

Risk factors for positive margin in breast conservative surgery for localized breast cancer

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Purpose

- To investigate factors associated with positive margins in breast cancer patients undergoing breast-conserving surgery for invasive localized breast cancer.

Background



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Breast Cancer

- A major global concern due to high incidence and prevalence
 - In 2022, there were 2.3 million diagnoses and 670,000 deaths globally
 - In the US alone, incidence of female breast cancer is expected to be 310,720 with an additional 2,800 cases in men for the year 2024
 - Accounts for 30% of newly diagnosed female cancers with a lifetime incidence of 1/8 in women
- Improved mortality and morbidity
 - 5-year relative survival rates (SEER)
 - Localized breast cancer – 99%
 - Distant breast cancer – 31%
 - All types/stages of breast cancer – 91%



Breast-conservative Surgery

- The removal of breast tumor tissue (invasive or in situ) surrounded by a margin of normal tissue
- Candidates typically have early-stage (stage 1 or 2) breast cancer, or DCIS, which is isolated to one area of the breast
- Neoadjuvant chemotherapy (option for larger tumors)
- Followed by adjuvant radiotherapy to tumor bed + surrounding tissue
- Procedures included:
 - Lumpectomy, partial mastectomy, wide excision, segmental mastectomy

Surgical Margins

- Negative margins
 - Necessary to avoid any breast cancer recurrence
 - Defined as no gross or microscopic disease evident at the resection border, also known as “no tumor on ink”
- Positive margins
 - Patients need additional surgeries with larger margins, or total mastectomy
 - Exposes patients to greater morbidity
 - Risk of surgical complications
 - Delays the start of adjuvant therapy
 - Worsened cosmetic appearance

Methods



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Study Design

- Retrospective cohort study
- Patients identified using CAMC Cancer Registry
- Queried from 2009-2022 for females diagnosed with invasive breast cancer who had surgery for localized disease

Study Design

- Inclusion Criteria:
 - Female breast cancer patients
 - Breast-conserving surgery performed at CAMC
 - Histology demonstrating invasive breast cancer

