



**GBCC2018**  
Global Breast Cancer Conference 2018

# **No Association of Positive Superficial and/or Deep Margins with Local Recurrence in Invasive Breast Cancer Treated with Breast-Conserving Surgery**

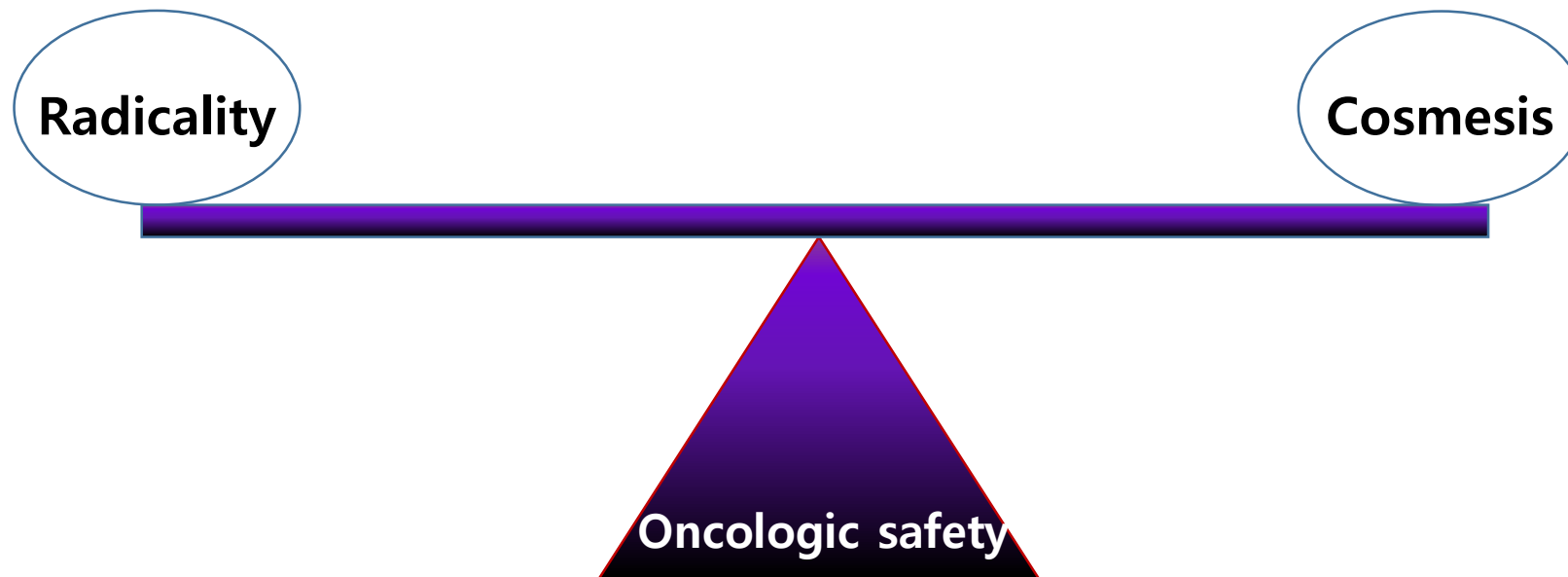
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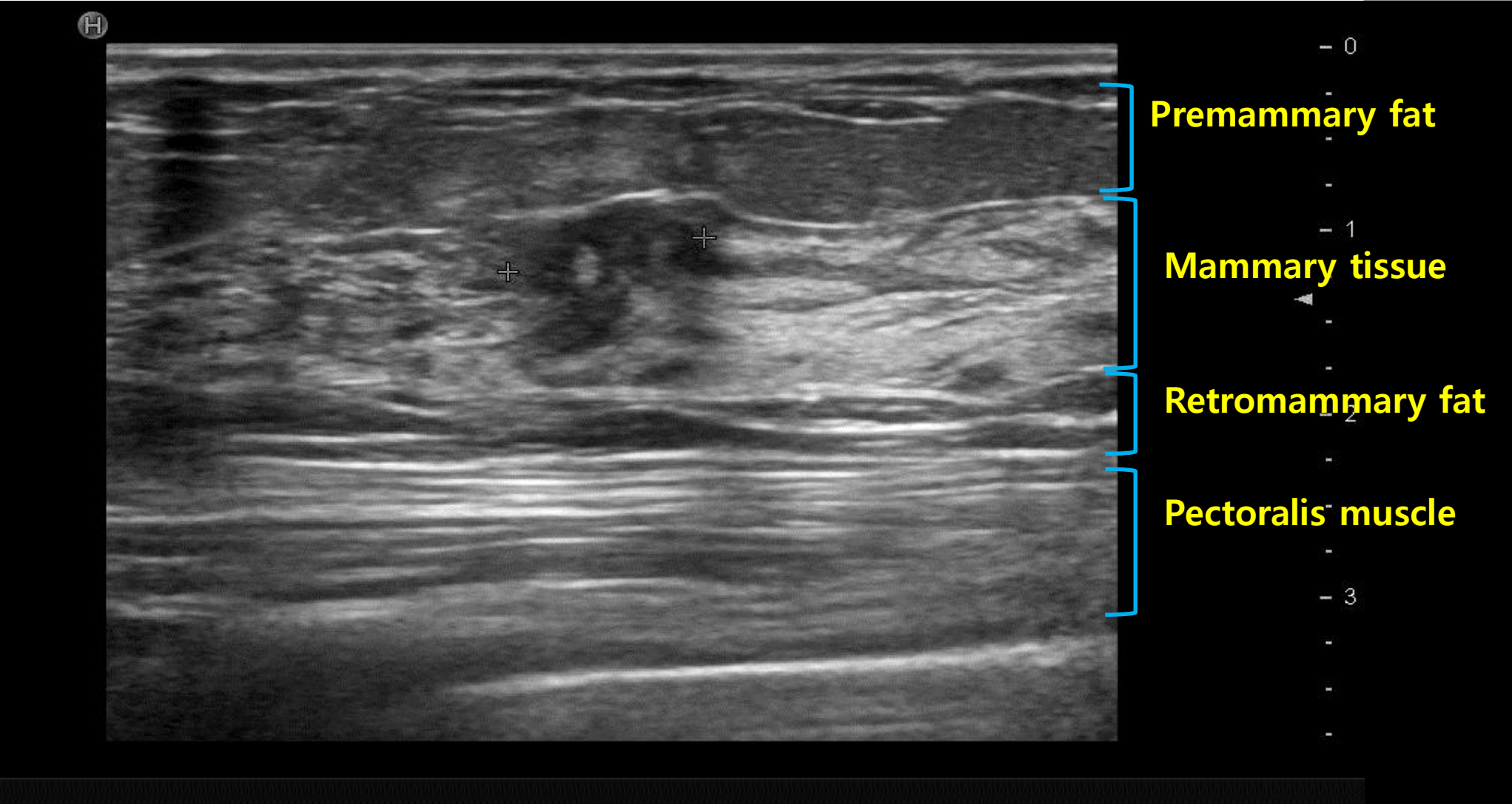
**Dongnam Institute of  
Radiological & Medical Sciences**

