Young age is associated with ipsilateral breast tumor recurrence after breast conserving surgery and radiation therapy in HER2 positive/ ER negative subtype

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Age and Breast conserving surgery

Can patient-, treatment- and pathology –related characteristics explain the high local recurrence rate following **breast conserving surgery In young patients**? *Eur J cancer 2003*

Prognostic factors of breast recurrence in the conservative management of early breast cancer *Int J Radiat Oncol Biol Phys (1989)*

Risk factors in breast conservation therapy *JCO (1994)*

Local recurrence after **breast conserving therapy** for invasive breast cancer: high incidence **in young patients** and association with **poor survival** *Int J Radiat Oncol Biol Phys (1998)*

The impact of young age on locoregional recurrence after **breast conservation therapy** in patients 40 years old or younger: **How young is young** ? *Int J Radiat Oncol Biol Phys (2006)*

Effect of age and **radiation dose** on local control after **breast conserving** treatment: EORTC trial *Radiother Oncol(2006)*

Age remains the **first prognostic factor** for locoregional breast cancer recurrence in young(<40yr) women treated with breast conserving surgery first *Radiotherapy and oncology (2007)*

Intrinsic subtype and local recurrence

Breast cancer subtype approximated by Estrogen receptor, progesterone receptor, and HER-2 is associated with local and distant recurrence after Breast Conserving therapy

Nguyen et al JCO 2008 26: 2373-2378

Breast cancer subtypes and risk of local and regional relapse

Voduc et al JCO 2010 28:1684-1691

Estrogen/progesterone receptor negativity and HER2 positivity predict locoregional recurrence in patients with T1a,b N0 breast cancer

Albert et al Int J Radiat Oncol Biol Phys 2010 77:1296-1302

Intrinsic subtype and local recurrence

Breast cancer subtype approximated by Estrogen receptor, progesterone receptor, and HER-2 is associated with local and distant recurrence after Breast Conserving therapy

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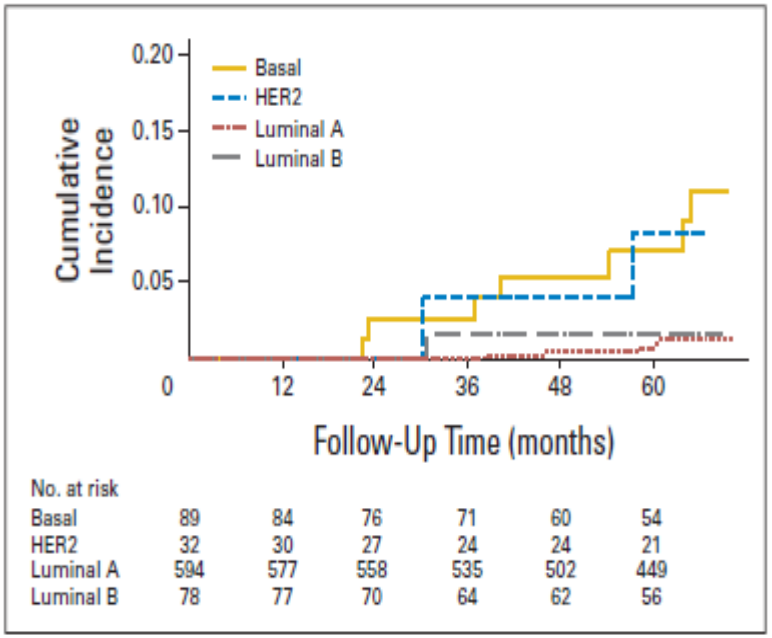
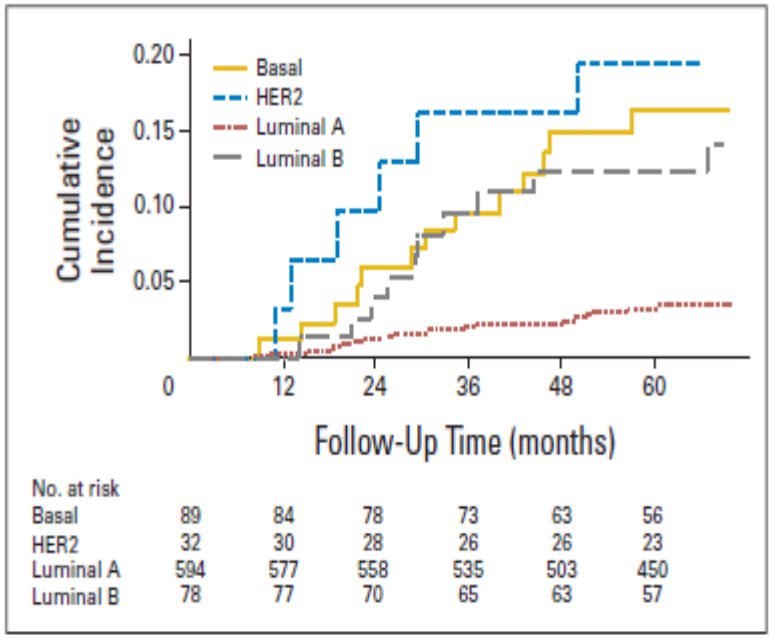
Local recurrence



