Q&A and Technical Support

- Please use the Q&A feature on the right-hand portion of your screen for any clinical questions and logistical concerns you have regarding the session. This is the only online method of communicating questions or concerns. Should you need additional assistance please e-mail **education@nccn.org** or call 215-690-0300 and ask to be connected with someone in the NCCN Conferences and Meetings Department.

- While NCCN is pleased to respond to as many questions as possible during this webinar, NCCN will not be able to respond to your individual questions of a clinical nature after the webinar has concluded. We are also not able to offer recommendations on patient care regarding specific cases.

Attendance Lists & Registration

- If you are participating with a group of peers, a list of everyone who attended in your group must be submitted within two weeks of the activity in order for the participants to be eligible to receive credit. This list is in addition to individual registration. Attendee lists will not be accepted after two weeks post-activity.

- Lists can be sent to **education@nccn.org** and should contain full contact information for each participant, including first and last name, credentials, mailing address, phone number, and e-mail address.

- If you have not individually registered, please register at: **http://www.cvent.com/d/9fqzgs.**

Accreditation Information

Intended Audience

This educational program is designed to meet the educational needs of oncologists, nurses, pharmacists, and other health care professionals who manage patients with breast cancer.

Learning Objectives

Following this program, participants should be able to:

- Discuss and debate the rationale for adjuvant radiation therapy to treat patients with DCIS.
- Assess the risk of recurrence and select optimal treatment strategies for patients with DCIS.

Accreditation Information

Physicians

National Comprehensive Cancer Network (NCCN) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

National Comprehensive Cancer Network designates this web-based activity for a maximum of 1.0 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses

National Comprehensive Cancer Network (NCCN) is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's (ANCC) Commission on Accreditation. NCCN designates this educational activity for a maximum of 1.0 contact hours. Accreditation as a provider refers to the recognition of educational activities only; accredited status does not imply endorsement by NCCN or ANCC of any commercial products discussed/displayed in conjunction with the educational activity.

Kristina M. Gregory, RN, MSN, OCN, is our lead nurse planner for this educational activity.

Accreditation Information

Pharmacists

Pharmacy Educational Objective: *After completing this activity, the participant should be able to:*
- Provide accurate and appropriate counsel as part of the treatment team.

Accreditation Statement

National Comprehensive Cancer Network is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Type of Activity: Knowledge

UAN: 0836-0000-16-018-L01-P

Credit Designation: National Comprehensive Cancer Network designates this continuing education activity for 1.0 contact hours (0.10 CEUs) of continuing education credit in states that recognize ACPE accredited providers.

Attention Pharmacists: ACPE and NABP have implemented CPE Monitor as a way to electronically track all ACPE-accredited CPE Units. In order to receive credit for this activity, please enter your six-digit NABP e-profile ID and birth date in the format of MMDD as part of the Overall Evaluation. If you have not already done so, please complete your e-profile at http://www.nabp.net to obtain your NABP e-Profile ID.

To comply with ACPE standards, pharmacists must complete all activity requirements within **30 days** of the live event date.

Accreditation Information

How to Claim Credit:

Within 5 business days after this educational program, you will receive an e-mail with information on how to claim credit for this activity. A statement of credit will be issued only upon completion of the activity evaluation form & immediate post-test within **30 days** of the activity date. A certificate will be electronically generated immediately upon completion of the evaluation.

All credit claiming must be done online through NCCN's continuing education portal at **https://education.nccn.org/node/78118.**

Should you not receive an e-mail within 5 days, please contact us at **education@nccn.org.**

Accreditation Information

- It is required by the ACCME that all educational activities are designed to change participant ***competence, performance, or patient outcomes.***
- To meet this requirement, NCCN asks that all participants complete the outcomes measures described below:
  - The post-test and evaluation as indicated in e-mail you will receive within 3-5 business days of the conclusion of this activity. This is required to receive credits or your certificate of completion. You must be registered in advance to receive credits or certificate. Certificates will be generated automatically upon successful completion of this step.
    - There will be a separate WebEx evaluation at the conclusion of this program, which is optional and does not go to NCCN.
  - The follow-up post test (to be sent 30 days after the activity has ended to demonstrate an increase in participant competence)
- NCCN greatly appreciates your compliance with completing the aforementioned post-test and surveys. All of these measures will be available by logging into your account at **http://education.nccn.org**. Reminder e-mails will be sent to the participants via e-mail. If you have any questions or concerns, please e-mail **education@nccn.org**.

Disclosures

The ACCME/ANCC/ACPE defines “conflict of interest” as when an individual has an opportunity to affect CE content about products or services of a commercial interest with which he/she has a financial relationship.

ACCME, ACPE, and ANCC focuses on financial relationships with commercial interests in the 12-month period preceding the time that the individual is being asked to assume a role controlling content of the CE activity. ACCME, ACPE, and ANCC have not set a minimal dollar amount for relationships to be significant. Inherent in any amount is the incentive to maintain or increase the value of the relationship. The ACCME, ACPE, and ANCC defines “'relevant financial relationships” as financial relationships in any amount occurring within the past 12 months that create a conflict of interest.

All faculty for this continuing education activity are competent in the subject matter and qualified by experience, training, and/or preparation to the tasks and methods of delivery.

Faculty Disclosures

Disclosure of Relevant Financial Relationships

All faculty and activity planners participating in NCCN continuing education activities are expected to disclose any relevant financial relationships with a commercial interest as defined by the ACCME's, ANCC's, and ACPE's Standards for Commercial Support. All faculty presentations have been reviewed for adherence to the ACCME's Criterion 7: The provider develops activities/educational interventions independent of commercial interests (SCS 1, 2, and 6) by experts on the topics. Full disclosure of faculty relationships will be made prior to the activity.

The faculty listed below have disclosed the following relevant financial relationships:

Jonathan B. Strauss, MD
AIM Specialty Health: Consulting Fees, Honoraria
The Osler Institute: Other financial benefit

NCCN Staff Disclosures

NCCN Staff Disclosures
The activity planning staff listed below has no relevant financial relationships to disclose:

Ann Gianola, MA; Mark Geisler; Kristina M. Gregory, RN, MSN, OCN; Kristin Kline Hasson; Rose Joyce; Joan S. McClure, MS; Diane McPherson; Deborah Moonan, RN, BSN; Liz Rieder; Shannon K. Ryan; Kathy Smith, CMP, CHCP; Jennifer McCann Weckesser

The NCCN clinical information team listed below, who have reviewed content, has no relevant financial relationships to disclose:

Kristina M. Gregory, RN, MSN, OCN; Rashmi Kumar, PhD; Dorothy Shead, MS

Faculty Biography

Jonathan B. Strauss, MD, is Assistant Professor in the Department of Radiation Oncology and Program Director of Residency in Radiation Oncology at Robert H. Lurie Comprehensive Cancer Center Northwestern University Feinberg School of Medicine.

Dr. Strauss received his medical degree from the Pritzker School of Medicine at the University of Chicago and his Master's in Business Administration from the University of Chicago Graduate School of Business. He later completed a residency at Rush University Medical Center. Dr. Strauss is board-certified in radiation oncology.

Dr. Strauss's clinical interests include breast and gynecological malignancies. He is an active and prolific clinical researcher and has focused more recently on adopting and studying new technologies in the treatment of breast and gynecological cancers to optimize cancer outcomes while minimizing the damage to normal tissues.

