AJCC 8th Edition Breast Cancer Staging Updates

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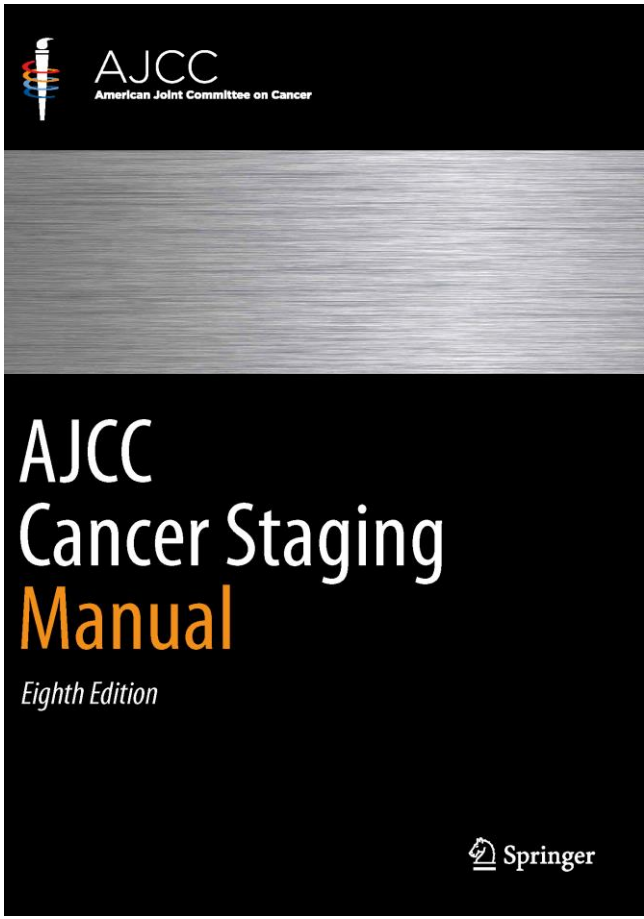
Pathology & Laboratory Medicine

AJCC 8th ed. Breast Cancer Staging Updates

- Background
- Key Changes
- “Personalized”Staging



AJCC 8th ed. Breast Cancer Staging Updates

Background

- (1959) Tumor (T), Lymph node (N), and Metastasis (M) staging system developed by the American Joint Committee on Cancer (AJCC) ➡ **anatomic extent**
- AJCC 1st edition (1977): TNM based primarily on the Halstedian view of tumor progression: tumor → regional nodes → distant sites
- AJCC 2nd-7th editions (1983, 1988, 1992, 1997, 2002, 2009): updated cancer classifications with associated outcomes prognostication
- AJCC 8th edition (2017) incorporates intrinsic tumor biology in risk stratification and personalized prognostication and treatment management ➡ **biomarker based (personalized) staging**
- January 1, 2018: Implementation of AJCC 8th edition staging system

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Evolution from a "population-based" to a more "personalized" approach to cancer staging in the era of precision medicine.

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Key Changes

	LOE
• Anatomic stage and prognostic stage groups	II
• LCIS is benign and removed from TNM	I
• (T):	
– Tumors >1mm and <2mm should be reported rounding to 2mm	I
– Maximum size of largest tumor focus is used for pT; synchronous foci are not added; use of (m) modifier	I

LOE I: based on multiple large, well-designed, prospective and retrospective studies in appropriate patient population
LOE II: based on at least one large, well-designed study

