Pathology After Neoadjuvant Chemotherapy

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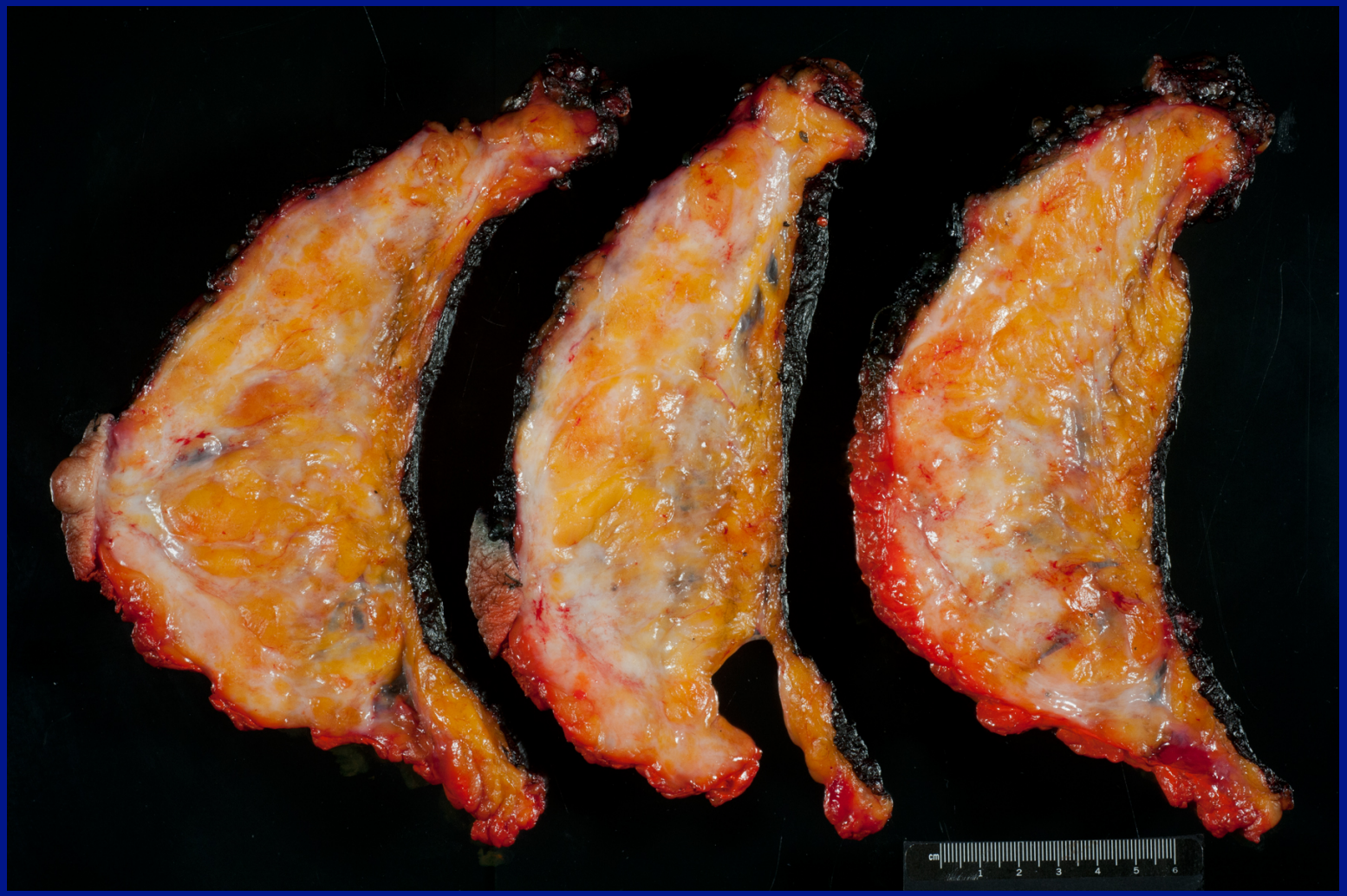
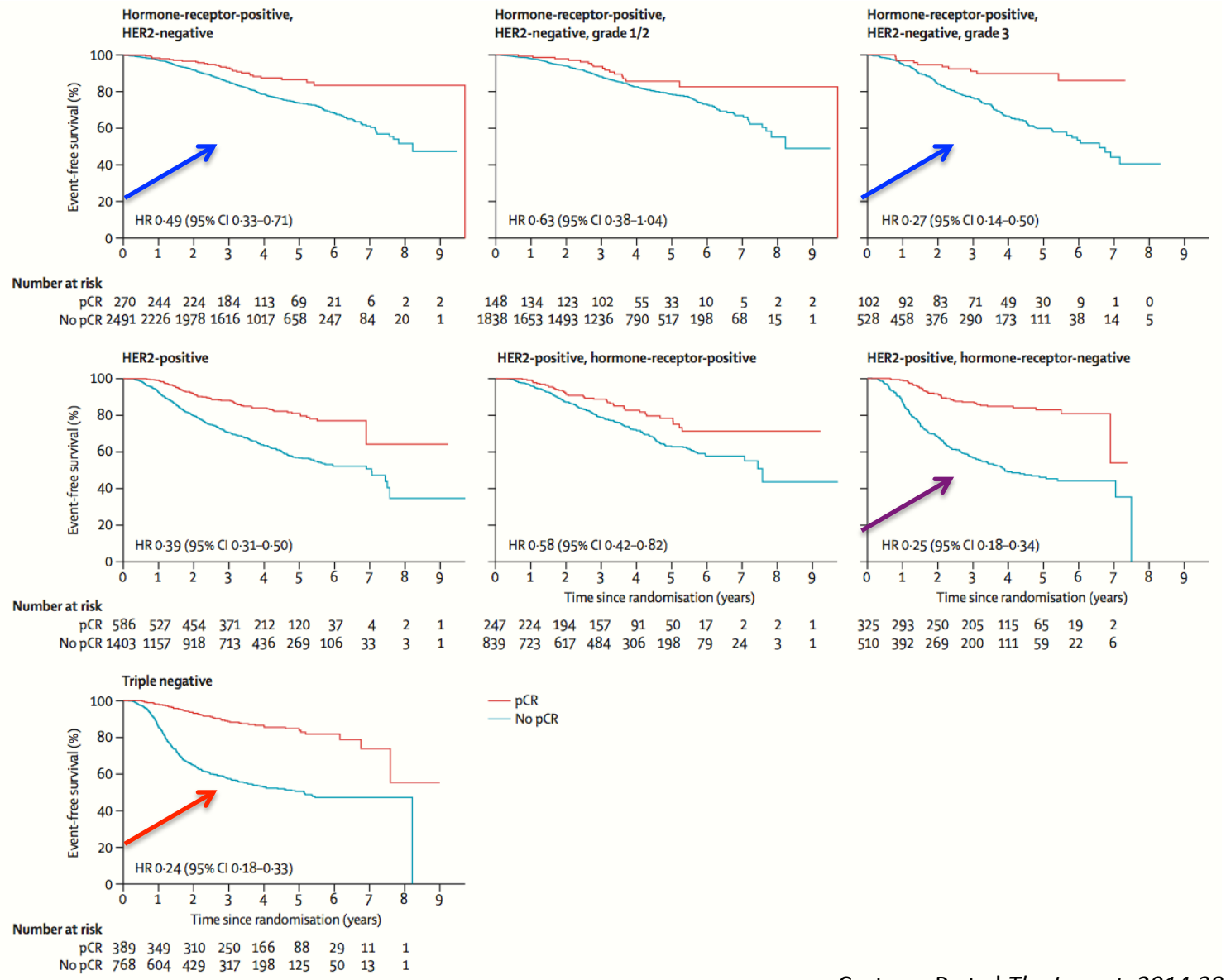
The 3 Informative Slices Of The 13 Slices From The Mastectomy After Neoadjuvant Chemotherapy



Can you imagine a primary endpoint for clinical trials that is defined by absence of disease, but relies on preferences of local sites to identify and sample the correct area within each resection specimen?

