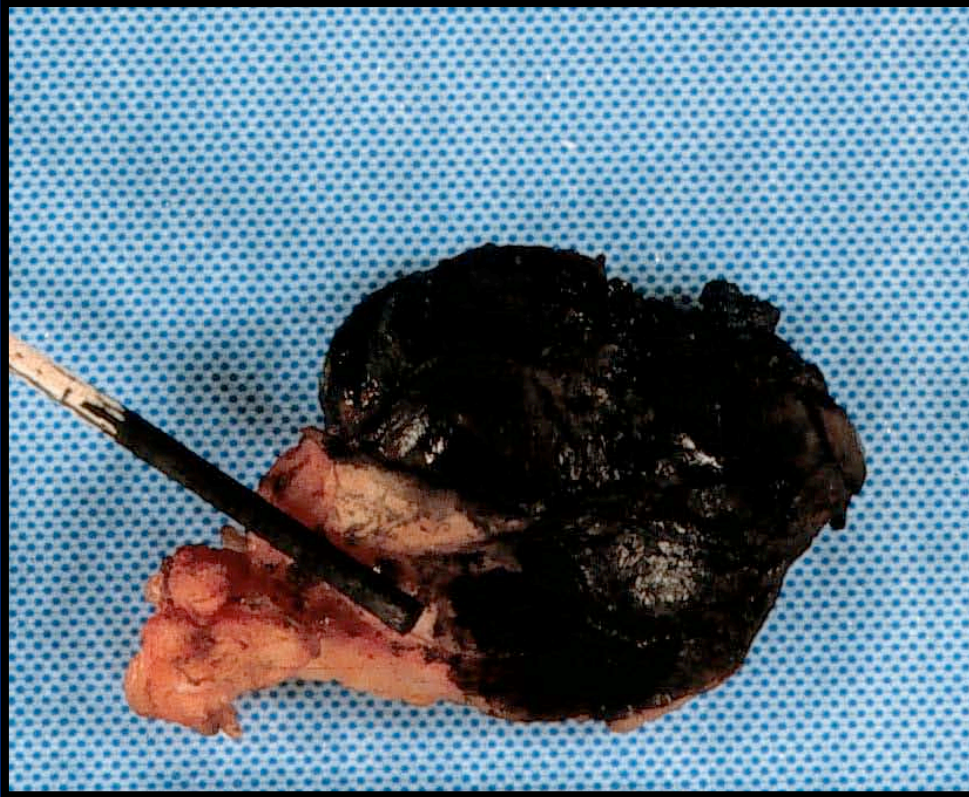


Margin Evaluation in Patients Undergoing Breast Conserving Therapy

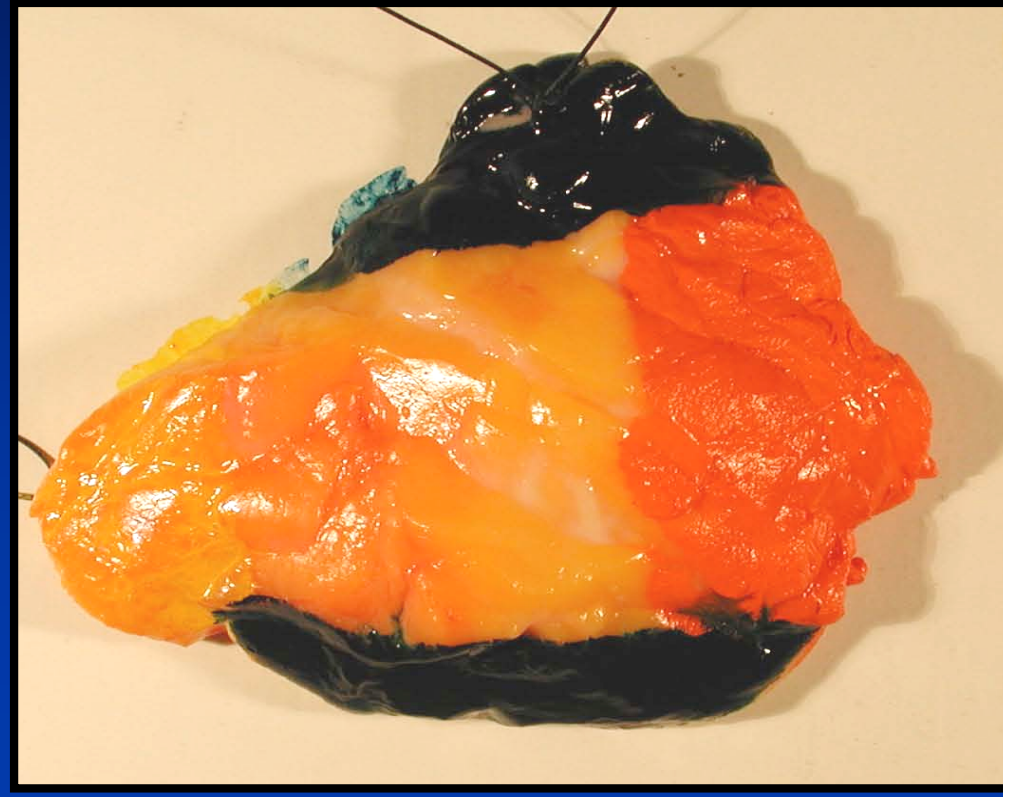
**Laura C. Collins, M.D.
Beth Israel Deaconess Medical Center
and Harvard Medical School
Boston, MA, USA**

