24th ANNUAL
ADVANCES IN ONCOLOGY CONFERENCE

NOVEMBER 11, 2023
THE KIMPTON SAWYER HOTEL
SACRAMENTO, CALIFORNIA

Distinguished Keynote Speaker

14th Annual Lois O'Grady Lectureship Recipient

Lori Pierce, MD, FASCO, FASTRO

Vice Provost for Academic and Faculty Affairs

Professor of Radiation Oncology

University of Michigan

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

Recent Advances in Radiation Treatment for Early-Stage Breast Cancer

Lori Pierce MD, FASCO, FASTRO
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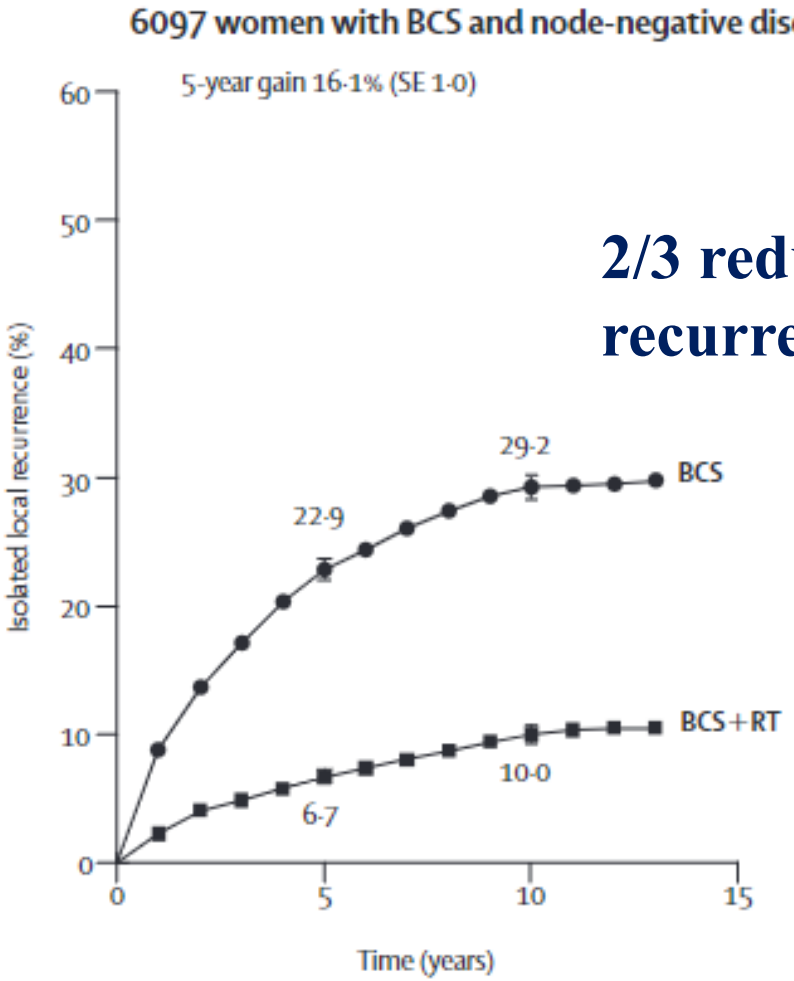
Effects of Radiotherapy on Local Recurrence: An Overview of the Randomised Trials



2/3 reduction in local recurrence with RT

EBCTCG. Lancet. 2005;365:1687.

Adjuvant RT after Lumpectomy

- Early Breast Cancer Trialists Collaborative Group (EBCTCG) Meta-Analysis:
  - Radiation after lumpectomy decreases the risk of any recurrence (local or distant) and impacts breast cancer survival

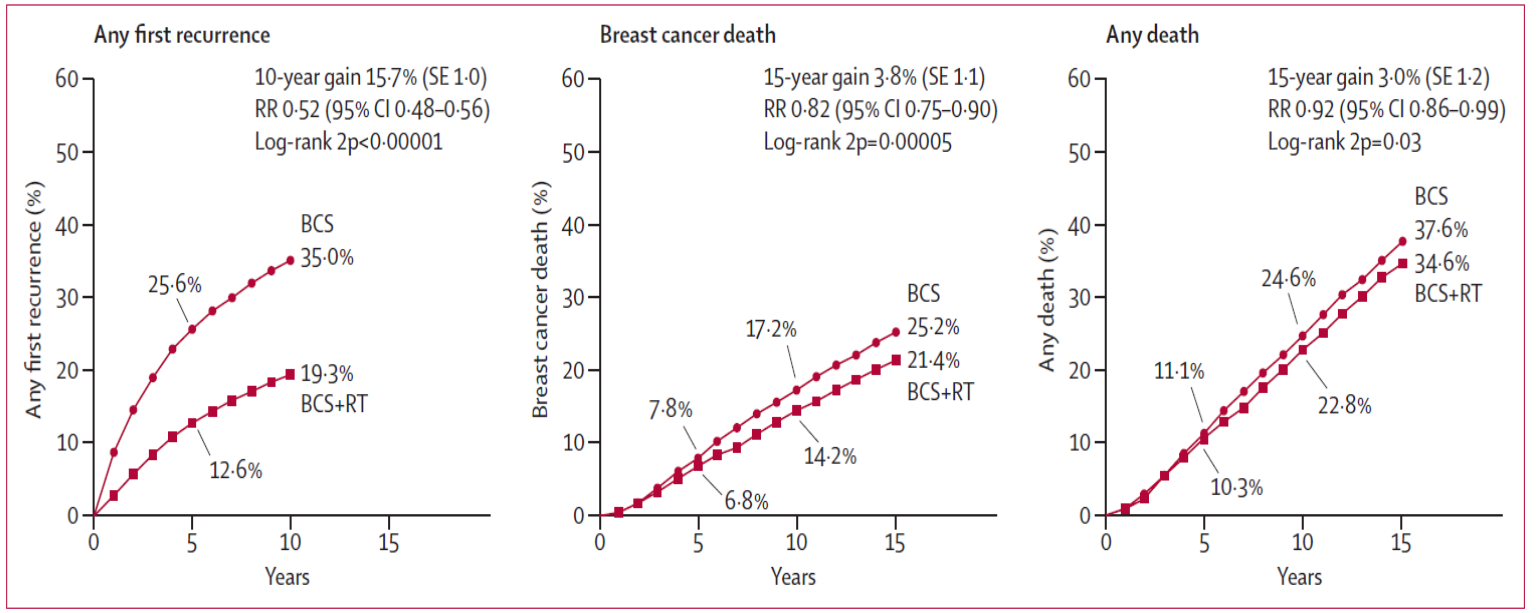


Figure 1: Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk of any (locoregional or distant) first recurrence and on 15-year risks of breast cancer death and death from any cause in 10 801 women (67% with pathologically node-negative disease) in 17 trials
Further details are in webappendix p 5. RR=rate ratio. Rate ratios in this figure include all available years of follow-up.

EBCTCG. Lancet 2011;378:1707.

Basics of tumor and normal tissue sensitivity to fraction size

- Long assumed that cancers were insensitive to fraction size
- Late reacting normal tissues known to be fraction size sensitive
- α/β (measure of fractionation sensitivity) modeling indicates breast cancer is more sensitive to fraction size than previously thought so using small fractions (1.8 – 2.0 Gy) could spare cancer as much as normal tissues.
- However, use of larger daily fractions requires reduction in total dose to reduce normal tissue toxicity.

Trials of Daily Conventional Fx vs. Moderate Hypofractionation

Trial			Treatment (Gy)		Local recurrence (%)		F/U (yrs.)
	n	Stage	CF	HF	CF	HF	
Ontario COG	1234	T_{1-2}, N_0	50/2	42.5/2.66	6.7	6.2	10
START B	2215	T_{1-3}, N_{0-1}	50/2	40/2.67	5.2	3.8	10
DBCG HYPO	1854	T_{is-2}, N_{0-1}	50/2	40/2.67 minority with boost	3.3	3.0	9
China	734	T_{1-2}, N_{0-3}	50/2	43.5/2.9 +boost	2	1.2	5
MD Anderson	287	T_{is-2}, N_{0-1}	50/2	42.5/2.66 +boost	2	1	5
BIG 3-07/TROG 07.01	1608	T_{is}	50/2	42.5/2.66 +/- boost	5.1	5.1	5

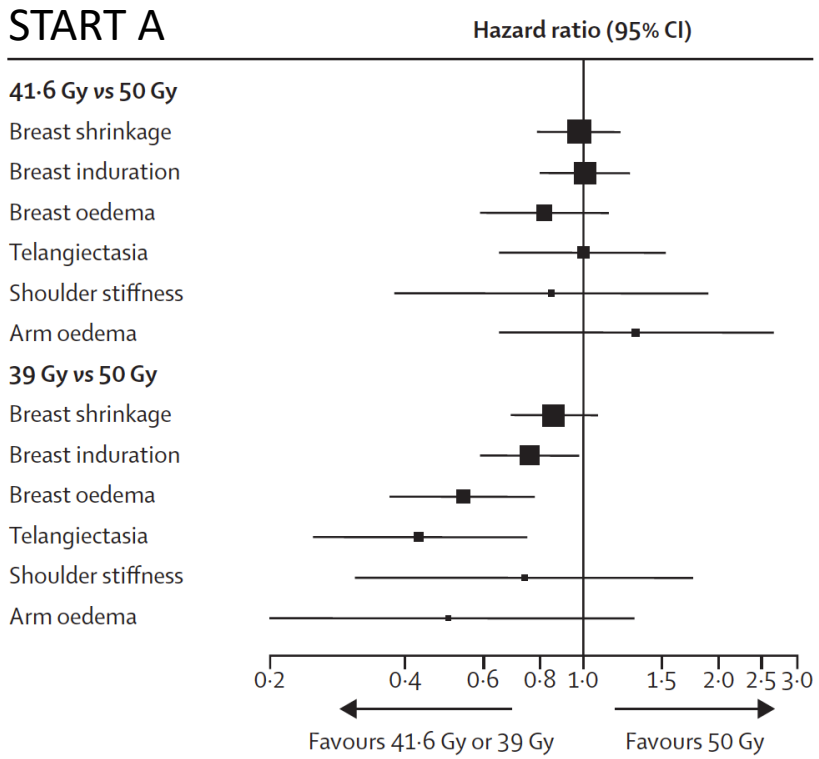
Hypofractionation: Equal/reduced late tissue effects

