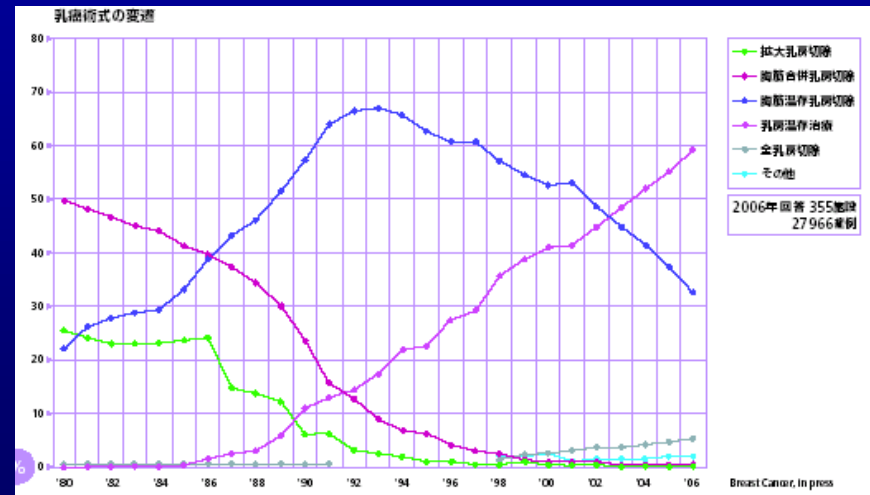


# Management for Ipsilateral Breast Recurrence after Breast Conservation Treatment

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# Background

- Breast conserving operation has been a standard treatment for early breast cancer since 2003 in Japan. About 60% of the patients underwent breast conserving operation in 2009. About five to ten percent of them developed ipsilateral breast tumor recurrence (IBTR). Relative incident of IBTR is low but the absolute amount is high. So it is an important issue how to manage IBTR. Indeed, many issues remain to be elucidated. We report here the actual conditions of IBTR, predictive factors of IBTR, relationship to the prognosis, and the factors which can predict outcome.



# Patients and Methods

- First series : Fifty-six local recurrence cases among 1372 patients with breast conserving operation between 1985 and 2005 in Keio University Hospital. Median follow up period was 73 months.
- Second series: Patients (N:1901) with unilateral breast cancer  $\leq 3$  cm in diameter who underwent BCT at 18 Japanese major institutes from 1986 to 1993. Median follow up period was 107 months.
- Third series: 172 patients with ipsilateral breast tumor recurrence after breast conserving operation done in 18 Japanese hospitals.

**First series**

# Characteristics of patients

	Local failure (n=56)	Local control (n=1316)	<i>p</i> value
Age	49 (28-79)	52 (21-93)	0.04
Primary tumor size*	2.2±1.1 cm	1.9±1.1 cm	0.01
DCIS	12.5%	11.7%	0.64
Estrogen receptor +	55.3%	68.8%	0.32
Progesterone receptor +	42.8%	58.3%	0.75
Lymphatic invasion +	32.1%	29.8%	0.16

\*Mean±SD

# Characteristics of patients

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\*Mean±SD

# Characteristics of patients

	Local failure (n=56)	Local control (n=1316)	p value
Pathological node +	23.2%	14.8%	0.32
Surgical margin +	8.9%	12.3%	0.49
Radiation	53.6%	76.8%	<0.01
Neoadjuvant therapy	3.6%	7.9%	0.57
Adjuvant therapy	48.2%	71.3%	0.02

\*Mean $\pm$ SD

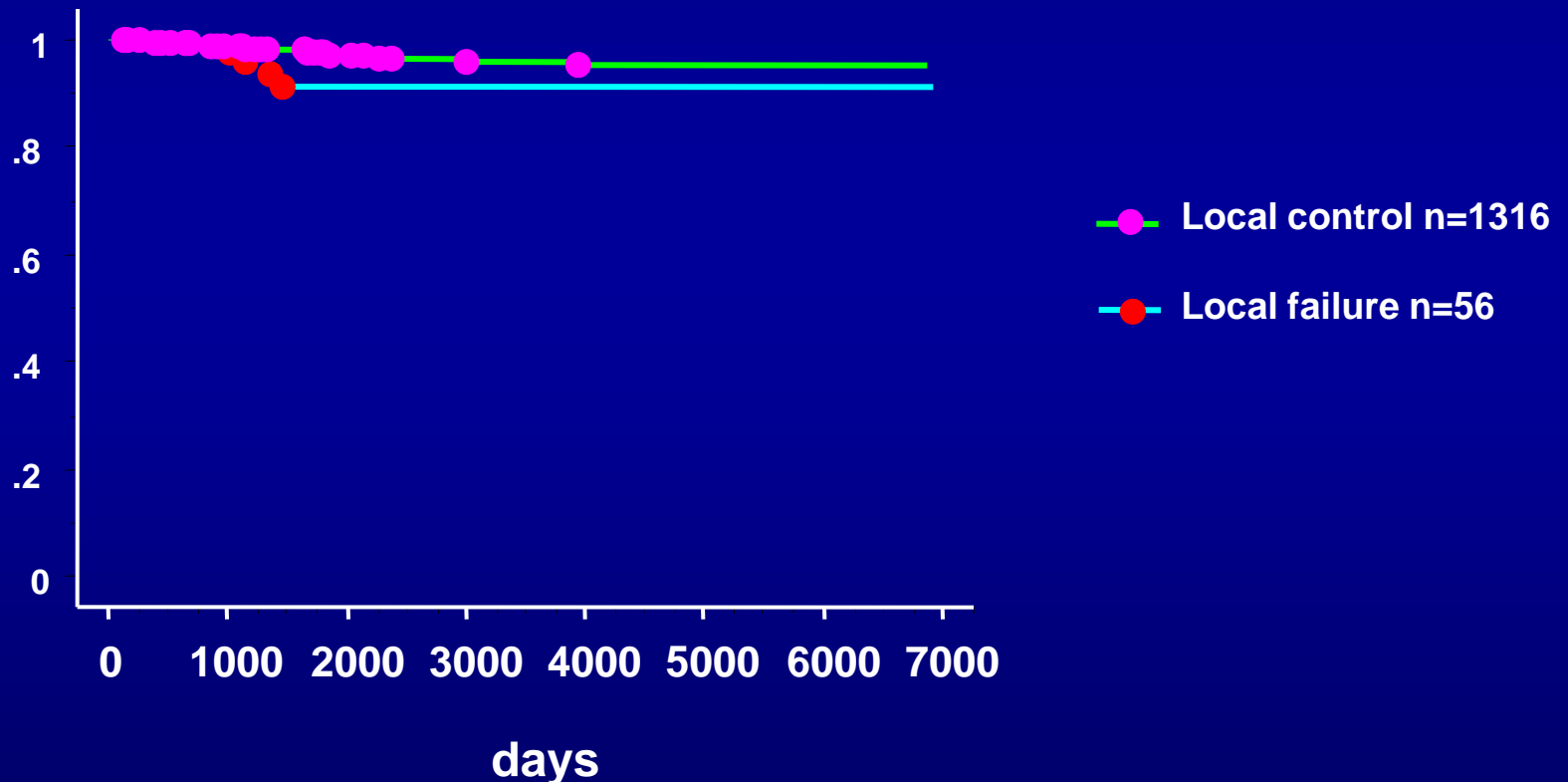
# Characteristics of patients

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Surgical margin +	8.9%	12.3%	0.49
Radiation	53.6%	76.8%	<b>&lt;0.01</b>
Neoadjuvant therapy	3.6%	7.9%	0.57
Adjuvant therapy	48.2%	71.3%	<b>0.02</b>

\*Mean $\pm$ SD



# Overall survival as a function of local failure



p=0.11

# Characteristics of patients with local failure (n=56)

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Age at the time of recurrence	52 (28-76)
Recurrent tumor size*	1.6±1.1 cm
Estrogen receptor +	46.3%
Progesterone receptor +	37%
Lymphatic invasion +	26.8%