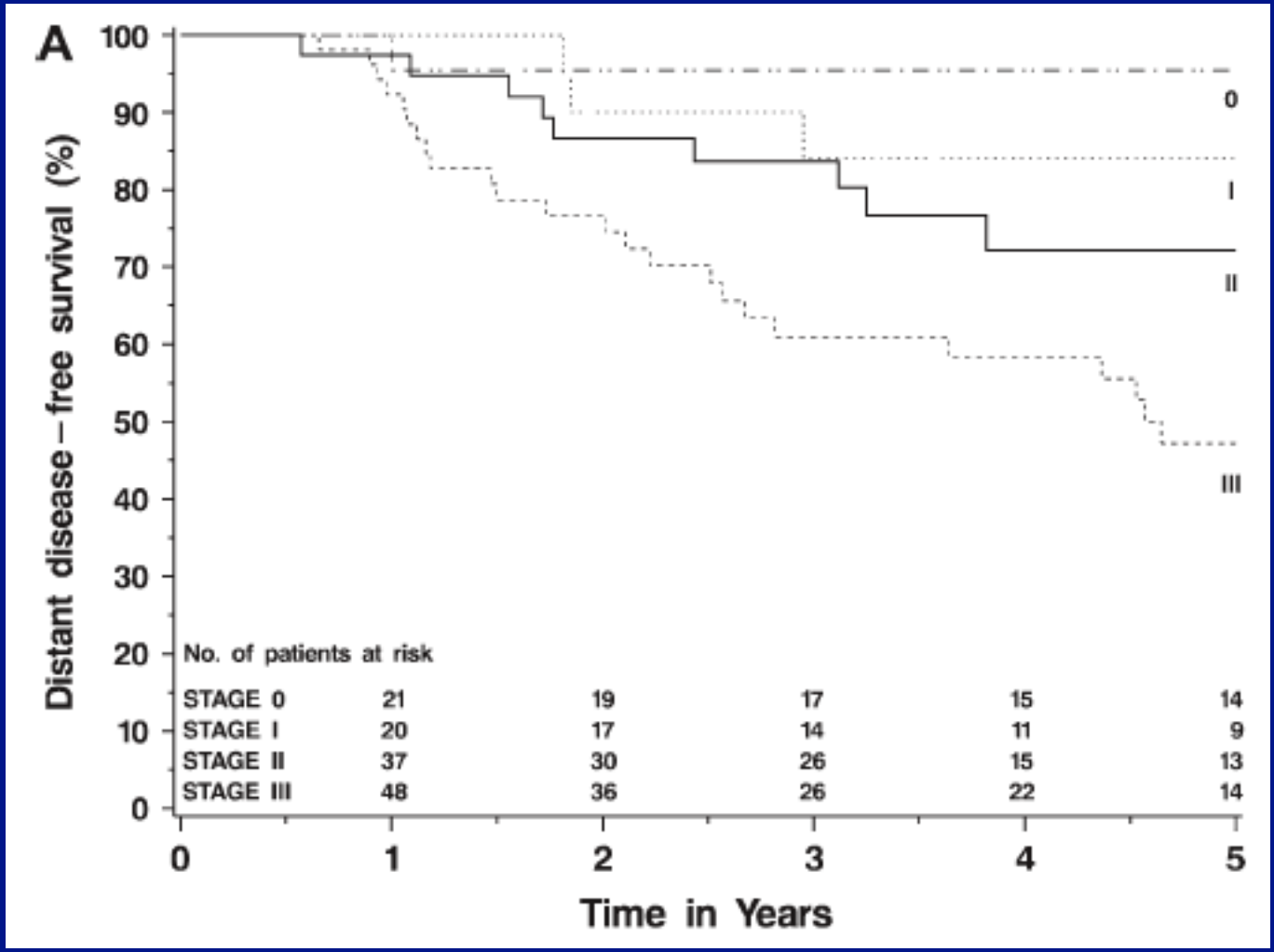
pCR is a good prognostic factor



Cortazar P et al *The Lancet. 2014;384:164-72*

Pathologic AJCC Stage After Preoperative Chemotherapy: UNC

N = 132

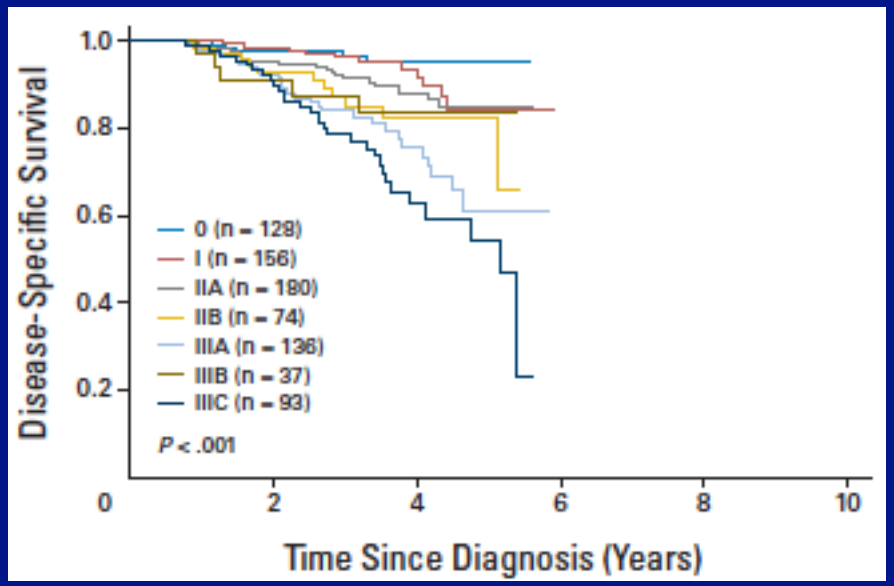


Based on 6th edition of AJCC Staging System (2003)

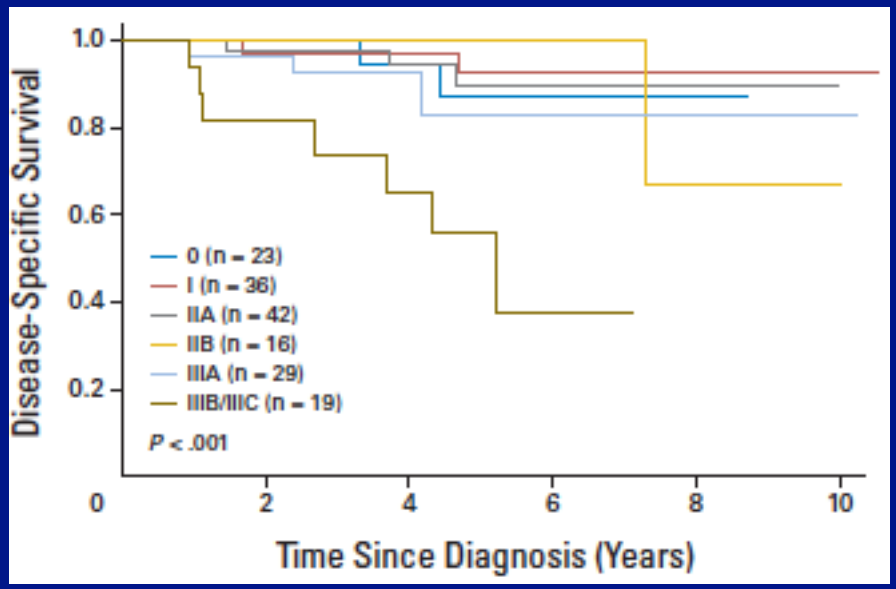
Carey et al JNCI 2005 97:1137-42

Pathologic Stage (yp) After Neoadjuvant Chemotherapy

Internal Validation Cohort (MDACC)