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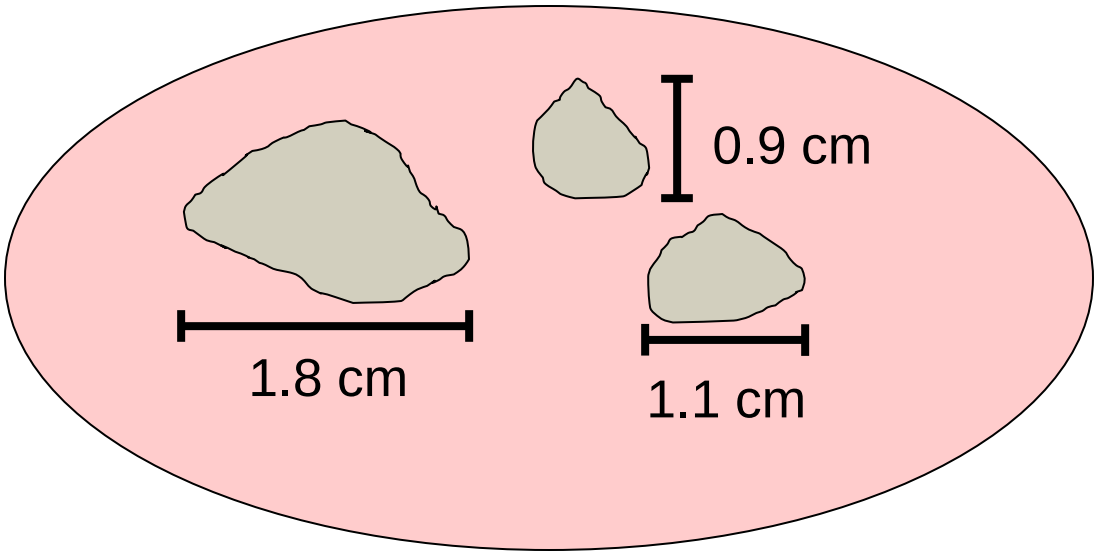
AJCC 8th ed: ~~pT2~~



T1a: >1mm but ≤ 5mm
T1b: >5mm but ≤1.0cm
T1c: >1.0cm but ≤2.0cm

T2: >2.0cm but <5.0cm
T3: >5.0cm
T4: chest wall and/or skin

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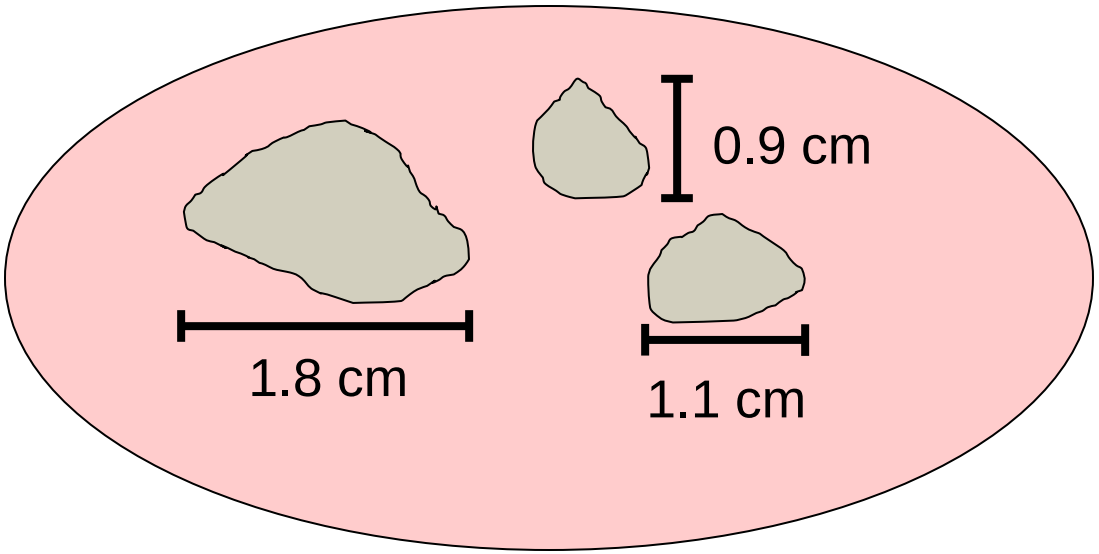
AJCC 8th ed: pT1c(m)



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- (N):
  - Maximum size of largest contiguous tumor deposit is used for pN; additional foci are not added.
- (M):
  - pM0 is not a valid category; if cM1 is histologically confirmed, then pM1 is used.
- (ypTNM):
  - ypT is based on largest focus of residual tumor; treatment fibrosis is not included. (m) is used for multiple foci of residual disease.
  - ypN is based on largest focus of residual tumor in the lymph node; treatment fibrosis is not included.