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\*Mean±SD

# Characteristics of patients with local failure (n=56)

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## Location

Same quadrant	41 (73.2%)
Other quadrant	12 (21.4%)

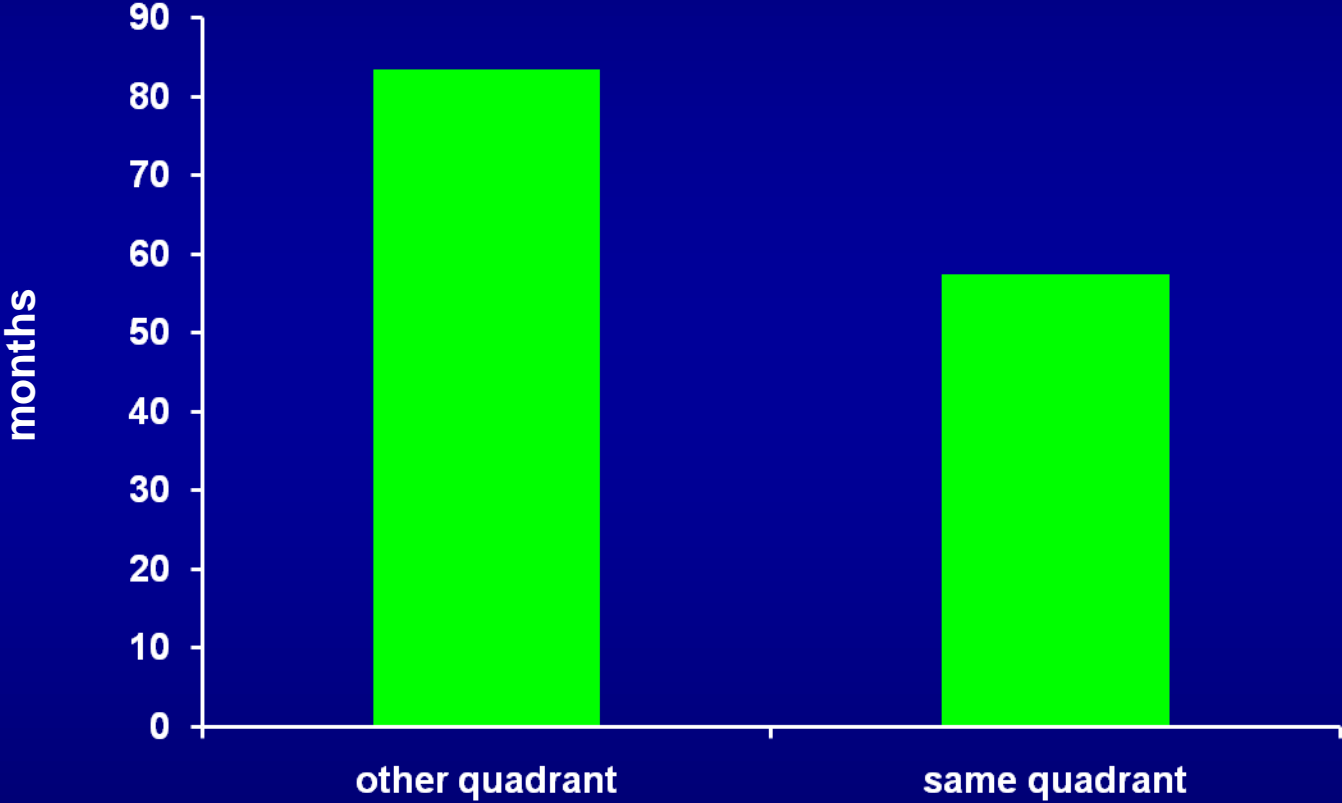
Inflammatory type 3 (5.6%)

Distant metastasis 1 (1.8%)

DFI 40.1 M (5.2-197 M)

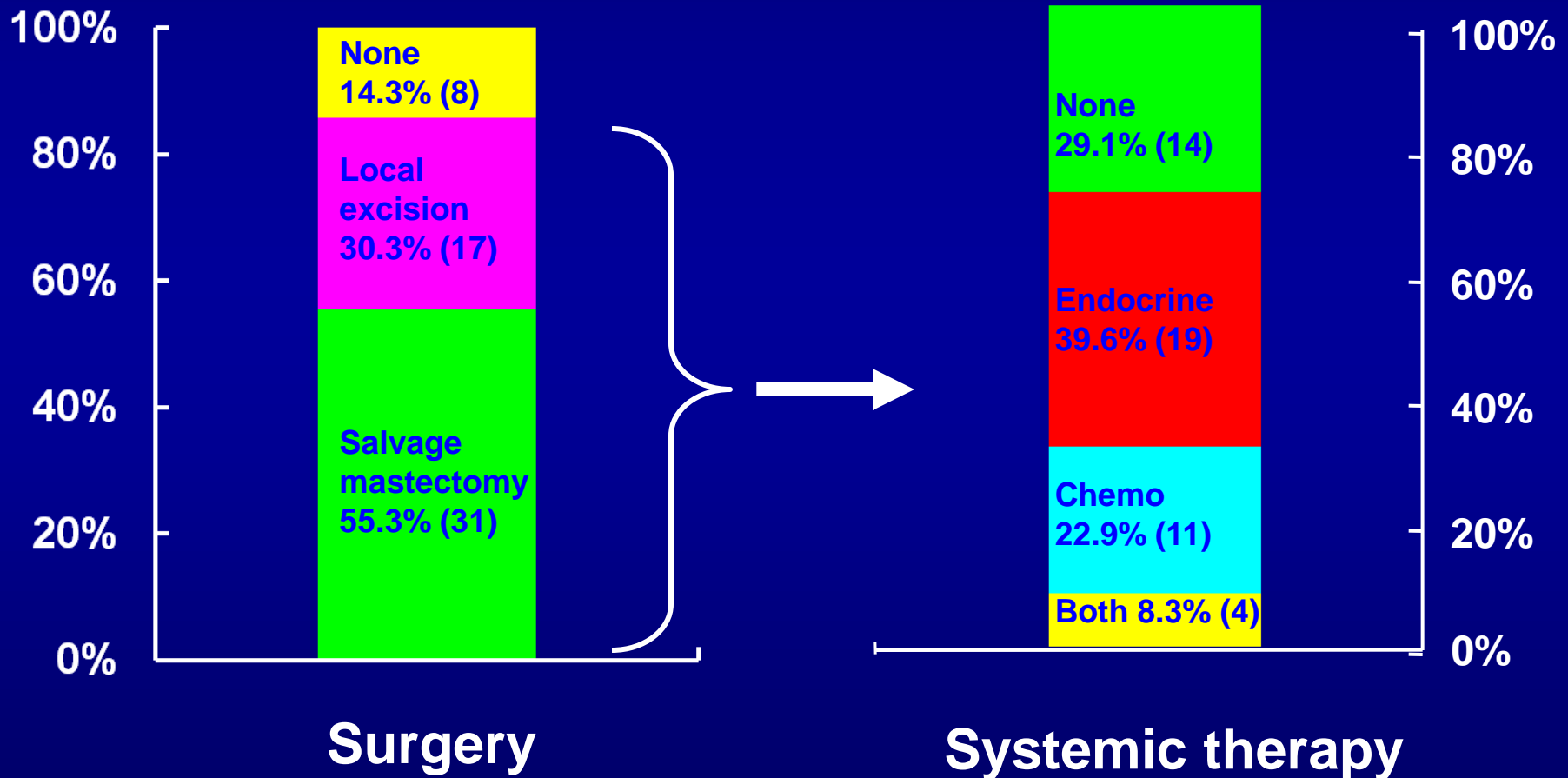
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# DFI according to the recurrence site