# Introduction

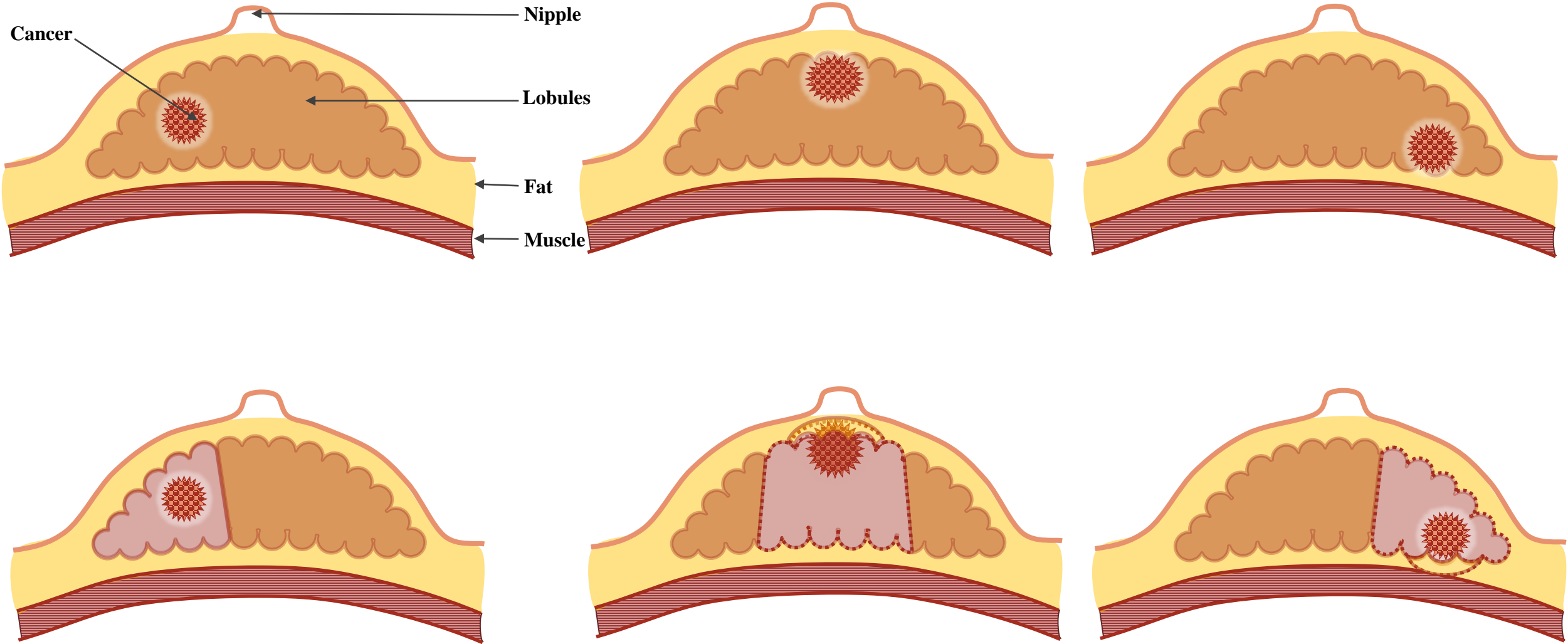
## Breast Conserving Surgery



# Introduction



# Introduction



# Introduction



National  
Comprehensive  
Cancer  
Network®

## NCCN Guidelines Version 2.2017 Invasive Breast Cancer

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### MARGIN STATUS IN INFILTRATING CARCINOMA

The use of breast-conserving therapy is predicated on achieving a pathologically negative margin of resection. The NCCN Panel accepts the definition of a negative margin as "No ink on the tumor," from the 2014 Society of Surgical Oncology-American Society for Radiation Oncology Consensus Guidelines on Margins.<sup>1</sup> Cases where there is a positive margin should generally undergo further surgery, either a re-excision to achieve a negative margin or a mastectomy. If re-excision is technically feasible to allow for breast-conserving therapy, this can be done with resection of the involved margin guided by the orientation of the initial resection specimen or re-excision of the entire original excision cavity.