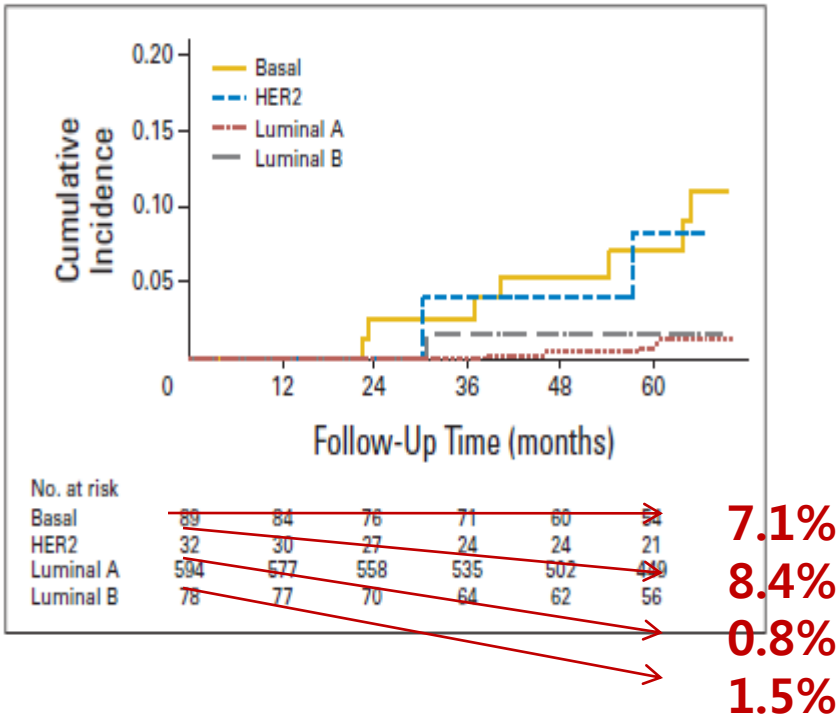
Distant metastasis



Breast cancer subtype approximated by Estrogen receptor, progesterone receptor, and HER-2 is associated with local and distant recurrence after Breast Conserving therapy

Nguyen et al JCO 2008 26: 2373-2378

Local recurrence (n=18)



Multivariate analysis

	HR	95% CI	P
Luminal A	1		
Her2	**9.2**	1.6 to 51	0.012
Basal	**7.1**	1.6 to 31	0.009

Intrinsic subtype and local recurrence

Breast cancer subtype approximated by Estrogen receptor, progesterone receptor, and HER-2 is associated with local and distant recurrence after Breast Conserving therapy

Nguyen et al JCO 2008 26: 2373-2378

Local recurrence was particularly low for the luminal A subtype, but was less than 10% at 5 yr for all subtypes. (70month)

Age ≤ 35 n=28 (3.5%), Age ≤ 45 n=152 (18.9%)

Breast cancer subtypes and risk of local and regional relapse

Voduc et al JCO 2010 28:1684-1691

Luminal A are associated with a low risk of local or regional recurrence (12yr)

Age <40 n=122 (8%)

IBTR after Conserving surgery

Young age

Intrinsic subtype

Aim to the study

The effect of patient age and breast cancer subtype on IBTR after treatment by BCS and RT