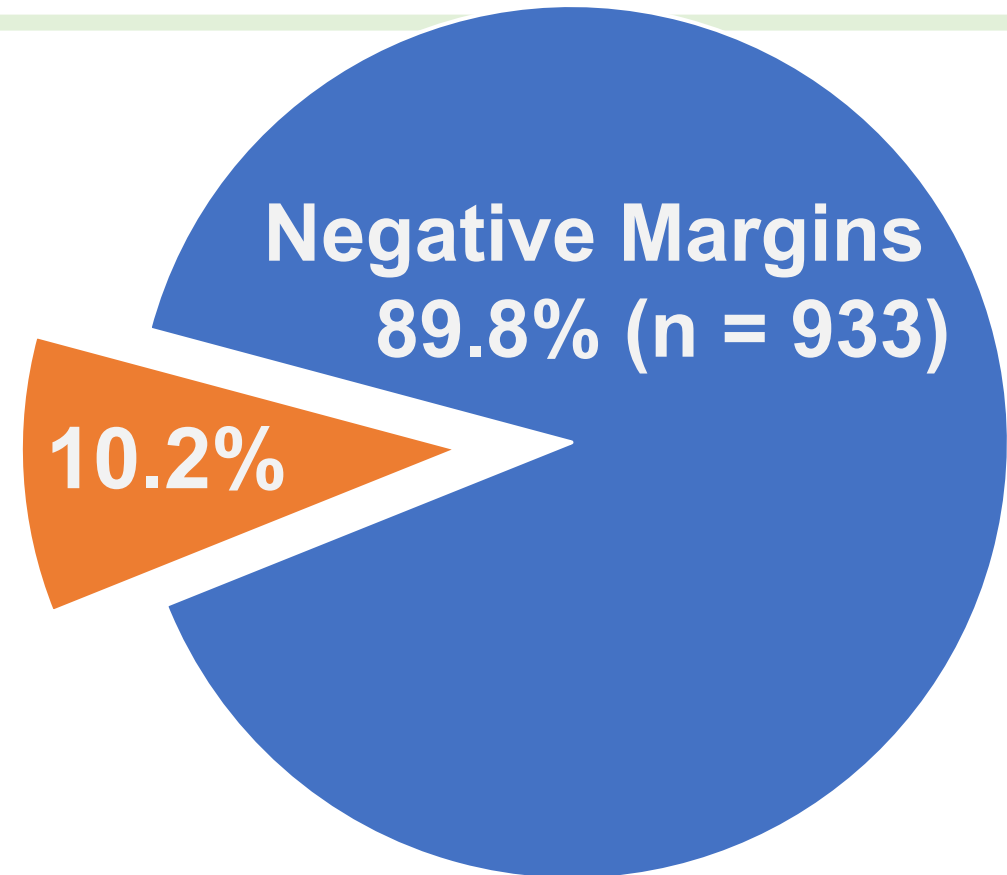
Study Design

- Exclusion Criteria:
 - Male breast cancer patients
 - Biopsy only: mammotome, core needle, FNA, excisional biopsy
 - Total mastectomy (any type)
 - Histology demonstrating non-invasive breast cancer
 - Patients with history of prior malignancy
 - Lymph node positive disease
 - Metastatic disease

Sample

- 5286 records of breast cancer patients were obtained from the CAMC Cancer Registry
- 1041 patients remained after applying inclusion and exclusion criteria

Positive Margins
(n = 108)



Variables

- Comorbidities
 - BMI, hypertension (HTN), hypothyroidism, diabetes, coronary artery disease (CAD), osteoporosis, cardiac arrhythmia, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), cerebrovascular accident (CVA), valvular disease, venous thromboembolism (VTE), congestive heart failure (CHF)
- Risk Factors
 - Tobacco use, hormone replacement therapy (HRT) use
- Tumor characteristics
 - Tumor size, laterality, breast location, stage (clinical/pathological)
- Histology
 - Histology type, multifocality, grade, Ki67
- Receptor status
 - ER, PR, HER2/neu

Statistical Tests

- SAS 9.4 was utilized to process the data for this investigation.
- Descriptive variables:
 - Means \pm standard deviation(SD) for continuous variables
 - Proportions (%) for categorical variables.
- Univariate analysis:
 - Mantel-Haenszel Chi-Square, Chi-square or Fishers Exact, students T-test, Kaplan Meier method
- Multivariate analysis:
 - Logistic regression (backwards selection), and Cox proportional hazards model.

Results



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Results

Variable		Negative Margins (mean ± SD)	Positive Margins (mean ± (SD)	P value
Age		64.1 ± 10.5	63.3 ± 12.2	.52
BMI		31.6 ± 7.4	30.5 ± 7.5	.15