A negative margin => “ No ink on the tumor ”



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# Introduction

- Concerns regarding the possible unfavorable prognostic effects of superficial and/or deep margin involvement
  - > still attempt to remove the skin to pectoral fascia to get clear margin status
- Conflicting personal opinions & a lack of evidence





# Purpose

- To evaluate the effect of positive superficial and/or deep margins on local failure in early breast cancer patients with BCS followed by radiotherapy.
- > If preserving sufficient fat layer would lead to good cosmesis, while ensuring oncological safety





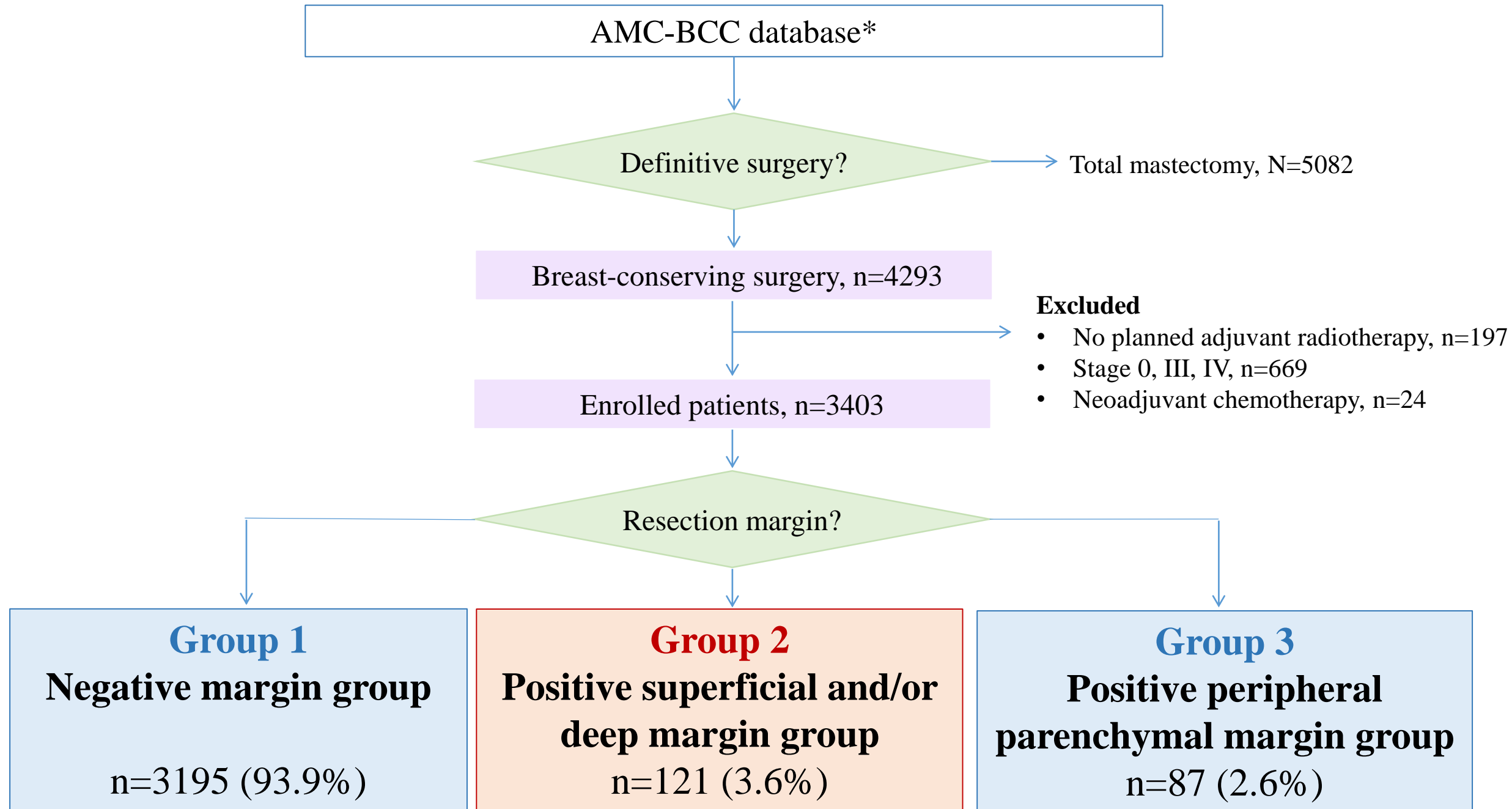
# Patients & Methods



# Patients

- Retrospective study
- Asan Medical Center, Seoul, Korea
- From Jan 2000 to Dec 2008
- Inclusion
  - BCS for stage 1 or 2 invasive breast cancer
  - Subsequent planned adjuvant radiotherapy
- Exclusion
  - Received neoadjuvant chemotherapy
- Enrolled patients : N = 3403, Median F/U = 88 months, F/U rate 97%





# Methods

- Specimen

- Oriented at the 12h,3h in the operation room
- Inked to the 6 margins
  - 4 parenchymal: medial, lateral, superior, and inferior
  - 2 non-parenchymal: superficial& deep

- Definition

- Negative margin; no ink on the tumor
- Positive margin; any invasive or in situ carcinoma on the inked margins of removed tissue



# Methods

- RM+ > further re-excised at the surgeon's discretion
- Final margin evaluation; re-excised specimen
- Postoperative RTx;
  - Whole-breast:
    - 50.4 Gy in 28 daily fractions
  - Boost:
    - Gr1 : 10 Gy in 4-5 daily fractions
    - Gr2 or 3 : 12.5 or 15 Gy in 5-6 daily fractions



# Methods

- Endpoint:
  - LR(local recurrence) according to RM groups
  - To identify superficial and/or deep margin involvement had no significance as a predictor of LR.
- Statistical analysis
  - Clinico-pathological characteristics: the chi-square test and ANOVA
  - Survival curves: the Kaplan-Meier method, the log-rank test.
  - Prognostic effect of the surgical resection margin status on LR: The Cox proportional-hazards model
  - SPSS version 21.0