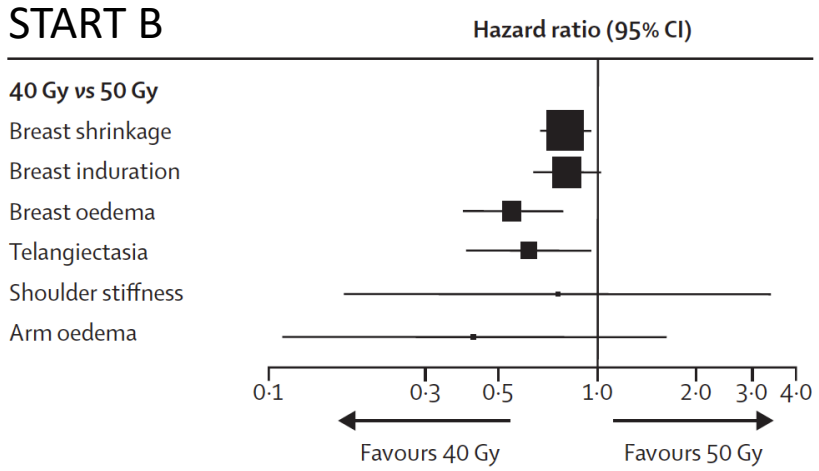
Ontario Clinical Oncology

Table 2. Global Cosmetic Outcome, Assessed According to the EORTC Scale.*

Rating	10 Yr		
	Standard Regimen (N=216)	Hypofractionated Regimen (N=235)	Absolute Difference (95% CI)
	percent of patients		*percentage points*
Excellent	27.8	30.6	
Good	43.5	39.2	
Fair	25.5	25.4	
Poor	3.2	4.8	
Excellent or good	71.3	69.8	1.5 (−6.9 to 9.8)

Whelan et al, NEJM 2010;362:513-520.





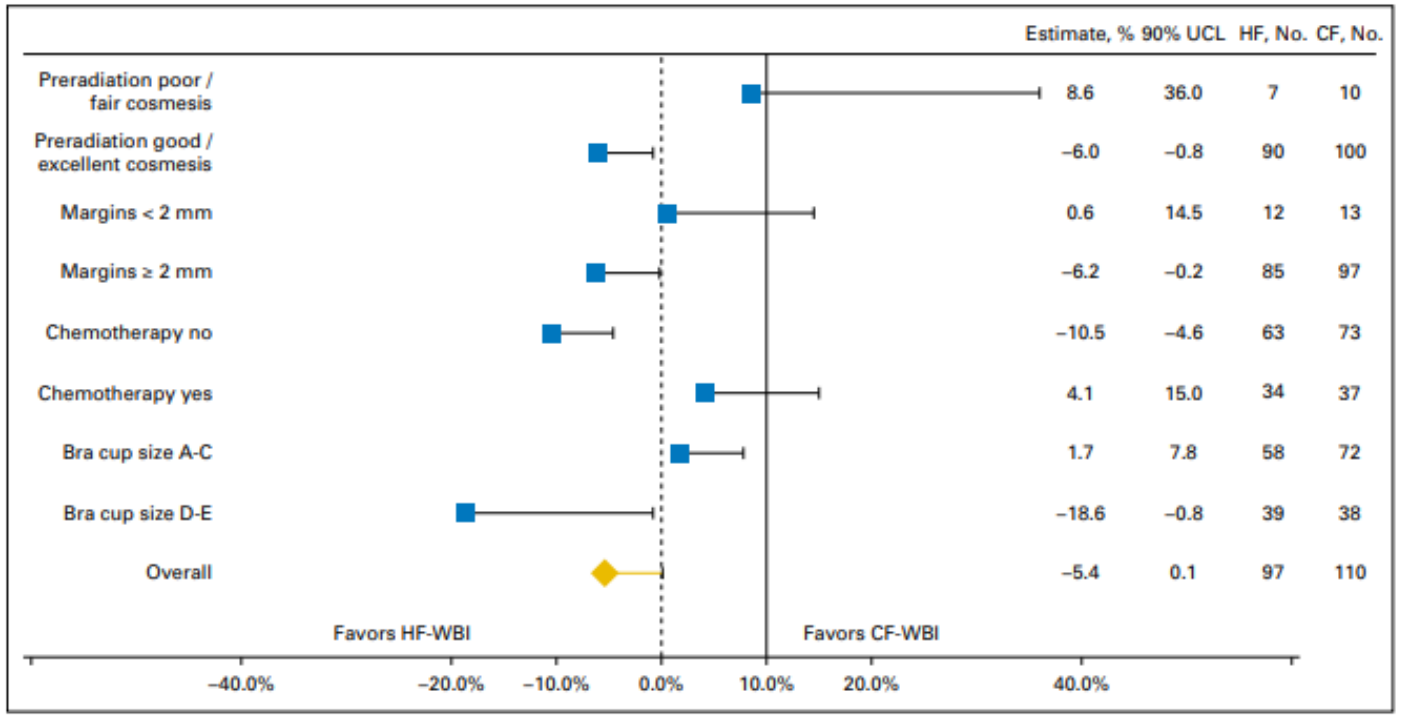
Haviland et al, Lancet Onc 2013;14:1086-94.

Three-year Outcomes with Hypofx vs. Conventional Whole Breast RT - Randomized Trial

MD Anderson: Primary endpoint was noninferiority of adverse cosmesis at 3 years

>99% patients received boost

~33% with bra cup size D-EE



Adverse cosmetic outcome

Shaitelman et al. JCO, 2018

MD Anderson trial: 3-year outcomes

Outcome	3-Year Estimate (95% CI)	4-Year Estimate (95% CI)	5-Year Estimate (95% CI)
Overall survival			
All (n = 287)	1	1 (0.97 to 1.00)	0.99 (0.94 to 1.00)
CF-WBI (n = 149)	1	1 (0.97 to 1.00)	0.98 (0.89 to 1.00)
HF-WBI (n = 138)	1	0.99 (0.93 to 1.00)	0.99 (0.93 to 1.00)
Local recurrence-free survival			
All (n = 287)	0.99 (0.97 to 1.00)	0.98 (0.96 to 0.99)	0.98 (0.96 to 0.99)
CF-WBI (n = 149)	0.99 (0.95 to 1.00)	0.98 (0.93 to 0.99)	0.98 (0.93 to 0.99)
HF-WBI (n = 138)	0.99 (0.95 to 1.00)	0.99 (0.95 to 1.00)	0.99 (0.95 to 1.00)
Distant recurrence-free survival			
All (n = 287)	0.99 (0.97 to 1.00)	0.99 (0.97 to 1.00)	0.99 (0.97 to 1.00)
CF-WBI (n = 149)	0.99 (0.95 to 1.00)	0.99 (0.95 to 1.00)	0.99 (0.95 to 1.00)
HF-WBI (n = 138)	0.99 (0.95 to 1.00)	0.99 (0.95 to 1.00)	0.99 (0.95 to 1.00)
Contralateral breast cancer–free survival			
All (n = 287)	0.98 (0.95 to 0.99)	0.98 (0.95 to 0.99)	0.98 (0.95 to 0.99)
CF-WBI (n = 149)	0.96 (0.92 to 0.99)	0.96 (0.92 to 0.99)	0.96 (0.92 to 0.99)
HF-WBI (n = 138)	0.99 (0.95 to 1.00)	0.99 (0.95 to 1.00)	0.99 (0.95 to 1.00)

Abbreviations: CF-WBI, conventionally fractionated whole-breast irradiation; HF-WBI, hypofractionated whole-breast irradiation.

Shaitelman et al. JCO, 2018

Differences in Acute Toxicities Following Breast Radiotherapy by Fractionation Schedule

Maximum Patient-Reported Toxicities

Toxic Effect	% Conventional fx	% Hypo fx	P value
Breast Pain (0-10) None (0) Mild (1 -3) Moderate (4-7) Severe (8-10)	 12.6 46.3 29.8 11.3	 27.7 48.1 20.2 4.0	.003
Moist desquamation, No.(%) Absent Present	 74.3 25.7	 96.2 3.8	<.001
Dry desquamation, No. (%) Absent Present	 48.2 51.8	 87.8 12.2	<.001
Your treated breast hurting No Yes	 66.5 33.5	 84.0 16.0	.001
Feel significant fatigue? No Yes Not answered	 70.3 29.7 43	 81.2 18.9 7	.02

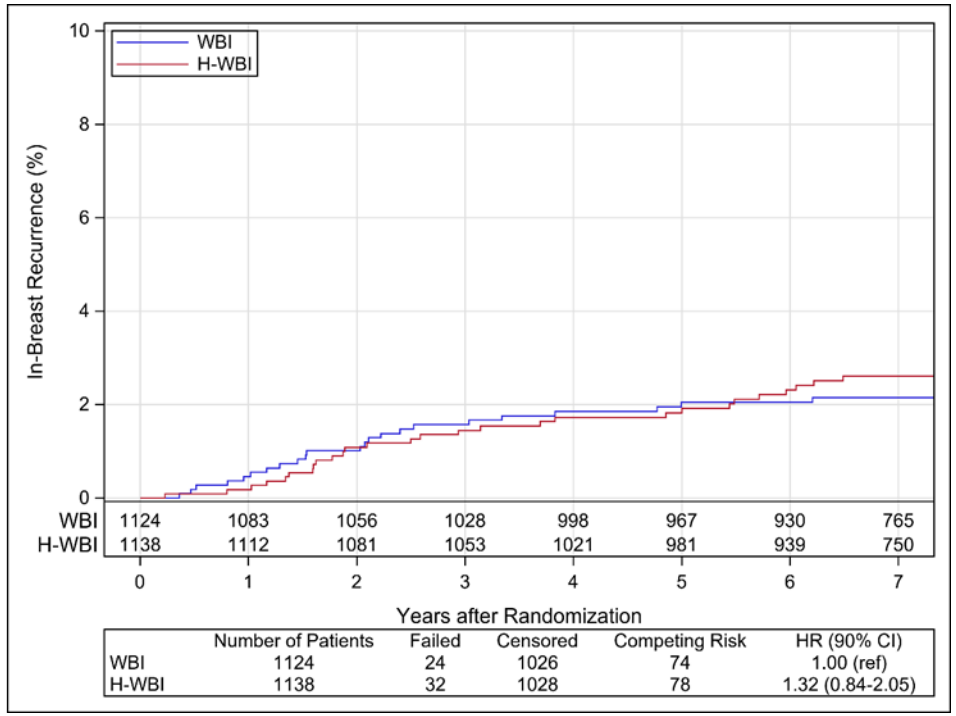
Jagsi et al. JAMA ONC 2015

RTOG 1005

Results: Primary Endpoint – IBTR

- Median follow-up: 7.4 years
- IBR events: 56

	WBI Sequential Boost (n = 1124)	H-WBI Concurrent Boost (n = 1138)
5-year estimate (90% CI)	2.0% (1.4%, 2.9%)	1.9% (1.3%, 2.7%)
7-year estimate (90% CI)	2.2% (1.5%, 3.0%)	2.6% (1.9%, 3.5%)



Vicini FA et al. Int J Radiat Oncol Biol Phys. 2022;114:S1.