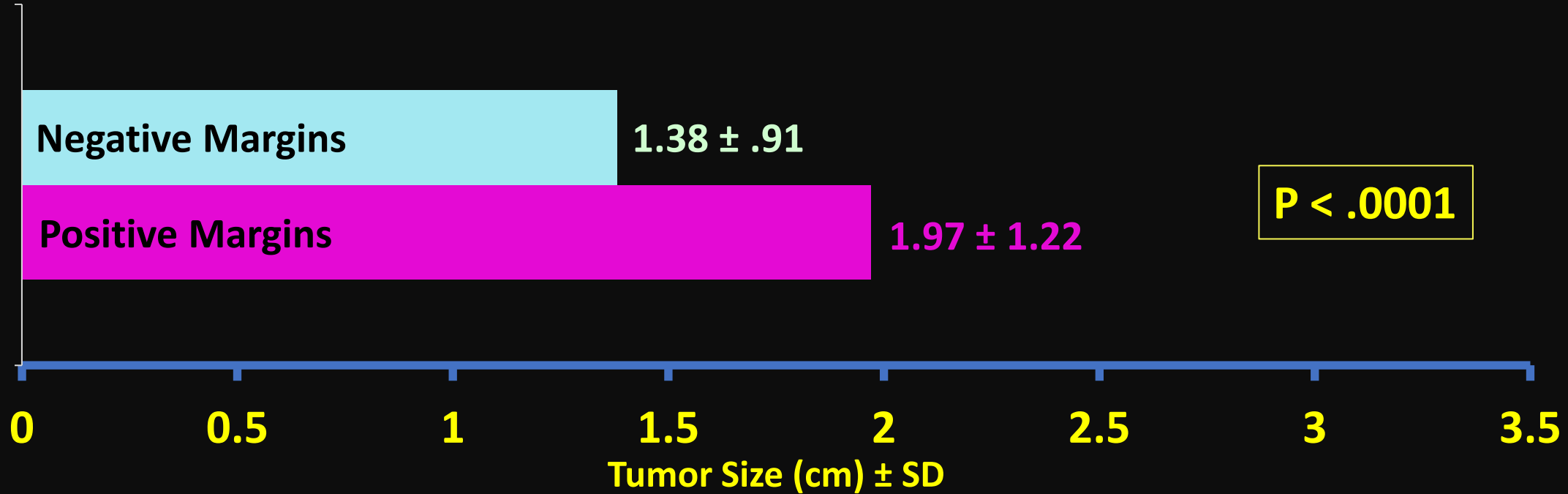
Comorbidities

Variable		Negative Margins (%)	Positive Margins (%)	P value
Hypertension		65.5%	61.1%	.37
Tobacco		32.6%	28.7%	.41
Tobacco (last 30 days)		14.6%	13.0%	.65
Hypothyroid		27.8%	30.6%	.54
Diabetes		21.5%	17.8%	.34
HRT		13.0%	19.4%	.07
CAD		12.2%	12.0%	.96
Osteoporosis		10.9%	8.4%	.42

Comorbidities

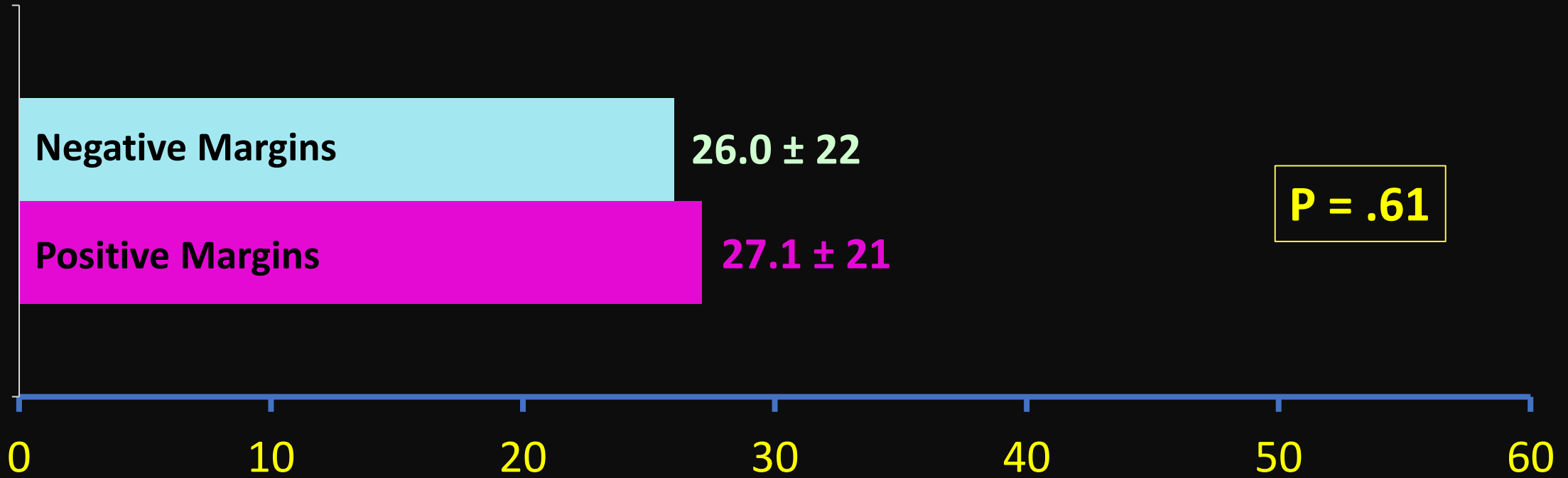
Variable	Negative Margins (%)	Positive Margins (%)	P value
Arrhythmia	7.5%	13.0%	.05
COPD	8.7%	4.6%	.15
CKD	5.7%	5.6%	.96
CVA	5.3%	2.8%	.26
Valvular disease	5.2%	3.7%	.51
VTE	2.8%	.93%	.25
CHF	2.7%	1.9%	.61

Tumor Size (cm)



Size Staging Category	Negative Margins	Positive Margins	P value
< 2 cm	78.7%	57.4%	P < .0001
2 to 5 cm	20.7%	38.9%	
> 5 cm	.5%	3.7%	

Ki-67



Variable	Negative Margins (%)	Positive Margins (%)	P value
Ki-67: >15.5	57.8%	60.2%	.64

Tumor Characteristics (Location)