Margin Evaluation

Unoriented Specimen

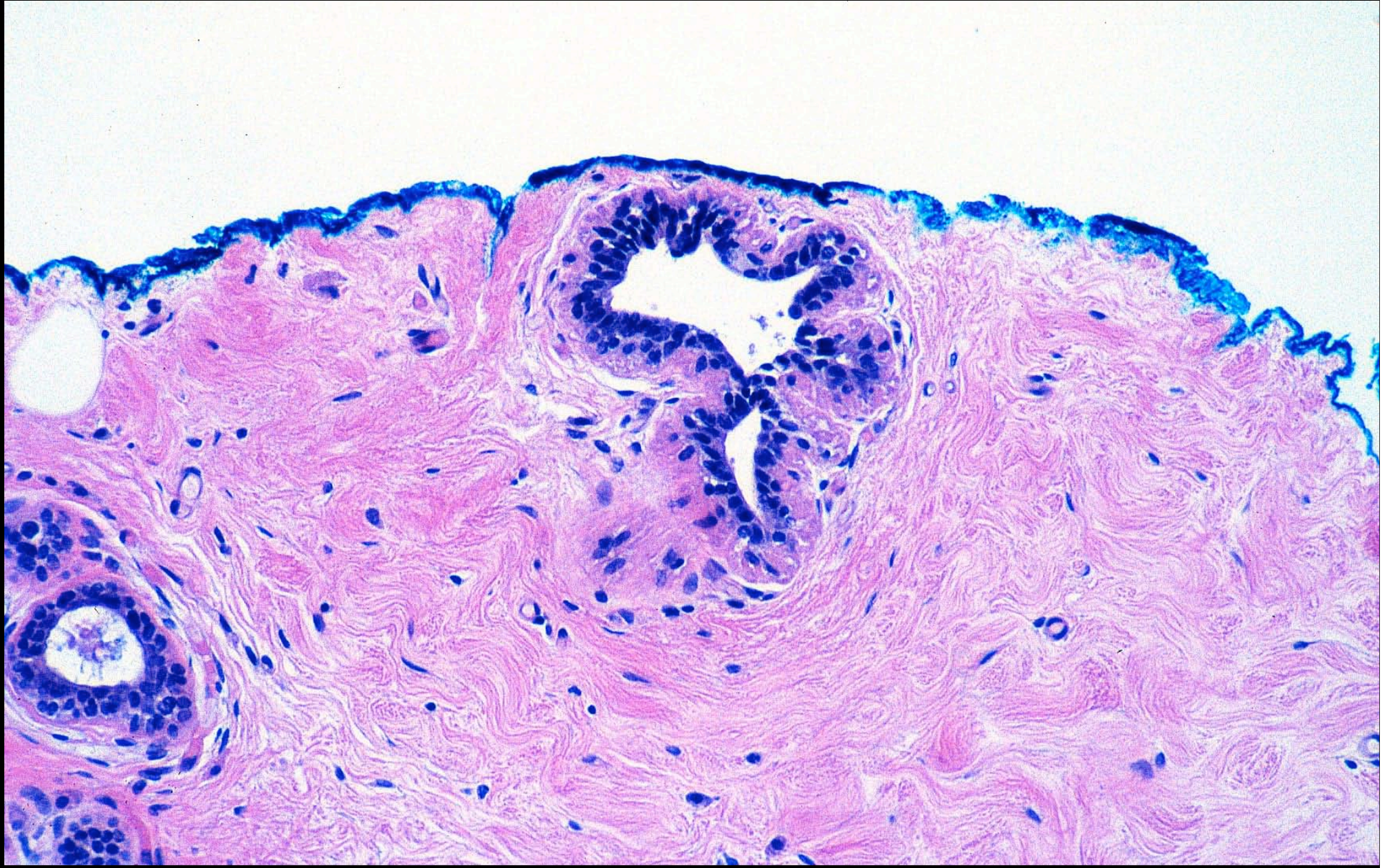


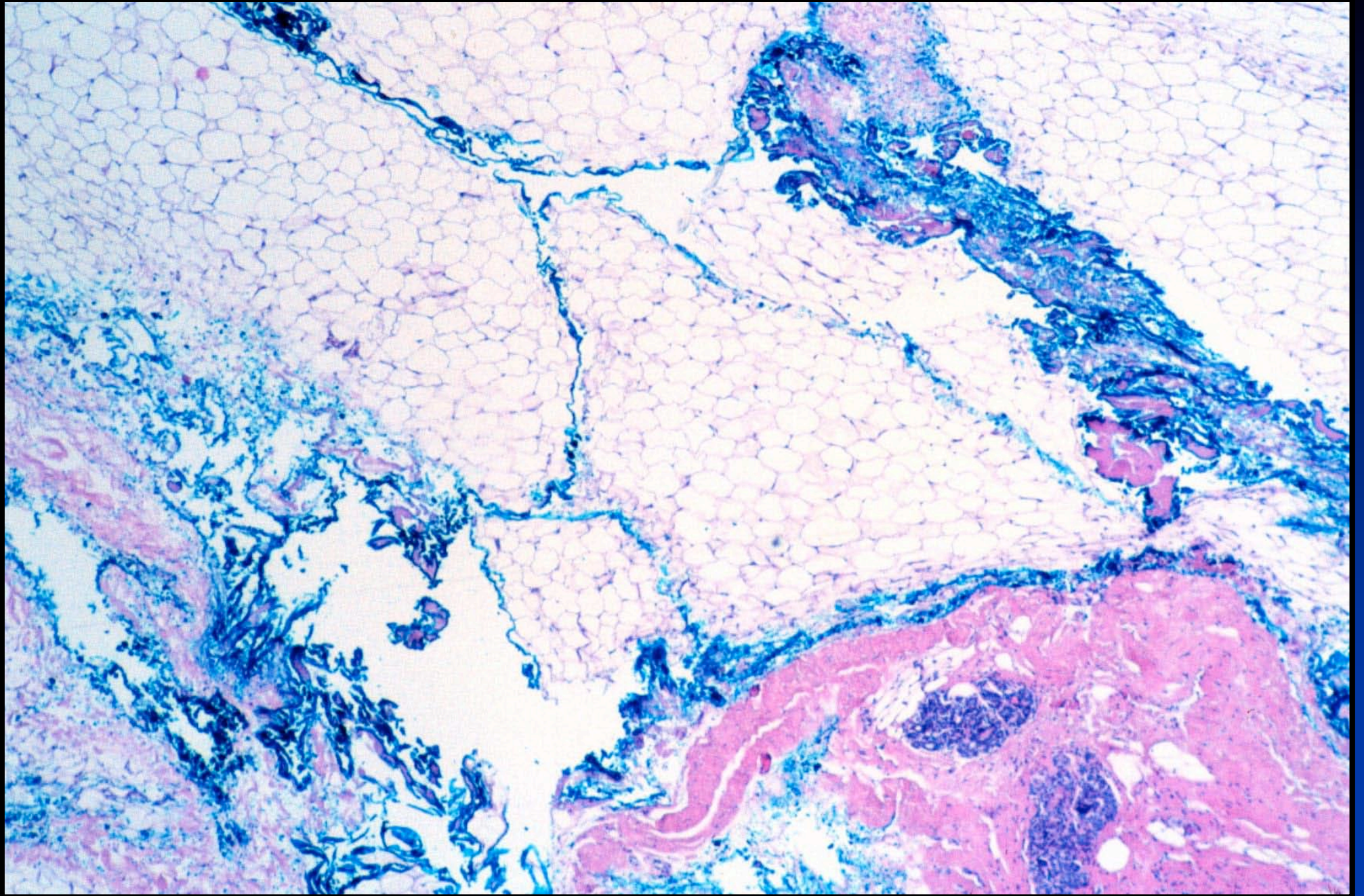