Dr. Strauss is a member of the American Brachytherapy Society (ABS), the American College of Radiology (ACR), the American Society of Clinical Oncology (ASCO), and the American Society for Therapeutic Radiology and Oncology (ASTRO). He also serves as Secretary/Treasurer/President-Elect of the Chicago Radiological Society and is an affiliate member of SWOG, an NCI-supported organization that conducts clinical trials in adult cancers. Additionally, Dr. Strauss has participated as an ad-hoc reviewer for a number of scientific publications, including the *American Journal of Clinical Oncology*, *Brachytherapy*, *Breast Cancer Research and Treatment*, the *International Journal of Gynecological Cancer*, the *International Journal of Radiation Oncology*, *Biology, and Physics*, and the *Journal of Thoracic Disease.*

2016

NCCN CONGRESS SERIES™

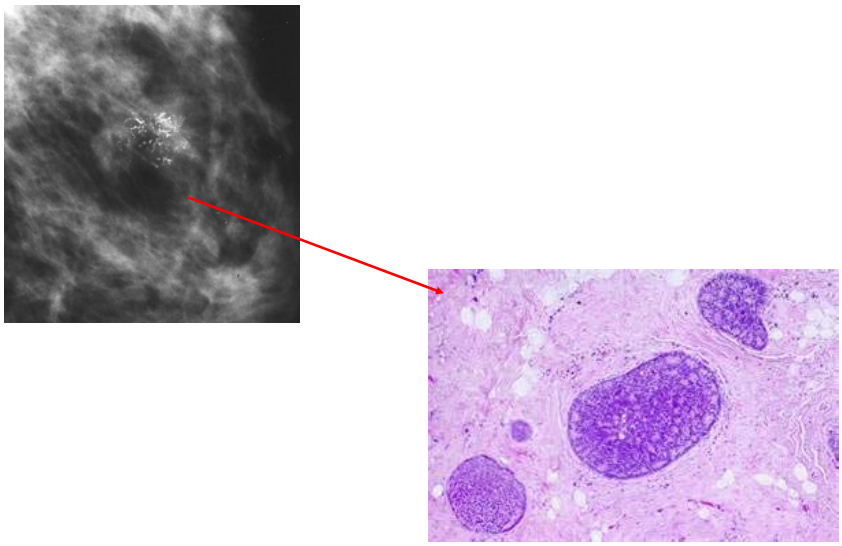
National Comprehensive Cancer Network

DCIS: Adjuvant Radiation Therapy & New Systemic Therapy Options

Jonathan B. Strauss, MD

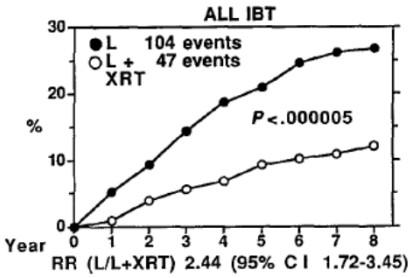
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

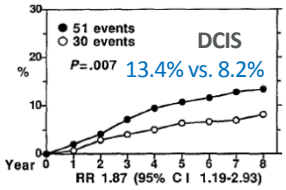
DCIS: Radiotherapy and Systemic Therapy

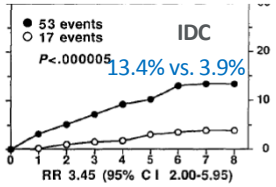


DCIS: RT Trial **NSABP B17**

- 818 women
  - 50 Gy/25 fx
  - No RT
- Excision and negative margins
- 17% palpable
- **8-year IBTR rate 27% vs. 12%**

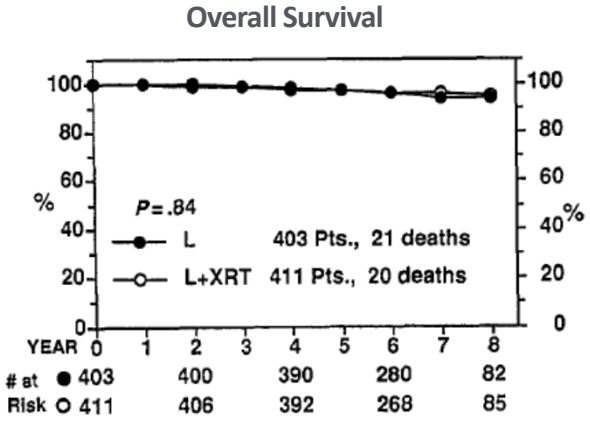






Fisher B, et al. N Engl J Med 1993;328:1581-1586
Fisher B, et al. J Clin Oncol 1998;16:441-452

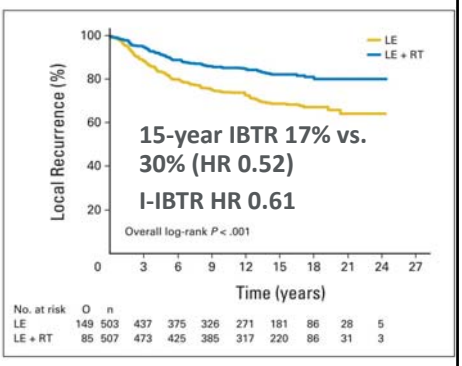
DCIS: RT Trial **NSABP B17**



Fisher B, et al. N Engl J Med 1993;328:1581-1586
Fisher B, et al. J Clin Oncol 1998;16:441-452

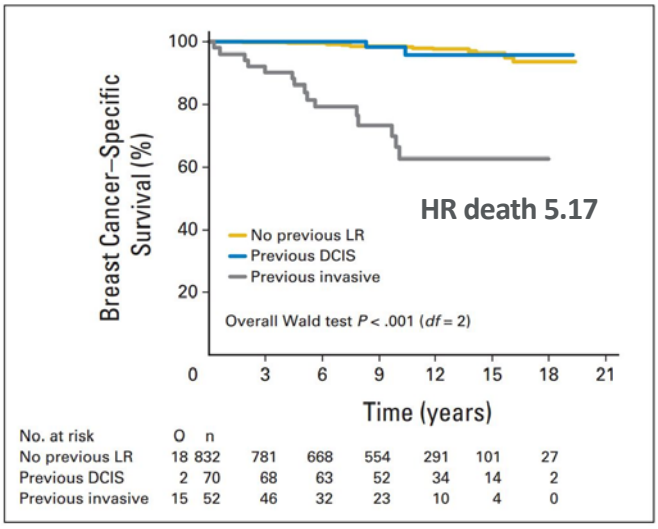
DCIS: RT Trial **EORTC 10853**

- 1,010 women <70 with DCIS <5cm
  - → 50 Gy/25 fx
  - → No RT
- Treated with excision
- In large subset 21% had close/+/NS margins
- 110 IBTRs: 48% DCIS and 52% invasive
- Prognostic Factors for IBTR
  - Age <40
  - Clinical detection (vs. mammographic)
  - + Margins
  - Solid or cribriform (vs. clinging or micropapillary)



Donker M, et al. JCO 2013;31(22):4054-4059

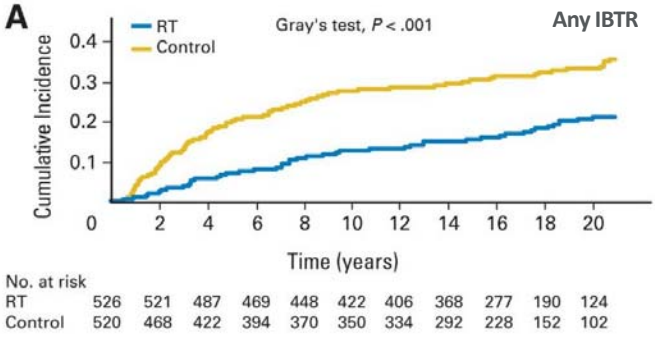
DCIS: RT Trial **EORTC 10853**



Donker M, et al. JCO 2013;31(22):4054-4059

DCIS: RT Trial **SweDCIS**

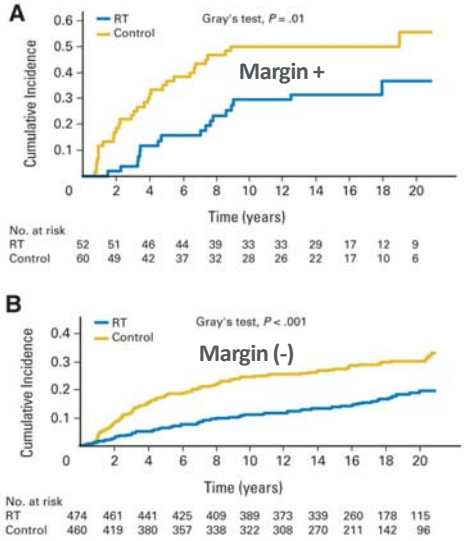
- 1,046 women with DCIS → RT / No RT
- ~10% + margins and ~9% unknown margins
- 20-yr CI IBTR: 20% vs. 32% -- relative risk reduction 37.5%



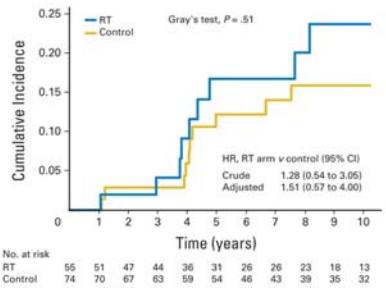
Ringberg A, et al. Eur J Cancer 2007;43:291-298
Warnberg F, et al. J Clin Oncol 2014;32:3613-3618