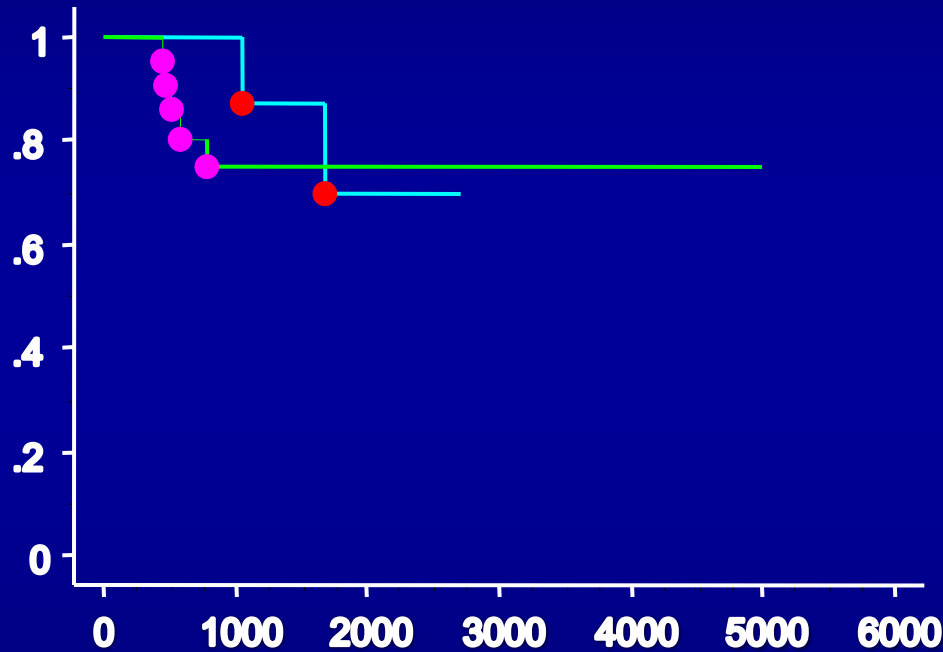
$p < 0.01$

# Treatment of patients with local failure



# Survival according to type of surgery

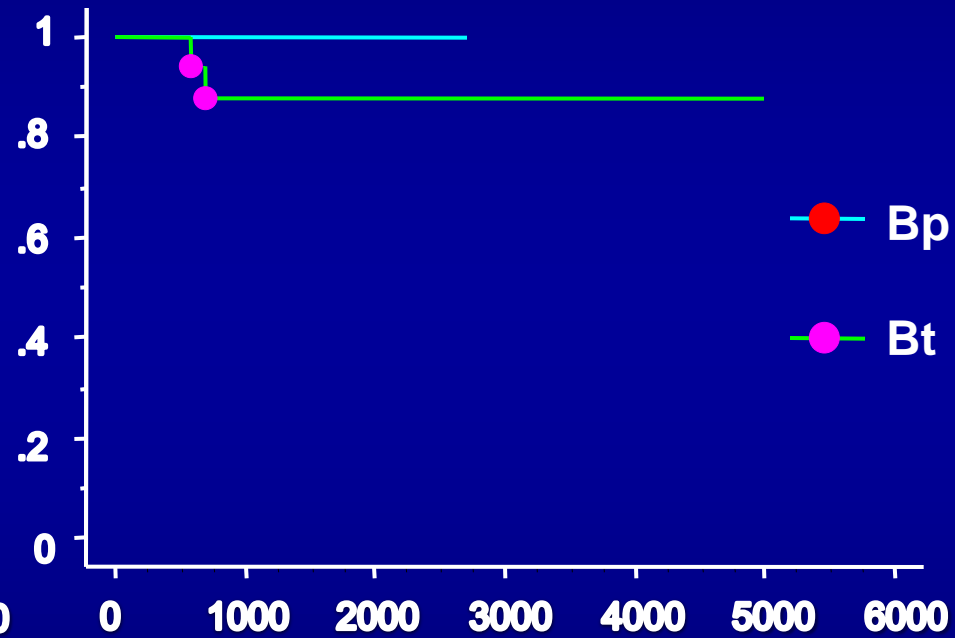
DFS



Days

p=0.6

OS



Bp

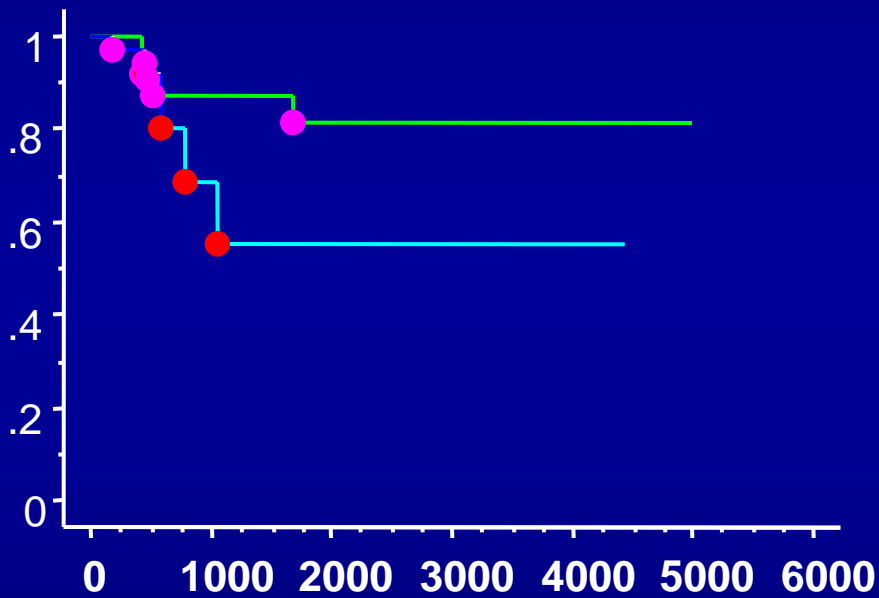
Bt