Trials of "Ultra" Hypofractionation in Early-Stage Disease

Trial			Treatment (Gy)		Local recurrence (%)		F/U (yrs.)
	n	Stage	Standard	UHF	HF	UHF	-
FAST	915	T_{1-2}, N_0	50/2	30/6 or 28.5/5.7 once weekly	.7	1.4 1.7	10
FAST-Forward	4096	T_{1-3}, N_{0-1}	40/2.67	27/5.4 26/5.2	2.1	1.7 1.4	5

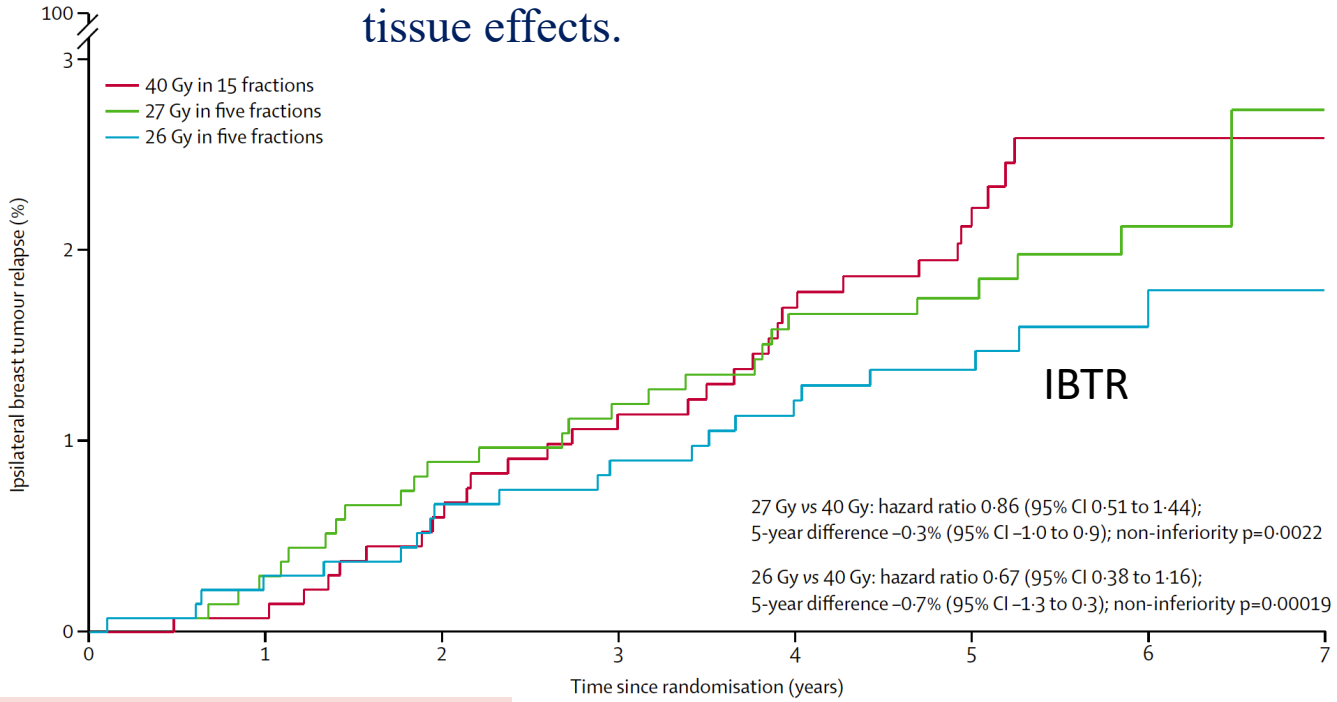
Ultrahypofractionation

UK Fast Forward Trial

- 2011-2014: 4,096 patients age ≥18 with pT1-T3 pN0-1 randomly assigned to whole breast/chest wall schedules (no regional nodal irradiation; lumpectomy boost at 2 Gy/F permitted):
  - 40 Gy at 2.67 Gy/F once daily
  - 26 Gy at 5.2 Gy/F ***once daily***
  - 27 Gy at 5.4 Gy/F ***once daily***

5-year results:

- 26 Gy at 5.2 Gy/F once daily has noninferior local control & similar normal tissue effects.
- 27 Gy at 5.4 Gy/F once daily had worse normal tissue effects.



	Number of moderate or marked events/total number of assessments over follow-up	Odds ratio for schedule (95% CI)	p value for comparison with 40 Gy	p value for comparison between 27 Gy and 26 Gy	Odds ratio for years of follow-up (95% CI); p value
Any adverse event in the breast or chest wall*	..	..	..	..	0·98 (0·96–1·00); 0·055
40 Gy	651/6121 (10·6%)	1 (ref)	..	..	..
27 Gy	1004/6303 (15·9%)	1·55 (1·32–1·83)	<0·0001	..	..
26 Gy	774/6327 (12·2%)	1·12 (0·94–1·34)	0·20	0·0001	..

Murray Brunt et al; Lancet 2020;395:1613-1626

Accelerated Partial Breast Irradiation: Randomized trials vs whole breast irradiation

	Hungarian[1]	GEC-ESTRO[2]	NSABP B39[3]	RAPID[4]	Barcelona[5]	IMPORT LOW[6]	U Florence[7]
PBI modalities	Multicath BT or electrons	Multicath BT	Multicath BT, single-entry BT, 3DCRT	3DCRT	3DCRT	Mini-tangents	IMRT
PBI duration	4 days (BT) 5 weeks (e-)	4 days	5 days	5 days	5 days	3 weeks	~2 weeks
IBTR	20Y 7.9% vs 9.6%	5Y 0.9% vs 1.4%	10Y 3.9% vs 4.6%	8Y 2.8% vs 3%	5Y 0%	5Y 1.1% vs 0.5%	10Y 2.5% vs 3.7%
No. pts	258	1,184	4,216	2,135	102	2,018	520

10,433 patients!

[1]*Polgar et al, IJROBP **2021**;109:998-1006.*
[2]*Strnad et al, Lancet 2016; 387:229-38.*
[3]*Vicini et al, Lancet **2019**;394:2155-64.*
[4]*Whelan et al, Lancet **2019**;394:2165-72.*
[5]*Rodriguez et al, IJROBP 2013; 87:1051-57.*
[6]*Coles et al, Lancet **2017**;390:1048-60.*
[7]*Meattini et al, JCO **2020**;38:4175-83.*

What patients were on these trials?

	Hungary (1)	GEC-ESTRO (2)	RAPID (3)	NSABP B-39 (4)	University of Florence (5)	IMPORT LOW (6)	Barcelona (7)
Number of Patients	258	1184	2135	4216	520	2018	102
Age	Mean 59 years 2.3% age ≤40	Median 62 years 14% age ≤50	Median 61 years	Median 54 years 38% age <50	15.8% age <50	Median 62 years	Mean 67.1 years
Tumor size	Median 1.3 cm 63.3% 1.1–2cm	Median 1.2 cm 49% 1.1–2 cm 11% >2 cm	29% 1.5–3 cm	30% 1.1–2 cm 9% >2cm	37.3% 1.1–2 cm 5.4% >2cm	Median 1.2cm	Median 1.0 cm 39.2% 1.1–2 cm 7.8% >2 cm
Nodal stage	2.3% N1mi	1% N1mi	<1% N1	10% N1	7.3% N1	2% N1	No N1
Margins	0% <2 mm 58.6% 2-<10 mm 37.5% ≥10mm	Median 8mm	–	–	–	–	–
Histology	No ILC No DCIS No Grade 3	13% ILC 6% DCIS 9% Grade 3	No ILC 18% DCIS 15% Grade 3	5% ILC 25% DCIS 26% Grade 3	8.1% ILC 8.8% DCIS 10% Grade 3	No ILC No DCIS	No ILC No DCIS
LVSI	2.3%	No LVSI	7%	–	7.3%	7%	–
Receptor Status	7.8% ER- 17.2% PR-	5% ER-/PR-	9% ER- 6% Her2+	19% ER-/PR-	4.6% ER- 10.8% PR- 2.5% Her2+	5% ER- 20% PR- 6% Her2+	3.9% ER- 15.7% PR- 1.9% Her2+
Endocrine therapy	69%	87%	61%	85% (ER+)	64%	91%	98%
Chemotherapy	2%	10%	12%	29%	1.5%	7%	2%