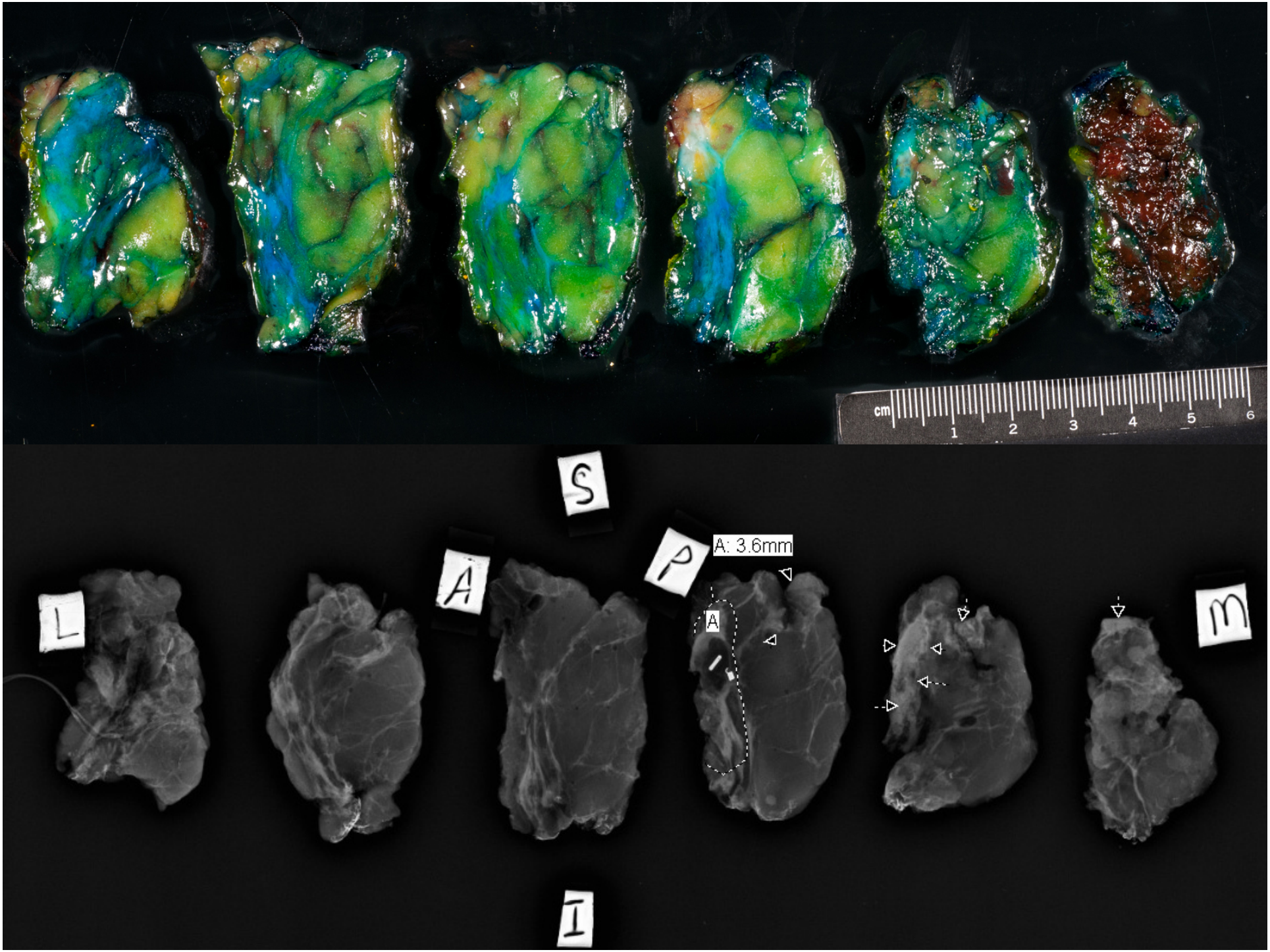


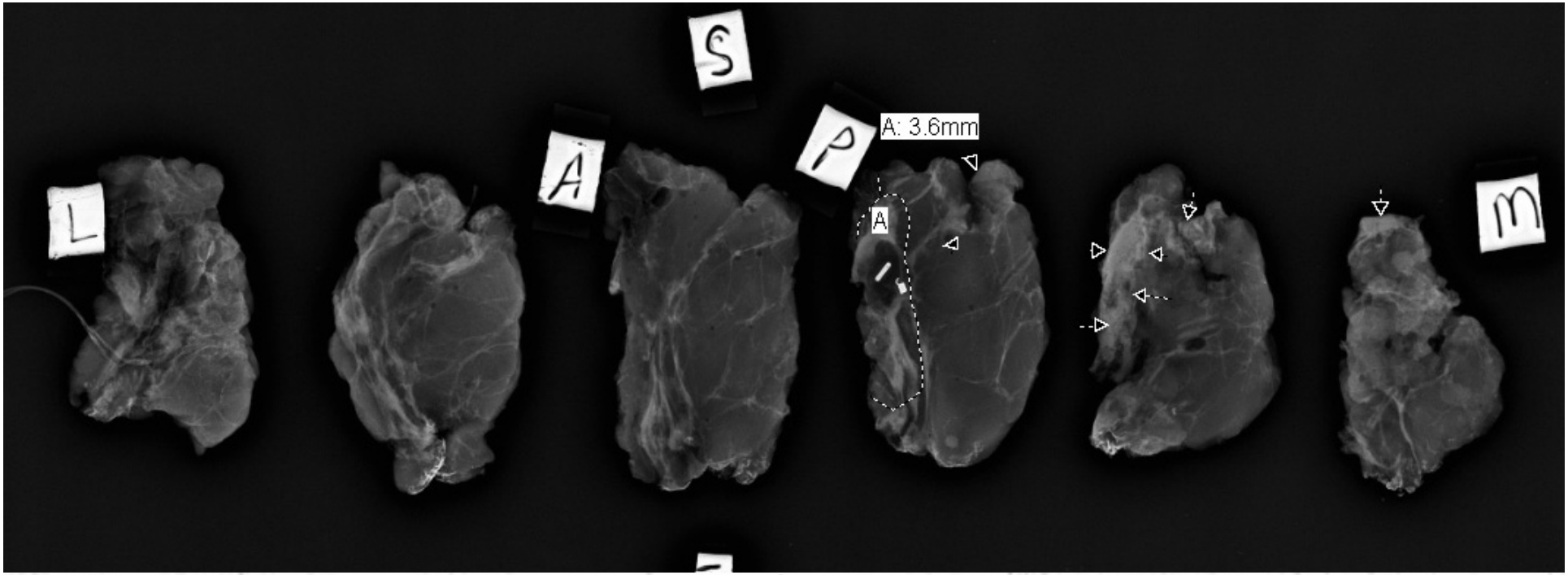
External Validation Cohort (U Mich)

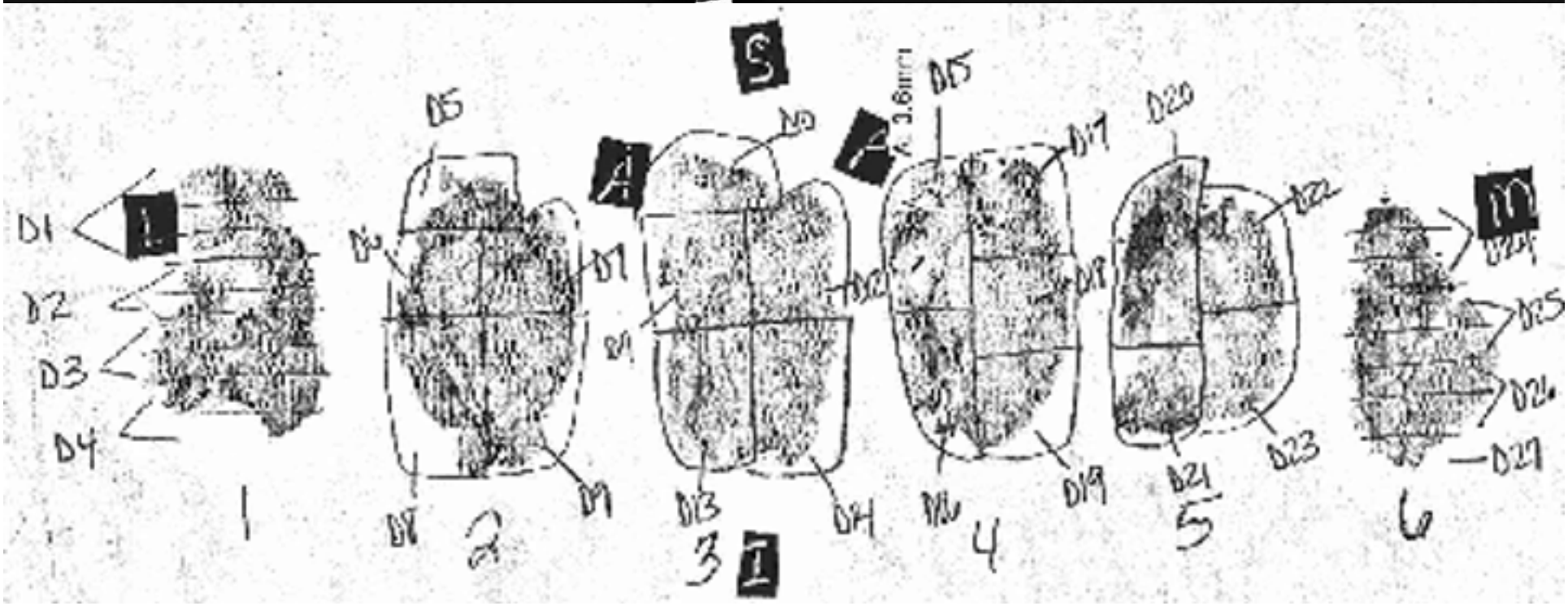


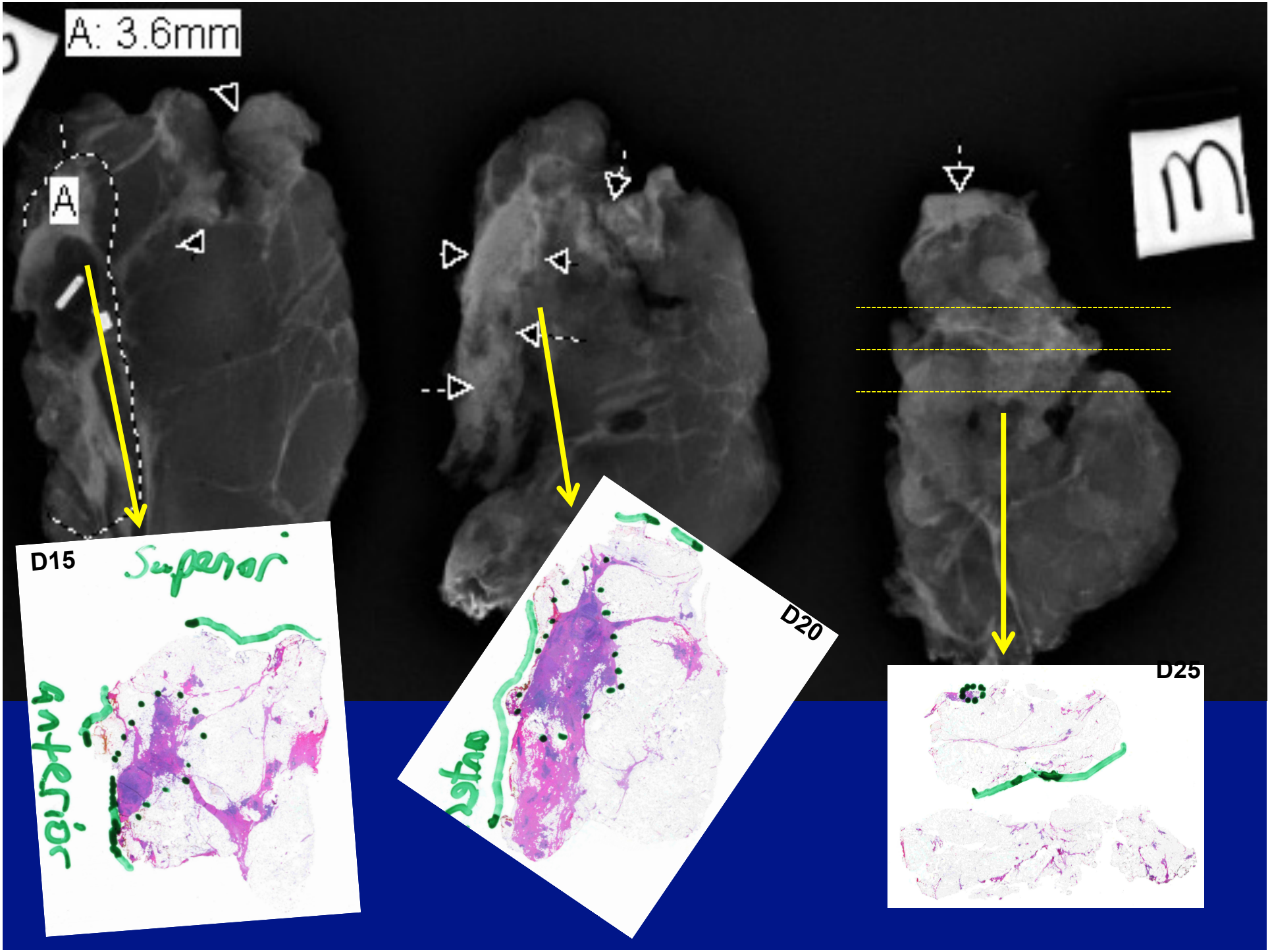
Based on 6th edition of AJCC Staging System (2003)