LOE

I

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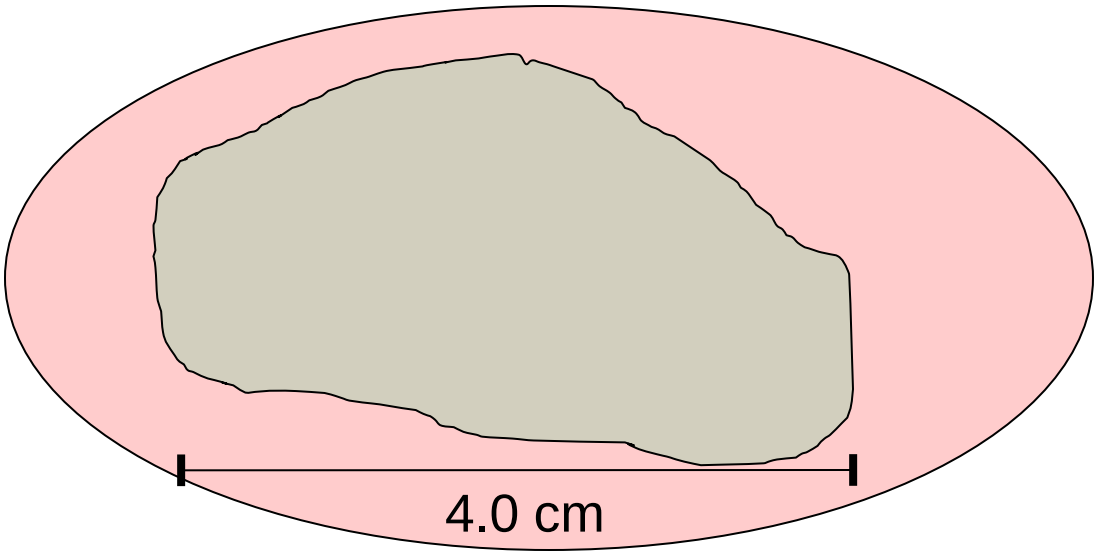
AJCC 8th ed: cT2

NEOADJUVANT THERAPY



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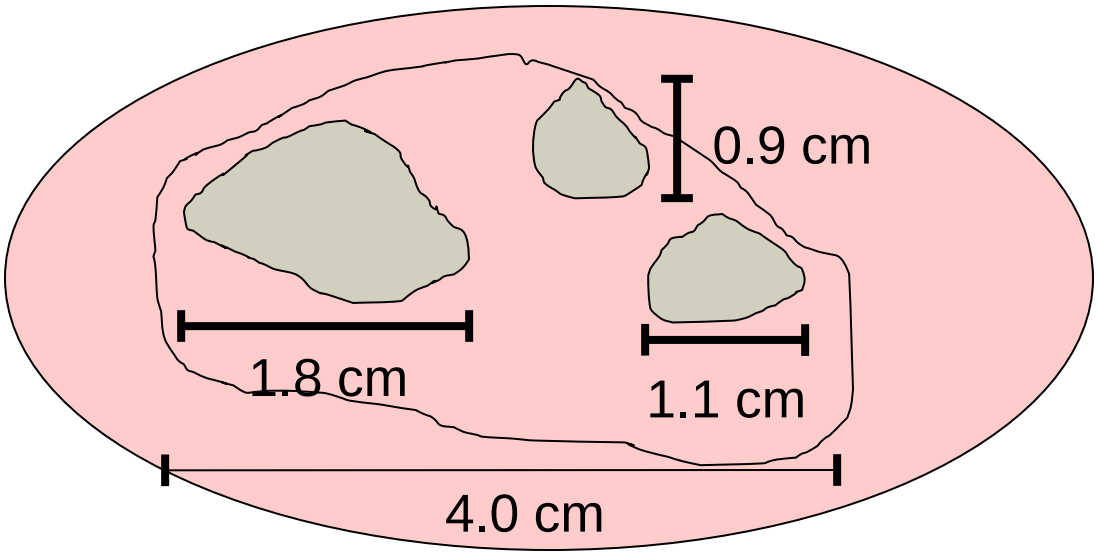
Post neoadjuvant AJCC 8th ed: ~~y~~ 2