DCIS: RT Trial **SweDCIS**

Any IBTR



CI Breast Cancer Specific Death after I-IBTR



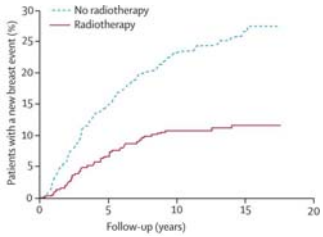
Ringberg A, et al. Eur J Cancer 2007;43:291-298
Warnberg F, et al. J Clin Oncol 2014;32:3613-3618

DCIS: RT Trial **UK/ANZ DCIS Trial (UKCCR)**

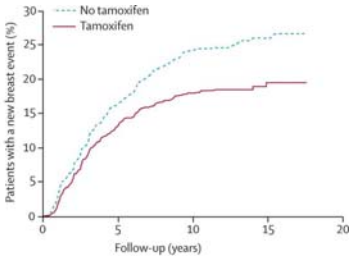
- 1,701 women with DCIS s/p excision
- Margins (-)
- Quasi 2X2 factorial design

→ 50 Gy/25 fx
→ No RT

→ Tam 20 mg qd x 5 year
→ No Tam

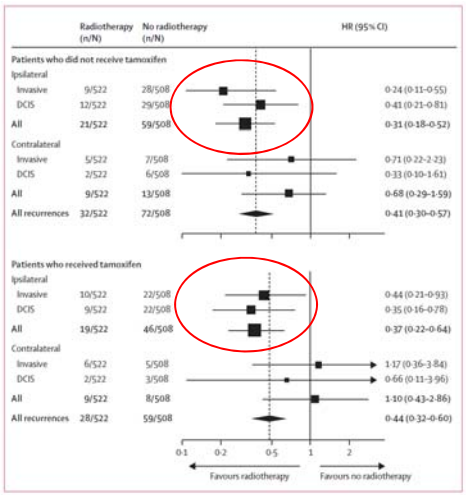


- RT reduced DCIS-IBTR (HR 0.38) and I-IBTR (HR 0.32)
- Tam reduced DCIS IBTR (HR 0.7) but not I-IBTR (HR 0.95)
- Tam reduced contralateral events (HR 0.44)



Cuzick J et al. Lancet Oncol 2011;12(1):21-29

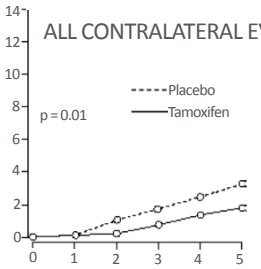
DCIS: RT Trial **UK/ANZ DCIS Trial (UKCCR)**

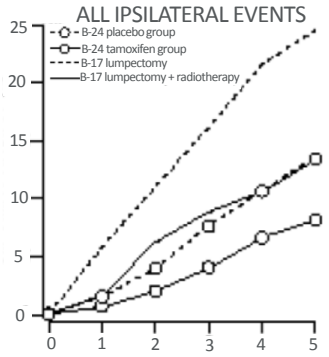


Cuzick J et al. Lancet Oncol 2011;12(1):21-29

DCIS: Endocrine Trial **NSABP B-24**

- 1,804 women with DCIS and 50 Gy/25 fx
  - → Tam 10 mg bid x 5 years
  - → Obs
- Treated with excision + or – margin
- 25% had + or unknown margins
- ER/PR status not specified
- **5-year breast cancer event 8.2% vs. 13.4%**

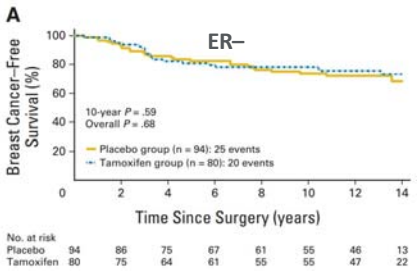


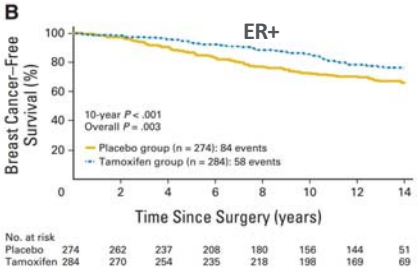


Fisher B, et al. Lancet 1999;353:1993-2000

DCIS: Endocrine Trial **NSABP B-24**

- Subset of patients for whom ER/PR status available
  - ER + 76%, PR + 66%





Allred D, et al. J Clin Oncol 2012;30(12):1268-1273

DCIS: **NSABP B-17 and B-24 Pooled Analysis**

- Median f/u 207 mo (B-17) and 163 mo (B-24)
- RT reduced I-IBTR by 52%
- Tam + RT reduced I-IBTR by 32% vs. RT alone

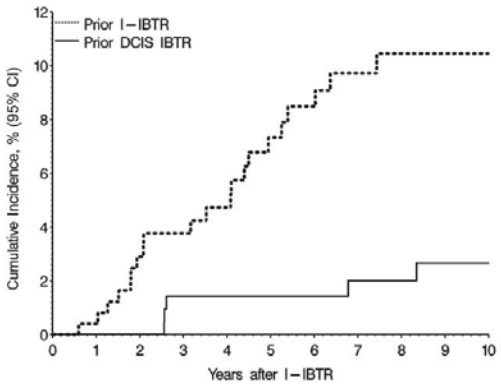
Table 3. Hazard ratios for invasive ipsilateral breast tumor recurrence (I-IBTR) or ductal carcinoma in situ (DCIS)-IBTR according to patient and disease characteristics*

	Ipsilateral breast tumor events			
	I-IBTR		DCIS-IBTR	
Characteristic	HR (95% CI)	P	HR (95% CI)	P
Age at diagnosis, y				
≥55	1.00 (reference)	.003	1.00 (reference)	<.001
<45	2.14 (1.40 to 3.26)		2.90 (1.84 to 4.56)	
45–54	1.80 (1.22 to 2.66)		1.81 (1.16 to 2.81)	
55–64	1.50 (1.00 to 2.26)		1.72 (1.10 to 2.70)	
Tumor size, cm				
≤1.0	1.00 (reference)		1.00 (reference)	
>1.0	0.94 (0.68 to 1.30)	.70	1.03 (0.73 to 1.44)	.89
Mode of detection				
Mammography only	1.00 (reference)		1.00 (reference)	
Clinically detected	1.37 (1.03 to 1.84)	.03	1.48 (1.09 to 2.01)	.01
Comedonecrosis†,‡				
Absent	1.00 (reference)		1.00 (reference)	
Present	0.87 (0.62 to 1.21)	.41	2.21 (1.52 to 3.20)	<.001
Treatment group, tumor margin status†,§				
LRT, margin-free	1.00 (reference)		1.00 (reference)	
LRT, involved/uncertain	2.61 (1.68 to 4.05)	<.001	1.65 (1.00 to 2.73)	.05
LRT + TAM, free	1.00 (reference)		1.00 (reference)	
LRT + TAM, involved/uncertain	1.27 (0.73 to 2.20)	.40	1.32 (0.77 to 2.28)	.31

Wapnir IL et al., JNCI 2011;103:478-488

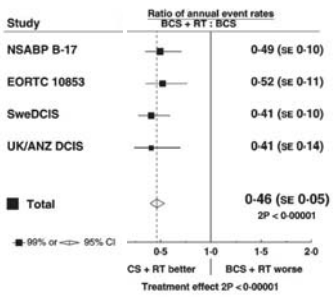
DCIS: **NSABP B-17 and B-24 Pooled Analysis**

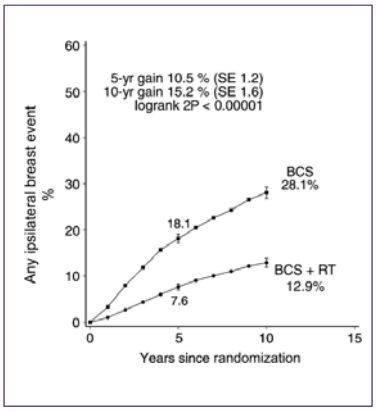
- 490 IBTR events (54% invasive)
- DCIS-IBTR not associated with increased mortality
- I-IBTR associated with increased mortality (HR 1.75)



Wapnir IL et al., JNCI 2011;103:478-488

DCIS: RT **Meta-Analysis**





- Every trial shows that RT cuts the risk of recurrence by at least half
  - Half of recurrences are DCIS – no compromise in survival
  - Half of recurrences are invasive – some decrease in survival

EBCTCG, JNCI 2010;41:162-177

DCIS: Clinical and Pathologic Risk Factors

- Imperfect information
- Some factors fairly consistent:
  - Age
  - Method of detection (clinical vs. mammographic)
  - Margin status (+ vs. -)
  - Histologic subtype/grade
  - Adjuvant therapy (RT, Tam)