Mittendorf et al JCO 2011;29:1956-62


cm
1
2
3
4
5
6
S
L
A
P
A: 3.6mm
A
I
M


S
L
A
P
A: 3.6mm
A
M

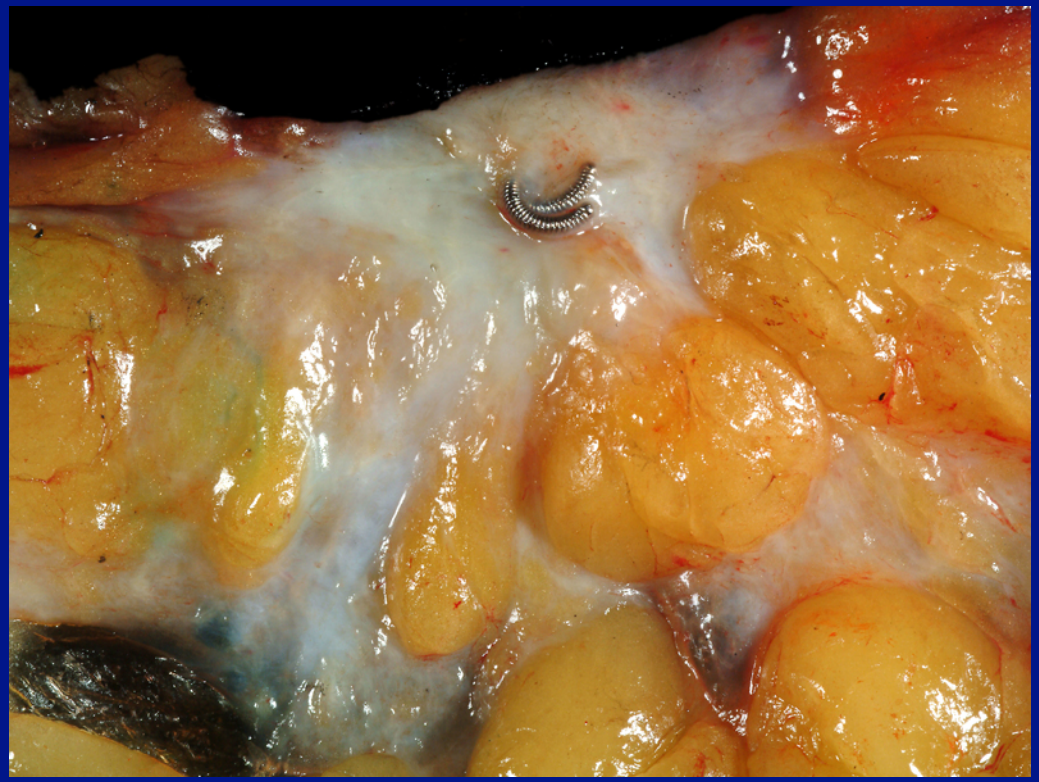

S
L
A
P
A: 3.6mm
M
D1
D2
D3
D4
D5
D7
D9
D11
D13
D15
D17
D19
D20
D21
D22
D23
D25
D27
1
2
3
4
5
6

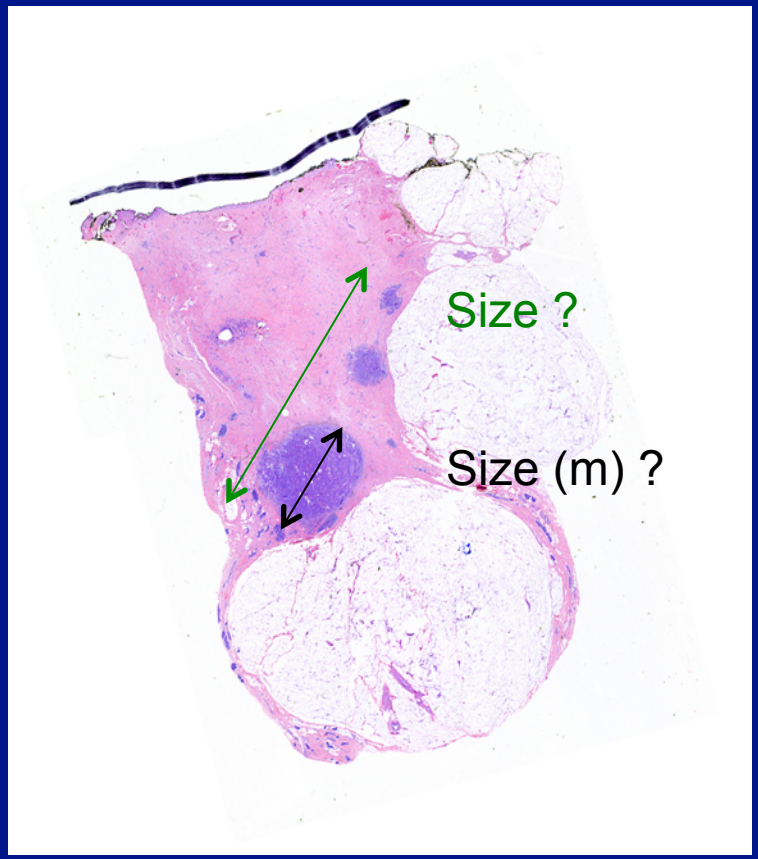

A: 3.6mm
A
B
D15
Superior
Anterior
D20
D25

AJCC Stage of Tumor and Neoadjuvant Treatment 7th edition, 2010

- Introduced the following specific recommendations:
- Postneoadjuvant therapy T Stage should be based on clinical or imaging (ycT) or pathologic findings (ypT)
- Estimate the size of tumors that are unapparent by clinical modalities or gross pathologic examination by carefully mapping the relative positions of the tissue sections and determining which contain tumor
- Pathologic (posttreatment) size should be estimated based on the best combination of gross and microscopic histological findings
- The posttreatment ypT will be defined as the largest continuous focus of invasive cancer as defined histopathologically with a subscript to indicate the presence of multiple tumor foci. Note: definition of posttreatment ypT remains controversial and an area in transition

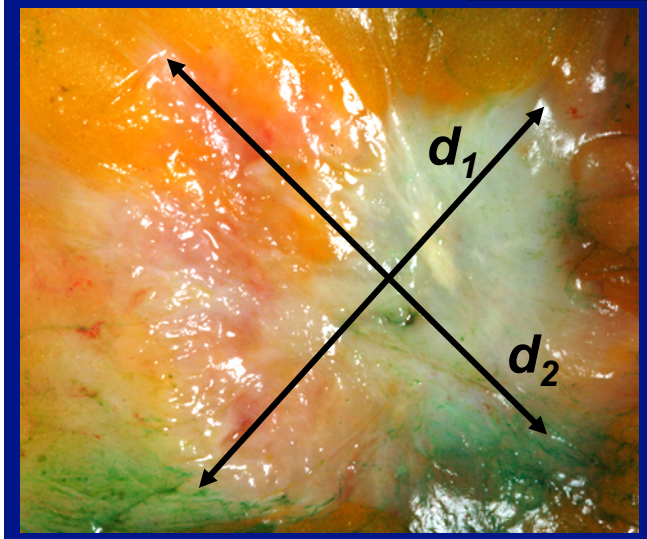
AJCC Staging Criteria, 7th Edition

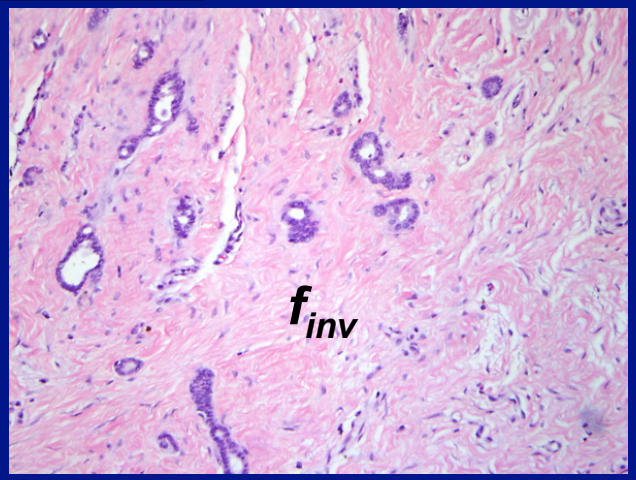




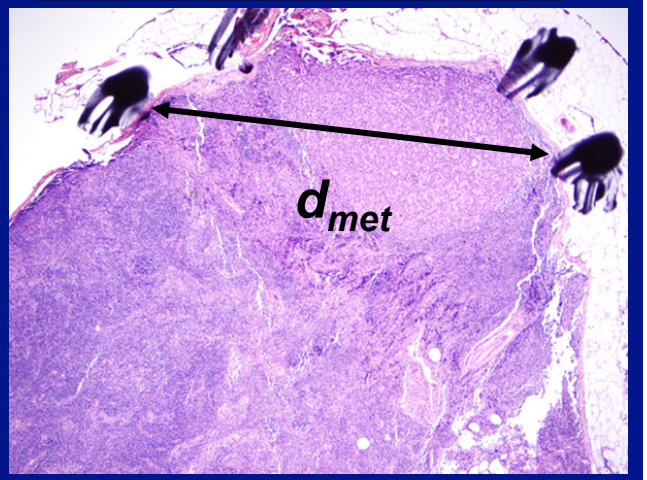
Residual Cancer Burden (RCB)