2000 -2005 ,
AMC data base=4984

2000 -2005 ,
SNU data base=2512

Inclusion criteria

Breast Conserving Surgery and radiotherapy
T1,T2

Exclusion criteria (n=2,102)
DCIS
T4, M1
Unknown T, N status
ER, PR , Her2/neu IHC unknown
IHC result of Her2/neu was 2+ , but no further study like FISH, SISH etc
Positive surgical margins

Total 2,102, median follow up =61 months
(≤40;513 , >40;1589)

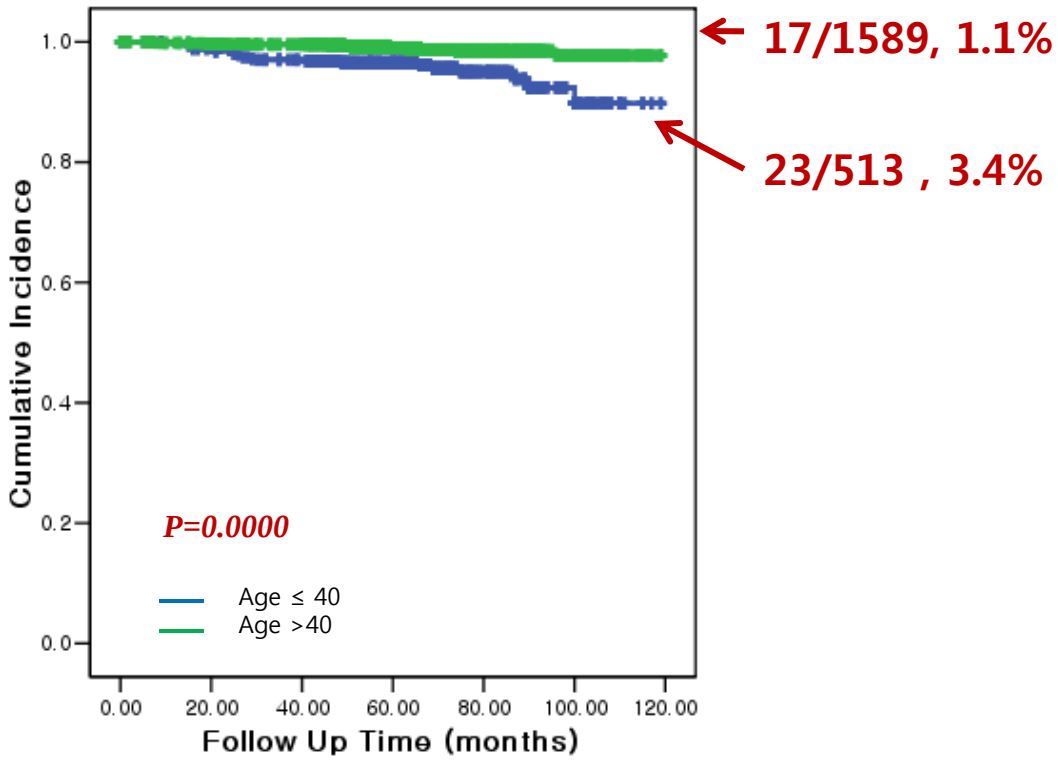
Prognostic Factor characteristics according to the age subgroup

Characteristics	Age≤40		Age >40		*P*
	No	%	No	%	
T stage					
T1	308	60	1123	70.7	0.000
T2	205	40	466	29.3	
Lymph node					
positive	339	66.1	1169	73.6	0.001
negative	174	33.9	420	26.4	
Grade					
1 /2	253	54.1	908	63.7	0.000
3	215	45.9	517	36.3	
Intrinsic subtype					
Luminal A	262	**51.1**	944	**59.4**	0.003
Luminal B	51	9.9	165	10.4	
HER2	52	**10.1**	119	7.5	
Triple negative	148	28.8	361	22.7	
Chemotherapy	410	83	1050	66.4	0.000
Hormone therapy	307	70.4	1136	71.8	0.310