Anderson et al, Brachytherapy 2022; Sept 15

Accelerated Partial Breast RT

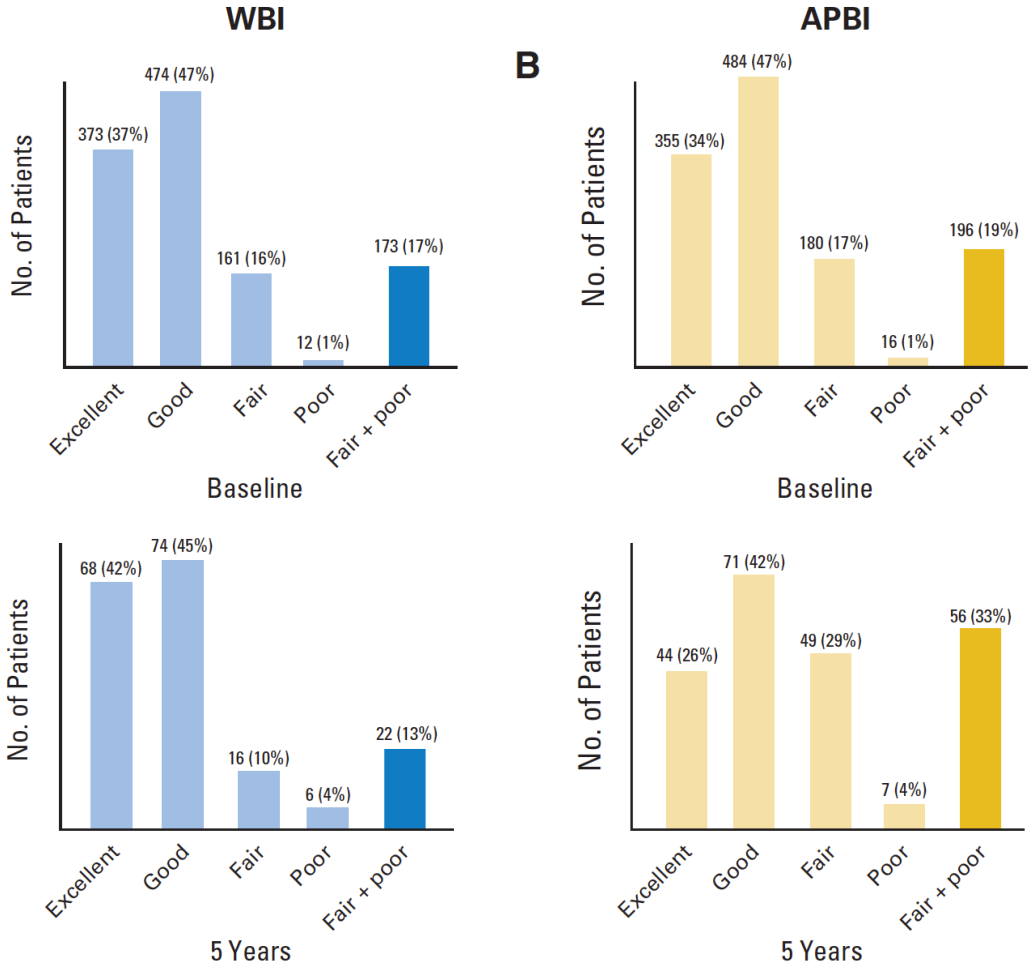
U. Florence: IMRT 6 Gy x 5 every other day vs. WBI

Assessment	**APBI (n=246)**	**WBI (n=260)**	**P**
Patient-rated cosmesis			
Excellent	44 (17.9)	13 (5.1)	.0001
Good	200 (81.3)	209 (80.3)	
Fair	2 (0.8)	38 (14.6)	
Poor	--------	---------	

Meattini et al. JCO, 2020

Accelerated Partial Breast Irradiation: Cosmesis concerns with bid fx

RAPID: 3DCRT 38.5 Gy bid vs WBI



Olivotto et al, JCO 2013;31:4038-45

	Baseline	3 years	5 years	7 years
Patient self-assessment APBI				
Excellent	314	313	244	175
Good	469	387	358	294
Fair	203	188	189	158
Poor	42	64	66	56
Fair + poor	245 (24%)	252 (27%)	255 (30%)	214 (31%)
Total	1034	963	873	690
Patient self-assessment WBI				
Excellent	289	370	329	250
Good	518	378	343	279
Fair	184	131	119	71
Poor	37	31	25	21
Fair + poor	221 (22%)	162 (18%)	114 (18%)	92 (15%)
Total	1028	910	816	621

Whelan et al, Lancet 2019;394:2165-72

Accelerated Partial Breast Irradiation:

Who can we treat?

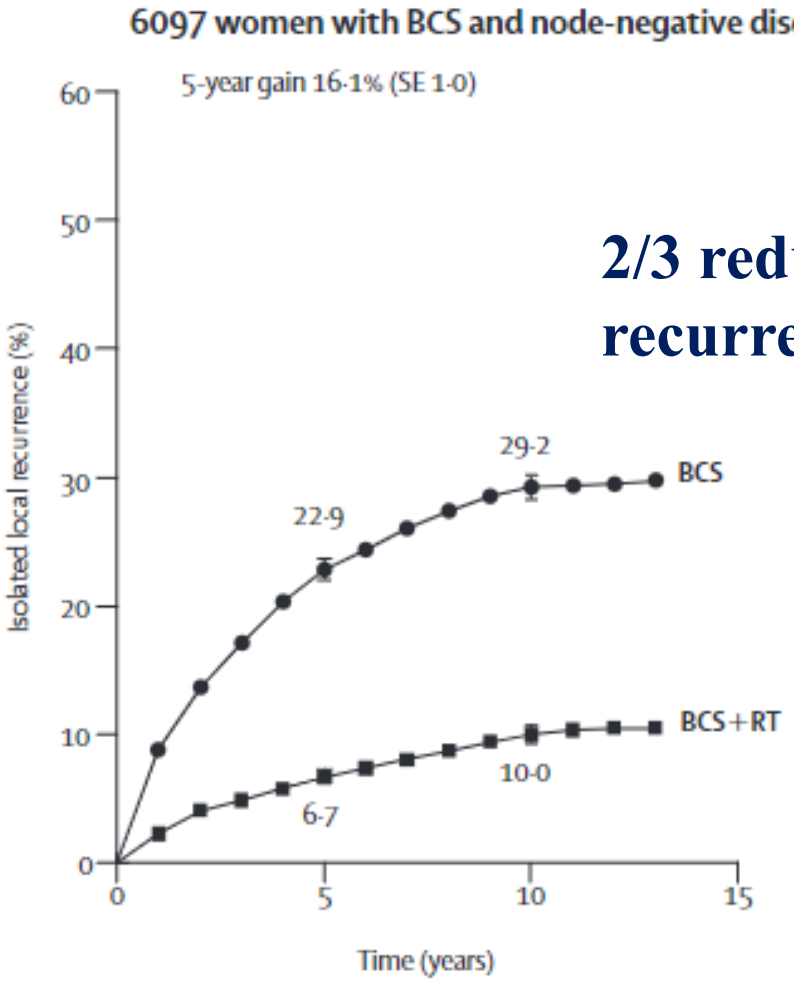
- Guidelines published by ASTRO, GEC-ESTRO, ABS, ASBS and more…
- Current NCCN guidelines endorse current ASTRO guidelines:

Patient group	Risk factor	Original	Update
Suitability	Age	≥60 y	≥50 y
	Margins	Negative by at least 2 mm	No change
	T stage	T1	Tis or T1
	DCIS	Not allowed	If all of the below: • Screen-detected • Low to intermediate nuclear grade • Size ≤2.5 cm • Resected with margins negative at ≥3 mm
Cautionary	Age	50-59 y	• 40-49 y if all other criteria for "suitable" are met • ≥50 y if patient has at least 1 of the pathologic factors below and does not have any "unsuitable" factors *Pathologic factors:* • Size 2.1-3.0 cm [a] • T2 • Close margins (<2 mm) • Limited/focal LVSI • ER(-) • Clinically unifocal with total size 2.1-3.0 cm [b] • Invasive lobular histology • Pure DCIS ≤3 cm if criteria for "suitable" not fully met • EIC ≤3 cm
	Margins	Close (<2 mm)	No change
	DCIS	≤3 cm	≤3 cm and does not meet criteria for "suitable"
Unsuitable	Age	<50 years	• <40 y • 40-49 y and do not meet the criteria for cautionary
	Margins	Positive	No change
	DCIS	>3 cm	No change

[a] The size of the invasive tumor component.
[b] Microscopic multifocality allowed, provided the lesion is clinically unifocal (a single discrete lesion by physical examination and ultrasonography/mammography) and the total lesion size (including foci of multifocality and intervening normal breast parenchyma) falls between 2.1 and 3.0 cm.

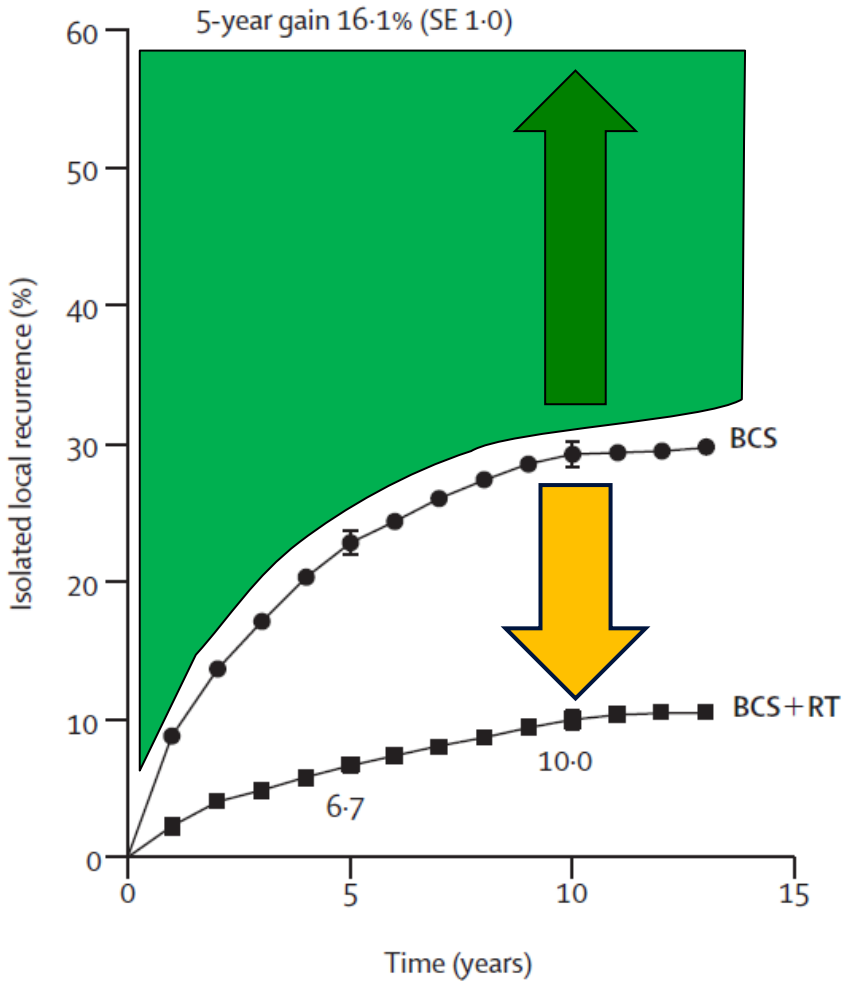
Correa et al, PRO 2017;7:73-79

Effects of Radiotherapy on Local Recurrence: An Overview of the Randomised Trials



2/3 reduction in local recurrence with RT

EBCTCG. Lancet. 2005;365:1687.