DCIS: Risk Factors and RT

- MSKCC prospective database 1978-2010
- 2996 cases with 363 recurrences

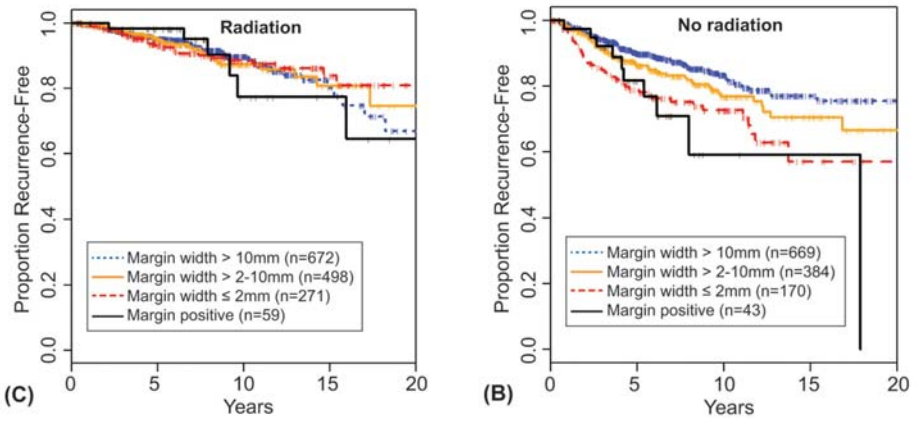
TABLE 5. Multivariable Cox Regression Analysis of Recurrence, Stratified by Use of Radiation

	No Radiation (N = 1225)*				Radiation (N = 1483)*			
Variable	**N**	**Events**	**HR**	***P***	**N**	**Events**	**HR**	***P***
Age at surgery								
Per year			0.987	0.02			0.956	<0.0001
Family history								
No	753	114	1	0.05	909	73	1	0.23
Yes	472	87	1.32		574	51	1.25	
Presentation								
Radiologic	1068	162	1	0.06	1326	102	1	0.43
Clinical	157	39	1.4		157	22	1.22	
Number of excisions								
1	688	100	1	0.0003	612	38	1	0.66
2	492	85	1.37		712	70	1.18	
≥3	45	16	3.18		159	16	1.30	
Endocrine therapy								
No	1026	180	1	0.003	1084	105	1	0.002
Yes	199	21	0.50		399	19	0.46	
Year of surgery								
1978–2000	459	123	1.60	0.003	367	65	1.18	0.44
2001–2010	766	78	1		1116	59	1	
Margin width								
Positive	40	10	1	<0.0001	58	6	1	0.95
Close (≤2 mm)	167	42	0.75		268	27	0.95	
>2–10 mm	369	62	0.58		492	35	1.00	
>10 mm	649	87	0.31		665	56	0.88	

*In entire population of 2996, 288 cases had at least one missing data point, resulting in population for multivariable analysis of 2708.

Van Zee KJ, et al. Ann Surg Oncol 2015;262:623-631

DCIS: Risk Factors and RT



Van Zee KJ, et al. Ann Surg Oncol 2015;262:623-631

Less is more ?

DCIS: Omission of RT: **Harvard Trial**

- Prospective single arm trial (BWH, MGH, BIDMC)
- DCIS, gr 1-2, size ≤ 2.5cm, margin ≥ 1cm or totally negative re-excision
- Planned accrual (n= 200); stopping boundary crossed at 158
- LR 1.9 % per patient-year (1.6% highest nuclear gr 1-2, 7.7% gr 3)

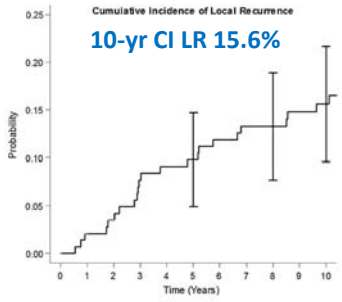


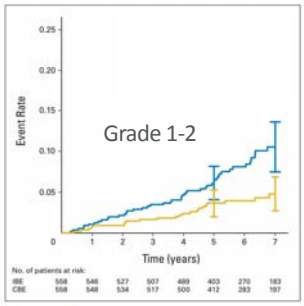
Fig. 1 Estimated cumulative incidence of LR

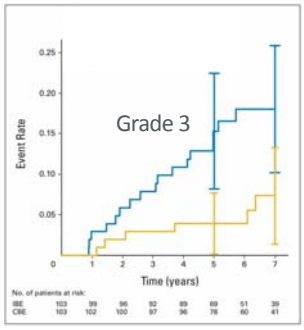
Wong J, et al. J Clin Oncol 2006;24(7):1031-1036
Wong J et al. Breast Cancer Res Treat 2014;143:343-350

DCIS: Omission of RT: **ECOG E-5194**

- Multi-institutional prospective single arm trial
- 665 women with DCIS s/p excision > 0.3cm margins
  - Gr 1-2: ≤ 2.5 cm (n=561)
  - Gr 3: ≤ 1 cm (n=104)
- Median size ~6mm
- Widely free margins (most >0.5cm)
- About 31% received tamoxifen

	5-year IBTR	12-yr IBTR	12-yr I-IBTR
Gr 1-2	6.1%	14.4%	7.5%
Gr 3	15.3%	24.6%	13.4%



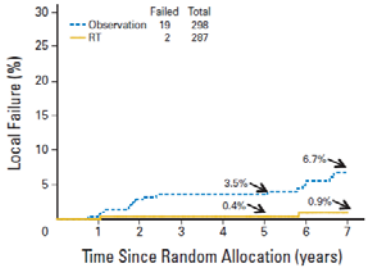


Hughes L, et al. J Clin Oncol 2009;27(32):5319-5324
Solin L, et al. J Clin Oncol 2015;33(33):3938-3944

DCIS: Omission of RT: **RTOG 9804**

- Closed due to slow accrual
- 636 women with DCIS treated with lumpectomy
  - Grade 1-2, >3mm clear margins, ≤ 2.5cm
- About 62% received tamoxifen → Whole breast RT ~ 50Gy
- Median size 5mm → No RT
- Widely free margins

	5-yr	7-yr
RT	0.4%	0.9%
No RT	3.5%	6.7%

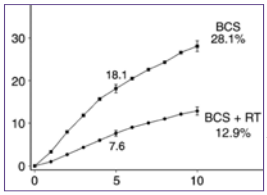


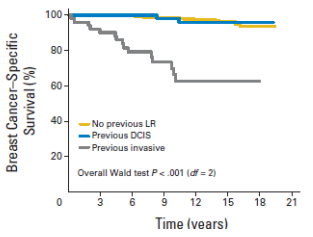
McCormick B, et al. J Clin Oncol 2015;33(7):709-715

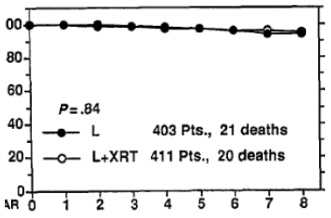
DCIS: Should we omit RT in low risk cohort?

- **NO! RT is needed**
- RT reduces the risk of IBTR in half
- All subsets of patients benefit, clinical variables → imperfect risk stratification
- Half of all recurrences are invasive
- Invasive recurrences associated with reduced survival

- **YES! RT is optional**
- In some patients, baseline risk of recurrence is low
- Especially as imaging, surgery, endocrine tx improving
- No proven survival advantage for RT
- RT carries potential for late toxicity (cardiac, second cancers)







EBCTCG, JNCI 2010;41:162-177
Fisher B, et al. N Engl J Med 1993;328:1581-1586
Donker M, et al. JCO 2013;31(22):4054-4059

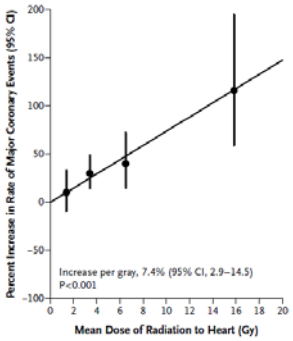
DCIS: Should we omit RT in low risk cohort?