Variable	Negative Margins (%)	Positive Margins (%)	P value
Laterality (left)	53.0%	51.9%	.82
Location (specific)			
12 o'clock	12.9%	15.7%	
3 o'clock left, 9 o'clock right	6.5%	4.6%	
3 o'clock right, 9 o'clock left	4.4%	4.6%	
6 o'clock	2.9%	6.5%	.047
LIQ	7.3%	6.5%	
LOQ	7.6%	8.3%	
UIQ	17.3%	13.0%	
UOQ	38.1%	38.0%	
Retroareolar	2.5%	2.8%	
Multiple locations	.5%	0%	

Tumor Characteristics (Histology)

Variable	Negative Margins (%)	Positive Margins (%)	P value
Ductal	86.2%	74.1%	.001
Lobular	7.2%	20.4%	<.001
Mucinous	3.2%	2.8%	
Microinvasive	0	.9%	
Other	.9%	.9%	
Ductal and lobular	.8%	.9%	
Tubular	.9%	0%	

Tumor Characteristics (Grade)

Variable	Negative Margins (%)	Positive Margins (%)	P value
Grade			
Grade 1	26.1%	21.3%	.56
Grade 2	45.0%	48.2%	
Grade 3	28.9%	20.6%	
Stage			
IA	79.4%	61.1%	< .0001
IB	2.5%	3.7%	
IIA	17.6%	34.5%	
IIB	.5%	3.7%	