70% need no additional radiation

2/3 relative risk reduction with RT

≥ 6000 women treated with breast conserving surgery

EBCTCG, Lancet 2005;366:2087-2106

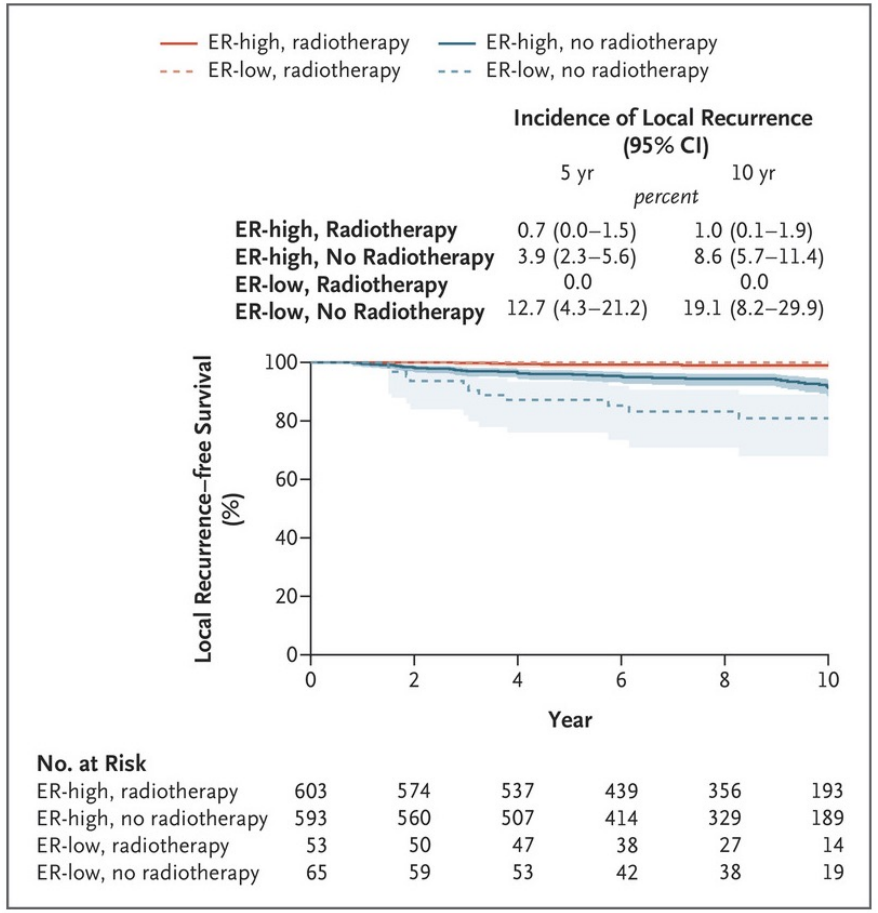
Examples of Lessons Learned in Omission Trials

	Milan (2001)	NSABP B21 (2002)	Princess Margaret (2004)
Age (yrs.)	≤70	any	≥50
Tumor size (cm)	≤2.5	≤1.0	≤5.0
Receptor status	any	any	any
Endocrine RT	for ER+ ds	yes	yes
Local recurrence (%) RT (+endocrine Rx) No RT (endocrine Rx only)	 5.8 23.5	 2.8 16.5	 0.6 7.7
F/U (yrs.)	10	8	5

Breast-Conserving Surgery, Endocrine Therapy With/Without RT

Trial	CALGB 9343	PRIME II
n	636	658
Age (yrs.)	$\geq$70	$\geq$65
Stage	clT_1N_0	p $\leq$ 3cm, N_0
Hormone Receptors	ER+	ER+ or PR+ or both
Endocrine RX	Yes	Yes
Local Recurrence (%) RT + ET ET alone	 2 9	 0.9 9.5
F/U (yrs.)	10	10

Breast-Conserving Surgery with or without Irradiation in Early Breast Cancer



Local Recurrence According to Estrogen Receptor (ER) Status and Receipt of Radiotherapy

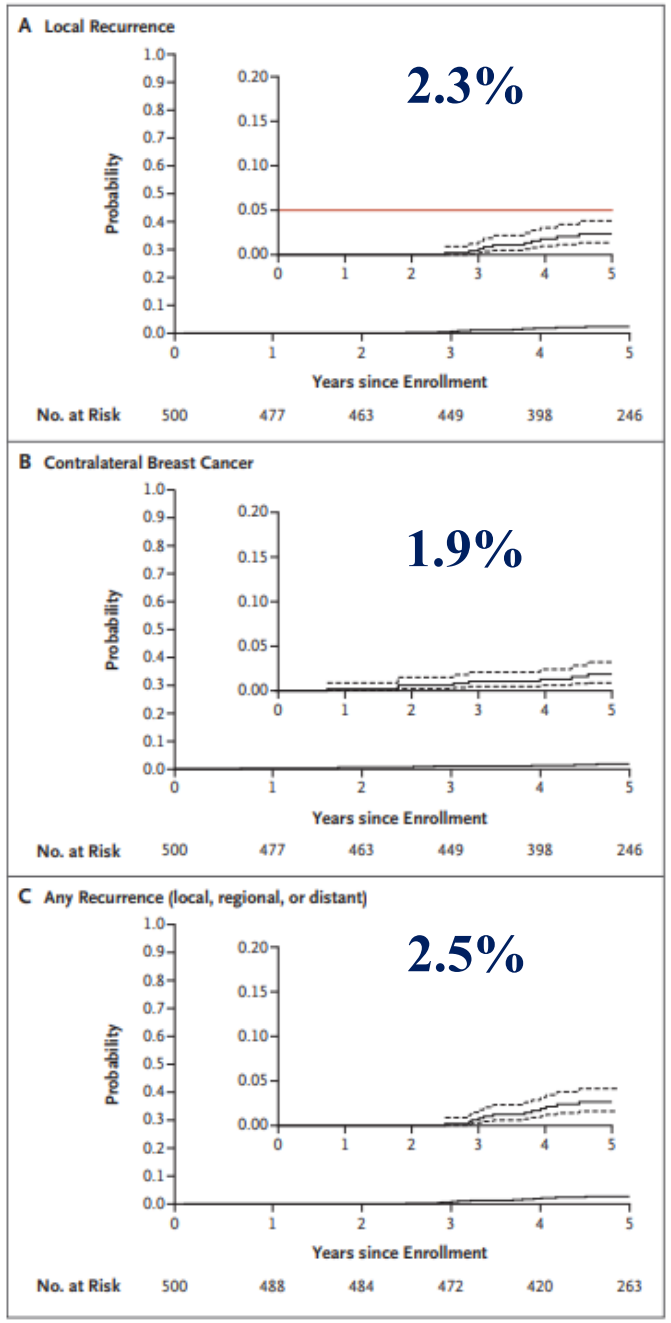
Kunkler et al. NEJM 2023;388: 585-94

Omitting Radiotherapy after BCS in Luminal A Breast Cancer: the LUMINA Study

Canadian Cancer Society/Canadian BCF

- 740 registered
- 500 enrolled
  - ≥ 55 years of age
  - T_1, N_0
  - Grade 1 or 2
  - ER+, PR+, Her2-
  - Ki67 ≤ 13.25%
  - receipt of endocrine therapy
- Primary endpoint: local recurrence in ipsilateral breast
- Acceptable risk defined as <5% LR at 5 years

Whelan et al. NEJM, 2023



Omitting Radiotherapy after BCS in Luminal A Breast Cancers: the LUMINA study

Whelan et al. NEJM, 2023

Ongoing prospective trials of precision medicine for early breast cancer

Name	EUROPA	EXPERT	NATURAL	DEBRA	PRECISION	PRIMETIME	IDEA	LUMINA
Study type	Randomized	Randomized	Randomized	Randomized	Single arm	Single arm	Single arm	Single arm
Age (yrs.)	≥70	≥50	≥60	≥50 and ≤70	≥50 and ≤75	≥60	≥50 and ≤69 (postmenopausal)	≥55
Stage	pT1 N0	pT1 N0	pT1 N0	pT1 N0	pT1 N0	pT1N0	pT1 N0	pT1 N0
Subtype	Luminal A	Luminal A	Luminal A	Recurrence Score ≤18	Luminal A	Very low risk Patients (based on IHC4 + C)	Recurrence Score ≤18	Luminal A
Assessment method	IHC FISH for HER2 2+	PAM 50 FISH for HER2 2+	IHC FISH for HER2 2+	Onctotype-DX FISH for HER2 2+	PAM 50 FISH for HER2 2+	IHC4 +4 FISH for HER2 2+	Onctoype-DX FISH for HER2 2+	IHC FISH for HER2 2+

Adapted from Meattini et al. J Geriatric One, 2021

Long-Term Outcomes of RT vs. RT + Endocrine Therapy in Low-Risk BC in Patients ≥ 70 years

Swedish Cancer Institute, Seattle, WA

Retrospective Analysis

- ≥70 years
- ER +/HER2- T, N_0 BC
- BCS
- 1995 – 2015
- Exclusion criteria: positive margins, multifocality, grade 3, LVI positive

Median age 76 years
Median F/U 9.6 years
Comparison of combined RT + ET (n=307) and RT alone (n=148)