Primary Tumor Bed





Lymph Nodes



$d_{prim} = \sqrt{d_1 d_2}$

f_{inv} = % area with invasive CA

LN = Number of Positive Nodes

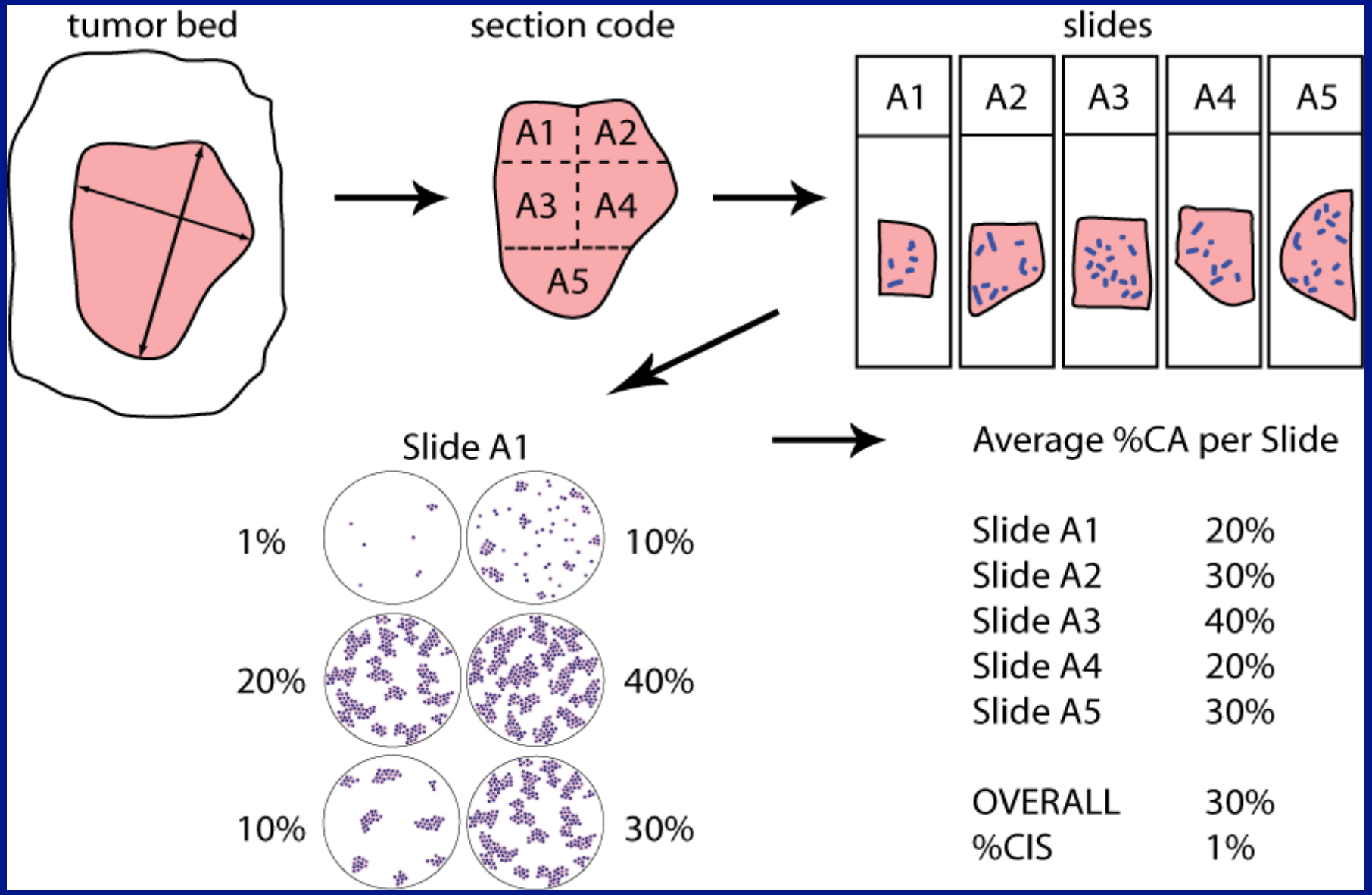
d_{met} = size largest metastasis

DRFS Following Neoadjuvant T/FAC Chemotherapy (N=241)

Variable	Hazard Ratio (95% CI)	P value
Primary tumor bed size (d_{prim})	1.24 (1.04-1.48)	0.02
Fraction of invasive cancer (f_{inv})	7.37 (2.16-25.1)	0.001
Number of positive lymph nodes (*LN*)	1.11 (1.04-1.19)	0.002
Size of largest metastasis (d_{met})	1.17 (0.99-1.38)	0.06

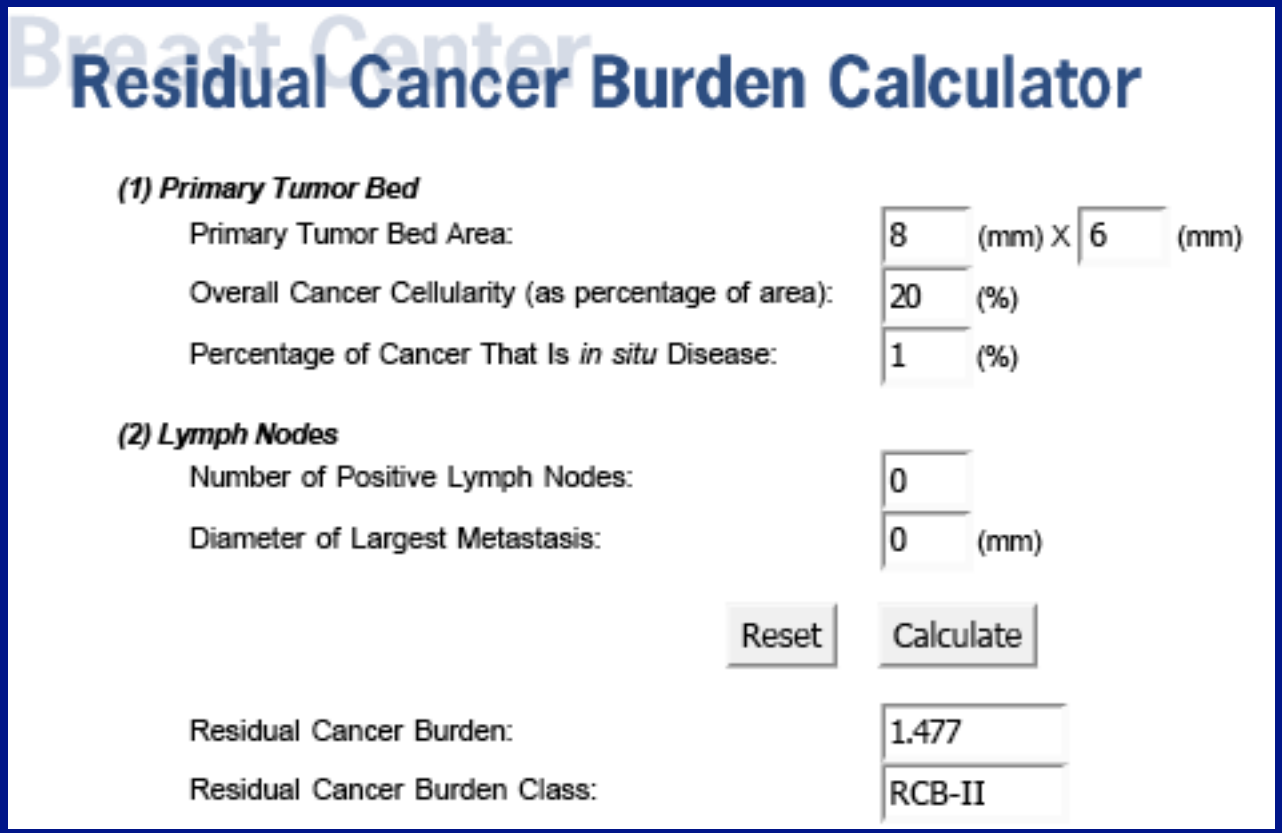
Symmans et al JCO 2007;25:4414-22

Pathologic Assessment Of The Primary Tumor Bed



See downloadable protocol and illustrations at www.mdanderson.org/breastcancer_RCB

www.mdanderson.org/breastcancer_RCB



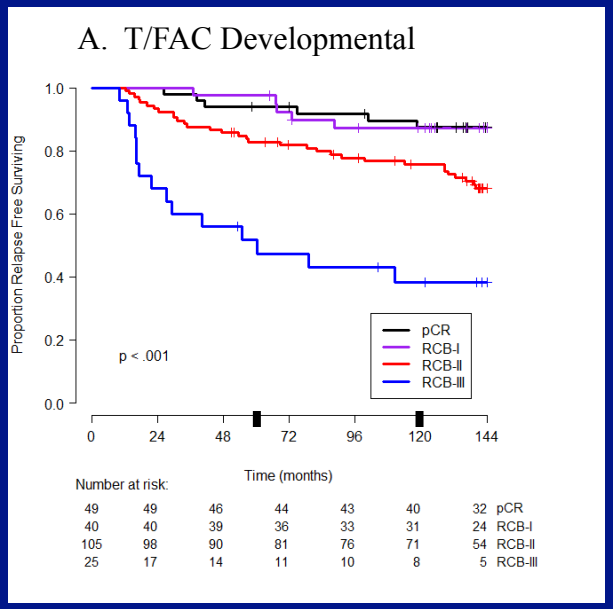
Symmans et al JCO 2007;25:4414-22

Prognostic Performance of RCB (continuous score)