Tumor Characteristics

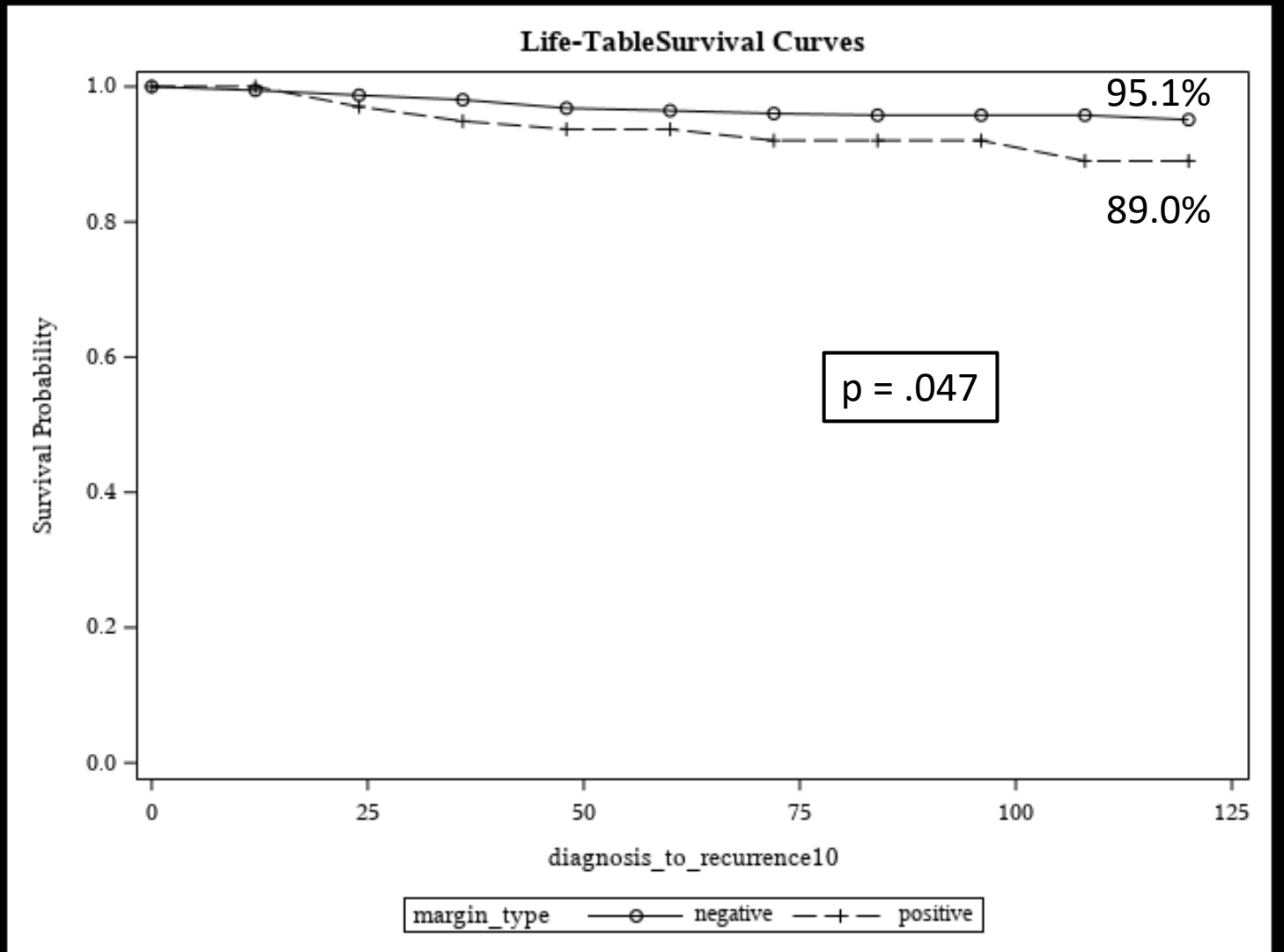
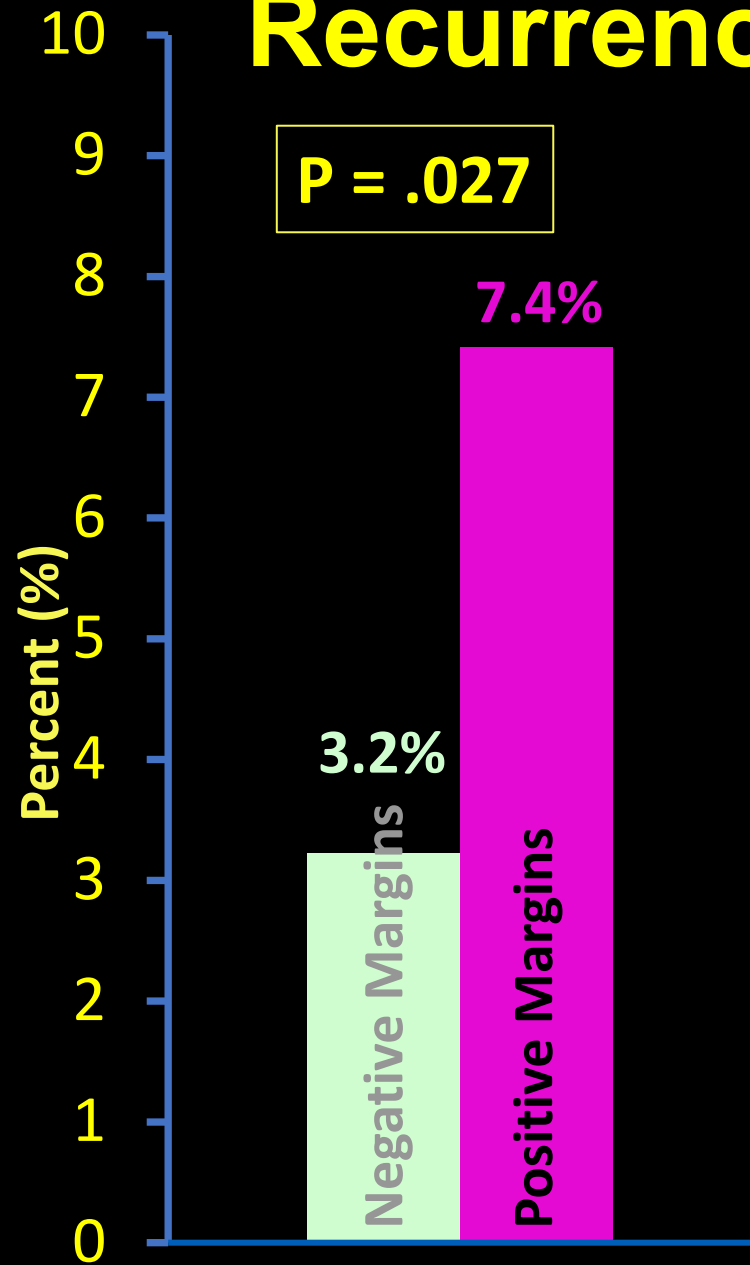
Variable		Negative Margins (%)	Positive Margins (%)	P value
Multiple tumors / One primary (Multifocality)		4.5%	17.8%	< .0001
Receptor Status				
ER (positive)		87.5%	88.0%	.88
PR (positive)		79.4%	84.3%	.23
HER2/neu (negative)		91.9%	87.0%	.22
Triple Negative (yes)		10.2%	9.3%	.76

Logistic Regression to Predict Positive Margin

Variable	Odd Ratio	95% Confidence Interval	P value
Stage	1.6	1.3-2.0	< .0001
Multifocality	4.2	2.3-7.8	< .0001
Lobular histology	2.7	1.6-4.7	.0005
6 o'clock position	2.6	1.0-6.4	.04