Morris et al. ASTRO 2023

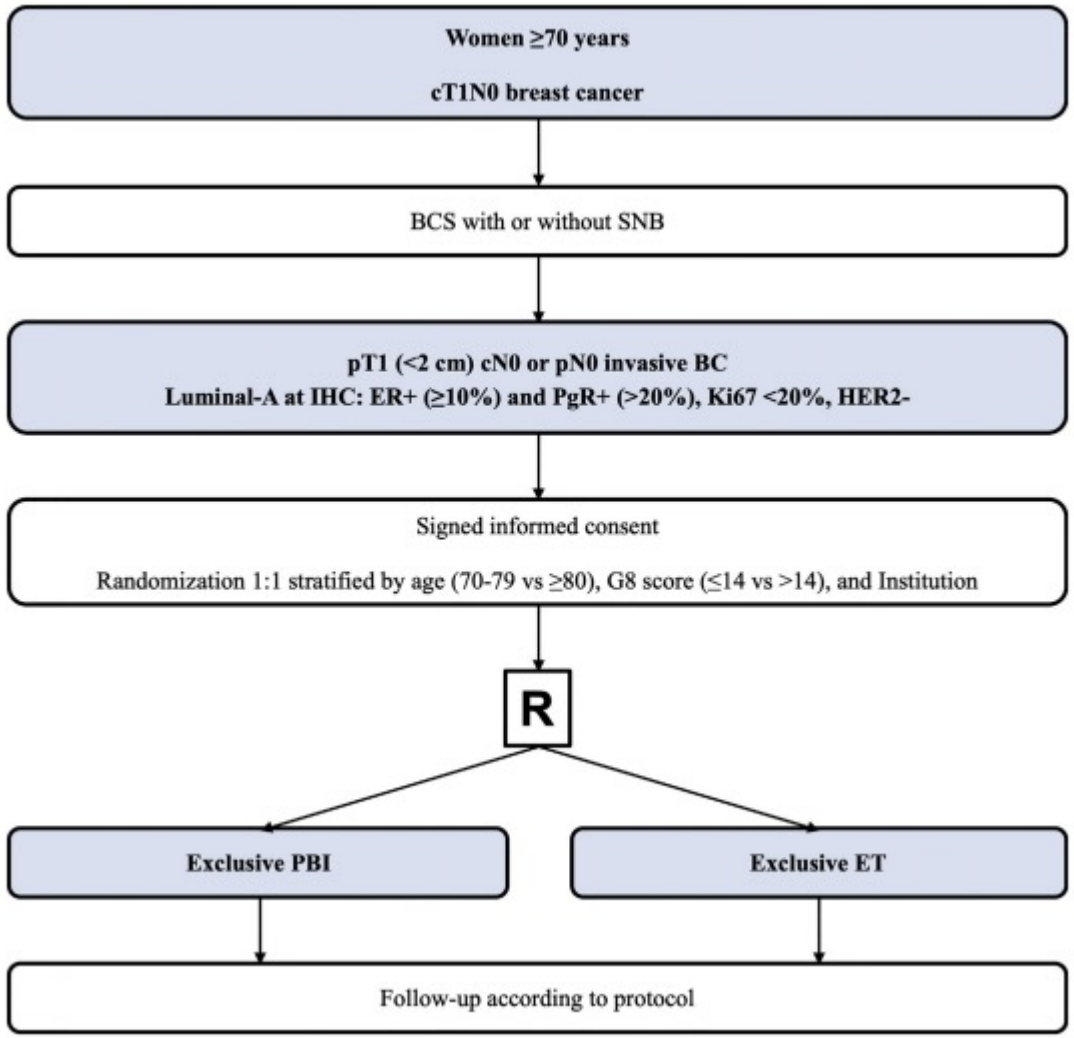
Long-Term Outcomes of RT vs. RT + Endocrine Therapy in Low-Risk BC in Patients ≥ 70 years

5, 10, and 15-year cumulative rates of outcomes for the RT monotherapy group and combined RT+ET group with *p* value for difference between treatments

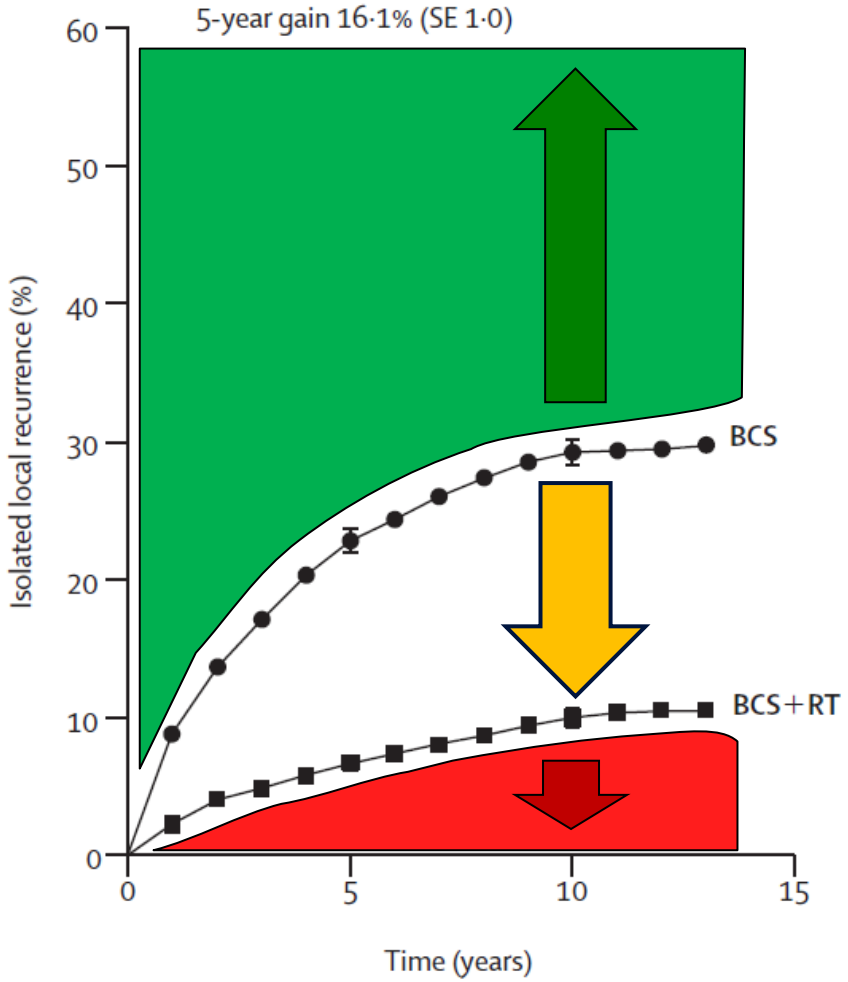
	LR			DM			DSS			OS			SBCEs		
	5yr	10yr	15yr	5yr	10yr	15yr	5yr	10yr	15yr	5yr	10yr	15yr	5yr	10yr	15yr
RT	0.00	0.00	0.00	0.00	1.37	1.37	100.00	99.29	98.24	89.84	57.95	33.69	2.03	2.72	3.64
RT+ET	0.00	0.37	0.37	0.00	0.73	1.23	100.00	99.57	99.06	91.79	69.49	39.29	1.98	2.62	4.02
***P* Value**	NS			0.78			0.80			0.55			0.99		

Morris et al. ASTRO 2023

EUROPA: Endocrine Therapy or Partial Breast RT for Women ≥ 70 years with Luminal A-like BC



Meattini et al. J Geriatric Onc, 2021



70% need no additional radiation

2/3 relative risk reduction with RT

10% develop recurrence despite standard therapy

≥ 6000 women treated with breast conserving surgery

EBCTCG, Lancet 2005;366:2087-2106

Previously Derived Signatures Applied to Radiation Questions

- Oncotype DX
- MammaPrint
- PAM 50 from ProSigna
- EndoPredict
- IHC surrogates for subtype

Radiation-Specific Signatures

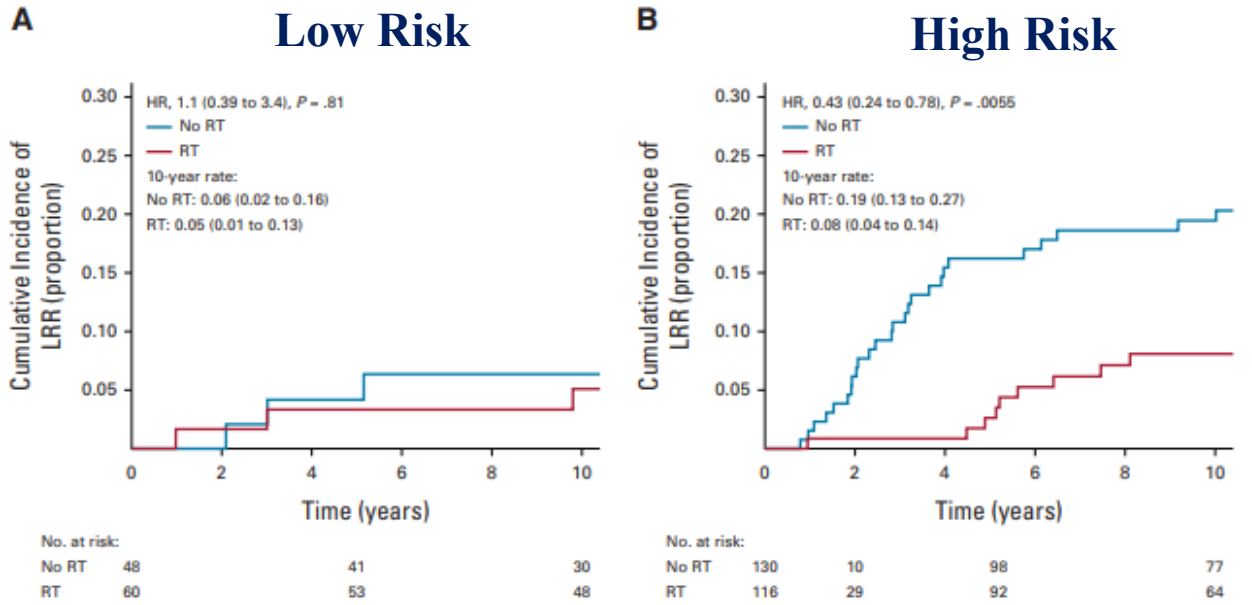
- Danish Breast Cancer Group – identifies RT benefit group
- Radiation Sensitivity Index – identifies RT resistant group
- Radiosensitivity and Immune Gene Signature – identifies RT benefit and sensitive group
- Adjuvant RadioTherapy Intensification Classifier (ARTIC) – identifies RT benefit and resistant group
- Profile for the Omission of Local Adjuvant Radiation (POLAR) – identifies patients at low risk of LRR who may be candidates for RT omission