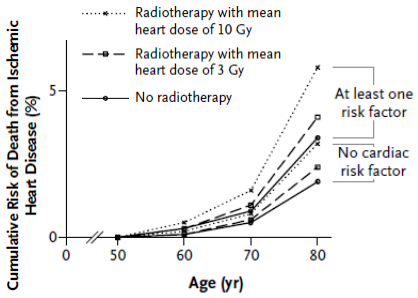
Better Radiotherapy

Better Patient Selection

DCIS: Late Toxicity of Radiotherapy

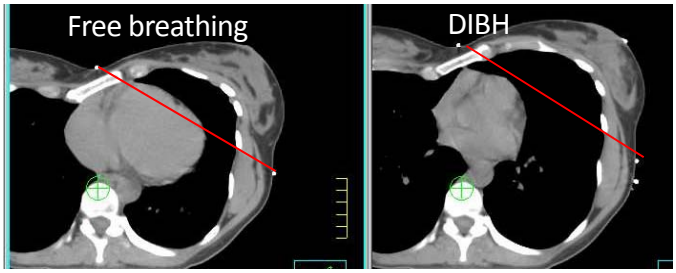
- 2168 women getting whole breast RT in Sweden/Denmark 1958-2001
- Major coronary events (MI, revascularization, death) increase linearly with mean heart dose – 7.4%/Gy for first 20 years
- Risk starts within 5 years, persists ≥ 20 years

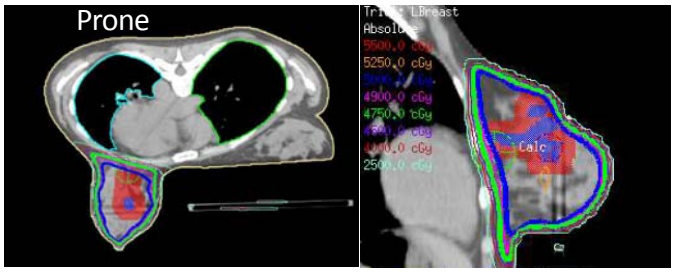




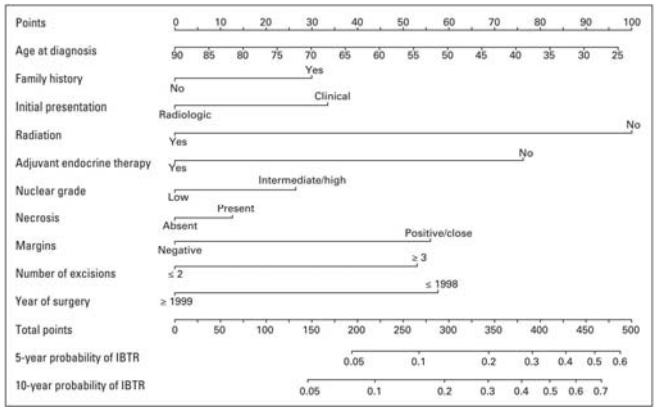
Darby S, NEJM 2013;368(11):987-998

DCIS: Better Radiotherapy





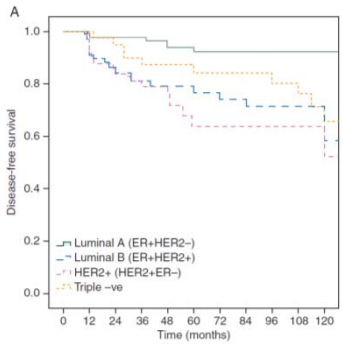
DCIS: Patient Selection via Nomogram



Rudloff U, et al. J Clin Oncol 2010;28(23):3762-3769

DCIS: Molecular Phenotypes

- 314 patients with DCIS screened for clinical trial
- Any surgery (~1/3 mastectomy), ~17% RT
- Molecular phenotypes determined by ER, PR, H2N staining



	HR IBTR	HR I-IBTR
Luminal B	5.1	13.4
Her-2	6.5	11.4
Triple (-)	3.3	10.3

Williams K, et al. Annals of Oncology 2015;26:1019-1025

DCIS: Genetic Profiling – **12-Gene RT-PCR Assay**

- Selected genes prognostic for LR in both ER+/ER- subsets
- Calculation of DS score:
  - 1) Expression of cancer-related genes normalized relative to ref genes
  - 2) Proliferation group score $(Ki67 + STK15 + Survivin + CCNB1 + MYBL2)/5$.
  - 3) $\text{DCIS Score}_u = +0.31 \times \text{proliferation group score} - 0.08 \times PR - 0.09 \times GSTM1.$
  - 4) DCIS Score = $(66.7 \times \text{DCIS Score}_u) + 10.0$

Proliferation group
Ki67
STK15
Survivin
CCNB1 (cyclin B1)
MYBL2

Hormone receptor group
PR

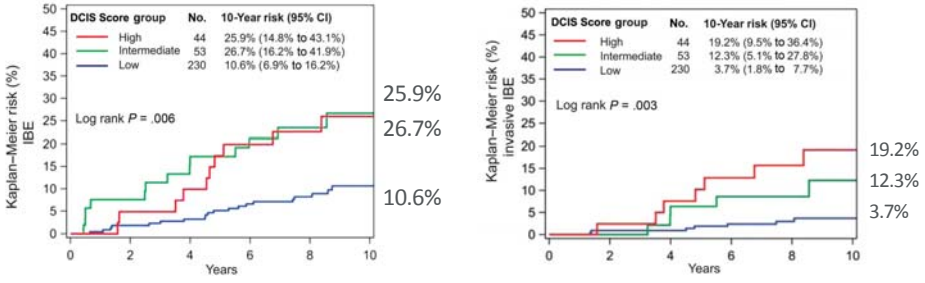
GSTM1

Reference group
ACTB (β-actin)
GAPDH
RPLPO
GUS
TFRC

Solin L, et al. JNCI 2013;105(10):701-710

DCIS: Genetic Profiling -- **ECOG E5194**

- Subset of highly selected ECOG E5194
- 12-Gene RT-PCR Breast Cancer Assay
- Continuous DCIS Score associated with risk of IBE (HR 2.31) and I-IBE (HR 3.68)



Solin L, et al. JNCI 2013;105(10):701-710

DCIS: Genetic Profiling -- **ECOG E5194**

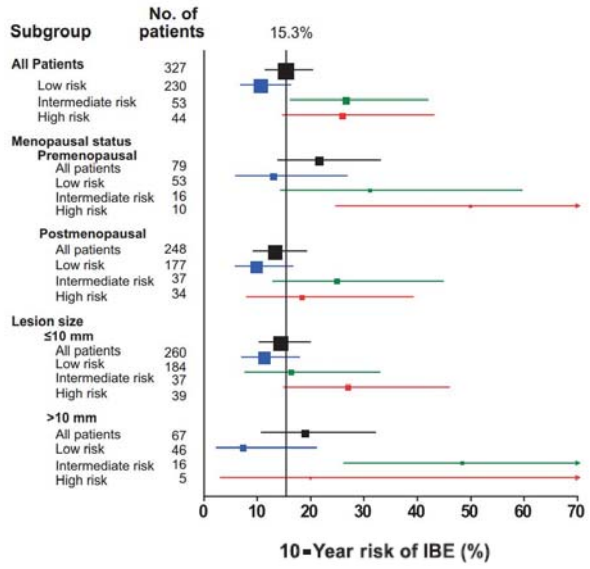
- Risk factors for IBTR: DCIS score, tumor size, menopausal status
- DS has independent prognostic value in addition to clinical variables
- DS is a compliment to, not a replacement for, clinical risk factors

Table 4. Multivariable Cox proportional hazards models for the risk of an ipsilateral breast event

Analyses and variables	Hazard ratio (95% CI)*	P†
Multivariable analysis of significant clinical and pathologic factors, including the DCIS Score		
Menopausal status		.02
Premenopausal	1.00 (referent)	
Postmenopausal	0.49 (0.27 to 0.90)	
Tumor size‡	1.52 (1.11 to 2.01)	.01
DCIS Score‡	2.37 (1.14 to 4.76)	.02

Solin L, et al. JNCI 2013;105(10):701-710

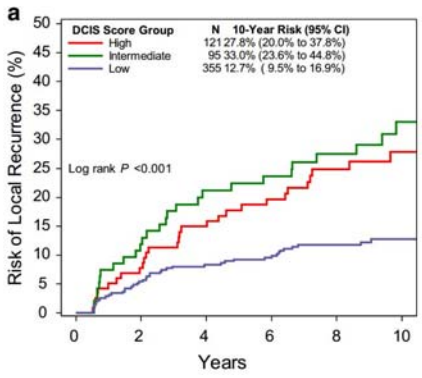
DCIS: Genetic Profiling -- **ECOG E5194**



Solin L, et al. JNCI 2013;105(10):701-710

DCIS: Genetic Profiling – **Ontario DCIS cohort**

- **Population-based cohort in Ontario, Canada**
- Not highly selected like ECOG E5194
- DCIS treated margin (-) excision (no RT) 1994-2003
- 12-Gene RT-PCR Breast Cancer Assay
- 571 pts, median f/u 9.6 years
- DS correlated to LR (HR 2.15)
  - I-IBTR: HR 1.78
  - DCIS-IBTR: HR 2.43