# Baseline Characteristics of the Patients

	Group1 (n=3195)	Group2 (n=121)	Group3 (n=87)	P-value
<b>Age</b> (median)	47	45	45	0.47
Range	19-78	29-71	30-73	
<b>Median Follow-up time</b> (months)	88	81	88	0.86
<b>Median tumor size</b> (cm)	1.60±0.85	1.63±0.80	1.52±0.83	0.66
Range(cm)	0-6	0-4	0-3.5	
<b>Tumor size</b>				
≤2cm	2356 (73.7%)	89 (73.6%)	70 (80.5%)	0.37
>2cm	839 (26.3%)	32 (26.4%)	17 (19.5%)	

# Baseline Characteristics of the Patients

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## Node metastasis

No metastasis	2419 (75.7%)	88 (72.7%)	71 (81.6%)	0.68
Metastasis	776 (24.3%)	33 (27.3%)	16 (18.4%)	

## Histologic grade

1 or 2	1959 (66.1%)	84 (74.3%)	63 (77.8%)	0.02
3	1003 (33.9%)	29 (25.7%)	18 (22.2%)	
Unknown	5			

## EIC present

No	2481 (81.3%)	86 (71.7%)	46 (55.4%)	<0.001
Yes	571 (18.7%)	34 (28.3%)	37 (44.6%)	
Unknown	143	1	4	

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# Baseline Characteristics of the Patients

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## HR status

Negative	993 (31.3%)	21 (17.4%)	16 (18.4%)	<0.001
Positive	2180 (68.7%)	100 (82.6%)	71 (81.6%)	
Unknown	21	0	0	

## Her2 status

Negative	2244 (80.4%)	86 (78.9%)	59 (80.8%)	0.89
Positive	546 (19.6%)	23 (21.1%)	14 (19.2%)	
Unknown	371	12	14	

## Hormone therapy

No	880 (27.8%)	20 (16.5%)	15 (18.6%)	0.005
Yes	2285 (72.2%)	101 (83.5%)	67 (81.4%)	
Unknown	30	0	1	

## Chemotherapy

No	1277 (40.0%)	61 (50.4%)	46 (52.9%)	0.005
Yes	1918 (60.0%)	60 (49.6%)	41 (47.1%)	
Unknown	1	0		

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# Results

# Results- Nature of margin and LR

Group	Nature of margin	No. of patients	No. of LR(%)	Type of LR (No. of patients)		
				IBTR	Skin	Chest wall
1	Negative	3195	89	IBTR, same quadrant(67)	Yes(1)	Yes(1)
				IBTR, other quadrant(20)		
		<b>3195</b>	<b>89 (2.8)</b>			
2	Invasive only	76	1	IBTR, other quadrant(1)	No	No
	In situ only	31	1	IBTR, same quadrant(1)	No	No
	Both	1	0			
	Unknown	13	0			
		<b>121</b>	<b>2 (1.7)</b>			
3	Invasive only	9	0			
	In situ only	73	7	IBTR, same quadrant(4)	No	No
				IBTR, other quadrant(3)		
	Both	4	1	IBTR, same quadrant (1)	No	No
Unknown	1	0				
		<b>87</b>	<b>8 (9.2)</b>			
Total		<b>3403</b>	<b>99 (2.9)</b>			