Development and Validation of a Genomic Profile for the Omission of Local Adjuvant RT in Breast Cancer (POLAR)

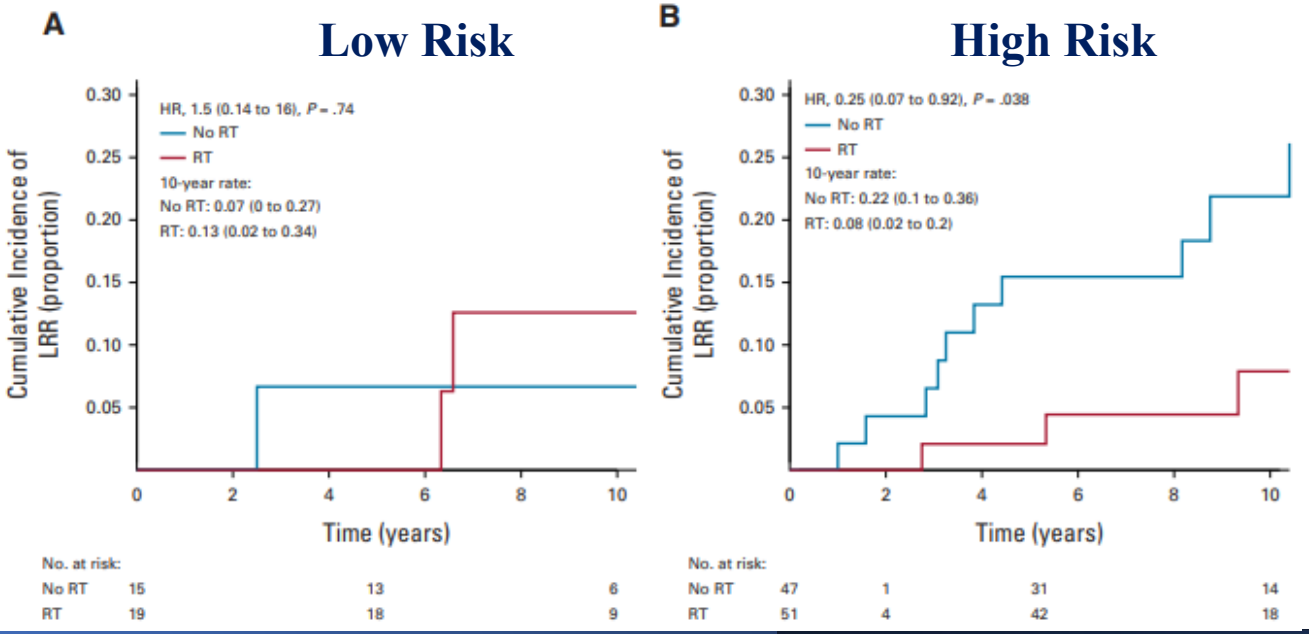
- Developed and validated from gene expression data from tumor samples in the SweBCG 91-RT and PMH +/- RT trials
- Only ER+, Her2- samples included
- Only samples from patients not treated with chemo +/- endocrine therapy used
- 16-gene signature developed and validated from tumors in patients treated on RT trials.
  Genes associated with higher risk of LRR involved cell cycle and proliferation.
  Genes associated with lower LRR risk were related to immune function.

Sjostrom et al. JOC, 2023

POLAR



Cumulative incidence of LRR with and without RT in SweBCG 91-RT validation cohort



Cumulative incidence of LRR with and without RT in Princess Margaret cohort

Sjostrom et al. JCO, 2023

A few comments on DCIS

Randomized Trials of Excision +/- RT

	N	FU	E alone	E + RT
NSABP B-17	814	17 y	35%	20%
			invasive: 20%	11%
			DCIS: 15%	9%
EORTC	1010	15.8 y	30%	17%
			invasive: 15%	9%
			DCIS: 15%	8%
UK	1030	12.7 y	19%	7%
			invasive: 7%	4%
			DCIS: 12%	3%
Swedish	1067	8 y	27%	12%
			invasive 12%	7%
			DCIS: 15%	5%

~50% reduction

Wapnir IL et al. J Natl Cancer Inst. 2011;103:478.
Donker M et al. J Clin Oncol. 2013;31:4054.
Cuzick J et al. Lancet Oncol. 2011;12:21.
Holmberg L et al. J Clin Oncol. 2008;26:1247.

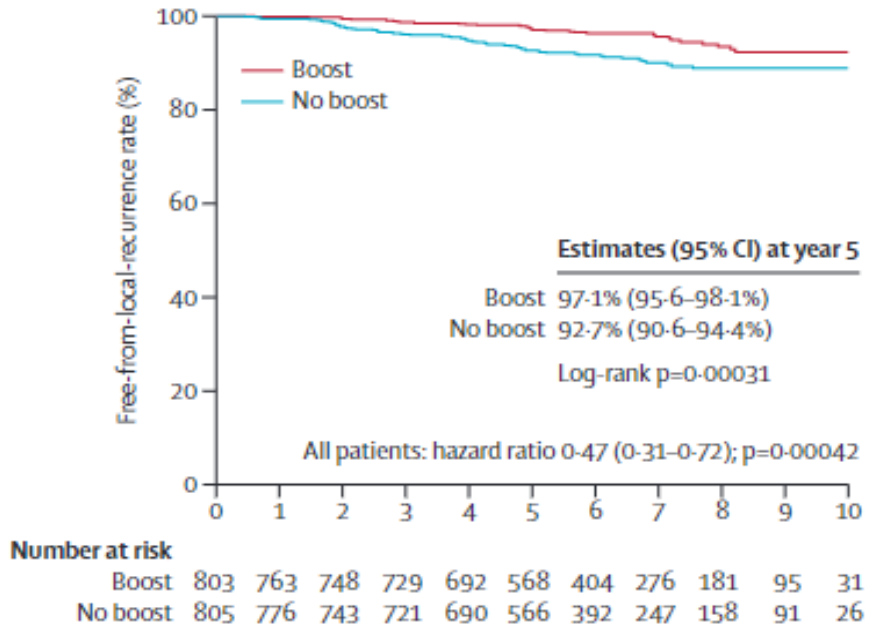
EBCTCG Meta-Analysis

- All 4 randomized trials of RT vs no RT
- RT reduced absolute 10-yr risk of ipsilateral breast events by 15.2%
- RT benefit regardless of age, extent of surgery, use of tamoxifen, margins, grade, size
- No effect on survival
- No excess mortality from RT

Correa C et al. J Natl Cancer Inst Monogr. 2010;2010:162.

Trial of Hypofractionation and Boost for DCIS BIG 3-07/TROG 07.01

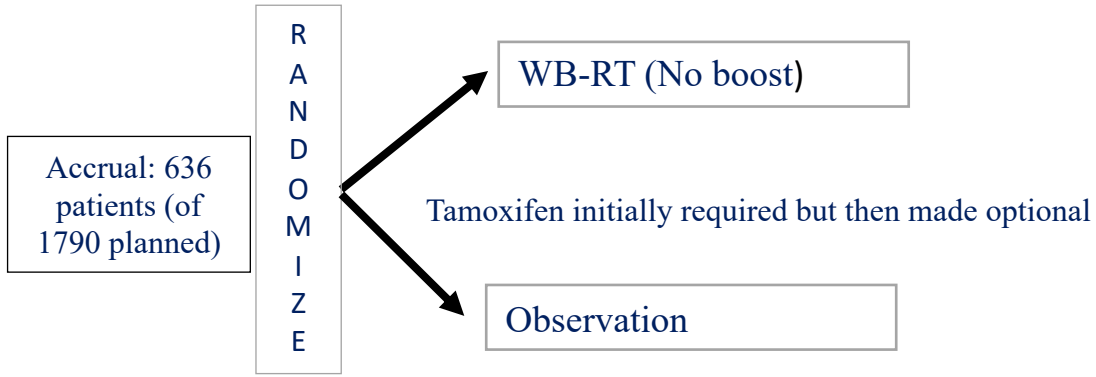
- Trial Design:
  - Randomized 2 x 2
  - Boost: 16 Gy/8fx or no boost
  - Fractionation: 50 Gy/25fx or 42.5 Gy/16 fx
- Results
  - Boost: higher rate of freedom from local recurrence at 5 years
  - No OS difference
  - No difference between conventional fx and hypofx



Chua BH et al. Lancet. 2022;400:431.