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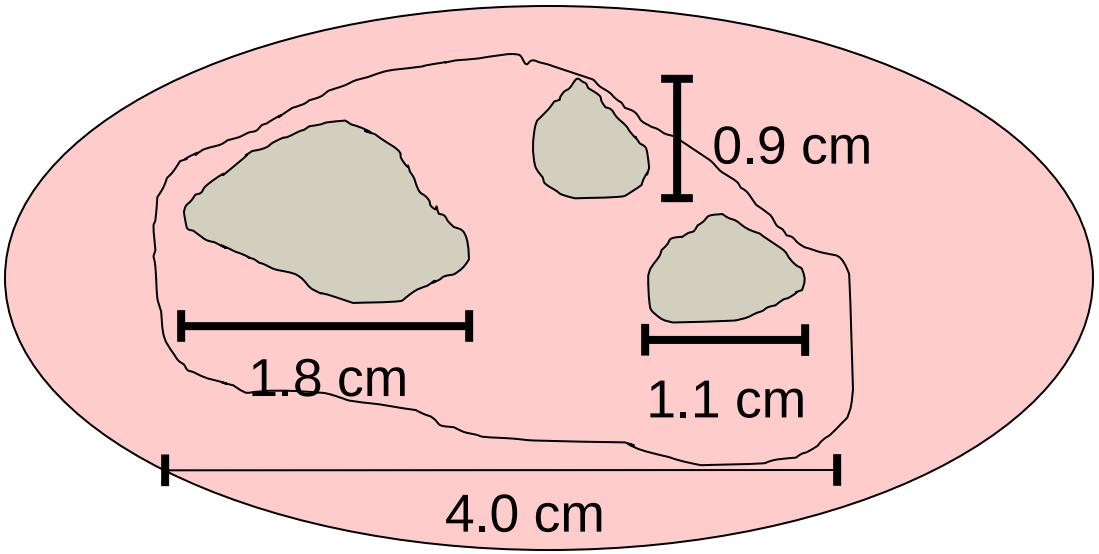
Post neoadjuvant AJCC 8th ed: ypT1c(m)



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	LOE
• Collection of biomarkers:	
– ER, PR, and HER2 on all invasive breast carcinomas.	I
• Inclusion of multigene panels as stage modifiers:	
– Oncotype Dx	I
– Mammaprint	II
– EndoPredict	II
– PAM50 (Prosigna)	II
– Breast Cancer Index	II

Anatomic Stage v. Prognostic Stage Groups

- AJCC Anatomic Stage Groups
  - Based solely on TNM
  - Utilized where biomarker studies are not available
  - Provides continuity and common language
- AJCC Prognostic Stage Groups
  - TNM plus tumor grade, ER, PR, HER2 status, and multigene panel
  - Prognostic subgroups according to calculated survival based on differing risk profiles with potential stage reassignment
  - Preferred for patient care and must be used by cancer registries for case reporting

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Development of Prognostic Stage Groups

Traditional TNM factors			Expanded Non-Anatomic Factors				TNM	PSG*
When T is	When N is	When M is	When G is	When HER2 is	When ER is	When PR is	7th Ed.	8th Ed.
T1	N0	M0					IA	
T1	N0	M0	1	Neg	Pos	Pos		IA
T1	N0	M0	Any	Neg	Neg	Neg		IIA
T2	N0	M0					IIA	
T2	N0	M0	1	Pos	Pos	Pos		IB
T2	N0	M0	1	Neg	Pos	Pos		IB
T2	N0	M0	3	Neg	Pos	Pos		IIA
T3	N0	M0					IIB	
T3	N0	M0	1	Neg	Pos	Neg		IIIA
T3	N0	M0	3	Neg	Neg	Neg		IIIC

* Prognostic Stage Groups

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Impact of Prognostic Stage Groups

" The inclusion of grade, HER2 and hormone receptor status for pathologic prognostic stage resulted in stage reassignment for 41% of the patients to a stage group higher or lower than would otherwise be assigned using the 7th Edition anatomic TNM stage."