Recurrence

P = .027

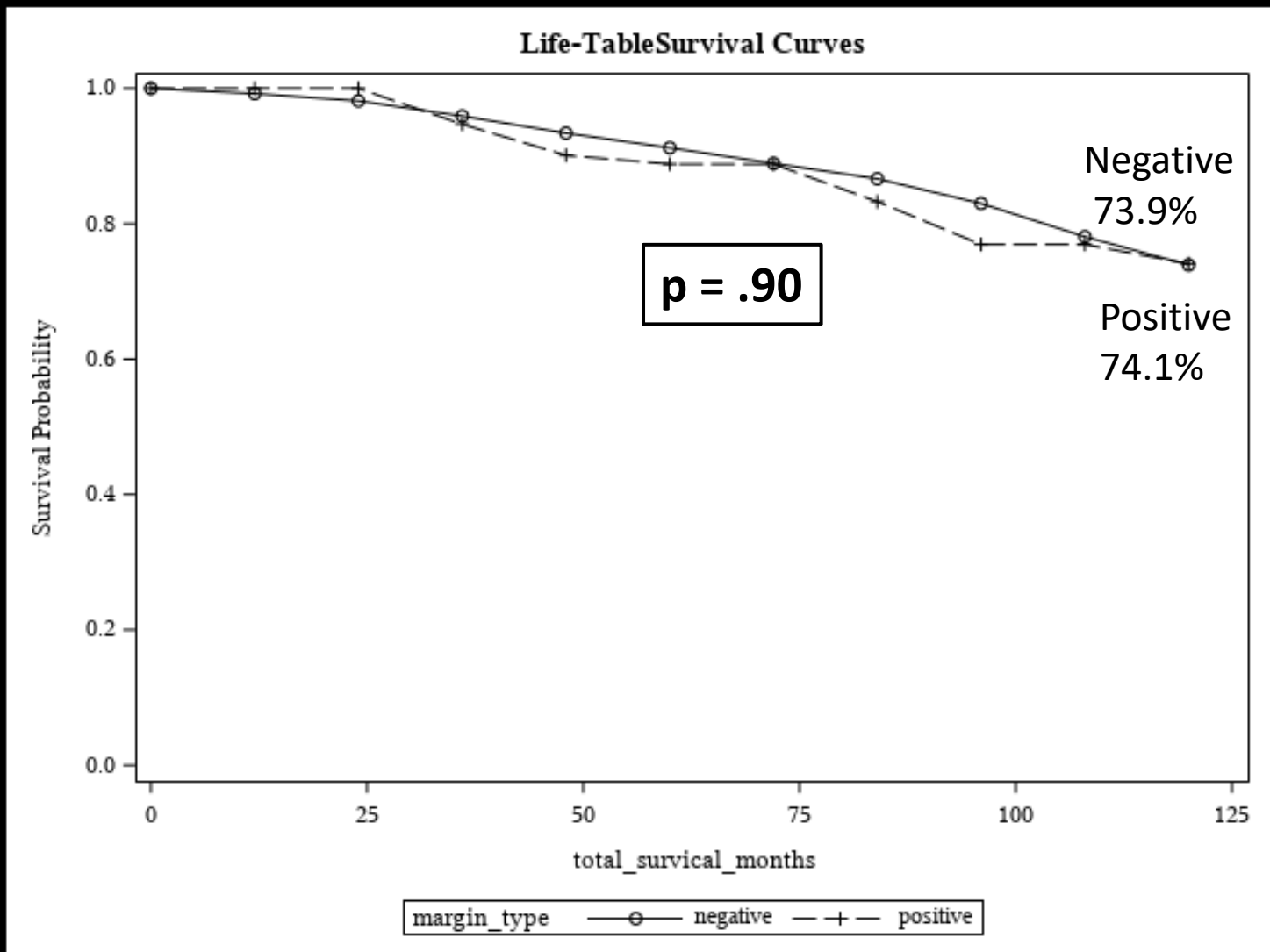
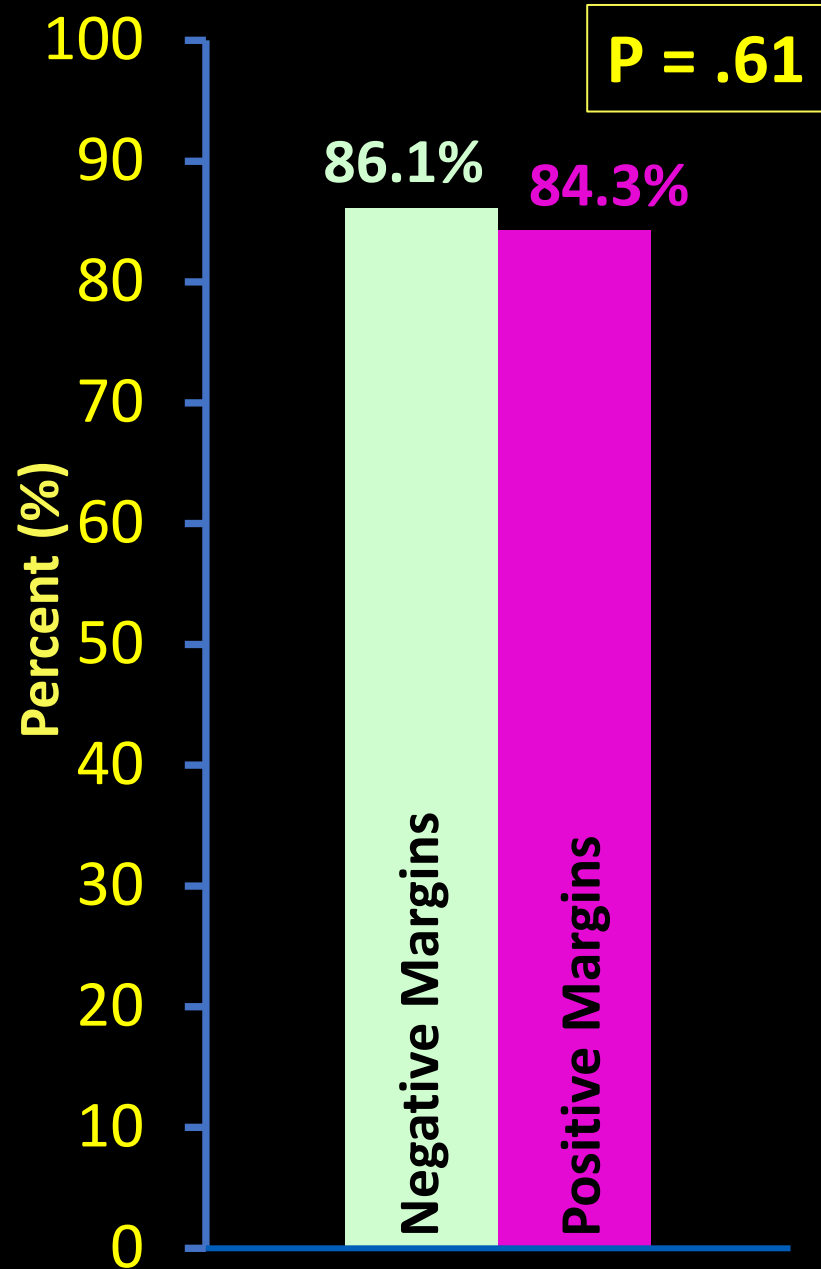