Days

NA

# Survival according to DFI

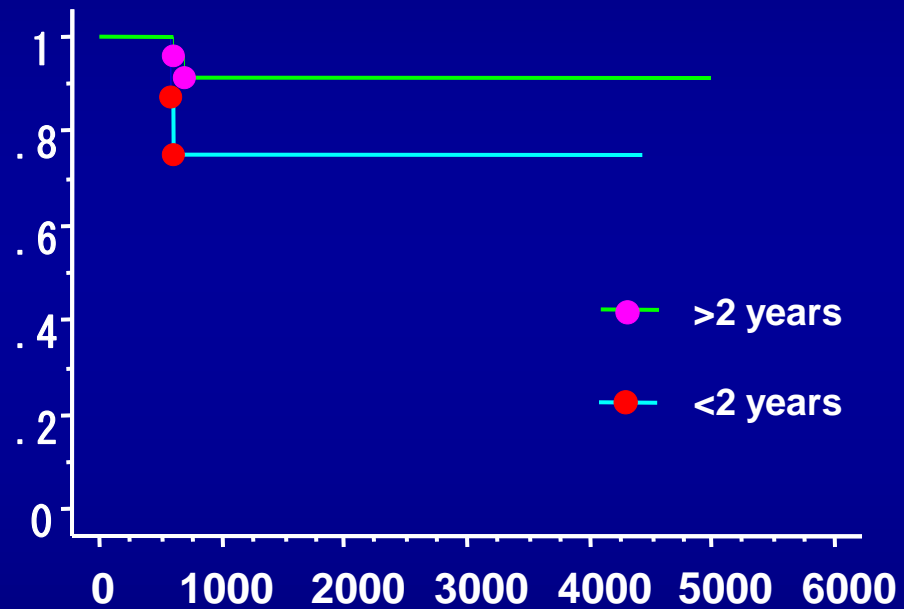
## DFS



Days

p=0.17

## OS

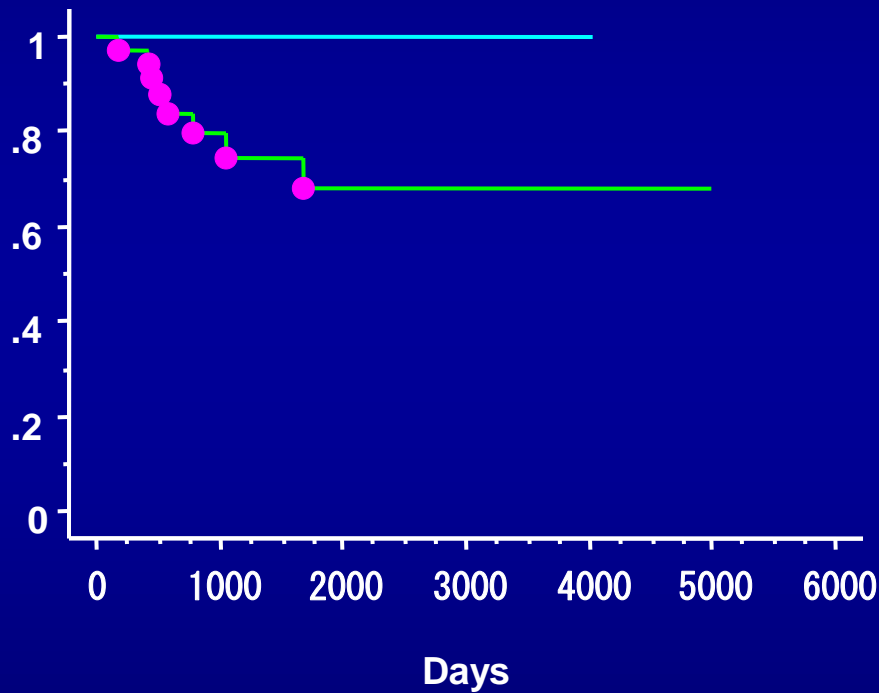


Days

p=0.19

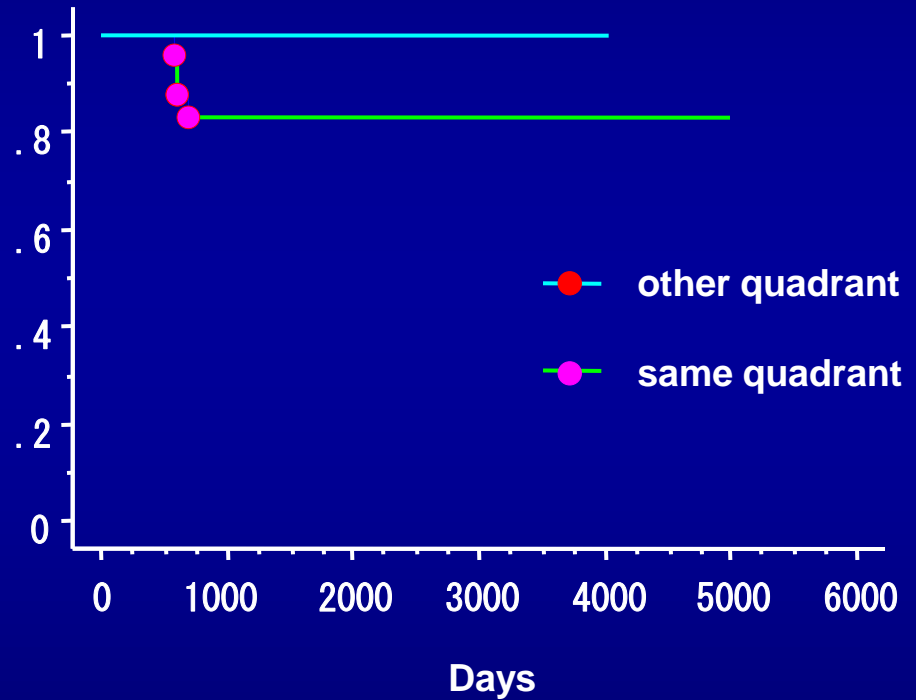
# Survival according to the recurrence site