Rakovitch E, et al. Breast Cancer Res Treat 2015;152(2):389-398

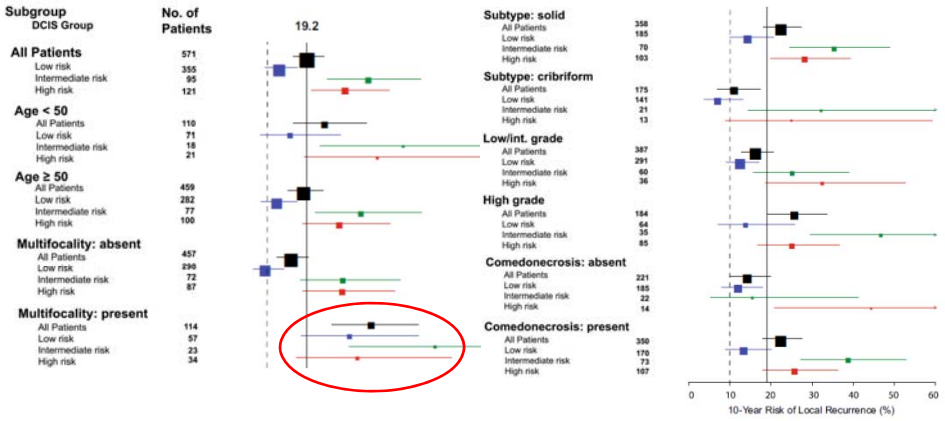
DCIS: Genetic Profiling – **Ontario DCIS cohort**

- DS independent prognostic info (adjusted HR 1.68) in addition to clinical variables

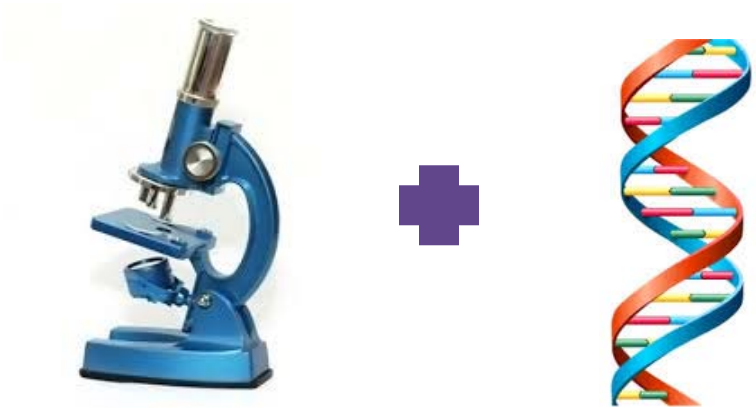
Characteristic	*N*	HR (95 % CI)*	*P* value*
DCIS Score (HR/50 U)	571	1.68 (1.08, 2.62)	0.02
Multifocality			0.003
Absent/unknown	457	1.0	
Present	114	1.97 (1.27, 3.02)	
Tumor size‡			0.01§
≤10 mm	150	1.0	
>10 mm	140	2.07 (1.15, 3.83)	
Age			0.03
≥50	459	1.0	
<50	110	1.75 (1.07, 2.76)	
DCIS tumor subtype			0.04
Cribriform	175	1.0	
Solid	358	1.63 (0.97, 2.88)	
Other	38	2.75 (1.17, 6.04)	

Rakovitch E, et al. Breast Cancer Res Treat 2015;152(2):389-398

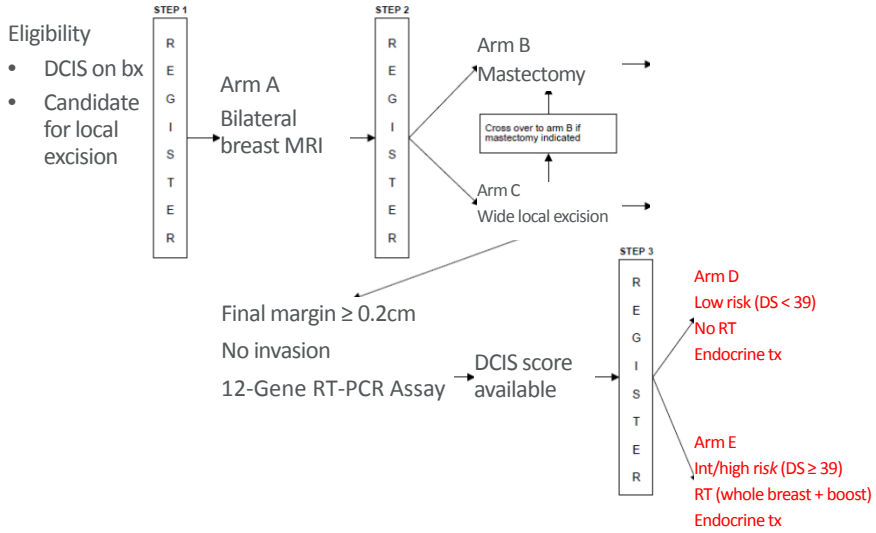
DCIS: Genetic Profiling – **Ontario DCIS cohort**



Rakovitch E, et al. Breast Cancer Res Treat 2015;152(2):389-398



DCIS: Genetic Profiling – **ECOG-ACRIN E4112**



DCIS: Endocrine Trial **NSABP B-35**

- 3,104 postmenopausal women with DCIS
  - Tam 20 mg qd x 5 yrs
  - Anast 1mg qd x 5 yrs
- ER or PR (+)
- Treated with excision (–) margin, 50 Gy RT
- Median follow-up 9 years
- AEs similar except thrombosis/embolism worse in tam group

(Await IBIS-II DCIS trial)

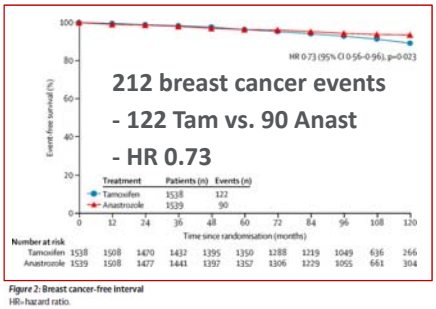


Figure 2: Breast cancer-free interval
HR=hazard ratio.

Margolese R, et al. Lancet 2015 Dec 10 [Epub ahead of print]

DCIS: Endocrine Trial **NSABP B-35**

- Anastrazole superior to Tam only in women <60

	Patients (n)	Tamoxifen (n=1538)	Anastrozole (n=1539)	Hazard ratio (95% CI)	p value
Breast cancer-free interval events					
<60 years	1447	63	34	0·53 (0·35–0·80)	0·0026
≥60 years	1630	59	56	0·95 (0·66–1·37)	0·78
Disease-free survival events					
<60 years	1447	104	74	0·69 (0·51–0·93)	0·0151
≥60 years	1630	156	161	1·03 (0·83–1·28)	0·79

Table 3: Breast cancer-free interval and disease-free survival events by age group

Margolese R, et al. Lancet 2015 Dec 10 [Epub ahead of print]

DCIS: Endocrine Trial **NSABP B-35**

- Of the 3,104 pts, 1,193 included in QoL substudy
- Tamoxifen worse for vasomotor sz, bladder control, gyne symptoms
- Anastrazole worse for M-skel pain, vaginal symptoms
- Younger age associated w/ more vasomotor, vaginal symptoms, weight problems, gyne symptoms

- **<60 years old: decision based on efficacy and toxicity profile**
- **>60 years old: decision on toxicity only**

Ganz P et al. Lancet 2015 Dec 10 [Epub ahead of print]

DCIS: Local Transdermal Endocrine Therapy

- Double-blind, Phase II, RCT
- 27 women with DCIS randomized
- Received tx for 6-10 weeks before surgery (med time 6 weeks)
- Oral tamoxifen vs. transdermal 4-hydroxytamoxifen gel (4-OHT)

	4-OHT	Oral Tam
Decrease in ki-67	3.4%	5.1%
Breast Adipose concentration (ng/g)	5.8	5.4
Mean Plasma concentration (ng/mL)	**0.2**	**1.1**
Effect on clotting factors	**No**	**Yes**

  - achieves therapeutic concentration in breast
  - exhibits anti-proliferative effect
  - Less systemic absorption

Lee O, et al. Clin Cancer Res 2014;20(14):3672-3682

DCIS: New Frontiers in Systemic Therapy

- **NSABP B-43**
  - 2000 women with DCIS Her-2 amplified
  - Treated with lumpectomy and RT
  - Endocrine tx if ER/PR +

