative patients
- T1 Tumours
- Normal pre-operative US or negative needle biopsy (FNAC)
- Randomized either *sentinel lymph node biopsy (+/-ALND**)* or