

***Impact of Pathology Practice on
Outcome in Published Studies of DCIS.
Recommendations for a Uniform
Pathology Protocol***

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Prognostic Factors for Local Recurrence

- ***Grade***
- ***Size (extent)***
- ***Margin width***
- ***Age <40***

Problems in Establishing Prognostic Features in DCIS

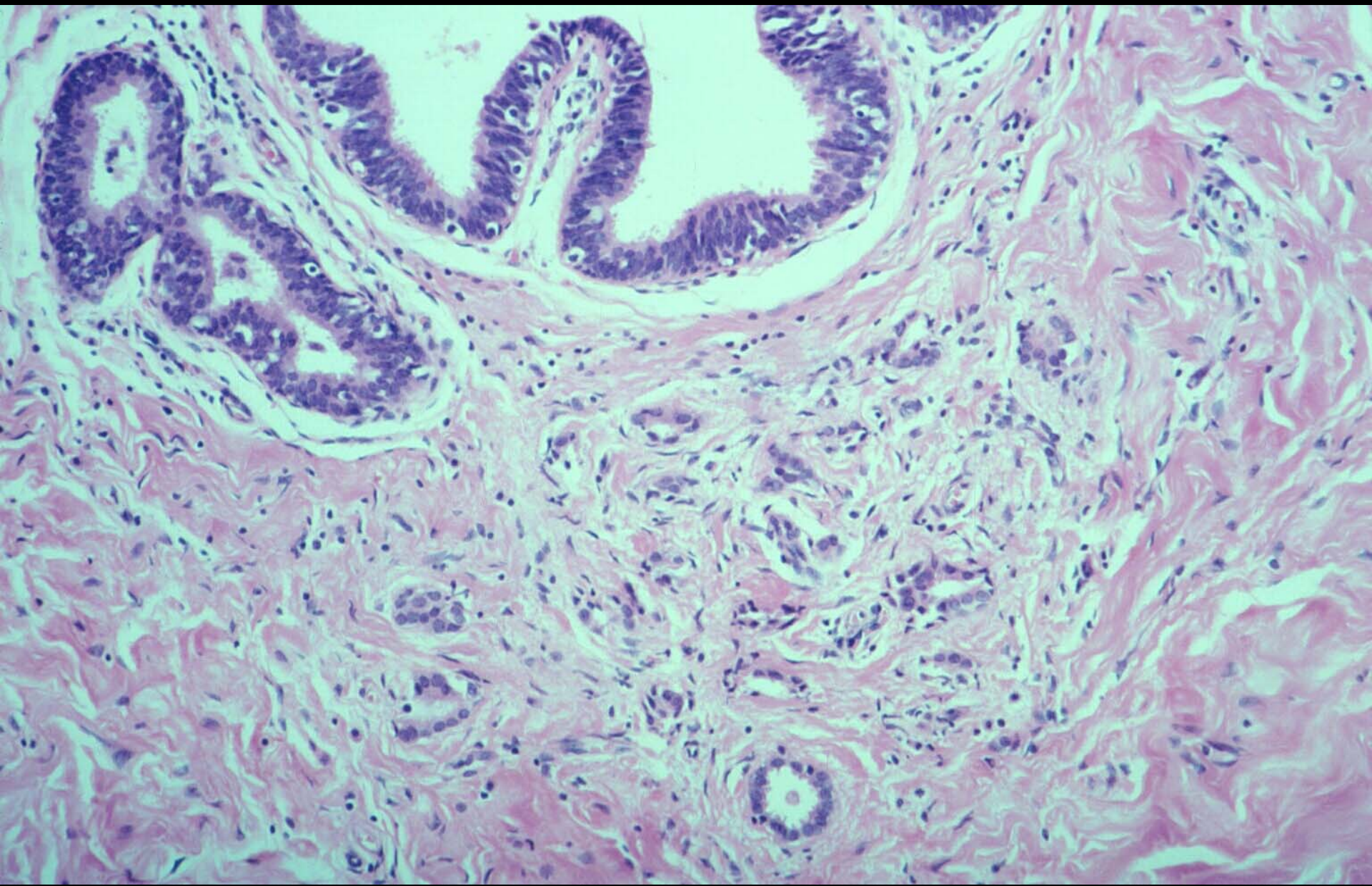
- *Invasion must be excluded*
- *Total extent (size) must be calculated*
- *All margins must be examined and margin widths measured*