Oriented Specimen



Problems with Microscopic Margin Evaluation

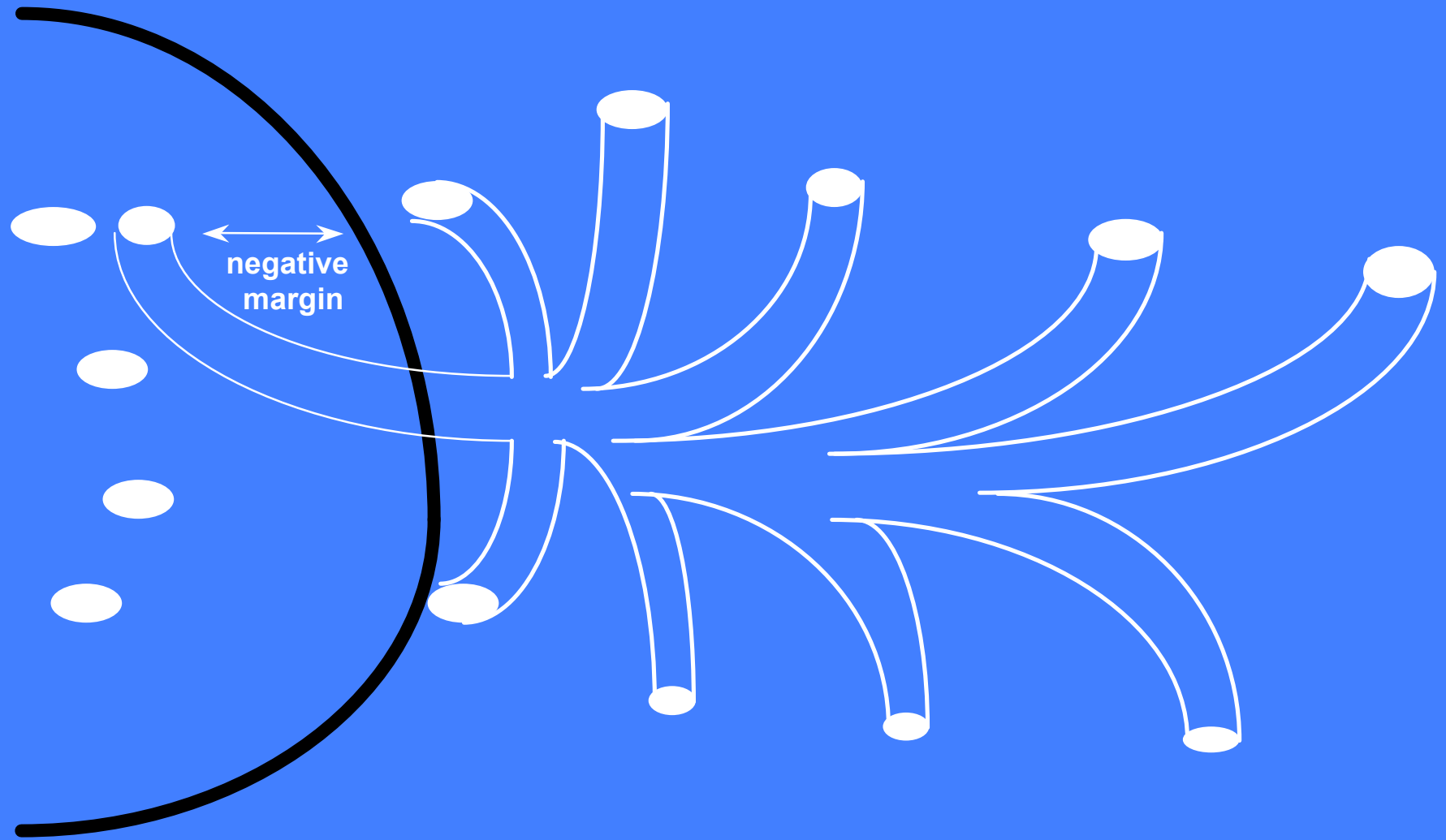
- Ink runs
- Anatomy of ductal system
- No uniform sampling method; sampling error
- No uniform definitions of “positive” and “negative” margins