Characteristics according to the Intrinsic subtype

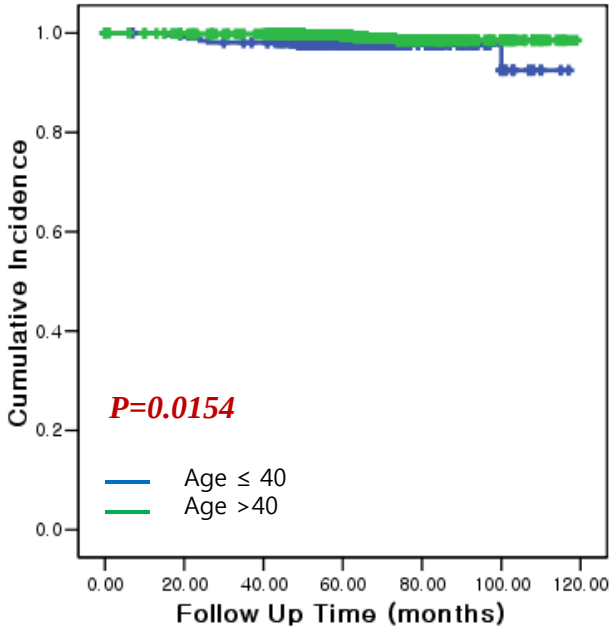
Characteristics	Age≤40		Age >40		*P*
	No	%	No	%	
Luminal A					
T1	174	66.4	684	72.5	0.034
Lymph node(+)	87	33.2	263	27.9	0.055
G3	47	20.2	155	18.3	0.292
Chemotherapy	176	70.7	516	55.0	0.000
Luminal B					
T1	32	62.7	121	73.3	0.102
Lymph node(+)	23	45.1	39	23.6	0.003
G3	26	54.2	54	36	0.020
Chemotherapy	43	91.5	86	52.4	0.000
HER2					
T1	32	61.5	81	68.1	0.255
Lymph node(+)	20	38.5	37	31.1	0.222
G3	29	61.7	67	63.8	0.471
Triple negative					
T1	70	47.3	237	65.7	0.000
Lymph node(+)	44	29.7	81	22.4	0.054
G3	113	80.7	241	74.2	0.079