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Inclusion of Multigene Panels into Prognostic Stage Groups

21-Gene Classifier

Oncotype DX

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Classifier Gene Set

PROLIFERATION
Ki-67
STK15
Survivin
Cyclin B1
MYBL2

INVASION
Stromolysin 3
Cathepsin L2

HER2
GRB7
HER2

GSTM1

CD68

BAG1

ESTROGEN
ER
PGR
Bcl2
SCUBE2

REFERENCE
Beta-actin
GAPDH
RPLPO
GUS
TFRC

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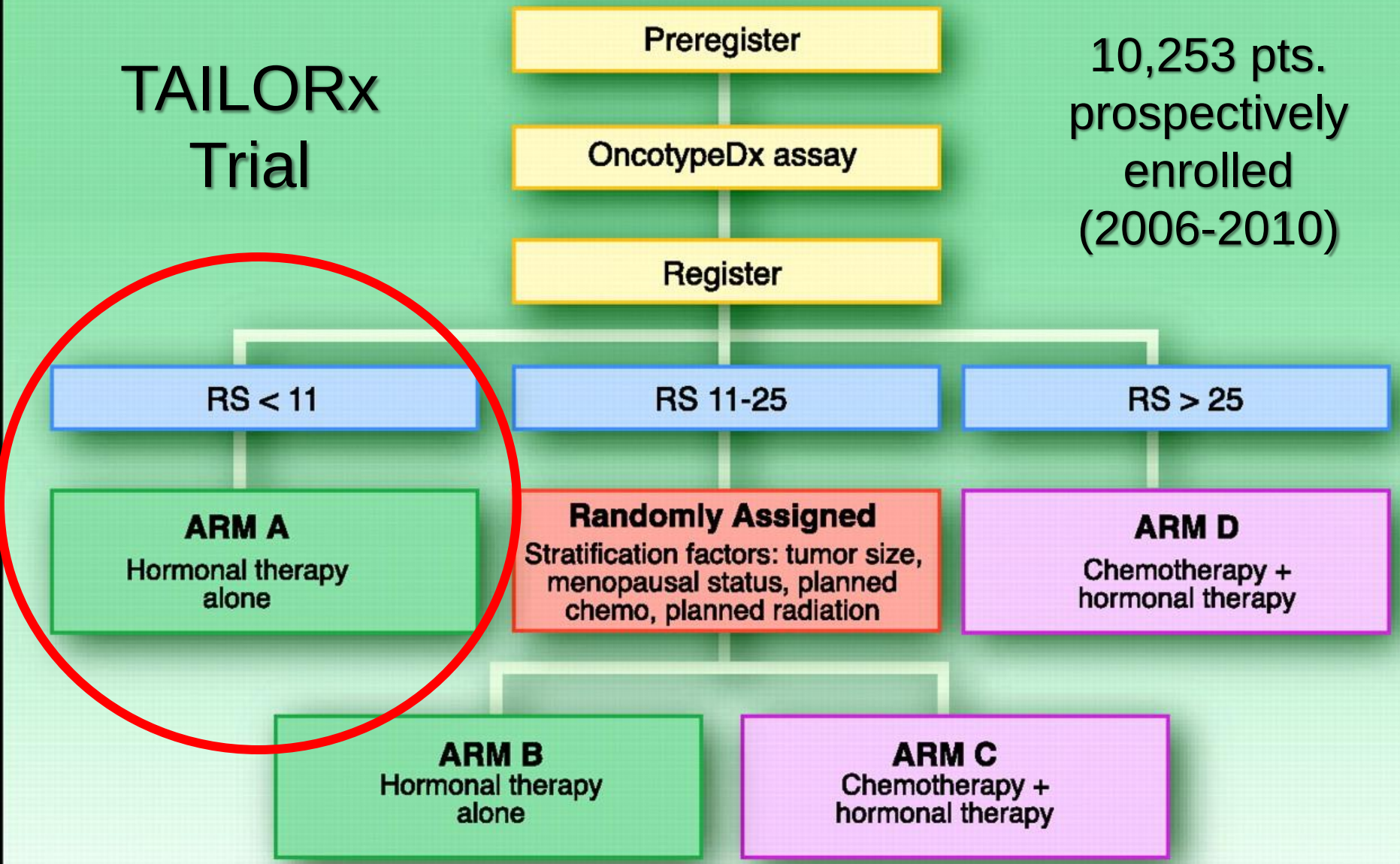
Kaplan-Meier Estimates of the Rate of Distant Recurrence at 10 years, according to recurrence-score risk categories