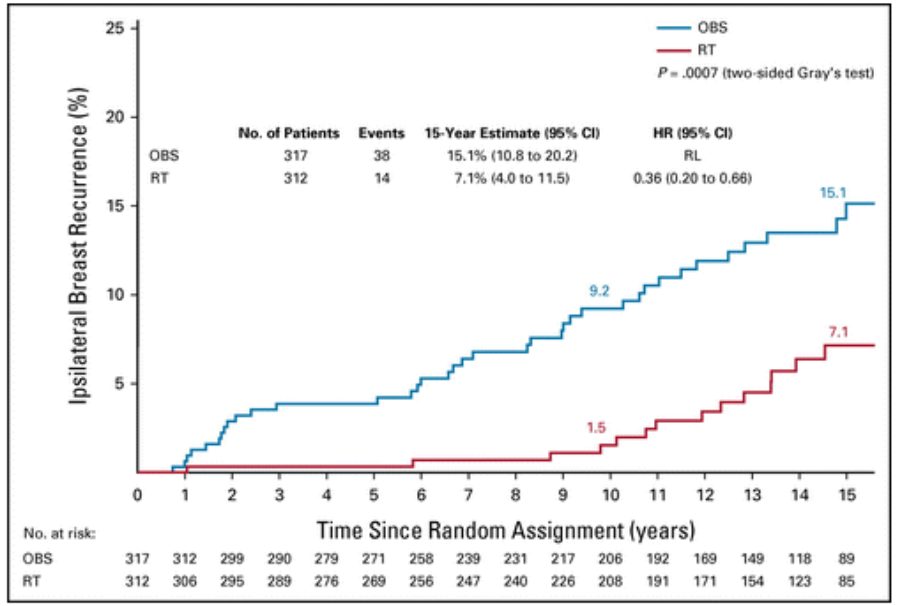
Can we select highly favorable DCIS for which there is no benefit with RT? RTOG 9804: RT vs Observation for Good-Risk DCIS

- Primary Objective: LF
- Secondary Objective: OS, CBF, DF, salvage mastectomy failure
- Inclusion:
  - *Patient Characteristics*: ≥ 26 y/o
  - *Tumor Features*: DCIS detected by mammogram or incidentally found
    - Unicentric
    - Low or intermediate nuclear grade
    - ≤ 2.5 cm
  - *Margin Status*: ≥ 3 mm
  - *Other*: Negative post-excision mammogram

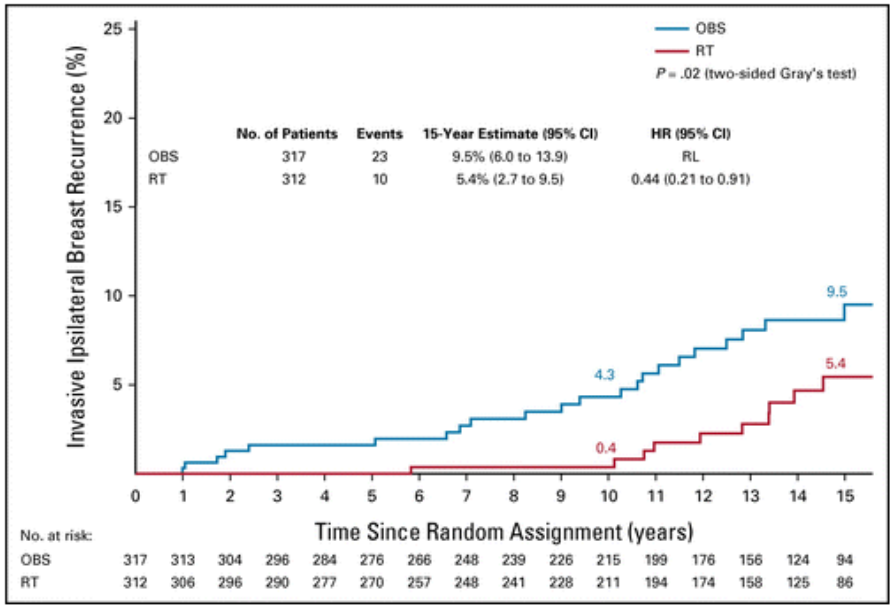


McCormick B et al. J Clin Oncol. 2015;33:709.
McCormick B et al. J Clin Oncol. 2021;39:3574.

Randomized Phase III Trial of +/- RT in Good Risk DCIS: RTOG 9804



15.1% vs 7.1%, *P* = .0007



9.5% vs 5.4%, *P* = .02

McCormick B et al. J Clin Oncol. 2021;39:3574.

ECOG 5194, Low Risk
(Low / Intermediate grade)

	Any Ipsi Breast Event (%)	Invasive Ipsi Breast Event (%)
5 years	**6 (4.0-8.1)**	**2.7 (1.3-4.1)**
7 years	**9.5 (7.0-12.0)**	**4.8 (2.9-6.6)**
10 years	**12.5 (9.5-15.4)**	**6.4 (4.2-8.6)**
12 years	**14.4 (CI 11.2-17.6)**	**7.5 (5.1-10.0)**

N = 561
Median follow-up 12.3 years

Solin LJ et al. J Clin Oncol. 2015;33:3938.

ECOG 5194, High Risk (High grade)

	Any Ipsi Breast Event (%)	Invasive Ipsi Breast Event (%)
5 years	15 (7.7-21.7)	5.3 (0.8-9.7)
7 years	18.2 (10.6-25.8)	7.6 (2.2-13.0)
10 years	24.6 (15.7-33.4)	13.4 (5.9-20.9)
12 years	24.6 (15.7-33.4)	13.4 (5.9-20.9)

N = 104

Solin LJ et al. J Clin Oncol. 2015;33:3938.

Can “Low Risk” DCIS be Safely Treated with Excision Alone?

- Prospective studies unable to identify a subset of patients treated with excision alone who have local recurrence rates of <10% after long-term follow-up based on conventional clinical-pathologic criteria
- Personal decision re: acceptable rate of IBTR without RT

Oncotype DX Recurrence Score for DCIS

- 327 patients (ECOG E5194)
- Median FU 8.8 yrs
- Recurrence score calculated using optimized gene expression algorithm
- 3 prespecified risk groups defined, score associated with LR at 10 yrs
  - "low risk" = 10.6% (invasive: **3.7%**)
  - "intermediate risk" = 26.7% (invasive: **12.3%**)
  - "high risk" = 25.9% (invasive: **19.2%**)

Solin LJ et al. J Natl Cancer Inst. 2013;105:701.

Routine Use of DCIS Score?

- Has not had nearly the same buy-in as Oncotype DX recurrence score for invasive breast cancer
- ? Another data point to consider in making treatment recommendations
- Not validated in specimens from randomized trials +/- RT
  - Is the added value sufficient to justify cost?
  - Cost effectiveness: using molecular testing in omission of RT decisions for DCIS does not confer a value advantage from a population perspective

Raldow AC et al. J Clin Oncol. 2016;34:3963.

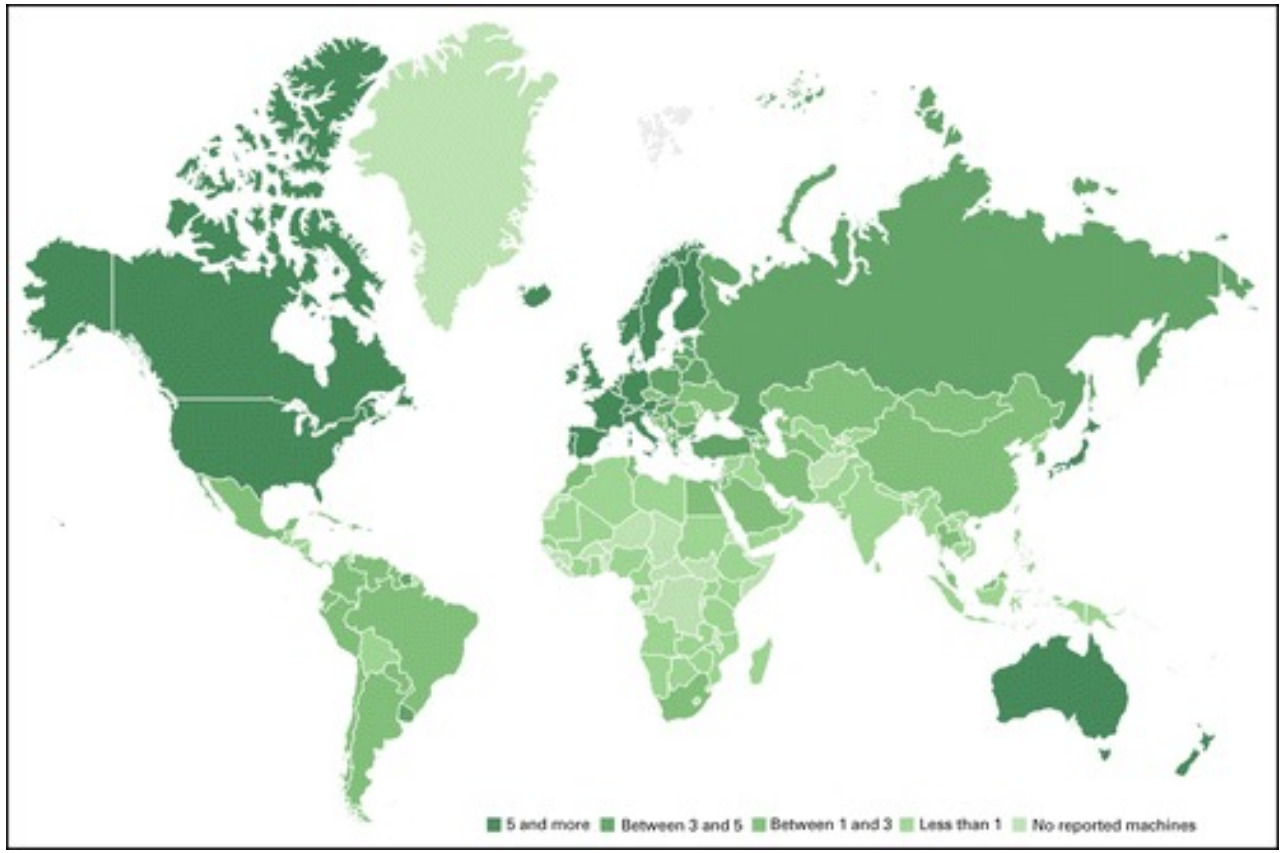
Are we ready to routinely use the DCISion RT (Prelude Dx)?

- 7 – gene assay
- DCISion RT reports a “decision score” (DS) based on biomarkers + clinicopathologic factors
- Is stated to be prognostic for recurrence risk after BCS and predictive for RT benefit

BUT

- No randomized data
- Results not presented from randomized cohorts other than inclusion of SweDCIS trial cohort mixed in
- Cut points have changed over time
- New biomarker added to mix (RRt) for residual risk subtype for high risk of LR after RT
- No prospective data showing markers are predictive of RT benefit

Global Radiotherapy: Current Status



Access to radiotherapy worldwide per million population

Abdel-Wahab et al. JCO Global Oncology, 2021

Work is ongoing to define biomarkers (i.e., IHC, PAM50, Oncotype DX, POLAR, Oncotype DX, DCISion RT, etc) that in conjunction with patient-specific characteristics will allow further de-escalation of therapy while achieving excellent rates of tumor control, cosmesis, and QOL for invasive and non-invasive disease.

These studies will benefit breast cancer patients in every part of the globe.