IBTR free survival according to the age groups-all subtype

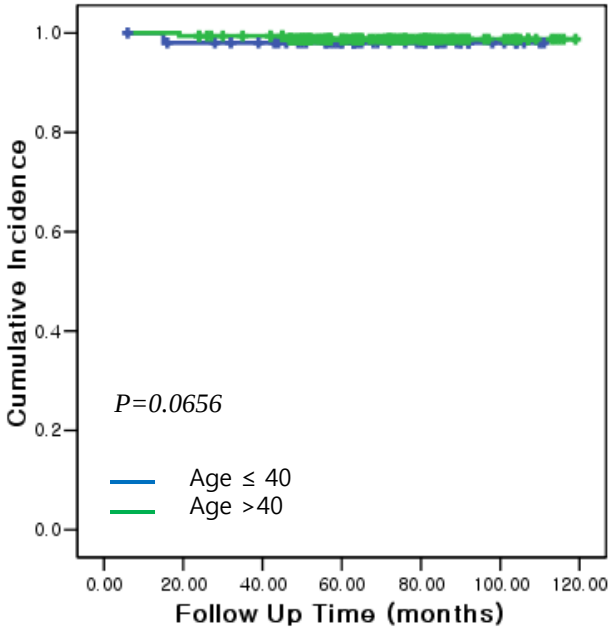


IBTR free survival according to the age groups

Luminal A subtype

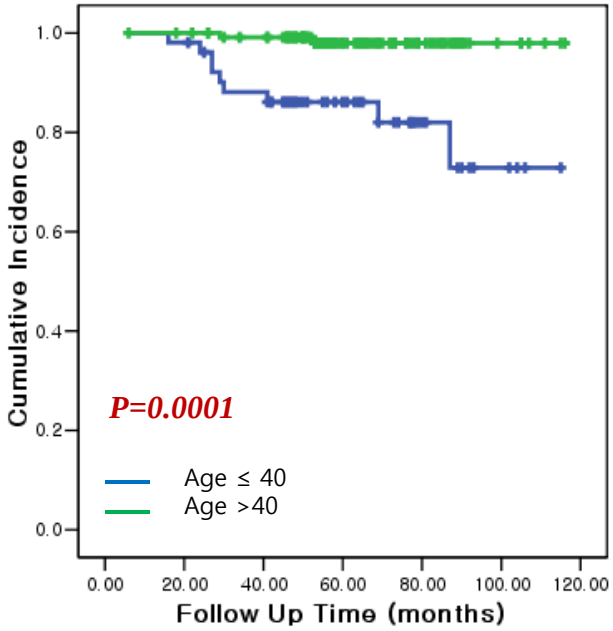


Luminal B subtype

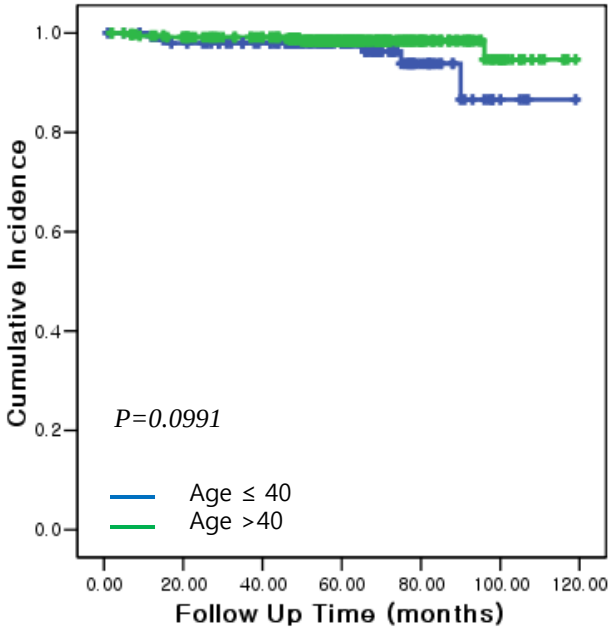


IBTR free survival according to the age groups

HER2 subtype

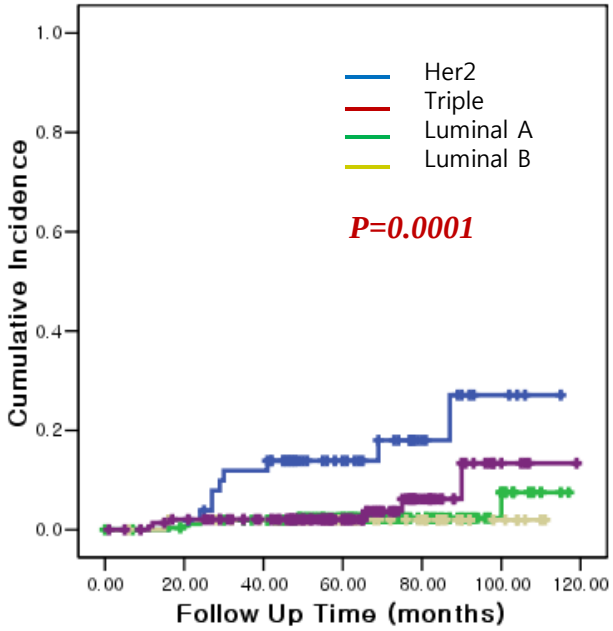


Triple negative subtype

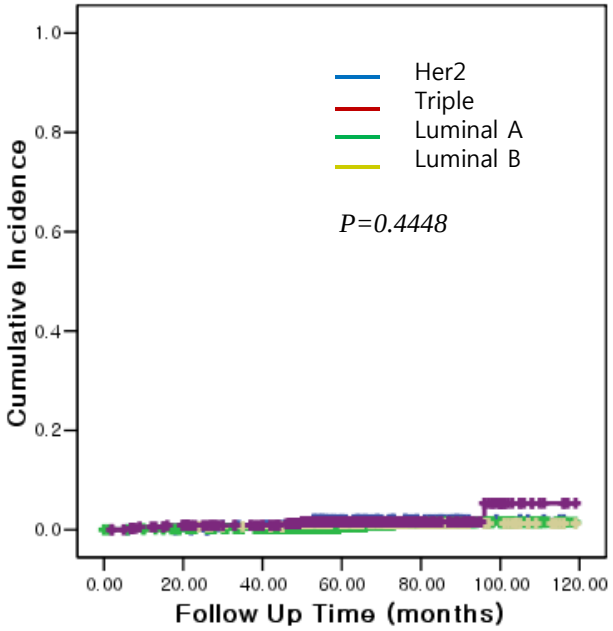


Cumulative Incidence of IBTR according to the combination of subtypes and age groups