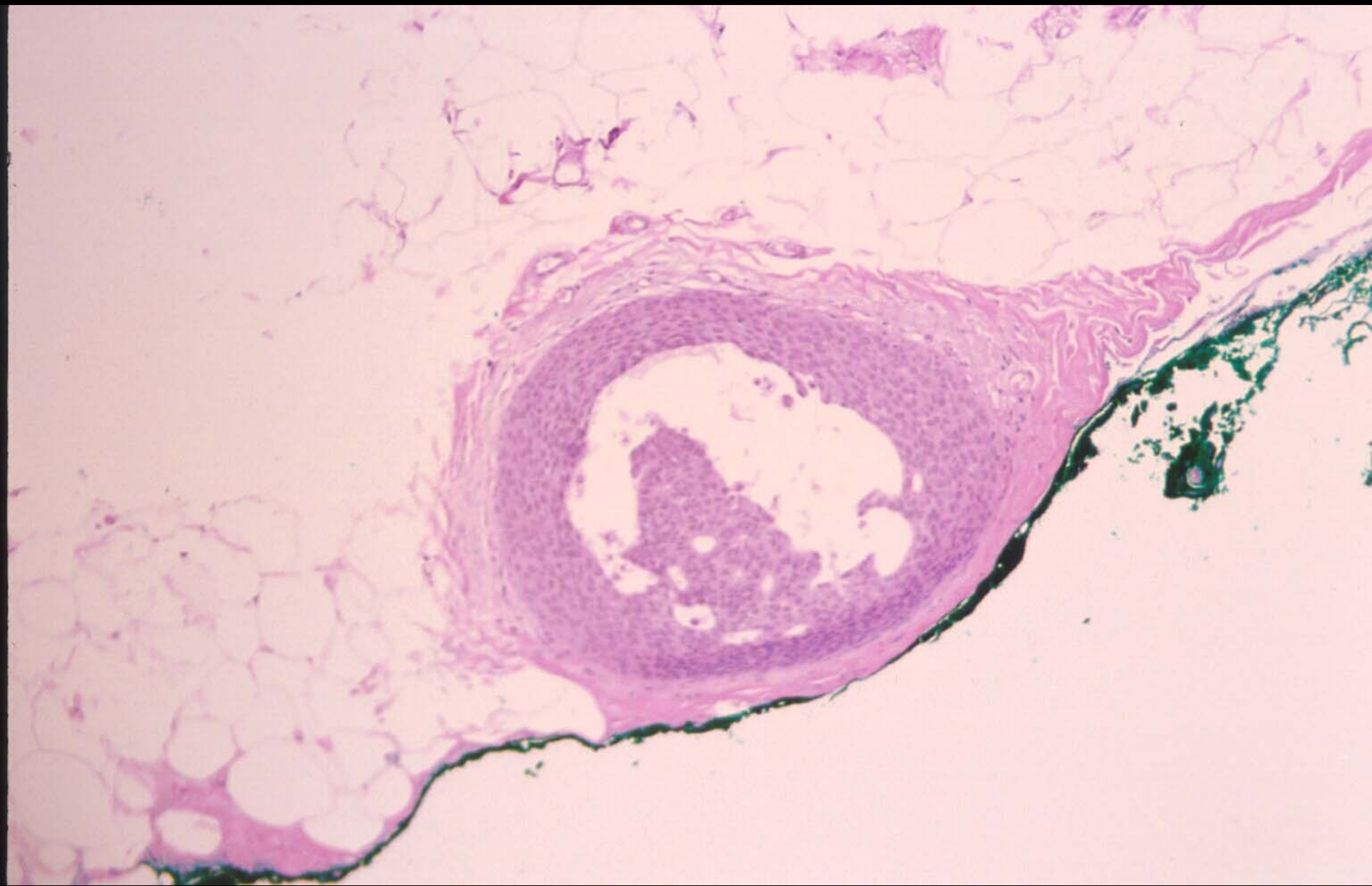
Tissue Sampling of DCIS

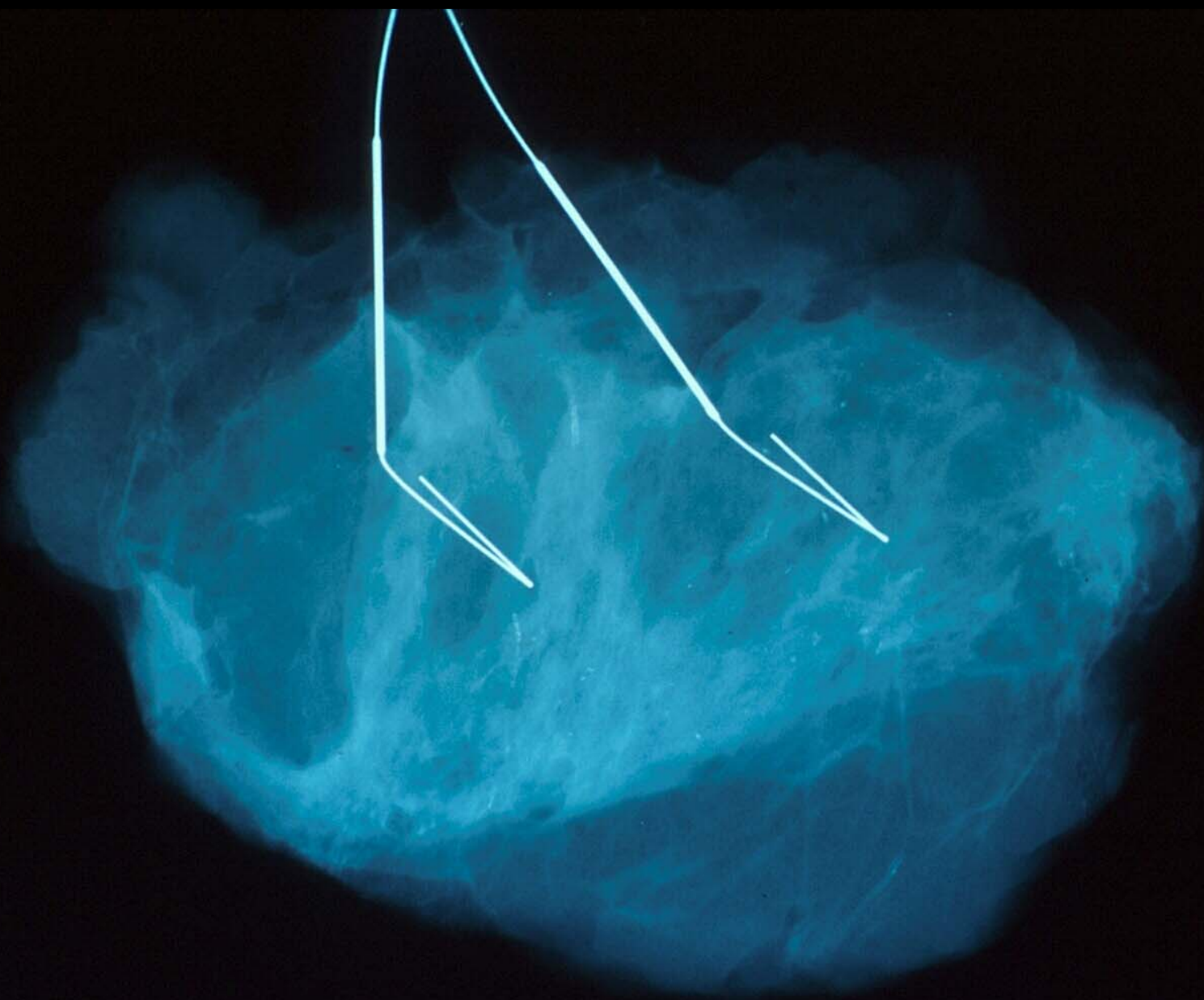
- *Cannot exclude invasion*
- *Extent (size) cannot be calculated*
- *Margins will only be sampled*