Cohorts	Median F-up (years)	Relapse-Free Survival		Overall Survival	
		Hazard Ratio (95% CI)	C-Index (95% CI)	Hazard Ratio (95% CI)	C-Index (95% CI)
Validation FAC	16.4	2.01 (1.54, 2.63)	0.74 (0.68, 0.81)	1.91 (1.45, 2.52)	0.74 (0.67, 0.82)
Development T/FAC	12.7	2.20 (1.74, 2.79)	0.73 (0.67, 0.80)	2.08 (1.61, 2.70)	0.72 (0.64, 0.80)
Validation T/FAC	8.3	1.87 (1.56, 2.25)	0.73 (0.67, 0.78)	1.94 (1.59, 2.38)	0.75 (0.68, 0.81)
Combined T/FAC	10.1	2.00 (1.72, 2.31)	-	2.01 (1.72, 2.35)	-

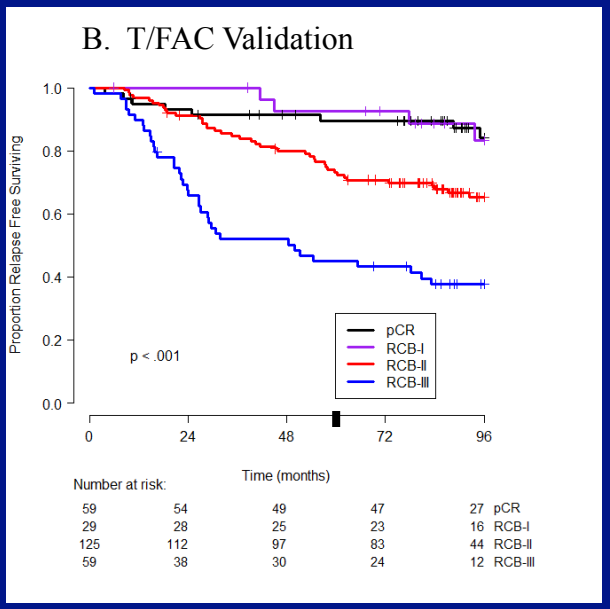
Prognosis According To RCB Categories (RFS)

Developmental Cohort T/FAC



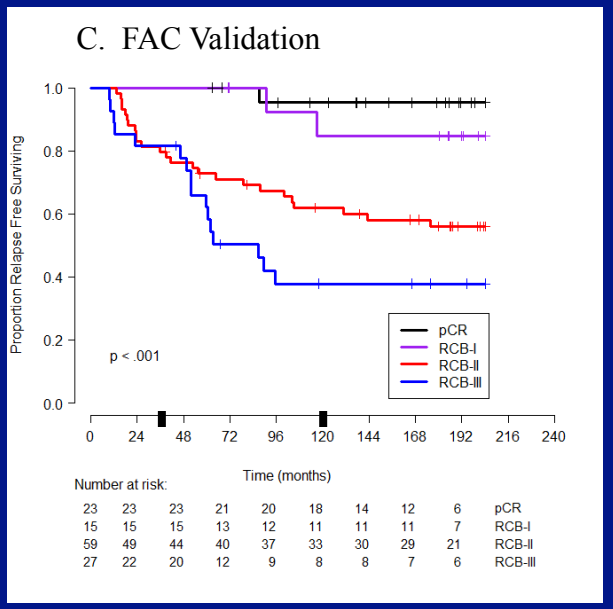
	Class	N	%
	pCR	49	22
	RCB-I	40	18
	RCB-II	105	48
	RCB-III	25	11

Validation Cohort T/FAC



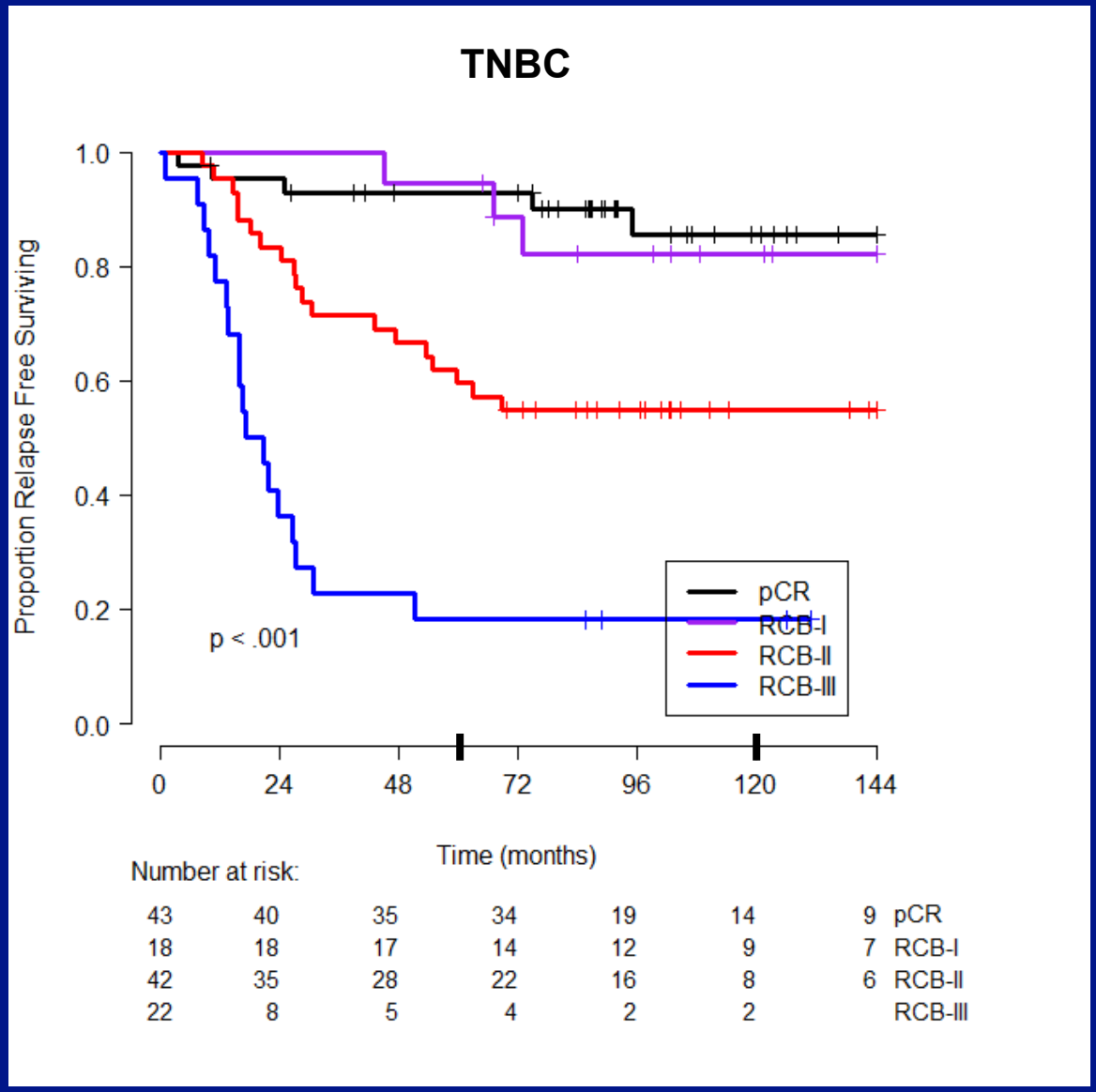
	Class	N	%
	pCR	59	22
	RCB-I	29	11
	RCB-II	125	46
	RCB-III	59	22

Validation Cohort FAC



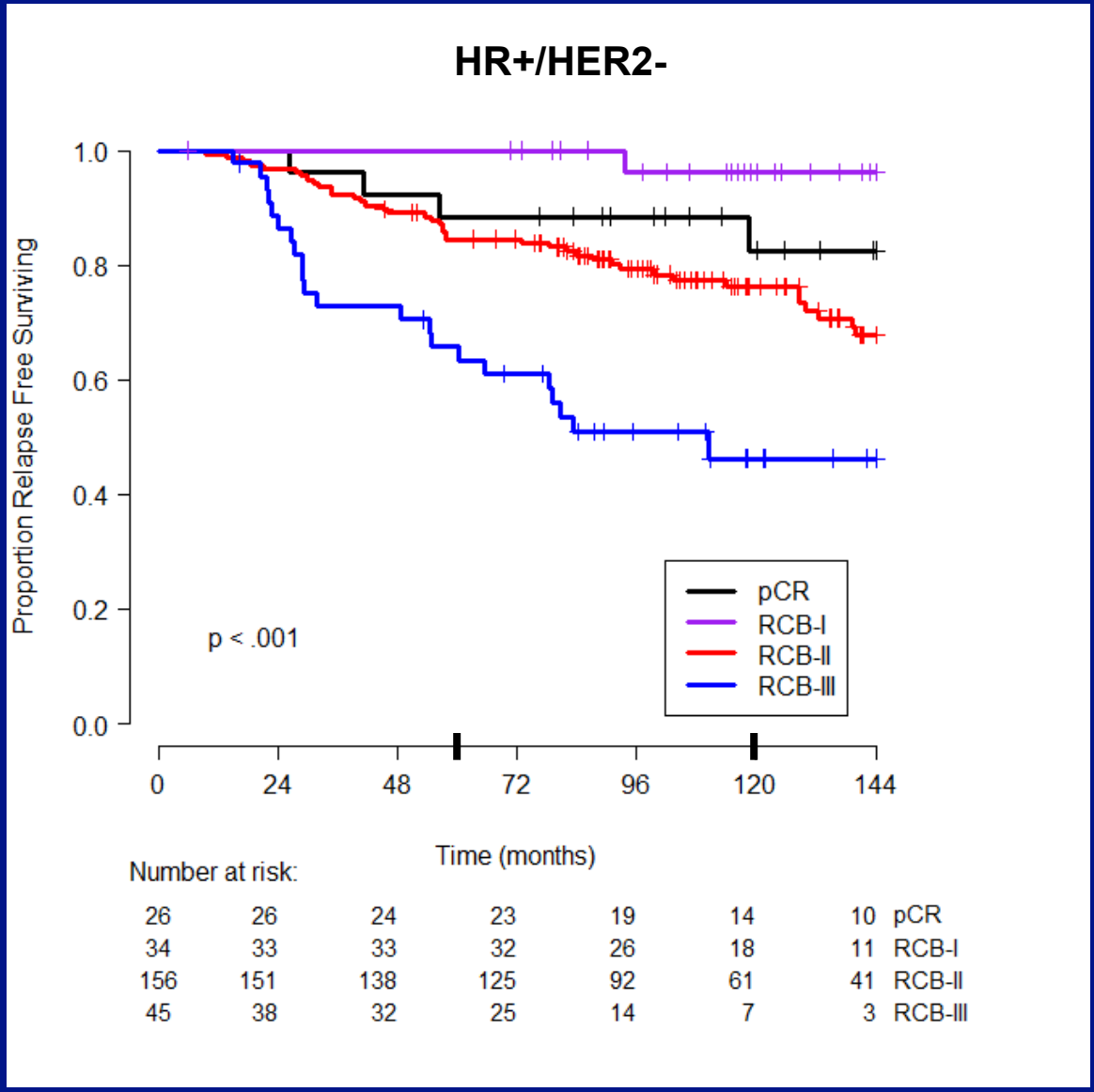
	Class	N	%
	pCR	23	18
	RCB-I	16	12
	RCB-II	60	46
	RCB-III	32	24