DFS



NA

OS



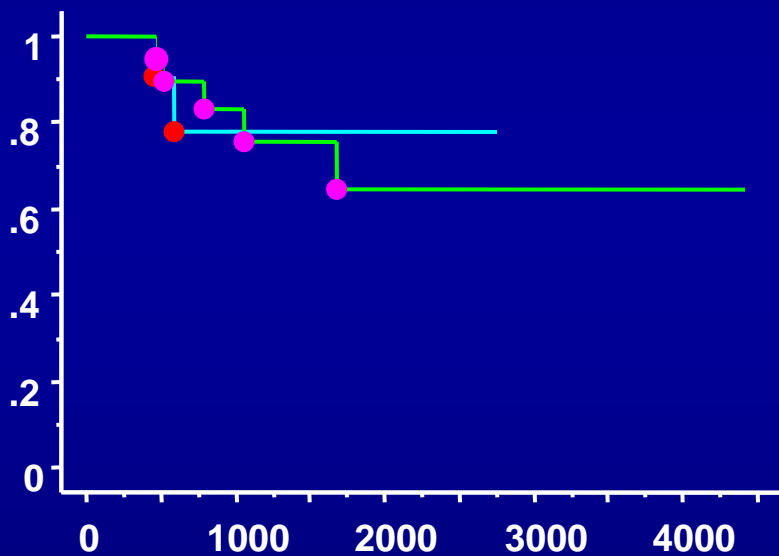
NA

- other quadrant
- same quadrant



# Survival according to hormone receptor status of the recurrent tumor

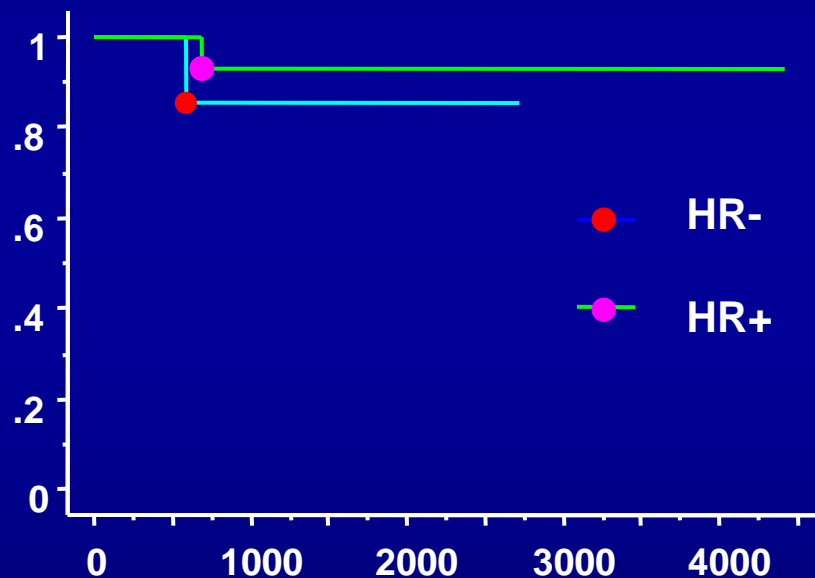
DFS



Days

p=0.9

OS



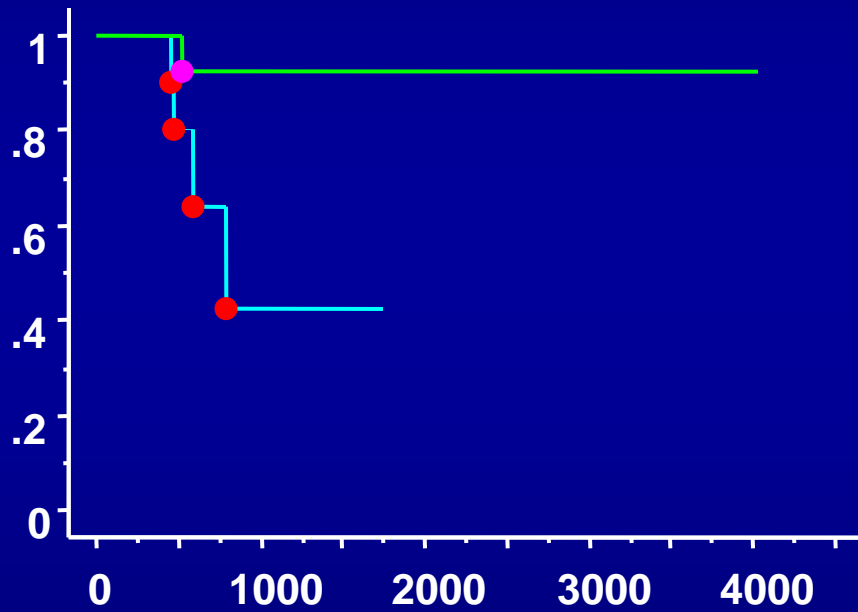
Days

p=0.4

● HR-  
● HR+

# Survival according to lymphatic invasion of the recurrent tumor

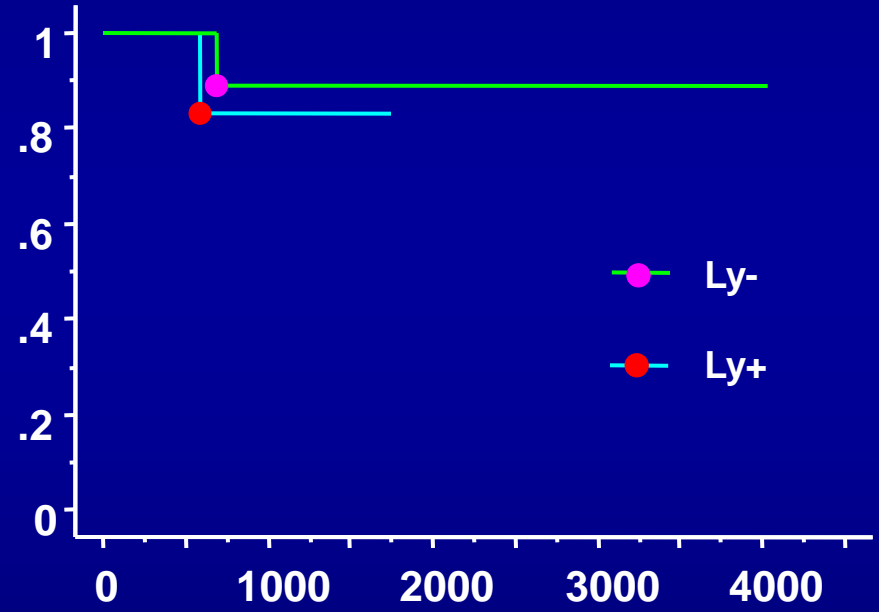
## DFS



Days

p=0.03

## OS



Ly-

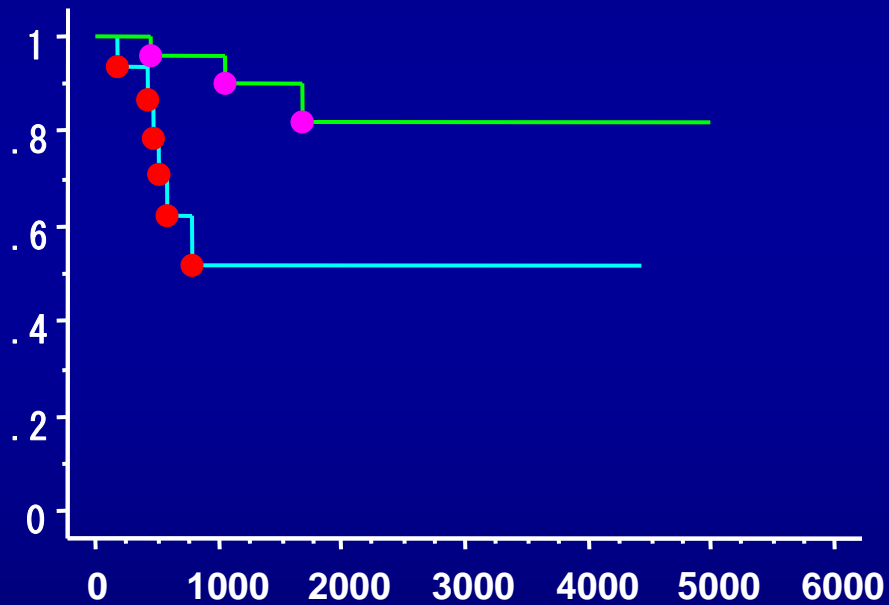
Ly+

Days

p=0.6

# Survival according to lymphatic invasion of the primary tumor

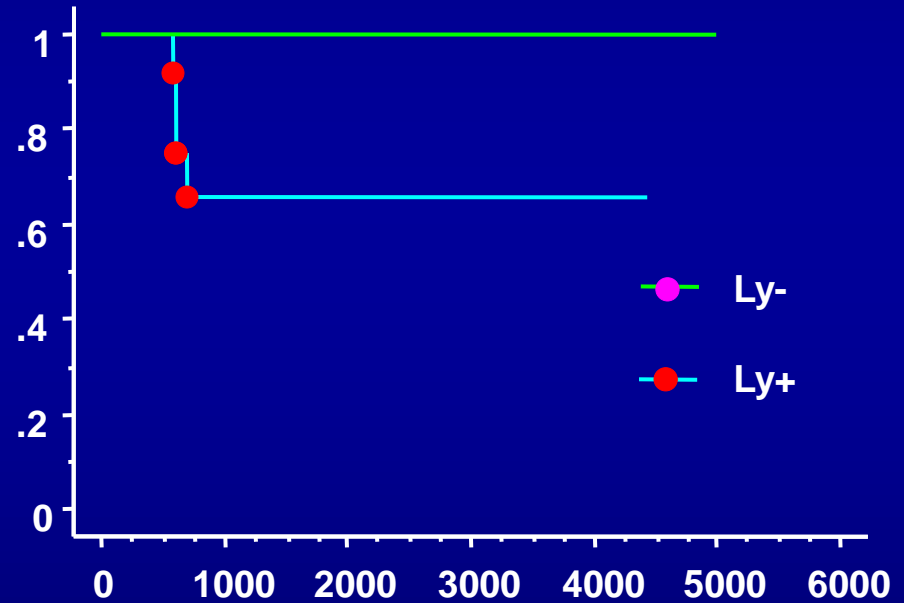
DFS



Days

p=0.018

OS

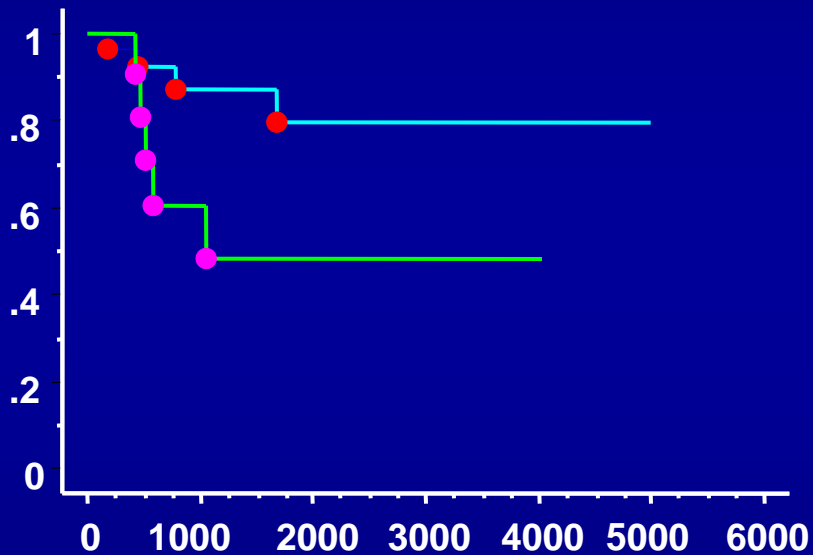


Days

NA

# Survival according to the pathological lymph node status

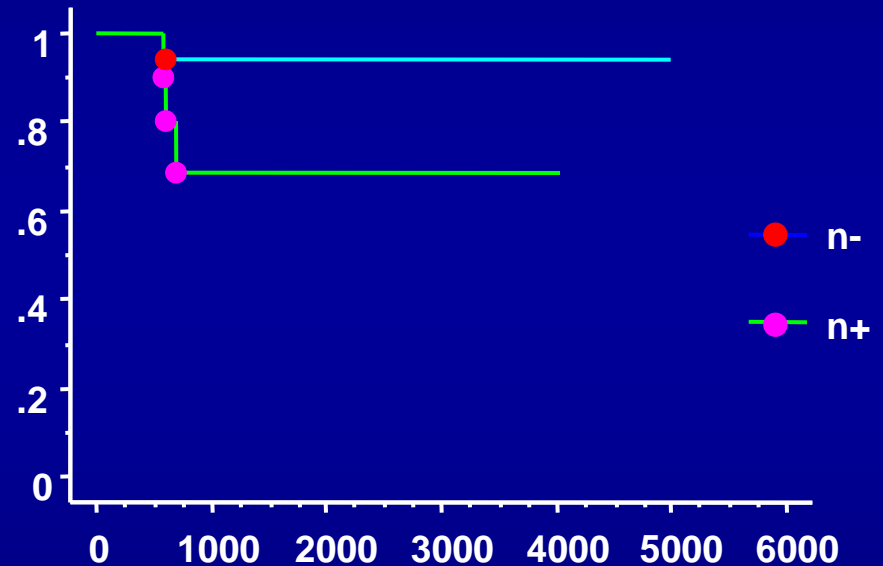
## DFS



Days

p=0.059

## OS



Days

P=0.069

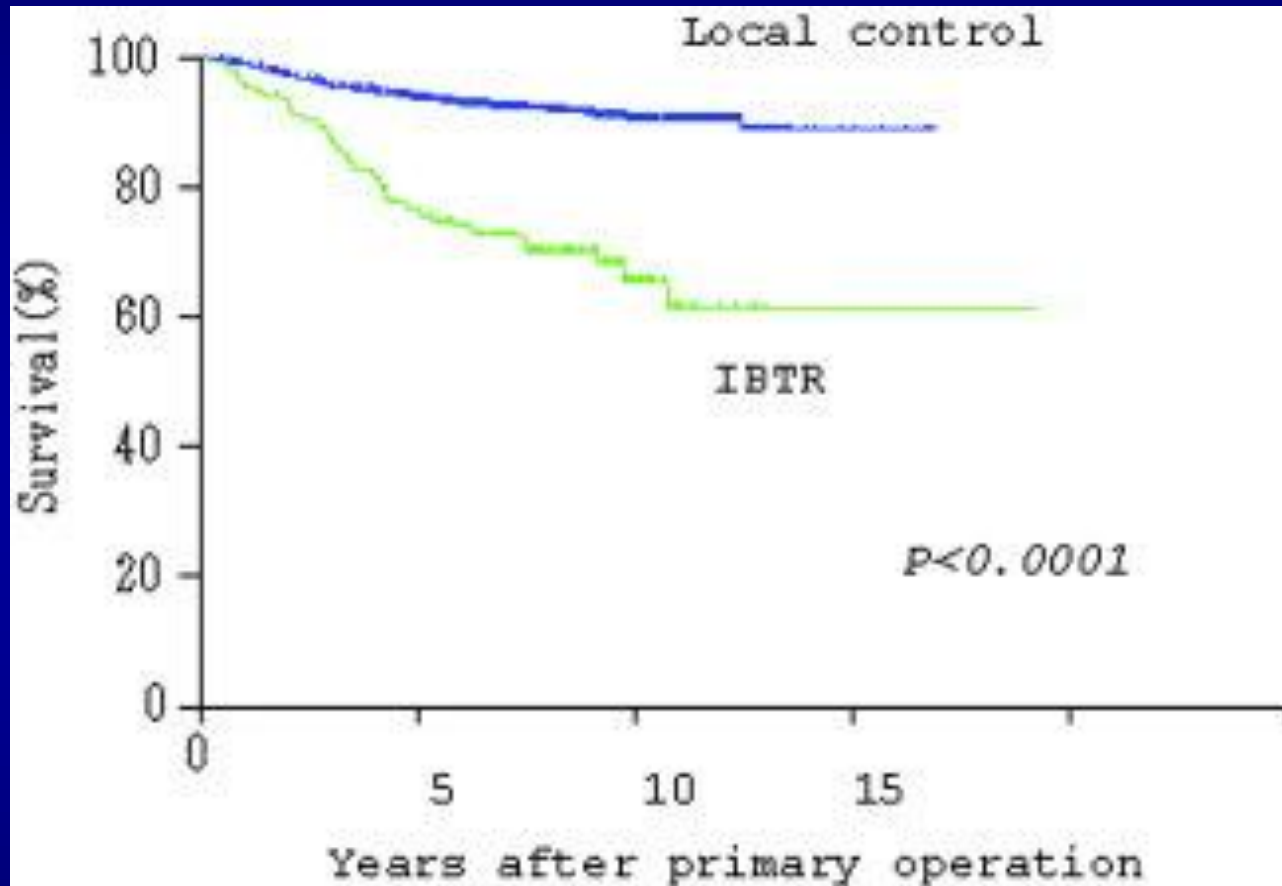
**Second series**

# Demographic factors of the patients

Characteristic	No. of patients
Age, yrs	
Median	49
Range	21–89
≤ 35	135
> 36	1766
Clinical tumor size, cm	
Median	17
Range	0–30
Lymph node metastasis	
Positive	380
Negative	1476
Unknown	45
ER status	
Positive	779
Negative	482
Unknown	640
PgR status	
Positive	510
Negative	430
Unknown	961
Surgical margin	
Positive	263
Negative	1503
Uncertain	135