	Survival %		
Margin Type	1-year	5-years	10-years
Negative	99.5%	96.4%	95.1%
Positive	100%	93.7%	89.0%

Logistic Regression to Predict Recurrence

Variable	Odd Ratio	95% Confidence Interval	P value
Ki-67 > 15.5	4.5	1.5-13.2	.006
Positive Margin	2.8	1.2-6.4	.018
PR (negative)	2.9	1.4-5.8	.003

Overall Survival



	Survival %		
Margin Type	1-year	5-years	10-years
Negative	99.2%	91.2%	73.9%
Positive	100%	88.8%	74.1%

Cox Proportional Hazards Model for Overall Survival

Variable	Hazard Ratio	95% Confidence Interval	P value
Recurrence	4.9	3.0-7.8	< .0001
Age \geq 80	3.8	2.5-5.7	< .0001

Discussion



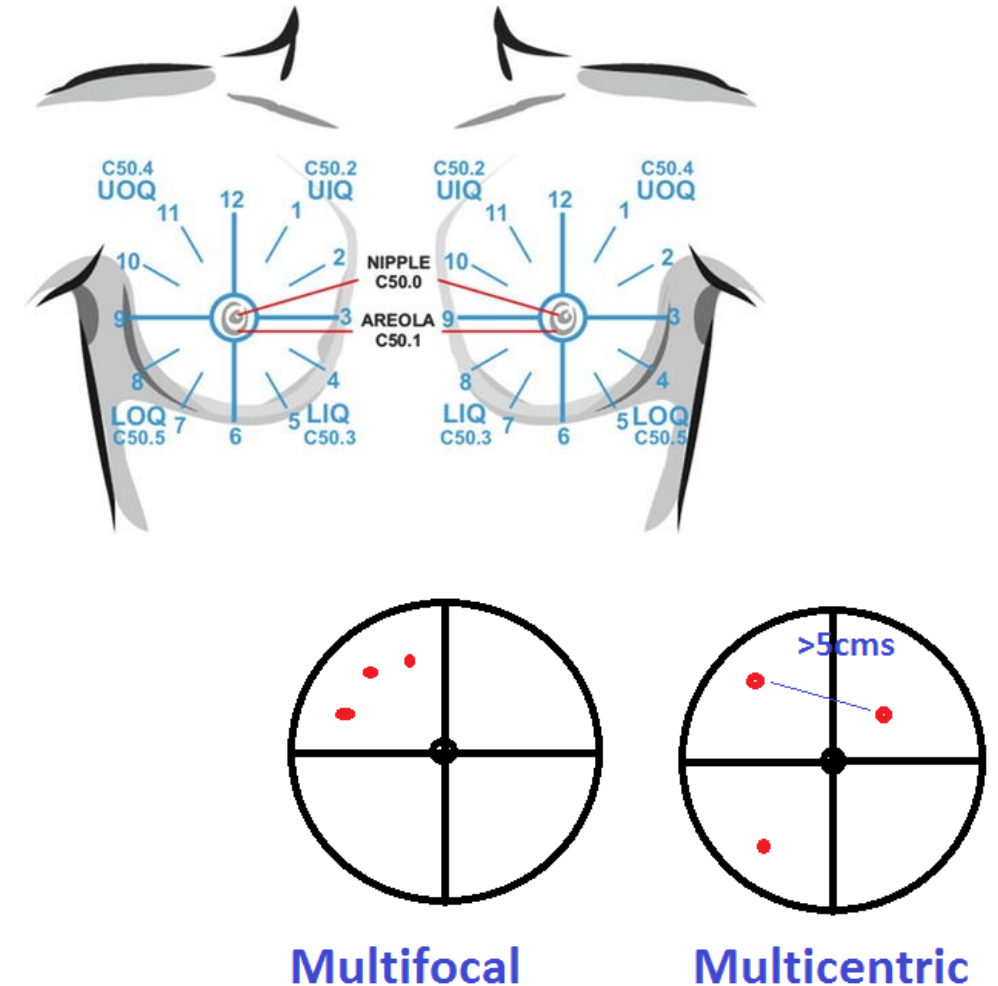
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Significant Findings

- Associated with positive margins
 - Arrhythmia
 - Tumor size (mean + categorical)
 - 6 o'clock position
 - Invasive ductal histology
 - Invasive lobular histology
 - Stage
 - Multifocality
 - Recurrence, local/distant



Previous Studies

- van Deurzen (2016)
 - Included [all patients with invasive breast cancer \(IBC\)](#)
 - Excluded DCIS, IBC after previous treatment
- Lombardi et al. (2019)
 - Included patients with [early breast cancer clinically N0](#), who [underwent BCS](#) and sentinel lymph node biopsy
 - Excluded mastectomy, DCIS, neoadjuvant therapy
- Hotsinpiller et al. (2021)
 - Included patients with [non-metastatic invasive breast cancer](#), who [underwent BCS](#)
 - Excluded radiation before surgery, unknown margin status, male breast cancer

Previous Studies

- Similarities:
 - Lobular histology, multifocality, tumor size
- Differences:
 - Age, ER+, grade, HER2/neu+, mixed histology
- Didn't Assess:
 - Angioinvasion, lymph node status, lympho-vascular invasion, presence/extent of DCIS, surgical technique (oncoplastic)
- Novel Findings:
 - Arrhythmia, 6 o'clock position

Conclusions

Positive margins were associated with recurrence (local + distant) but were not associated with overall survival.

The results of this study may help to guide surgeons and oncologists in the management of localized, invasive breast cancer

- 1) In planning appropriate surgeries based on tumor histology, focality, and breast location
- 2) In emphasizing timely follow-up in higher risk patients
- 3) In the education of patients regarding their care

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Questions?



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