RCB Categories: Combined T/FAC Cohorts (RFS)



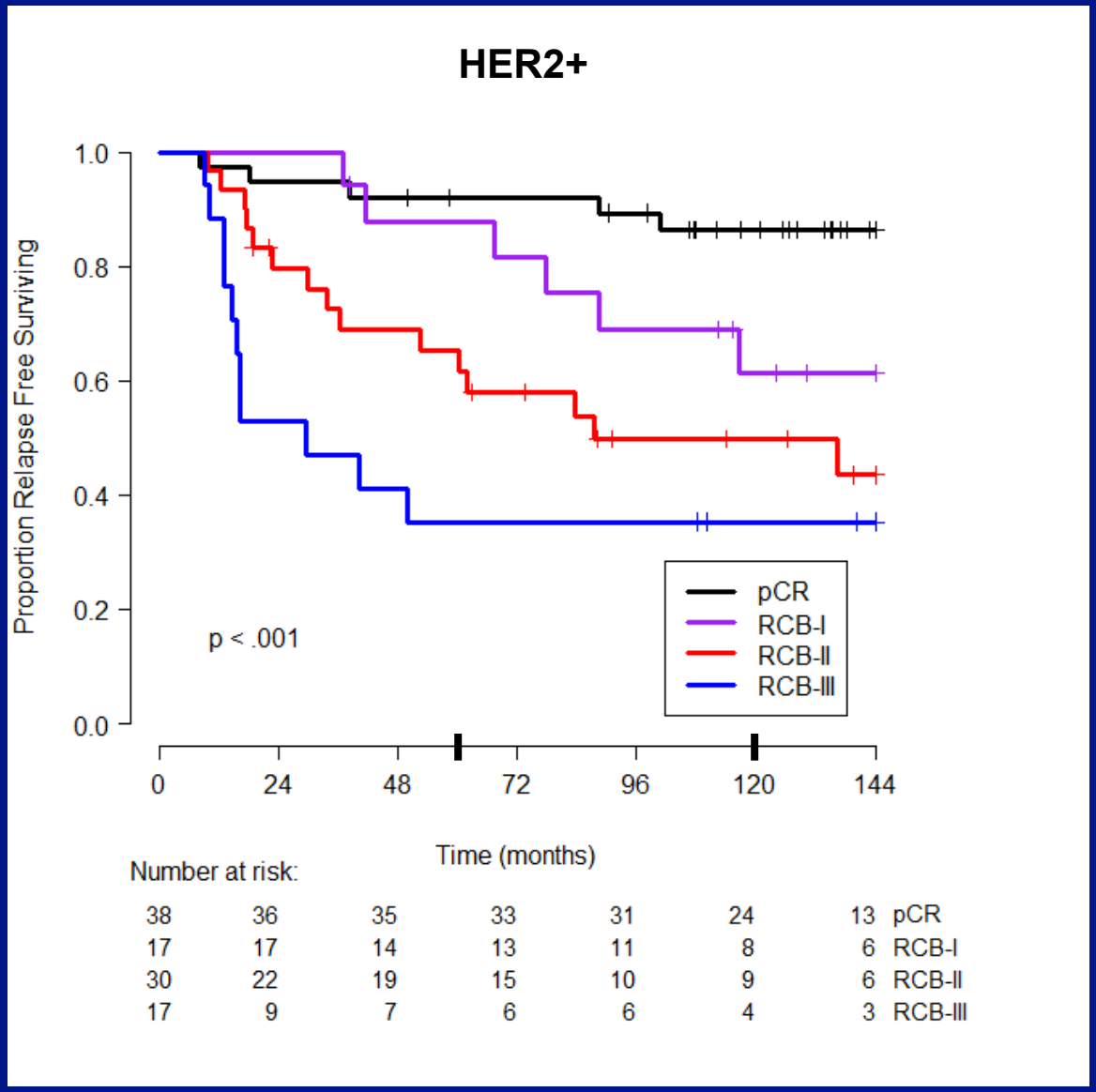
Class	N	%
pCR	43	34
RCB-I	18	14
RCB-II	42	34
RCB-III	22	18

RCB Categories: Combined T/FAC Cohorts (RFS)



Class	N	%
pCR	26	10
RCB-I	34	13
RCB-II	156	60
RCB-III	45	17

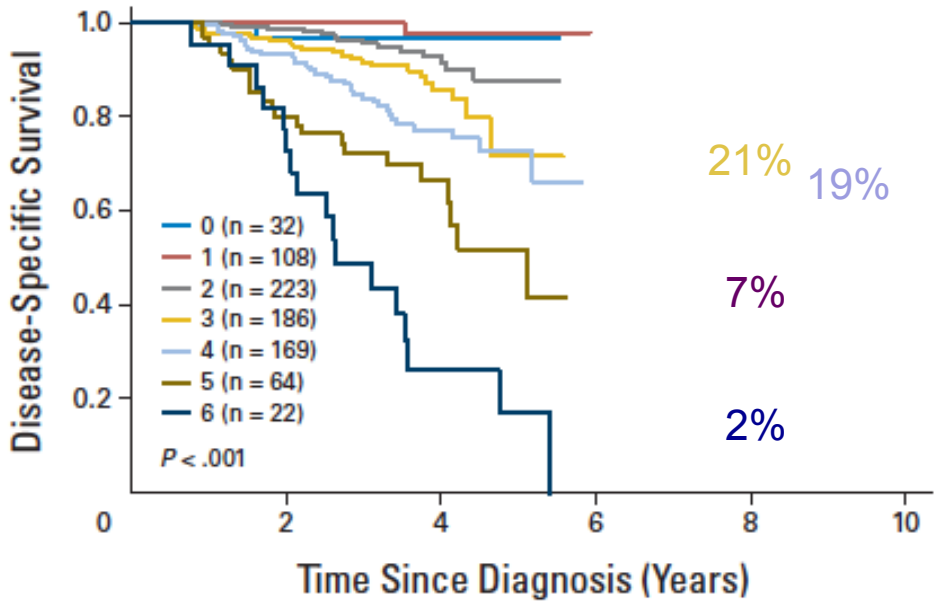
RCB Categories: Combined T/FAC Cohorts (RFS)

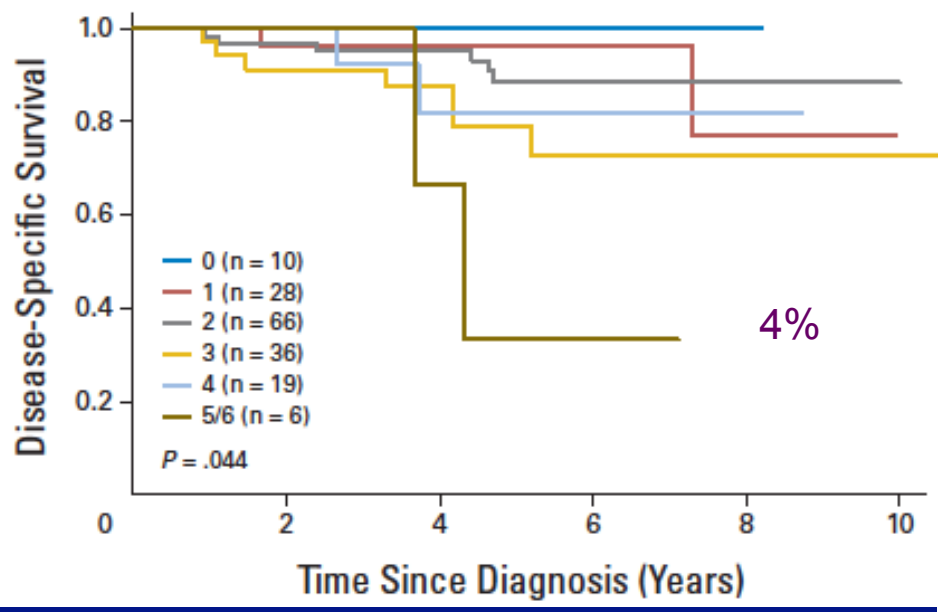


Class	N	%
pCR	38	37
RCB-I	17	17
RCB-II	30	29
RCB-III	17	17

Clinical Stage + ER Status + Grade + Pathologic Stage (CPS-EG)