Variable	Univariate analysis <i>P</i> value	Multivariate analysis		
		HR	<i>P</i> value	95% CI
Age	< 0.0001	0.943	< 0.0001	0.917–0.970
Size	0.0257	1.017	0.2557	0.988–1.047
Histologic type				
DCIS/IDC/special	0.6053			
Lymph node metastasis				
+/-	0.141			
Surgical margin				
+/-	< 0.0001	2.849	0.0004	1.587–5.012
ly +/-	0.8768			
v +/-	0.5236			
Nuclear grade				
3/1, 2	0.0650			
EIC +/-	0.0106	1.422	0.1857	0.847–2.398
ER -/+	0.0493	0.696	0.1464	0.427–1.135
PgR -/+	0.0036			
Chemotherapy				
-/+	0.0878			
Endocrine therapy				
-/+	0.0180	1.543	0.0824	0.397–1.057
Radiation therapy				
-/+	< 0.0001	3.861	< 0.0001	0.155–0.433

# Distant disease-free survival after primary operation according to local relapse





## Risk Factors for Distant Metastases After Breast Conserving Surgery, Results of Univariate and Multivariate Analysis

Variable	Univariate analysis		Multivariate analysis		
	HR	P value	HR	P value	95% CI
Age	0.979	0.004	0.99	< 0.30	0.978–1.008
Size	1.013	0.10			
Lymph node metastasis <u>+/-</u>	3.55	< 0.0001	3.34	< 0.0001	2.365–4.724
Surgical margin +/-	1.46	0.03	1.30	0.20	0.873–1.926
ly +/-	2.16	< 0.0001			
v +/-	1.98	0.002			
Nuclear grade 3/1, 2	3.32	0.006			
EIC +/-	0.57	0.03			
ER -/+	0.79	0.16			
PgR -/+	0.64	0.01			
<u>IBTR +/-</u>	3.72	< 0.0001	3.93	< 0.0001	2.676–5.771