Risk Category (RS*)	Percentage of Patients	Rate of Distance Recurrence at 10 yr (95% CI)
Low (0-17)	51	6.8 (4.0-9.6)
Intermediate (18-30)	22	14.3 (8.3-20.3)
High (31-100)	27	30.5 (23.6-37.4)

*Recurrence score

NEJM 2004;351:2817-26, Table 1

TAILORx Trial



10,253 pts. prospectively enrolled (2006-2010)

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 19, 2015 VOL. 373 NO. 21

Prospective Validation of a 21-Gene Expression Assay in Breast Cancer

J.A. Sparano, R.J. Gray, D.F. Makower, K.I. Pritchard, K.S. Albain, D.F. Hayes, C.E. Geyer, Jr., E.C. Dees, E.A. Perez, J.A. Olson, Jr., J.A. Zujewski, T. Lively, S.S. Badve, T.J. Saphner, L.I. Wagner, T.J. Whelan, M.J. Ellis, S. Paik, W.C. Wood, P. Ravdin, M.M. Keane, H.L. Gomez Moreno, P.S. Reddy, T.F. Goggins, I.A. Mayer, A.M. Brufsky, D.L. Toppmeyer, V.G. Kaklamani, J.N. Atkins, J.L. Berenberg, and G.W. Sledge