→ Trastuzumab x 2 during RT

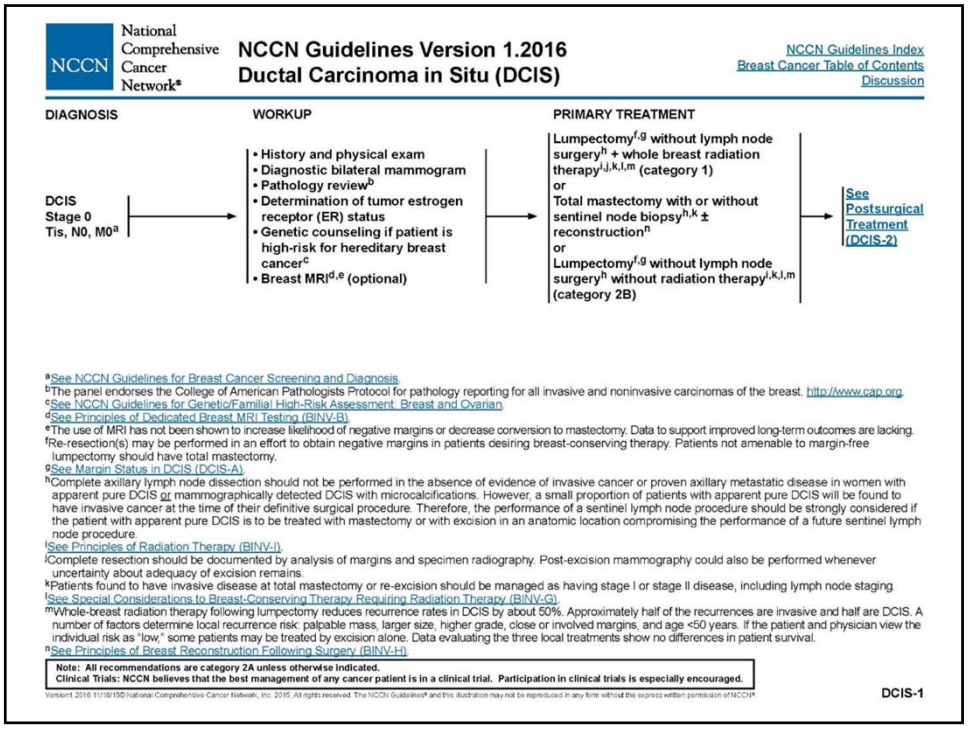
→ RT alone

- **CALGB 40903**
  - Phase II study neoadjuvant letrozole x 6 months in postmenopausal women with DCIS
  - Estimate mean change in MRI tumor volume, change in ki-67

DCIS: New Frontiers in Radiotherapy

- **EORTC 22085-10083**
  - DCIS, margin (-) excision, "high risk"
  - 2x2 factorial design:
    - Breast 50 Gy / 25 fx
      - Boost 16 Gy / 8 fx
      - No Boost
    - Breast 42.5 Gy / 16 fx
      - Boost 16 Gy / 8 fx
      - No Boost
- **BONBIS Trial**
  - DCIS, excision
  - 50 Gy to breast
    - Boost 16 Gy / 8 fx
    - No Boost
- **Multiple Trials of APBI in DCIS**

NCCN Guidelines



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Ductal Carcinoma in Situ (DCIS)

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DIAGNOSIS

DCIS
Stage 0
Tis, N0, M0[a]

WORKUP

- History and physical exam
- Diagnostic bilateral mammogram
- Pathology review[b]
- Determination of tumor estrogen receptor (ER) status
- Genetic counseling if patient is high-risk for hereditary breast cancer[c]
- Breast MRI[d,e] (optional)

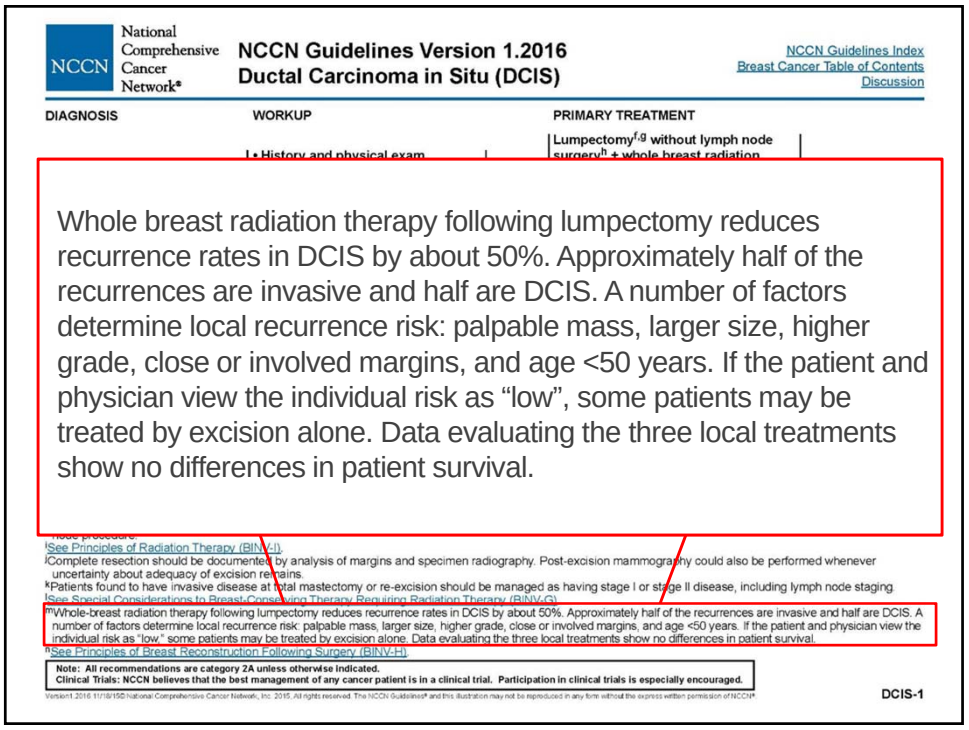
PRIMARY TREATMENT

Lumpectomy[f,g] without lymph node surgery[h] + whole breast radiation therapy[i,j,k,l,m] (category 1)
or
Total mastectomy with or without sentinel node biopsy[h,k] ± reconstruction[n]
or
Lumpectomy[f,g] without lymph node surgery[h] without radiation therapy[i,k,l,m] (category 2B)

→ See Postsurgical Treatment (DCIS-2)

[a] See NCCN Guidelines for Breast Cancer Screening and Diagnosis.
[b] The panel endorses the College of American Pathologists Protocol for pathology reporting for all invasive and noninvasive carcinomas of the breast. http://www.cap.org.
[c] See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian.
[d] See Principles of Dedicated Breast MRI Testing (BINV-B).
[e] The use of MRI has not been shown to increase likelihood of negative margins or decrease conversion to mastectomy. Data to support improved long-term outcomes are lacking.
[f] Re-resection(s) may be performed in an effort to obtain negative margins in patients desiring breast-conserving therapy. Patients not amenable to margin-free lumpectomy should have total mastectomy.
[g] See Margin Status in DCIS (DCIS-A).
[h] Complete axillary lymph node dissection should not be performed in the absence of evidence of invasive cancer or proven axillary metastatic disease in women with apparent pure DCIS or mammographically detected DCIS with microcalcifications. However, a small proportion of patients with apparent pure DCIS will be found to have invasive cancer at the time of their definitive surgical procedure. Therefore, the performance of a sentinel lymph node procedure should be strongly considered if the patient with apparent pure DCIS is to be treated with mastectomy or with excision in an anatomic location compromising the performance of a future sentinel lymph node procedure.
[i] See Principles of Radiation Therapy (BINV-I).
[j] Complete resection should be documented by analysis of margins and specimen radiography. Post-excision mammography could also be performed whenever uncertainty about adequacy of excision remains.
[k] Patients found to have invasive disease at total mastectomy or re-excision should be managed as having stage I or stage II disease, including lymph node staging.
[l] See Special Considerations to Breast-Conserving Therapy Requiring Radiation Therapy (BINV-G).
[m] Whole-breast radiation therapy following lumpectomy reduces recurrence rates in DCIS by about 50%. Approximately half of the recurrences are invasive and half are DCIS. A number of factors determine local recurrence risk: palpable mass, larger size, higher grade, close or involved margins, and age <50 years. If the patient and physician view the individual risk as "low," some patients may be treated by excision alone. Data evaluating the three local treatments show no differences in patient survival.
[n] See Principles of Breast Reconstruction Following Surgery (BINV-H).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Ductal Carcinoma in Situ (DCIS)

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DIAGNOSIS
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Whole breast radiation therapy following lumpectomy reduces recurrence rates in DCIS by about 50%. Approximately half of the recurrences are invasive and half are DCIS. A number of factors determine local recurrence risk: palpable mass, larger size, higher grade, close or involved margins, and age <50 years. If the patient and physician view the individual risk as "low", some patients may be treated by excision alone. Data evaluating the three local treatments show no differences in patient survival.