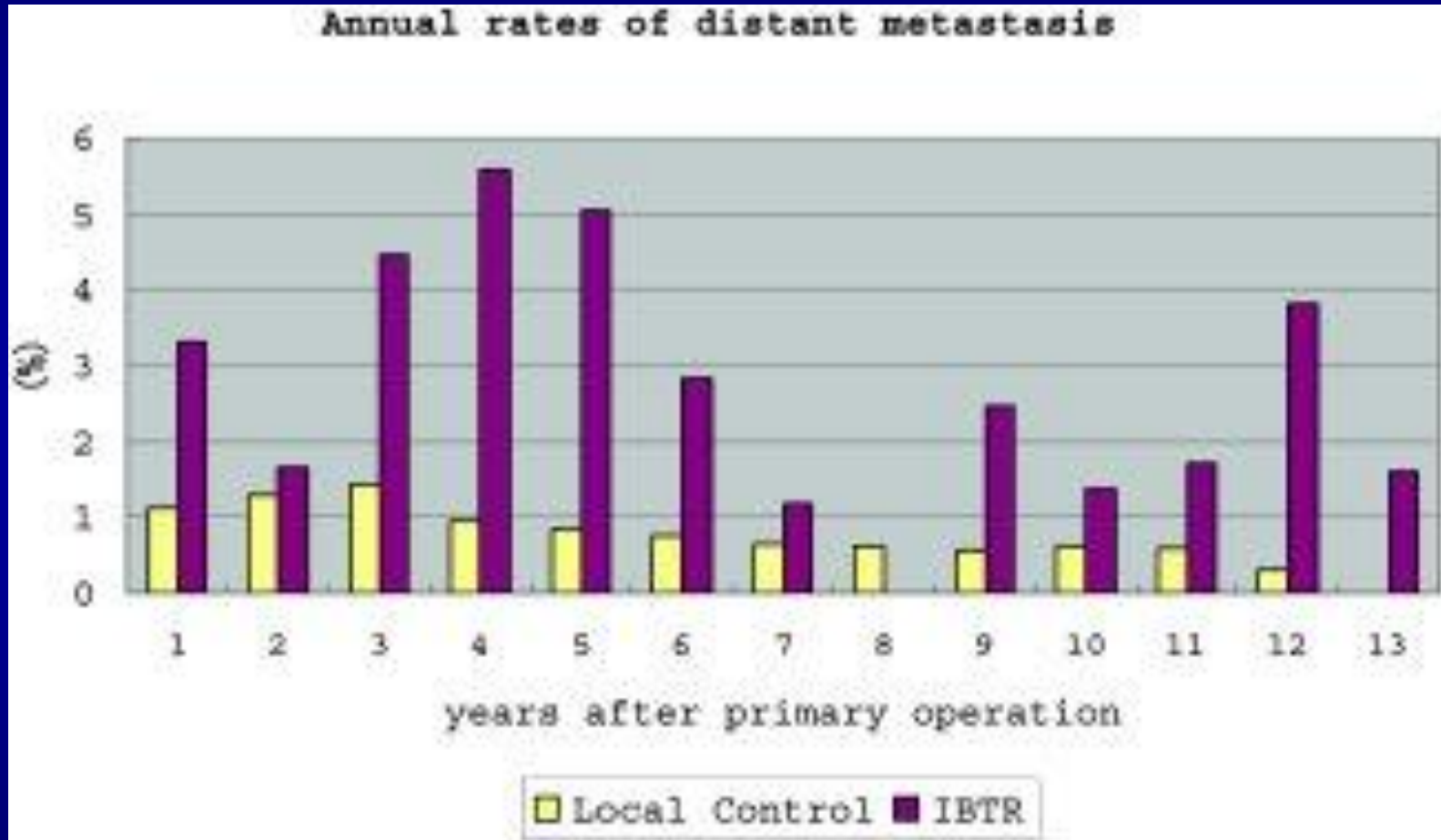
# Annual and cumulative rates of ipsilateral breast tumor recurrence after primary operation



## Risk Factors for Subsequent Distant Metastases After IBTR, Results of Univariate and Multivariate Analysis

Variable	Univariate analysis <i>P</i> value	Multivariate analysis		
		HR	<i>P</i> value	95% CI
Age	0.1724			
Size	0.5618			
Lymph node metastasis +/-	< 0.001	2.68	0.008	1.291-5.574
Surgical margin +/-	0.3113			
ly +/-	0.0161	1.21	0.599	0.888-2.506
v +/-	< 0.0001			
Nuclear grade 3/1, 2	NE			
EIC +/-	0.2134			
ER -/+	0.4057			
PgR -/+	0.2230			
DFI	< 0.0001	0.99	0.008	0.999-1.000

# Annual rates of distant metastasis according to Ipsilateral breast tumor recurrence (IBTR) status

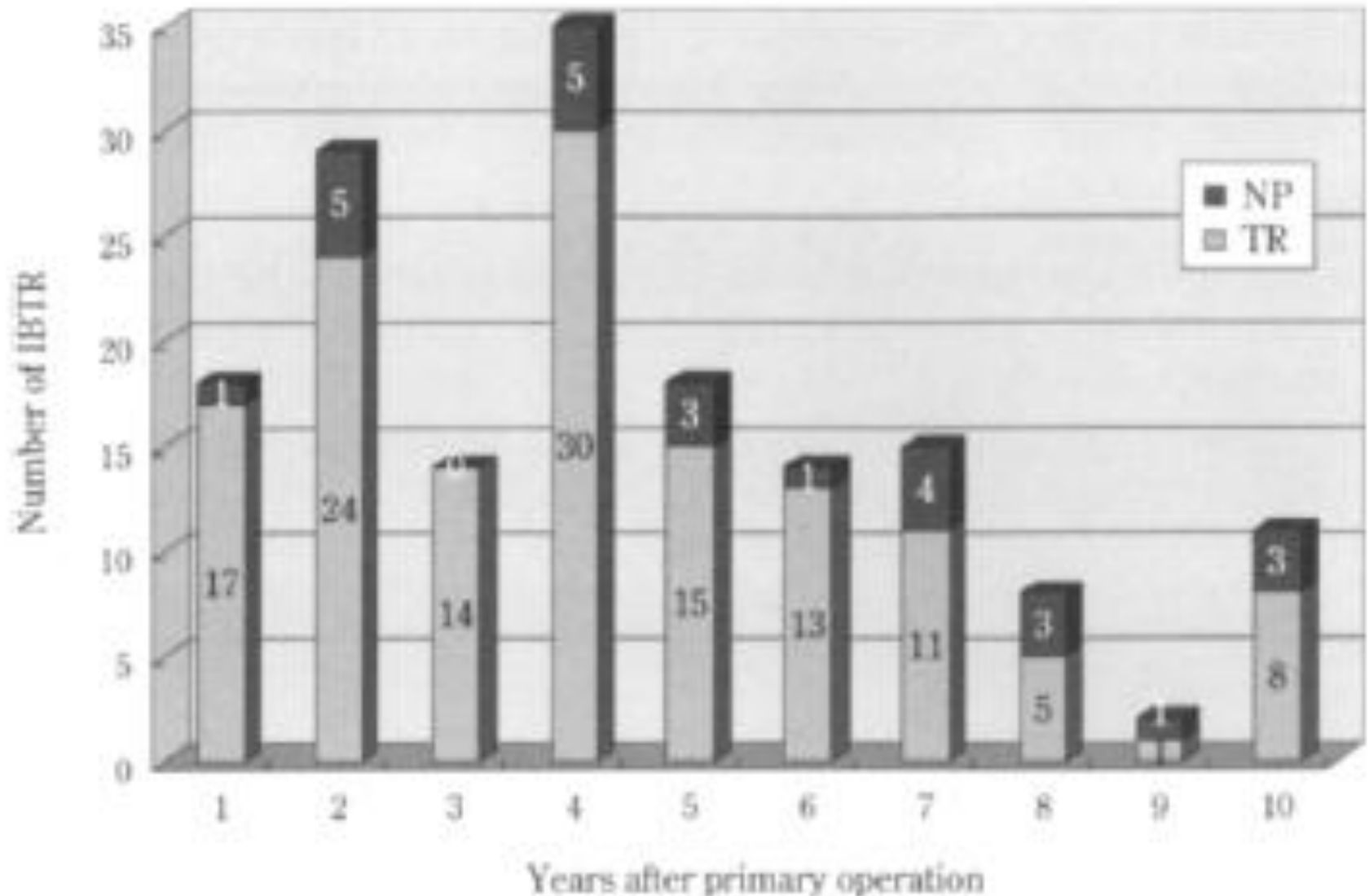


Third series

# Type of IBTR

- Classification of True recurrence (TR) /New primary (N)P was based on the location of the primary and secondary tumor, initial surgical margin and other pathologic features. Ambiguous cases were principally classified as TR.
- TR: 135/172 (78%), NP: 26/172 (15%)  
(Eleven cases were difficult to classify.)