Problems with Microscopic Margin Evaluation

- Ink runs
- **Anatomy of ductal system**
- **No uniform sampling method; sampling error**
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Problems with Microscopic Margin Evaluation

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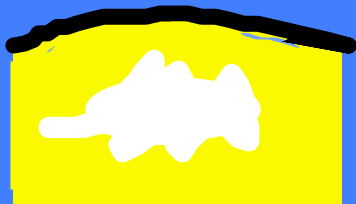
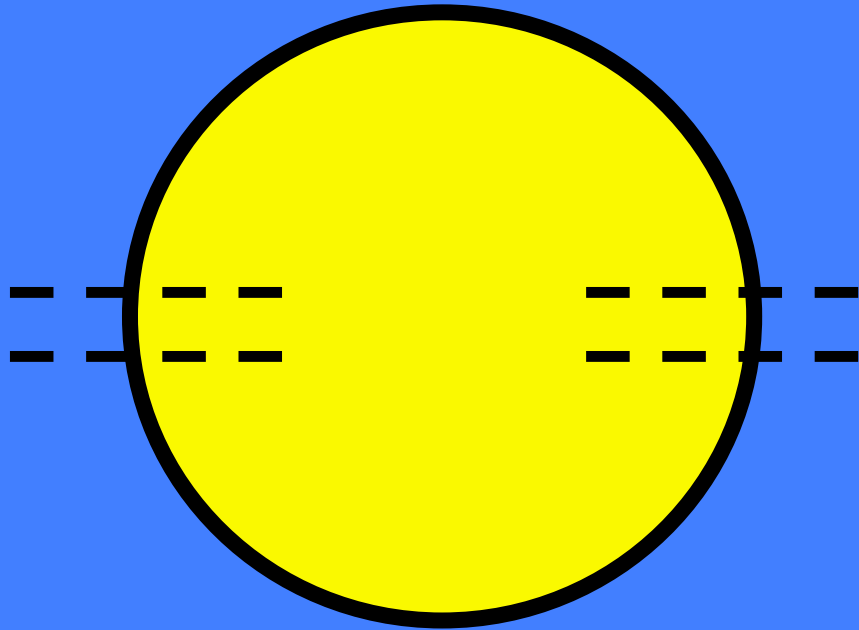
Methods to Evaluate Margins

- ***Histologic***

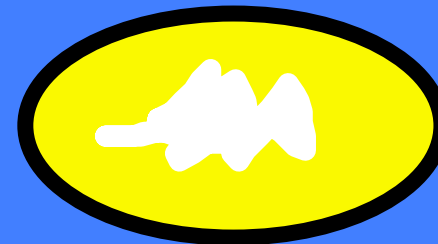
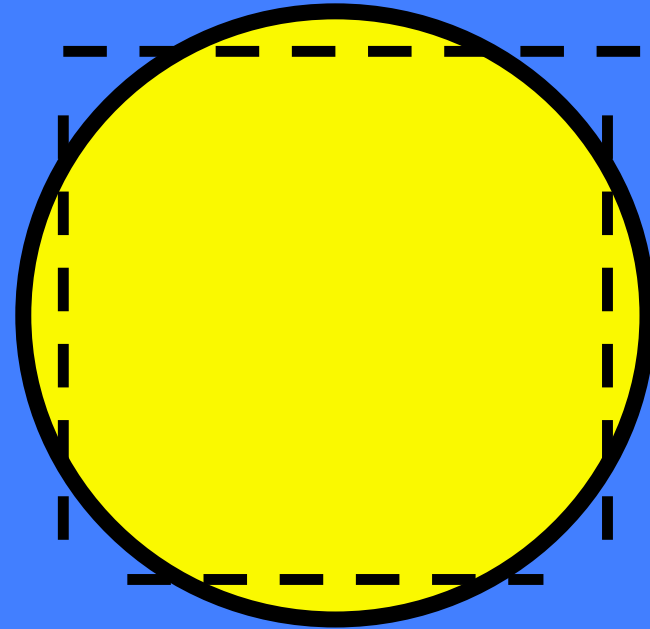
- Sections perpendicular to inked surface
- Margins shaved from specimen
- Margins shaved from biopsy cavity walls
- Large sections (macrosections)