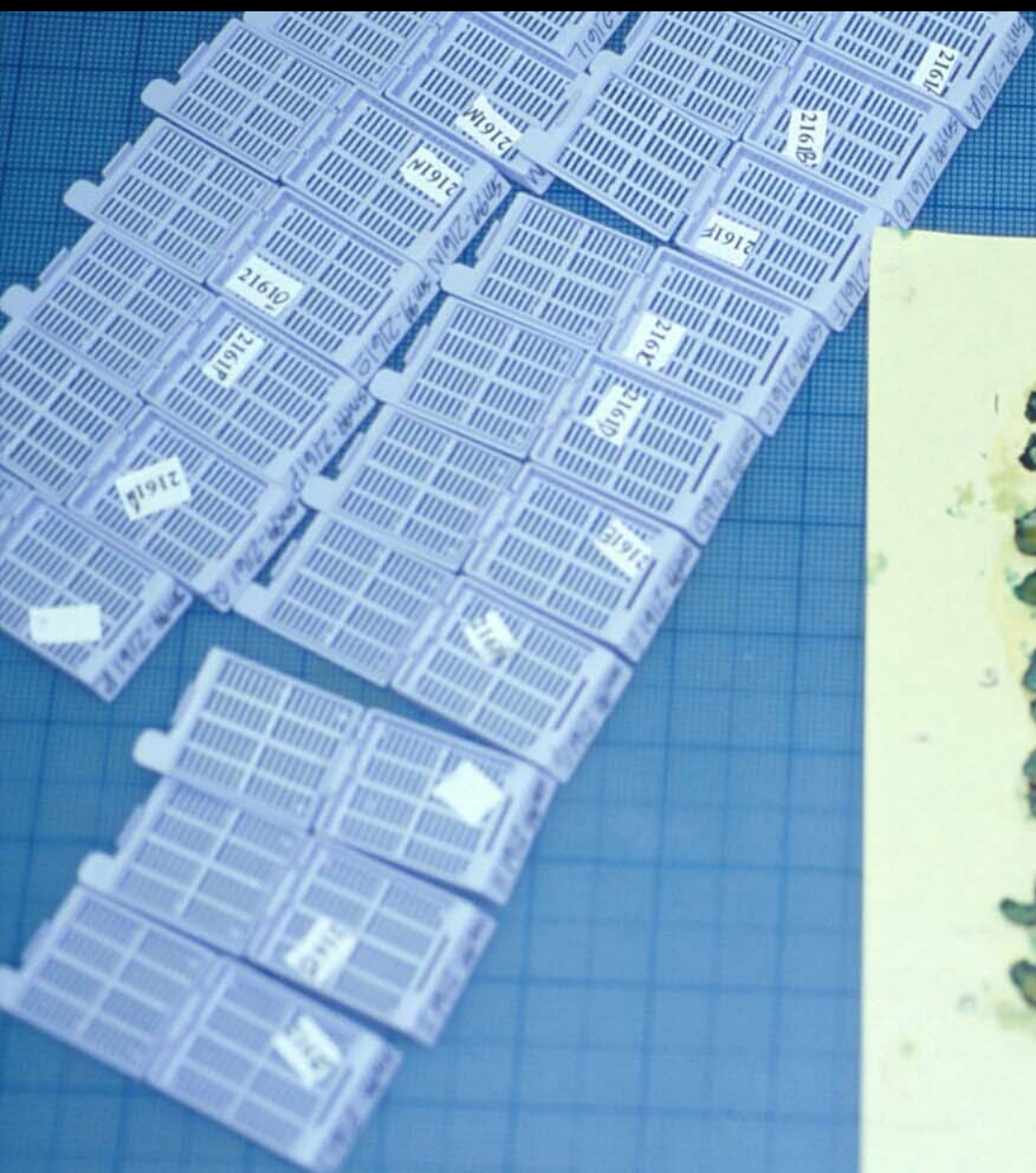


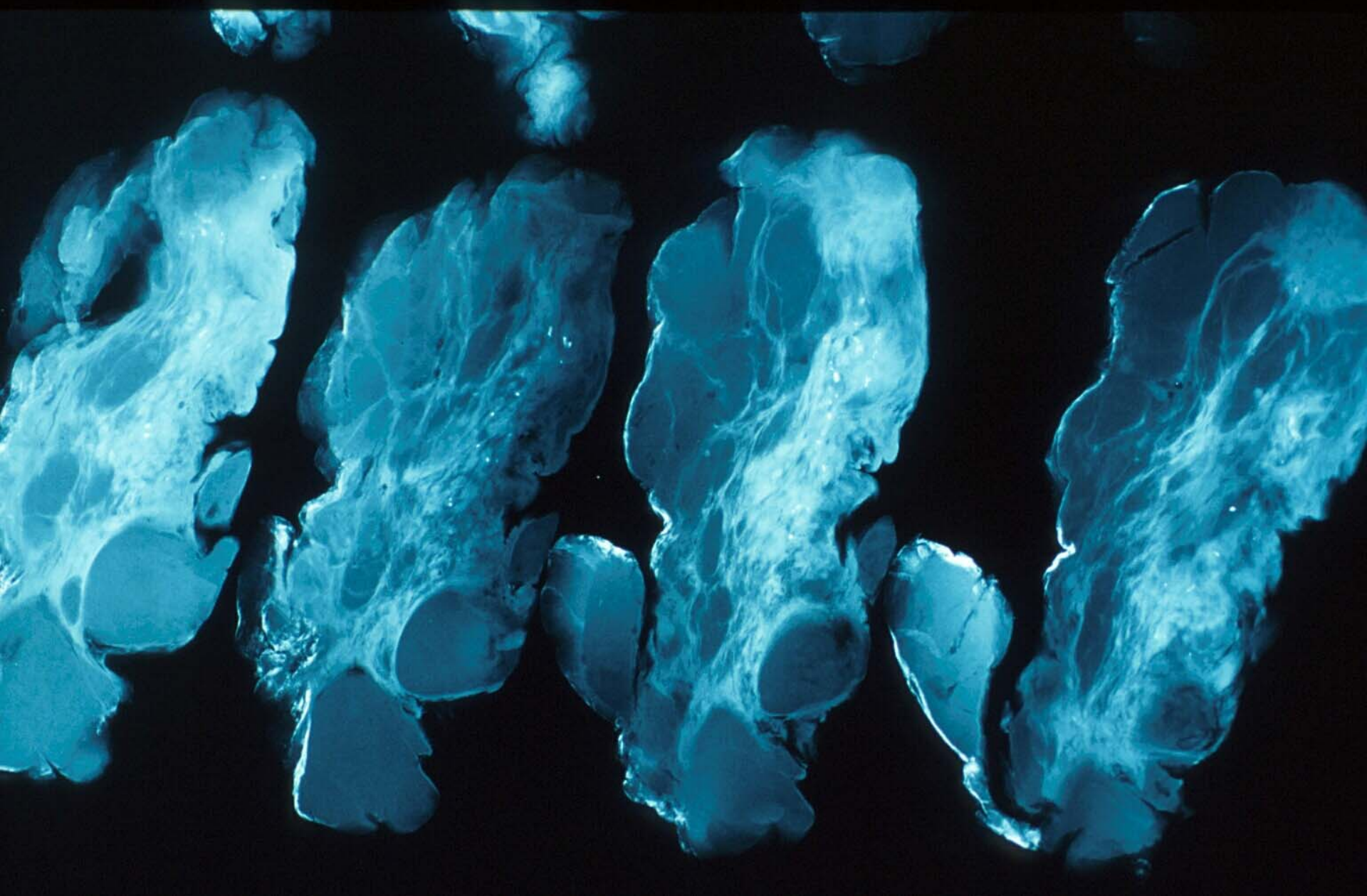












***Problems in Pathologic
Examination in Published Trials
on DCIS:***

***NSABP B17, EORTC 10853,
Wong et al, 2006***

DCIS Comparative Study Designs

B-17

USC/Van Nuys

<u>Grade/Classification</u>	Retrospective	Prospective
<u>Size/Extent</u>	Retrospective <u>No microscopic</u>	Prospective <u>Microscopic</u>
<u>Margins</u>	Non-transection Inking optional	Measured Specific Inks
<u>Mammographic Correlation</u>	Retrospective Specimen xray optional	Prospective Specimen xray required
<u>Tissue Processing</u>	Sampling	Complete/sequential
<u>Central Review</u>	Retrospective 75% cases available	Prospective 100% cases <u>all slides</u>

Limitations of Bijker et al, 2006

Pathology Review in 863 cases (85%):

-Invasive or suspicious 4.6%

-Benign 5.5%

***Tissue sampling – not sequentially
processed***

Size: from reports – cited in 193 (22%)

Margins: transected/non-transected

Limitations of Wong JS et al, 2006

Pathology

- ***Tissue sampling – not sequentially processed***
- ***Grade: Predominant – not highest grade used***
- ***Size: 96% estimated from number of blocks***
– no measured size