# Results- Multivariate Analysis of prognostic factors for LR

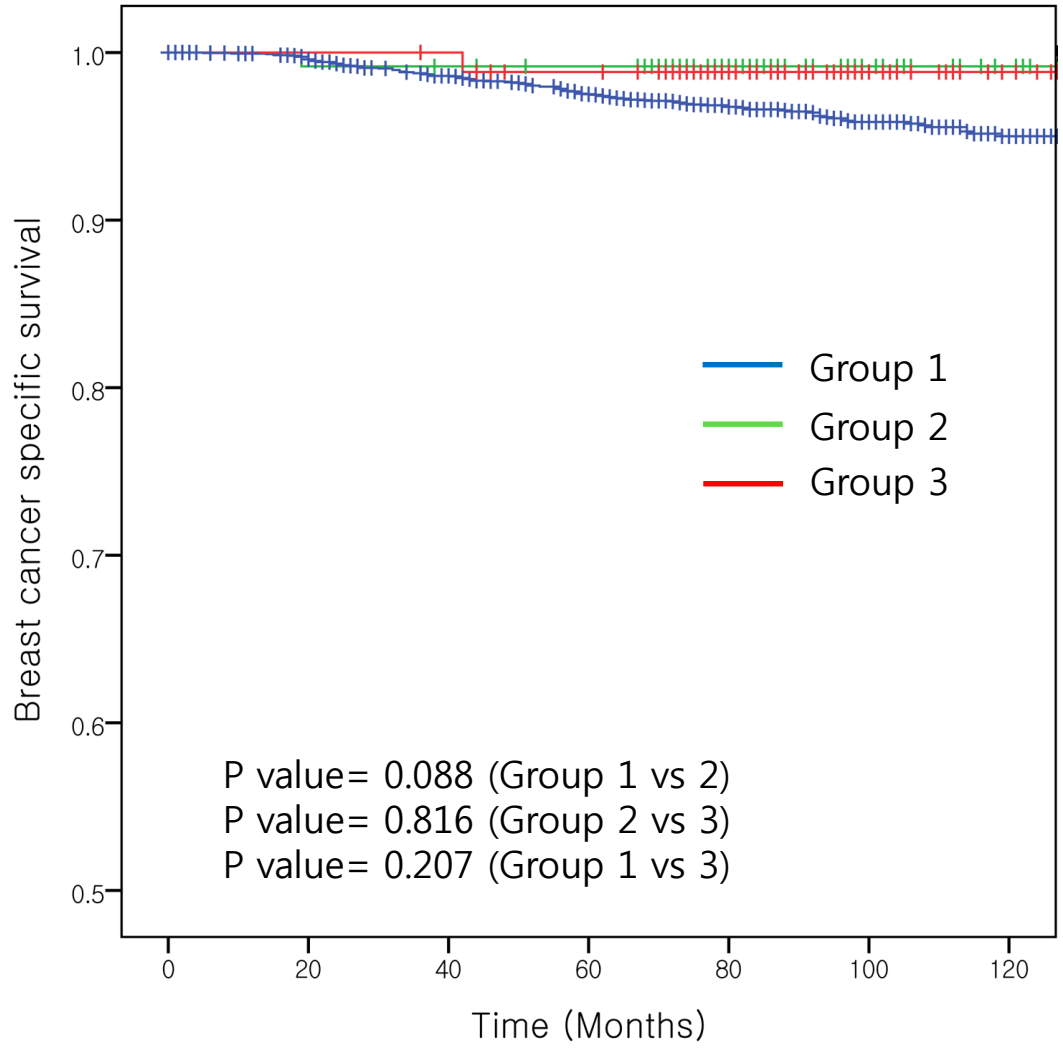
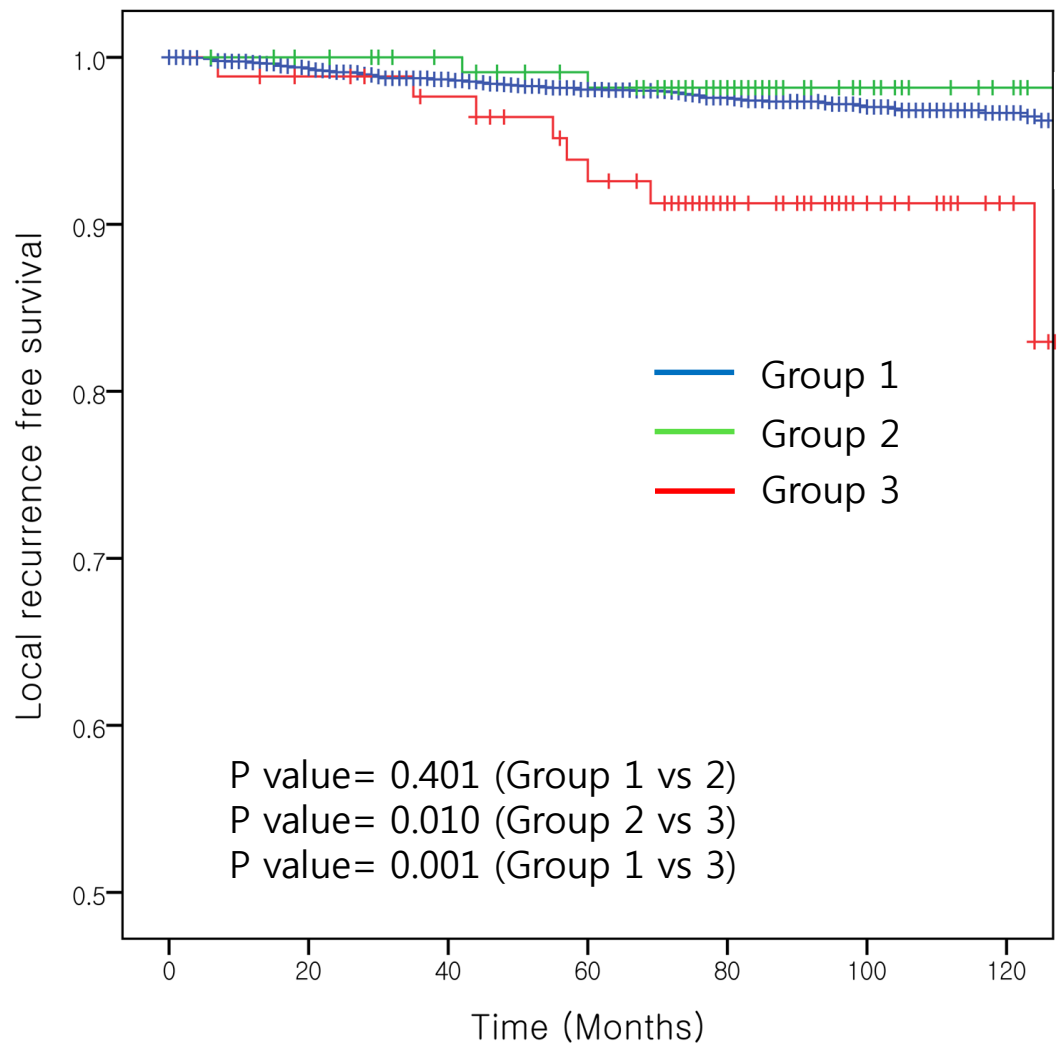
Variable	HR (95% CI)	<i>p-value</i>
<b>Age at diagnosis (years)</b>		<b>&lt;0.001</b>
>40	1	
≤40	2.59 (1.64-4.10)	
<b>Tumor size</b>		<b>0.022</b>
≤2cm	1	
>2cm	1.78 (1.09-2.92)	
<b>Node metastasis</b>		0.613
No	1	
Yes	0.86 (0.48-1.54)	
<b>Histologic grade</b>		0.880
1/2	1	
3	0.96 (0.57-1.63)	
<b>EIC presence</b>		0.410
No		
Yes	1.26 (0.73-2.17)	0.410

\*cox proportional hazard model.