# Annual incidence of ipsilateral breast tumor recurrence according to recurrence type



# Comparison of clinicopathological factors between TR and NP

	TR	NP	<i>p</i> -value
Age	44.8	47.1	N.S.
Size (cm)	1.7	1.8	N.S.
LN (+/-)	37/98	2/23	*0.031
ly (+/-)	44/53	5/13	N.S.
ER (+/-)	47/44	9/4	N.S.
DFI (months)	46.6	62.1	**0.025



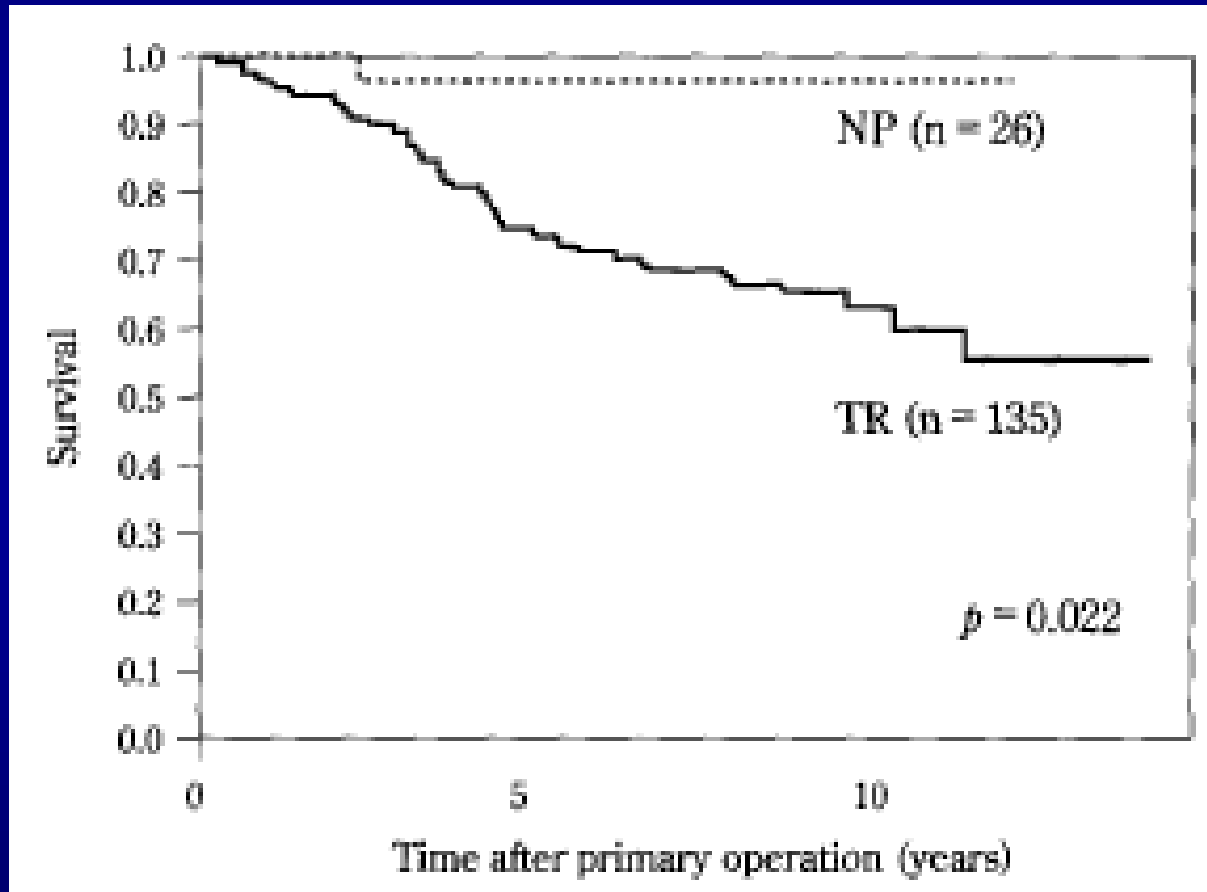
# Risk factors for true recurrence detected by uni- and multivariate analysis

Variable	risk/reference	univariate		multivariate	
		p-value	R.R.	p-value	95%C.I.
Age	≤35/>35	<0.0001	5.932	<0.0001	3.031-10.867
Size	>1 cm/≤1 cm	0.048	1.657	0.281	0.627-3.646
LN meta	positive/negative	0.028	2.064	0.009	1.205-3.457
Margin	positive/negative	<0.0001	2.921	<0.0001	1.562-5.341
EIC	positive/negative	0.0304	1.422	0.217	0.807-2.433
ER	negative/positive	0.0352	1.626	0.058	0.983-2.675
RT	(-)/(+)	<0.0001	3.491	<0.0001	2.024-6.033

# Risk factors for new primary detected by uni- and multivariate analysis

Variable	risk/reference	univariate		multivariate	
		p-value	R.R.	p-value	95%C.I.
Age	younger/older	0.017	1.046	<0.045	1.0028-1.1271
Ly	negative/positive	0.048	1.116	0.842	0.6556-7.3288
CBC	yes/no	0.004	4.950	0.036	1.8639-19.731
Endocrine therapy	(-)/(+)	0.0047	2.196	0.174	0.8163-21.881
Chemotherapy	(-)/(+)	0.0016	2.000	0.270	0.4921-17.374
Radiation	(-)/(+)	0.0002	3.090	0.023	1.3940-8.4595

# Survival rates of patients with true recurrence and new primary after primary operation



# Salvage surgery

- Local recurrence 172 cases
  - Salvage operation 136 cases
    - Repeat lumpectomy 55 cases
      - Five year distant-free survival rate 75.0%
      - Five year local control rate: 80%
    - Salvage mastectomy 81 cases
      - Five year distant-free survival rate 74.6%
      - Five year local control rate: 93%

## Risk factors for secondary local relapse after repeat lumpectomy (Univariate analysis)

Variable	risk/reference	<i>p</i> -value
Age	younger/older	0.335
menopause	pre-/post-	0.810
location	elsewhere/near	0.726
type of recurrence	NP/TR	0.003
size	> 1 cm/≤ 1 cm	0.405
LN	positive/negative	0.506
margin	positive/negative	0.861
ly	positive/negative	0.233
v	positive/negative	0.256
grade	3/1, 2	N.E.
EIC	positive/negative	0.073
ER	positive/negative	0.131
PgR	positive/negative	0.772
Endocrine therapy	(-)/(+)	0.058
chemotherapy	(-)/(+)	0.227
CBC	(-)/(+)	0.778
DFI	(-)/(+)	0.156

# Summary

- **The 10-year cumulative rate of IBTR was 9.6% (8.5% in the group with postoperative irradiation and 17.2% without radiation).**
- **Risk factors for IBTR include young age, positive margin, omission of postoperative radiation and endocrine therapy.**
- **IBTR is a risk factor for prognosis and the 10 year distant-free survival rate was 70%.**
- **The methods of salvage operation did not affect survival.**
- **Two peaks in the incidence of distant metastasis were observed among patients with IBTR.**
- **Classifying IBTR into true recurrence and new primary contributes to predict outcome.**



Thank you for your attention!



# SLN in the patients Re-operation

SLN procedure success rate	n	%	p
<b>By procedure</b>			
Modified radical surgery	3/11	45.5	0.106
Total mastectomy and SLN	4/4	100	
Total mastectomy alone	4/5	80	
<b>By no of previous LN excised</b>			
<5	8/9	88.9	0.134
≥5	5/11	45.5	
<b>By previous radiotherapy</b>			
No	8/11	61.1	0.509
Yes	2/2	100	
<b>By previous reconstruction</b>			
No	7/8	87.5	0.147
Yes	6/12	50	
<b>By stage</b>			
0	5/7	71.4	0.786
1	4/7	57.1	
2	3/4	75	