- ***Cytologic***

Options for Histologic Margin Evaluation



Inked, Radial



Shaved, En Face

Options for Histologic Margin Evaluation

- **Inked**

positive = tumor at inked tissue edge

- **Shaved**

positive = tumor anywhere on section

Potential Advantage of Shaved (en face) Margins

- Examination of greater surface area of margin with fewer sections

Shaved vs. Inked Margins

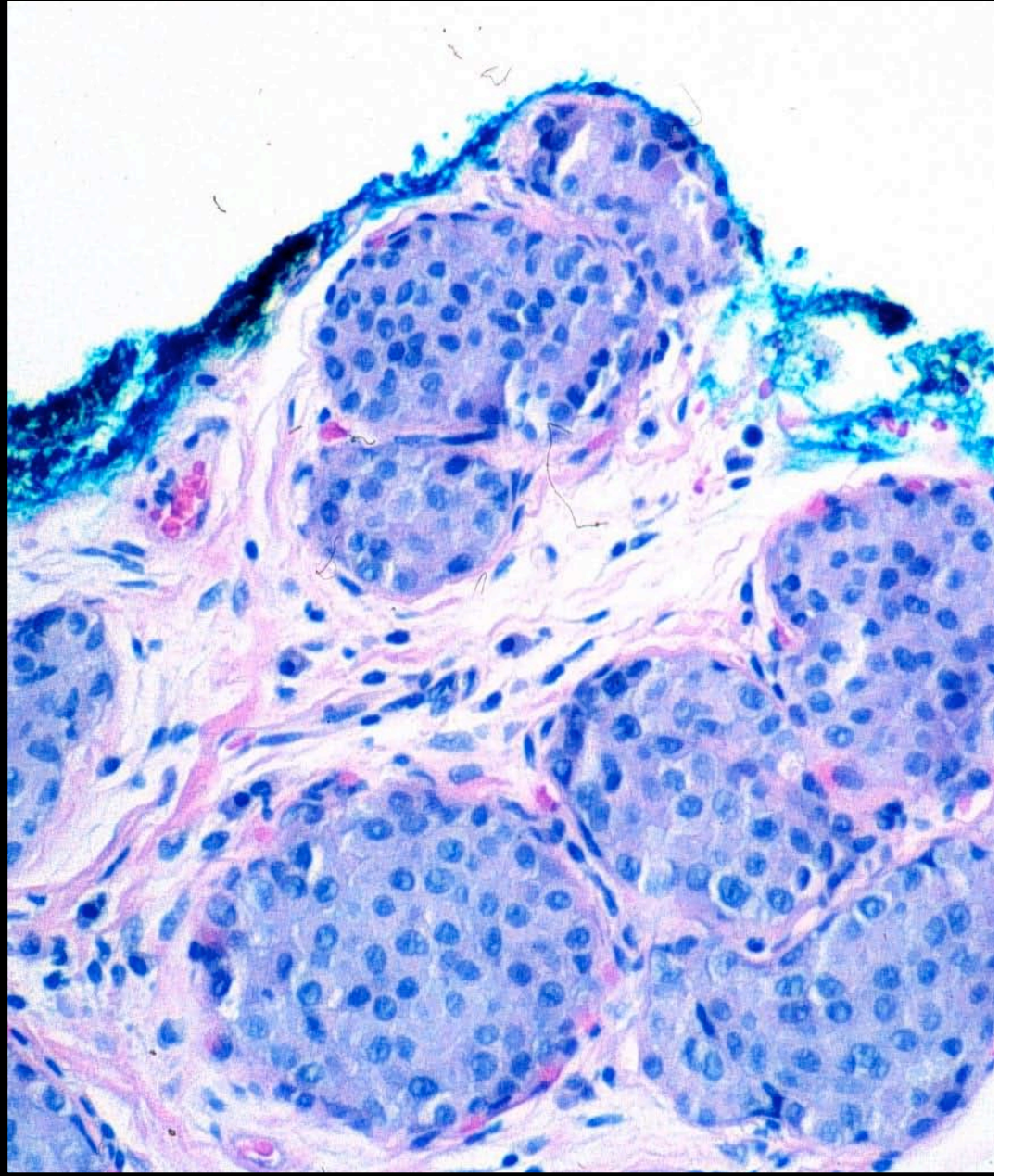
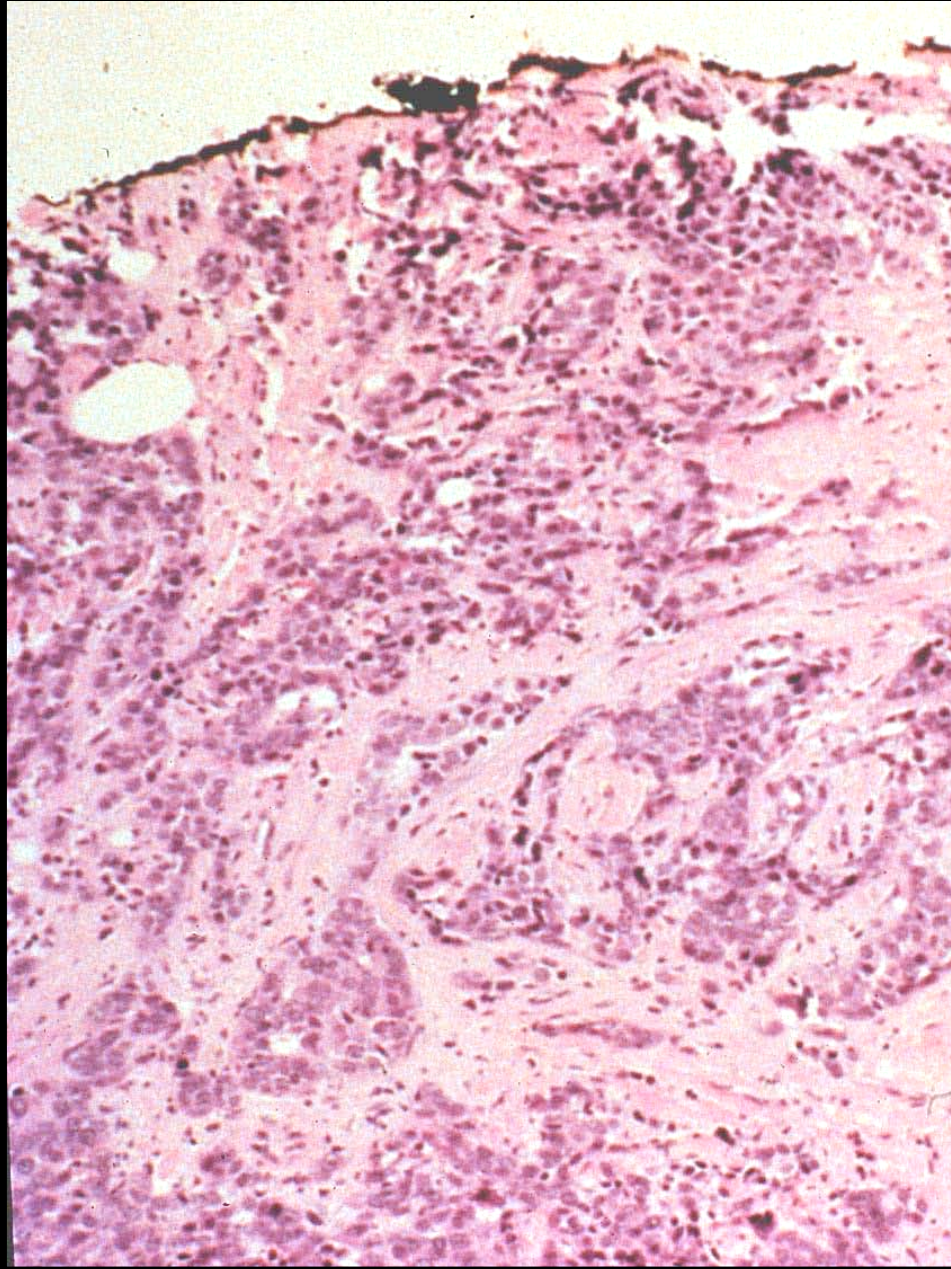
- Many patients with positive shaved margins do not have positive inked margins
- Use of shaved margins could result in improved local control, but unnecessary additional surgery (or even mastectomy) in some patients