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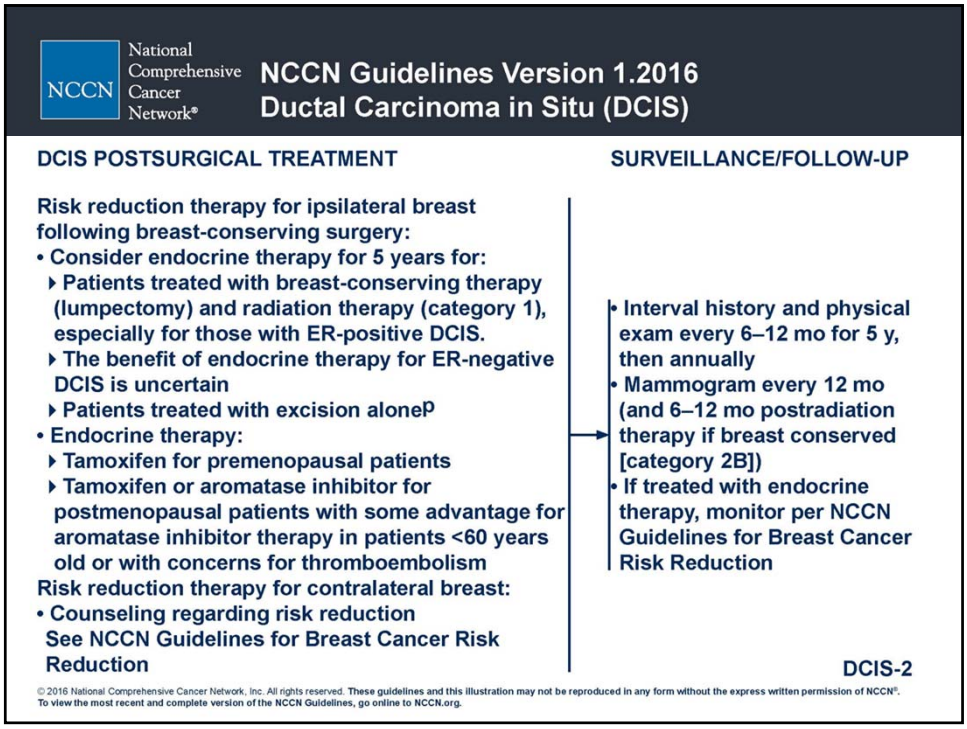
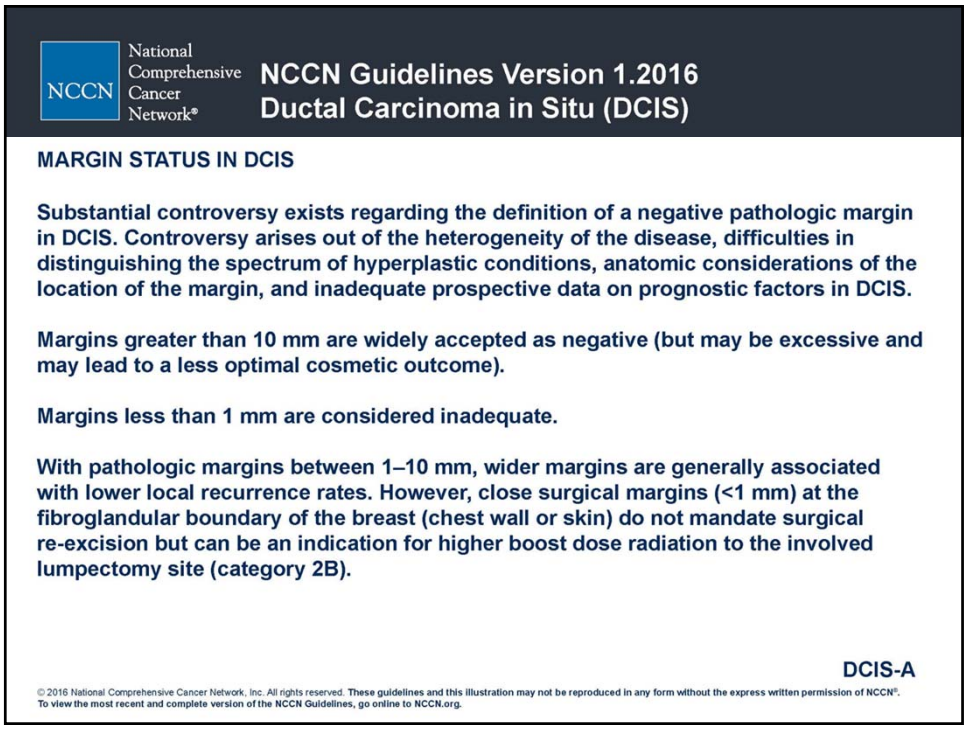
DCIS-1





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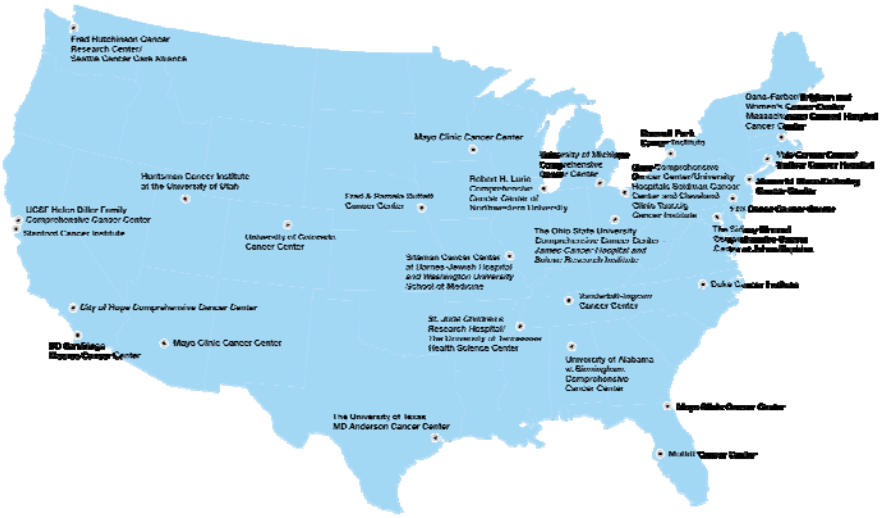

Q&A SESSION

Upcoming Webinars – Register at NCCN.org/events

- **Late Stage Breast Cancer, Including SABCS Updates**
  Thursday, March 3 at 1:00 PM [EST]
  William J. Gradishar, MD, *Robert H. Lurie Comprehensive Cancer Center of Northwestern University*
- **Recognition and Management of Toxicities Associated with the Treatment of Renal Cell Carcinoma Supportive Care: Fertility Preservation & Use of Bone Modifying Agents in Patients with Breast Cancer**
  Thursday, March 17 at 2:00 PM [EDT]
  Joanne Frankel Kelvin, MSN, RN, CNS, AOCN, *Memorial Sloan Kettering Cancer Center*
  John H. Ward, MD, *Huntsman Cancer Institute at the University of Utah*
- **Early Stage Breast Cancer: Role of Multigene Assays & SABCS Updates on Adjuvant & Neoadjuvant Therapies**
  Friday, April 8 at 2:30 PM [EDT]
  Matthew Goetz, MD, *Mayo Clinic Cancer Center*
  Sarika Jain, MD, MSCI, *Robert H. Lurie Comprehensive Cancer Center of Northwestern University*
  Cesar A. Santa-Maria, MD, *Robert H. Lurie Comprehensive Cancer Center of Northwestern University*
- **Early Stage Breast Cancer: Adjuvant Radiation, Surgical Management, & SABCS Updates on Local Therapy**
  Friday, April 22 at 8:45 AM [EDT]
  Benjamin O. Anderson, MD, *Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance*
  Seema A. Khan, MD, *Robert H. Lurie Comprehensive Cancer Center of Northwestern University*
  Kilian E. Salerno, MD, *Roswell Park Cancer Institute*

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Thank you for your participation in today's program!