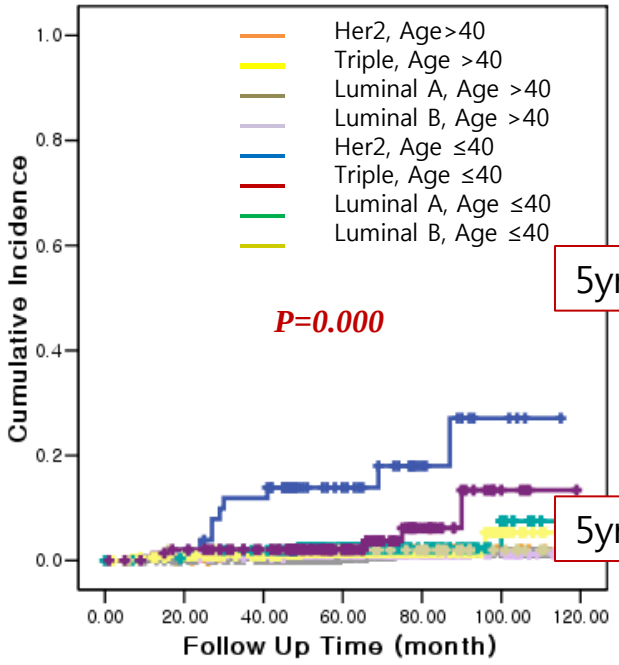
Age ≤ 40yr



Age >40 yr



Cumulative Incidence of IBTR according to the combination of subtypes and age groups