- ***Margins: only sampled***

Clinical Evaluation

- ***23% of "recurrences" were de novo events in other quadrants – 76% were true***

DCIS – Breast Conservation Metastatic First Events (regional and distant)

	<u><i>Mean FU, yrs</i></u>	<u><i>N/Total - %</i></u>
<i>Lagios et al, 1989</i>	<i>15</i>	<i>0/79 – 0</i>
<i>Silverstein, 2007</i>	<i>12</i>	<i>0/1289 – 0</i>
<i>Solin et al, 1996</i>	<i>15</i>	<i>1/270 – 0.37</i>
<i>Fisher et al, 2001</i>	<i>12</i>	<i>17/813 -2.09</i>
<i>Bijker et al, 2006</i>	<i>10.5</i>	<i>7/1010 – 0.69</i>

Comparative DCIS Trials Metastatic Events (MET) and Cause-Specific Mortality (CSM)

	<u>NSABP-B17</u>		<u>EORTC 10853</u>	
	12 years		10.5 years	
	<i>L</i>	<i>RTX</i>	<i>L</i>	<i>RTX</i>
	403	410	503	507
<i>Met-N</i>	-	-	20	23
<i>CSM-N</i>	12	15	15	17
<i>Total</i>				
<i>CSM-N(%)</i>	27 (3.3)		32 (3.1)	

Impact of Pathologic Methodology

- ***Definition and identification of pathologic prognostic factors is highly dependent on methodology***
- ***Van Nuys database is based on resections which are entirely and sequentially embedded with rigorous mammographic-pathologic correlation***

- ***Randomized trials did not demand such methodology. As a result NSABP – B17 did not find that NG, size or margins were statistically significant prognostic indicators. EORTC 10853 was able to define NG but not other features as statistically significant.***

Conclusion: Prognostic value of specific features can only be assessed within a pathologic protocol which permits complete analysis: Total sequential, correlated tissue processing

Minimal Pathologic Requirements for Evaluation of DCIS

***Resection Must be Completely
and Sequentially Examined
Microscopically***

Recommendations for Future DCIS Intervention Trials

- ***Correlation of preoperative imaging, specimen radiography and post-excision studies***
- ***Complete sequential tissue processing of oriented specimen***
- ***Calculation of size, measurement of margin widths, exclusion of microinvasive foci, classification by grade (NG and necrosis)***

Penny-wise Pound-foolish Cost Benefit Analysis/100 patients RTX-Tamoxifen vs. Complete Tissue Processing

- ***Assume 32.5% of DCIS patients, those with VNPI 4-6 are spared RTX-TAM***
- ***32.5% of RTX/TAM cost/100***
 - =\$524,062***
 - \$24,000 (costs CPT/100)***
- ***Potential cost savings/100 = \$500,000***
- ***Cost savings are 20X the costs of CTP for all 100 patients***