# Results- Multivariate Analysis of prognostic factors for LR

Variable	HR (95% CI)	<i>p</i> -value
<b>Hormone receptor status</b>		<b>&lt;0.001</b>
Positive	1	
Negative	2.90 (1.65-5.12)	
<b>Adjuvant chemotherapy</b>		0.139
No	1	
Yes	0.62 (0.33-1.17)	
<b>Resection margin involvement</b>		<b>&lt;0.001</b>
Group 1	1	
Group 2	0.66 (0.16-2.72)	0.566
Group 3	4.78 (2.27-10.09)	<b>&lt;0.001</b>

# Results- LRFS / BCSS according to margin status



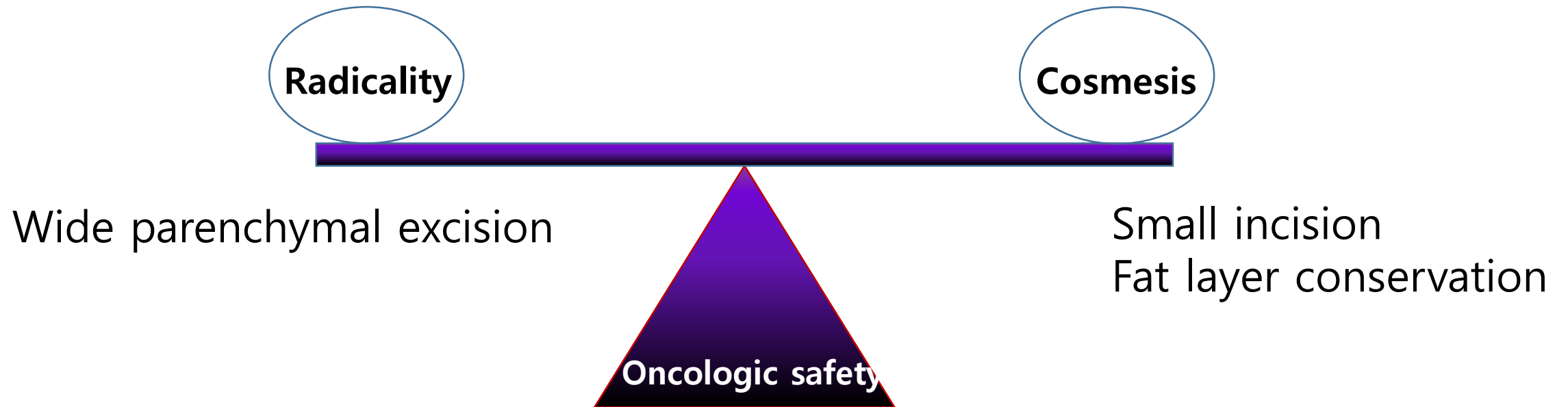
# Discussion

- Superficial/ deep margin  $\neq$  peripheral parenchymal margin
- In some cases of positive superficial and/or deep margin might be exposed in the process of tissue preparation
- In most cases, it does not mean that there are remaining cancer tissue in breast, skin, or muscle