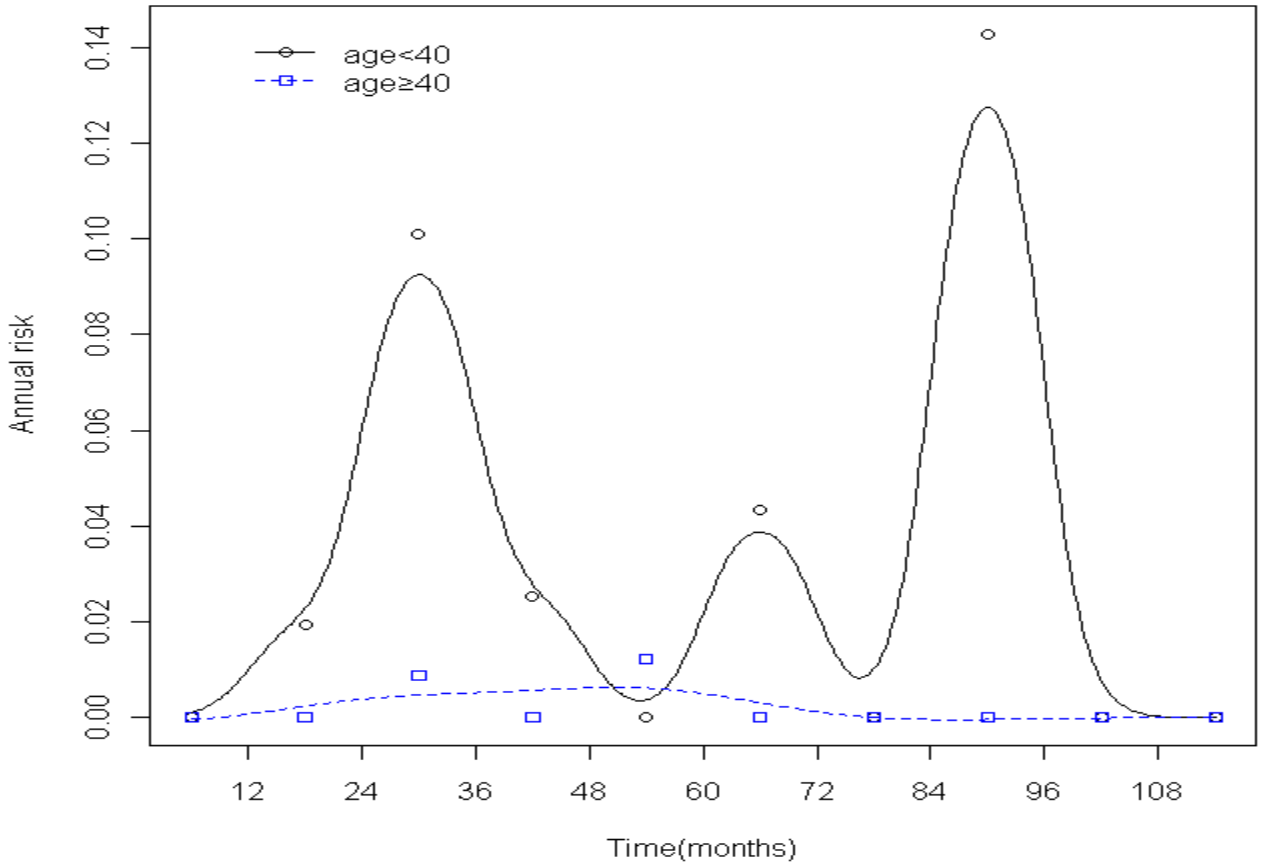
5yr IBTR 13.9%

5yr IBTR 1.3%

	HR	95% CI	*P*
Age>40			
Luminal A	1		
Luminal B	1.55	0.32-7.51	0.588
HER2	0.55	0.05-6.34	0.635
Triple negative	1.17	0.22-6.26	0.856
Age ≤ 40			
Luminal A	2.97	0.99-8.96	0.053
Luminal B	1.92	0.22-16.84	0.557
HER2	**12.14**	**2.54-57.96**	**0.002**
Triple negative	1.22	0.16-9.05	0.849

Adjusted by tumor size, node positivity, grade, chemotherapy, hormone therapy

Smoothed annual risk of IBTR after primary surgery with HER2 subtype



Conclusion

Younger breast cancer patients with the HER2 subtype have an increased risk of IBTR after BCS and RT

Aggressive local control and adjuvant therapy should be considered for young patients with HER2 subtype breast cancer

Back up slide

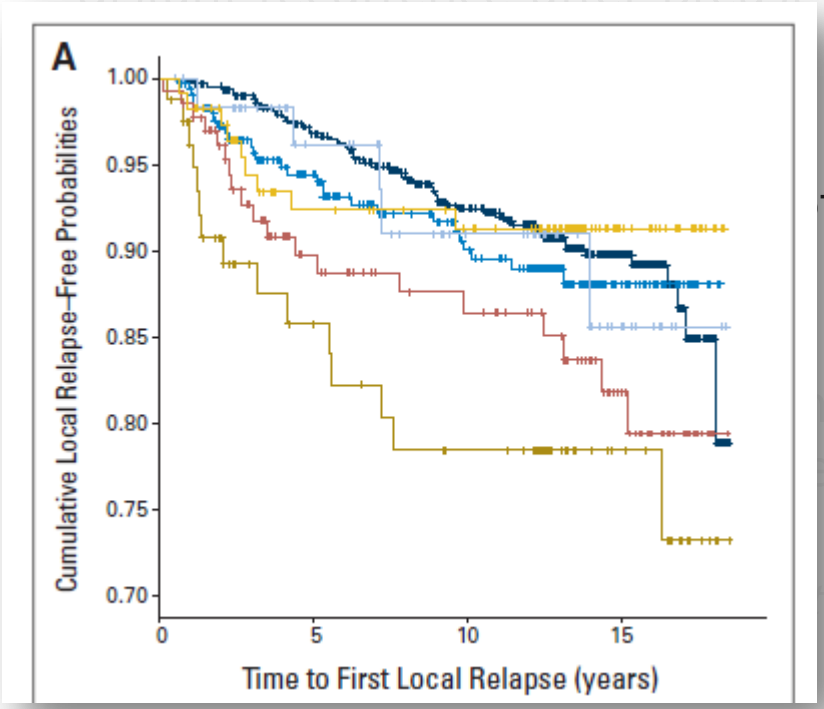
Summary

5 yr rate of IBTR who underwent BCS and RT was low (1.6%) , but higher in young women (≤40yrs;3.4%) than in old women (>40yrs;1.1%)

Summary

- The rate of IBTR varied according to the breast cancer subtypes, as assessed by IHC staining for ER, PR, and HER2
- Multivariate analysis showed that the presence of the HER2 subtype in younger patients was significantly and independently associated with increased local recurrence

Local recurrence



Regional recurrence