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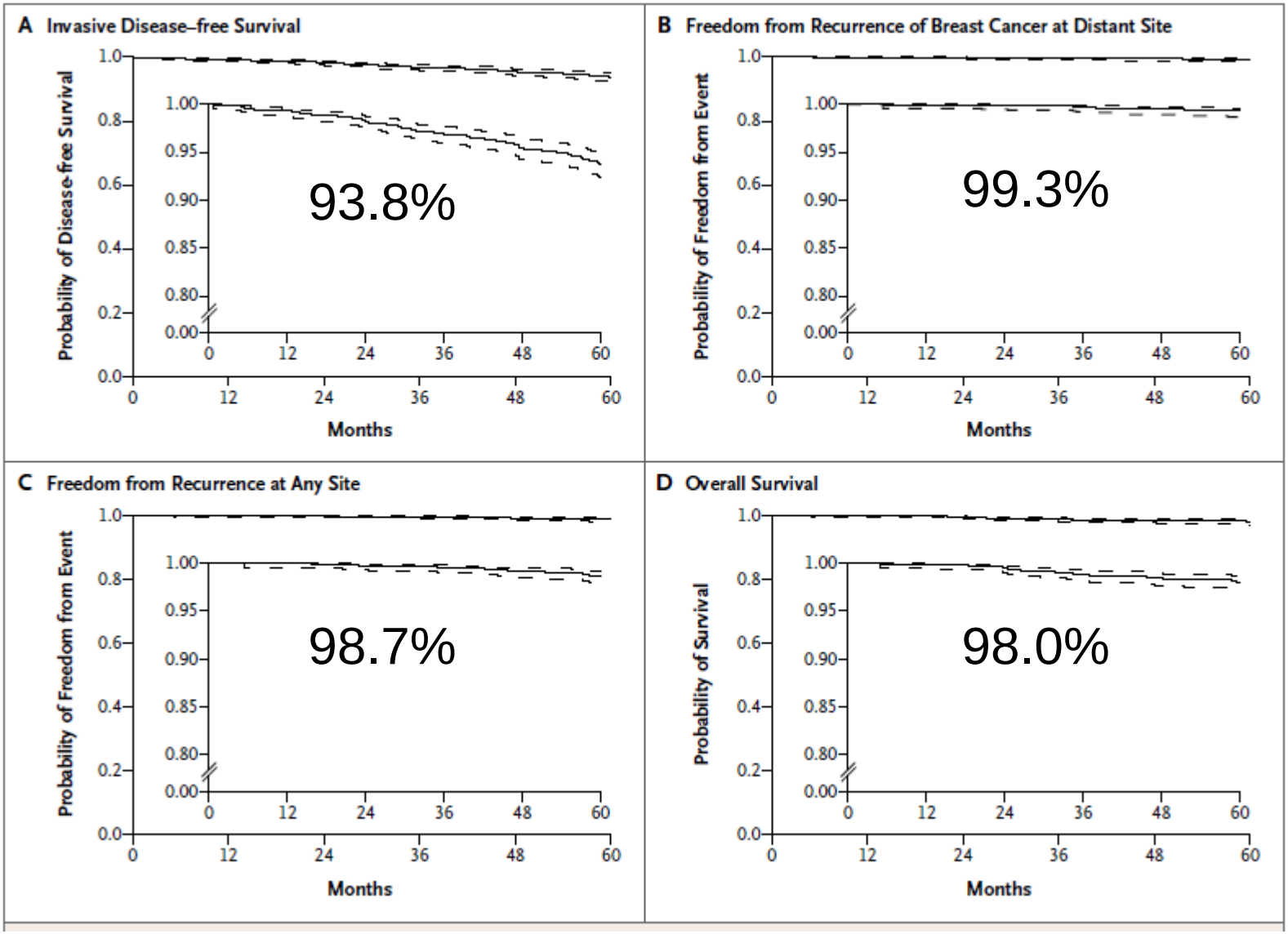
1,626 pts with T1-2, N0, ER+, HER2-, RS<11 at 5 years



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Inclusion of Multigene Panels into Prognostic Stage Groups

Traditional TNM factors			Expanded Non-Anatomic Factors				21-gene	PSG +RS*
When T is	When N is	When M is	When G is	When HER2 is	When ER is	When PR is	RS*	8th Ed.
T1-2	N0	M0	1-3	Neg	Pos	Any	<11	IA

When incorporating Oncotype DX into the Prognostic Stage Groups, the following patients are downstaged to Pathological Stage IA (T1N0):

TNM	PSG	PSG + RS <11
T2 N0 M0 IIA	Grade 1, HER2-, ER+, PR+ (IB)	**IA**
T2 N0 M0 IIA	Grade 2, HER2-, ER+, PR- (IIB)	**IA**
T2 N0 M0 IIA	Grade 3, HER2-, ER+, PR+ (IIA)	**IA**
T2 N0 M0 IIA	Grade 3, HER2-, ER+, PR- (IIIA)	**IA**

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- Oncotype Dx is supported by prospective level I data and is the only multigene panel included in the prognostic stage group table of the AJCC 8th ed.
- It is likely that other multigene panels provide prognostic information regarding low risk biology but thus far, available data has achieved level II evidence.
- Prognostic and predictive models should not be used for staging without prior knowledge of ER, PR, and HER2.
- Multigene panels should only be incorporated into the staging system for selected subsets of breast cancer.

AJCC 8th ed. Breast Cancer Staging Updates

The 8th edition of the AJCC staging system for breast cancer:

- Introduces Biomarker-Based" Staging
- Refined staging reflective of the prognostic and predictive significance of biologic factors
- Anticipates frequent online modifications as peer reviewed, validated information becomes available

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