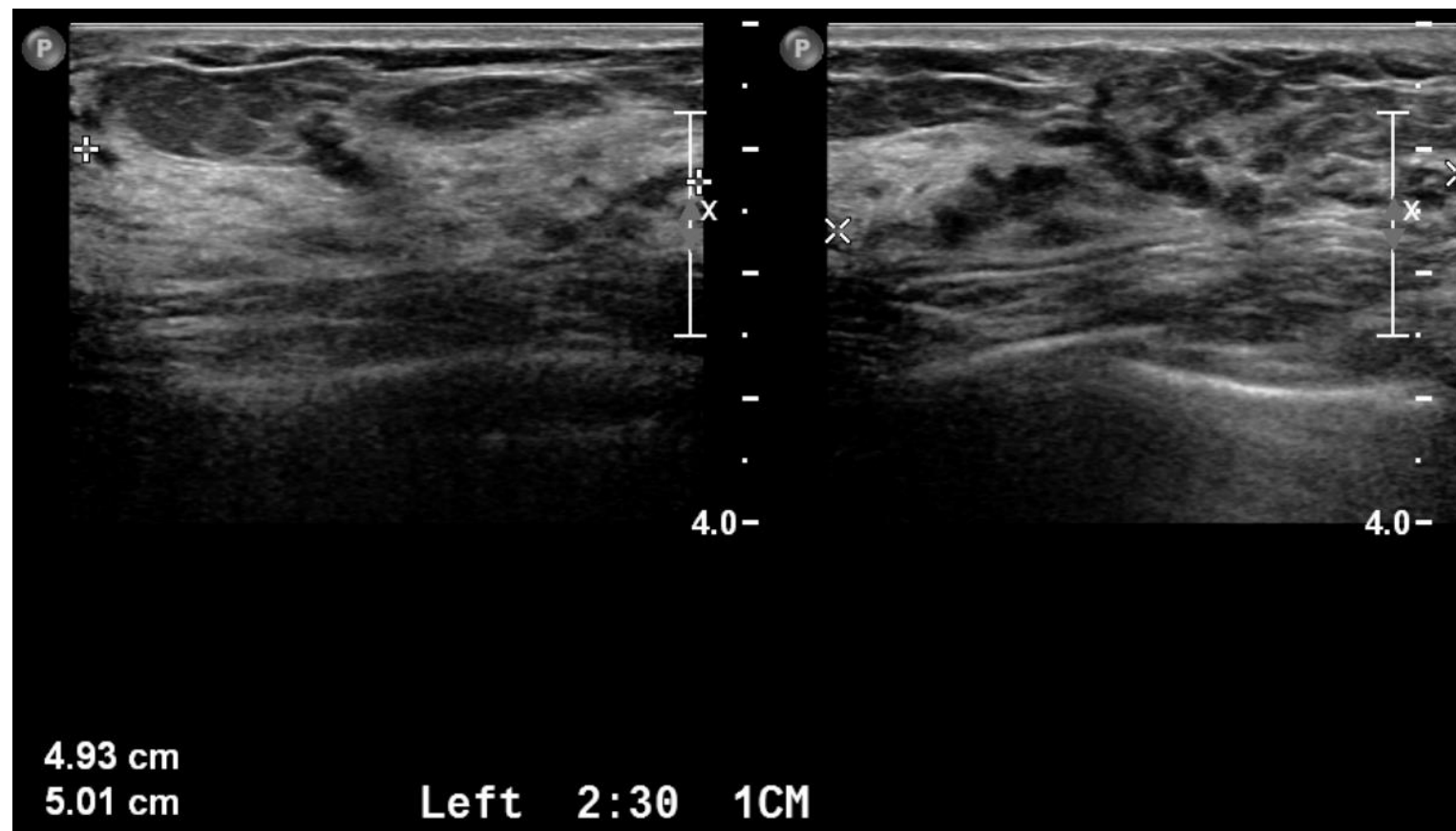
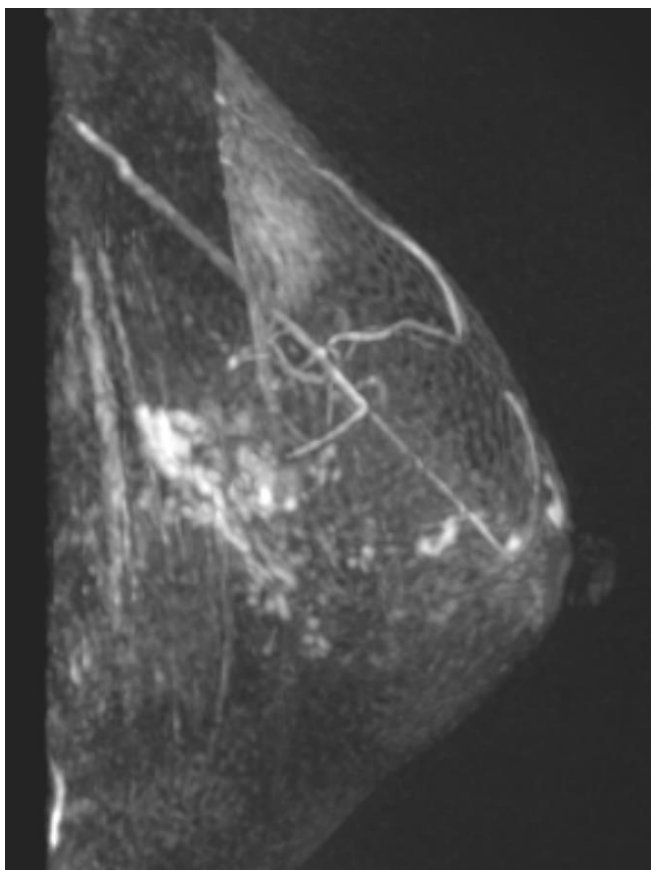


# Discussion



# Case #1, F/42

## #1. Lt breast DCIS



# Case #1, F/42

Specimen: A lump of breast ( 10 x 9.6 x 2 cm, 75 gm )

Lesion:

A well-demarcated, lobulated mass ( 4.3 x 2.5 x 1.6 cm )

- Cut surface: yellowish white, firm, nodular with focal hemorrhage without necrosis

Resection margins: Not involved

( safety margin: superficial, abutting; deep, abutting;  
3 o'clock, 2.3 cm; 6 o'clock, abutting;  
9 o'clock, 4.9 cm; 12 o'clock, 6.5 cm )

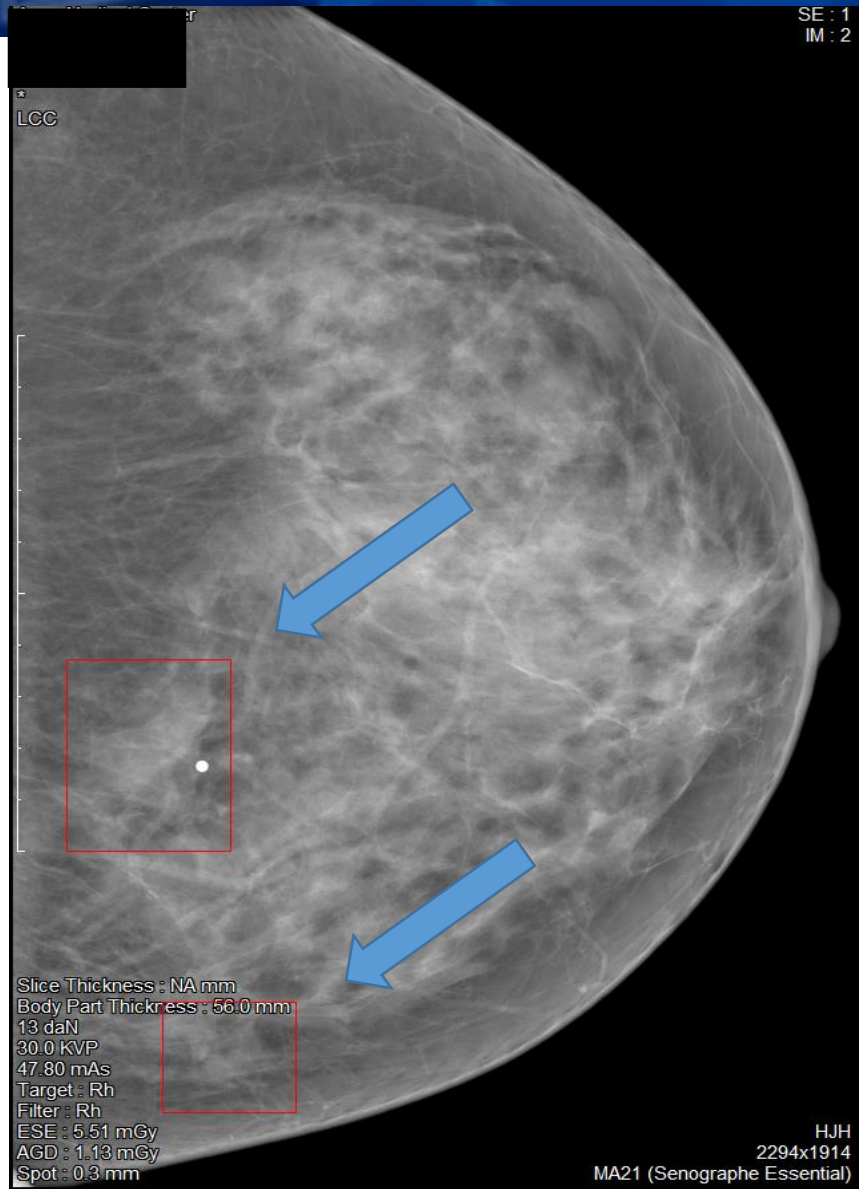
DIAGNOSIS:

A-G) Breast, ( left ), breast conserving operation with axillary staging:

- DUCTAL CARCINOMA IN SITU, NUCLEAR GRADE 2/3, WITHOUT NECROSIS, 4.3 x 2.5 x 1.6 cm,
  - with 1) no involvement of resection margins ( < 0.1 mm from closest deep and 6 o'clock resection margins ).
  - 2) no metastasis in 1 lymph node ( 0/1 ) ( sentinel LN #1, 0/1 ). ( See note )
- Microcalcification present.



# Case #2, F/55





# Case #2, F/55

## #1. Lt multifocal breast cancer

Specimen: A lump of previously disrupted breast ( 11 x 7.7 x 1.5 cm,  
55 gm )

### Lesions:

- 1) An ill-defined, irregular mass ( 1.8 x 1.2 x 0.8 cm )  
- Cut surface: grayish white, firm, fibrotic with hemorrhage and necrosis
- 2) An ill-defined, irregular mass ( 1.6 x 1.2 x 0.8 cm ), 2.5 cm from first mass  
- Cut surface: grayish white, firm, fibrotic with hemorrhage and necrosis

### Resection margins:

- 1) Not involved  
( safety margin: superficial, abutting; deep, 0.6 cm;  
3 o'clock, 4.7 cm; 6 o'clock, 4.5 cm;  
9 o'clock, 2.3 cm; 12 o'clock, 2.3 cm )
- 2) Not involved  
( safety margin: superficial, 0.1 cm; deep, 0.8 cm;  
3 o'clock, 3.4 cm; 6 o'clock, 1.8 cm;  
9 o'clock, 3.5 cm; 12 o'clock, 6 cm )

### Breast Cancer (Lt)

\*

Specimen: A. Sentinel lymph node #1 ( FS ),  
B. Sentinel lymph node #2 ( FS ),  
C. 3 o'clock left breast resection margin ( FS ),  
D. Left breast cancer.

### DIAGNOSIS:

A-D) Breast, ( left ), breast conserving operation with axillary staging:  
- INVASIVE DUCTAL CARCINOMAS ( x2 ), ( See note #1 )  
NUCLEAR GRADE 2/3, HISTOLOGIC GRADE 2/3,  
1.8 x 1.2 x 0.8 cm AND 1.6 x 1.2 x 0.8 cm  
with 1) intraductal component: < 5 % / EIC (-),  
nuclear grade 2/3, without necrosis  
2) lymphovascular invasion: not identified  
3) tumor infiltrating lymphocytes: 10-20 %  
4) no involvement of resection margins  
( < 1 mm from closest superficial resection margin )  
5) no metastasis in 2 lymph nodes ( 0/2 )  
( sentinel LN #1, 0/1;  
sentinel LN #2, 0/1 ). ( See note #2 )  
- Microcalcification present



# Summary

- A significant risk factor for LR
  - Younger age at diagnosis of breast cancer (HR 2.59)
  - Negative hormone receptor (HR 2.90)
  - Tumor size (>2cm) (HR 1.78)
  - Pph margin involvement (HR 4.78)
  - EIC more presented positive resection margins than without EIC.

However, the presence of EIC was not associated with an increased risk of local failure.



# Summary

- Total IBTR rate : 2.8% (97/3403)
- Positive Superficial and/or deep margin involvement was not a significant predictor for LR (HR 0.66, P=0.566)
- No significant difference in the LRFS between the G1 and the G2 (P = 0.401).





# Conclusion

- Superficial and/or deep margin involvement following BCS does not affect LR.
- Extensive excision of skin, premammary fat, retromammary fat, or pectoral fascia does not need to be routinely performed to achieve negative superficial and/or deep margin status during BCS.



A night-time photograph of a modern university campus. The scene is dominated by several tall, multi-story buildings with glass facades and numerous lit windows, creating a warm glow against the dark blue twilight sky. A wide, paved road with white lane markings and streetlights runs through the center of the campus, flanked by green trees. In the background, more campus buildings and distant city lights are visible under a deep blue sky with some light clouds. The overall atmosphere is serene and modern.

**Thank you**

# Discussion

- Median duration for LR: 45m / mean 52m
- Peripheral parenchymal margin involvement
  - DCIS only(84%), No residual tissue(7%), Refuse (2%), Unknown (7%)
- Limitations
  - Retrospective
  - The small number of LR events