Pre-Rx Stage (c)		Pre-Rx Pathobiology				Post-Rx Stage (yp)	
c Stage	=	ER Status	=	N Grade	=	yp Stage	=
I - IIA	0	Positive	0	1 - 2	0	0 - I	0
IIB - IIIA	1	Negative	1	3	1	IIA - IIIB	1
IIIB - IIIC	2					IIIC	2

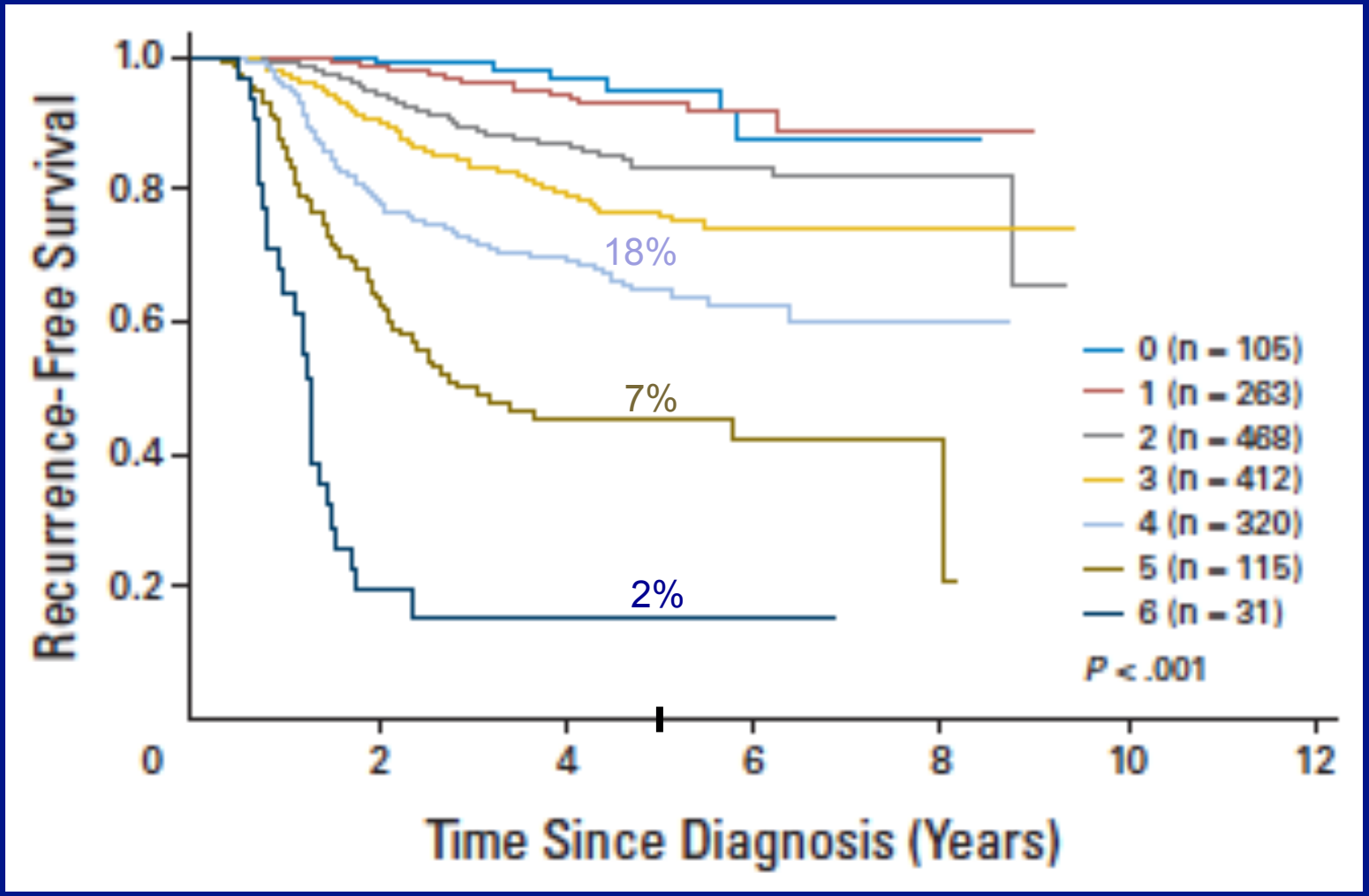




Based on 6th edition of AJCC Staging System (2003)

Mittendorf et al JCO 2011;29:1956-62

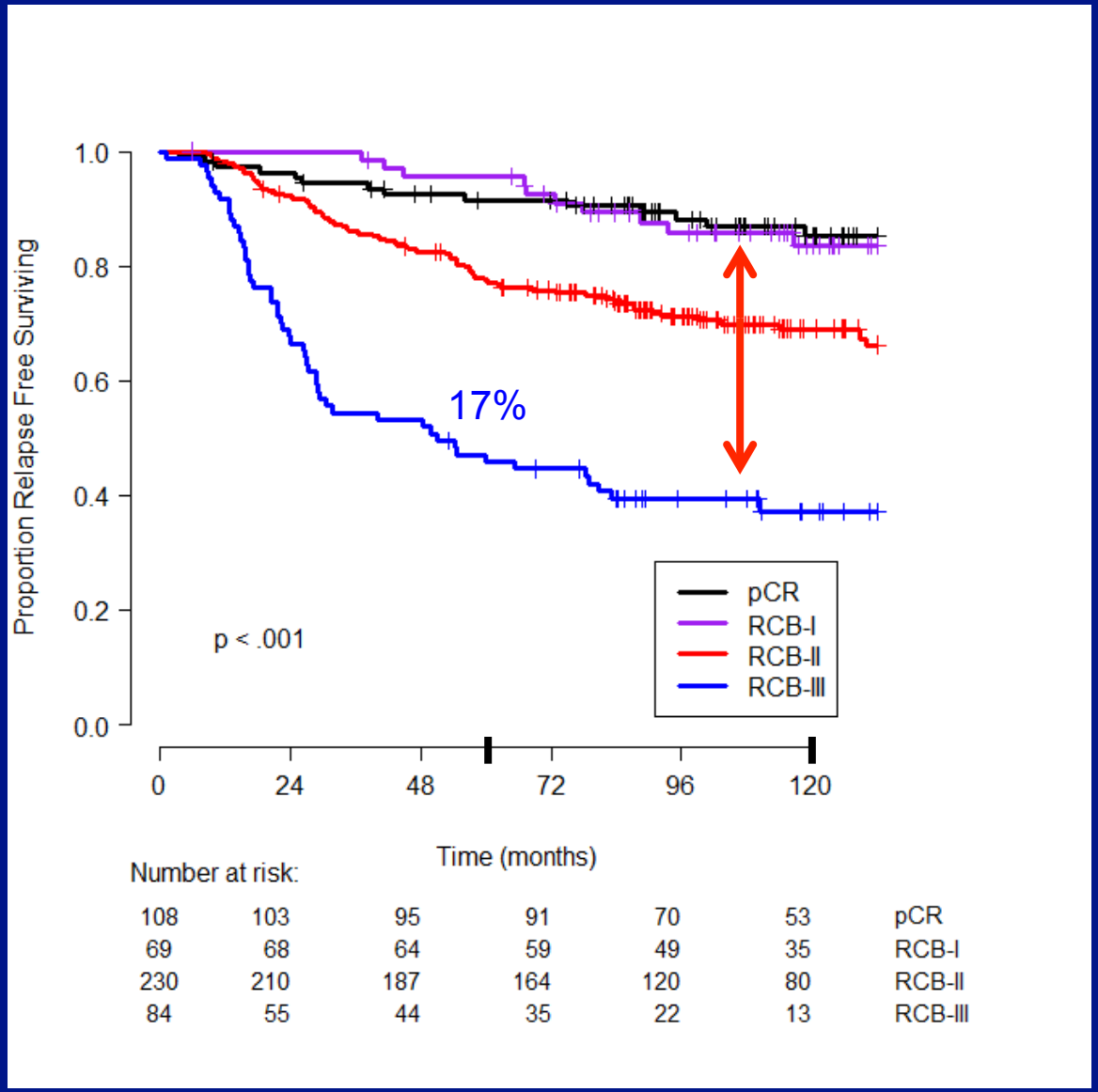
Prognosis (DFS) of CPS-EG Groups In MDACC T/FAC Cohorts: Development (n=932) and Validation (n=969)



Based on 6th edition of AJCC Staging System (2003)

Mittendorf et al JCO 2011;29:1956-62

Prognosis (RFS) of RCB Categories MDACC T/FAC Cohorts



Class	N	%
pCR	108	22
RCB-I	69	14
RCB-II	230	47
RCB-III	84	17

Recommendations

- Record pretreatment cStage from clinical records
- Record pretreatment phenotype and grade
- pCR
  - pCR in breast and nodes
  - Report presence and extent of in situ residual disease
- Require standardized procedures to evaluate the gross specimen, record a map of the tissue sections related to the gross & imaging findings, and relate the histopathologic findings to that map
  - Multidisciplinary teamwork from surgeons, radiologists, and pathologists
- Then it becomes very easy to interpret and report
  - ypT Stage defined by largest continuous extent of invasive cancer
  - RCB from the dimensions and cellularity of primary tumor bed
  - Multifocality