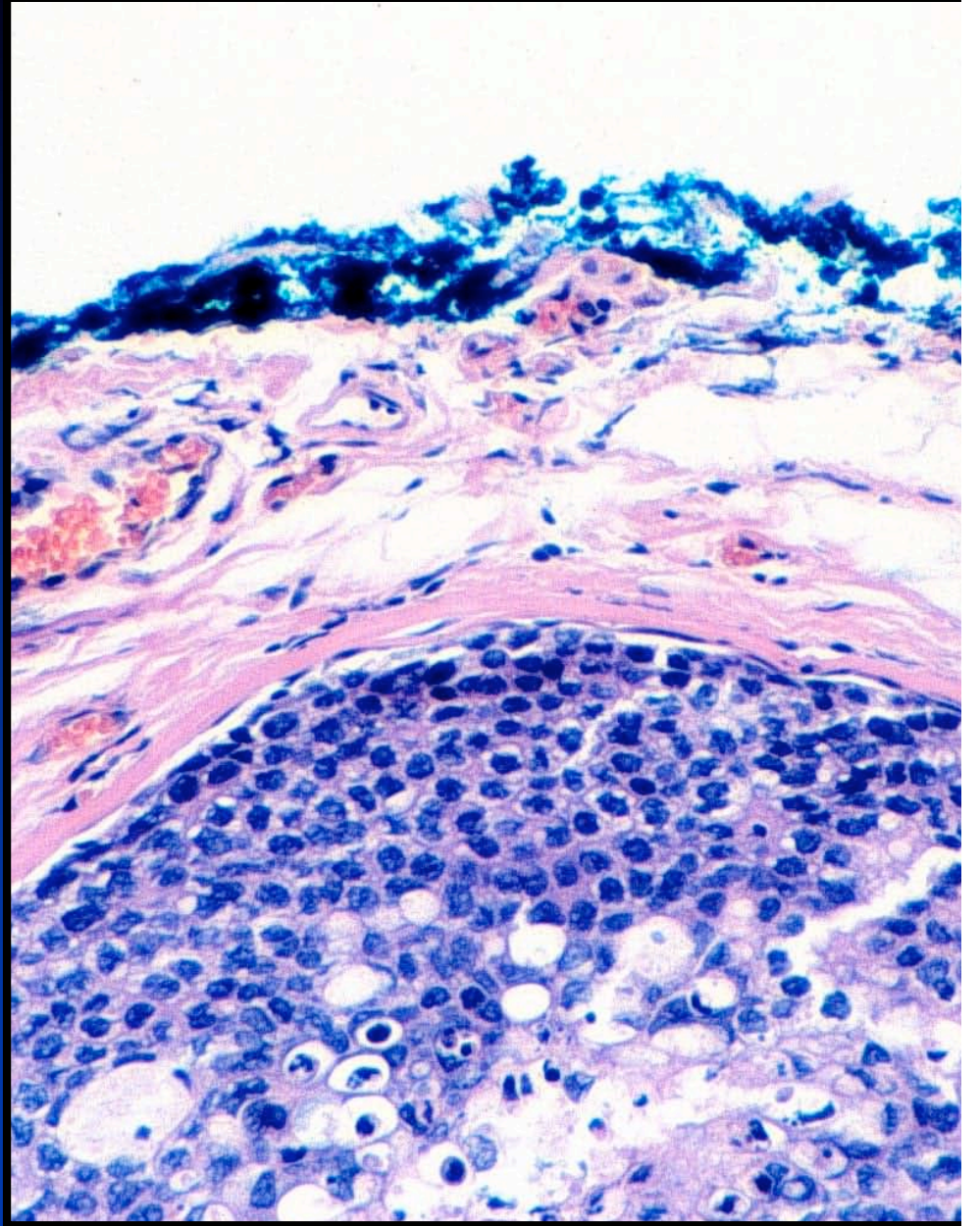
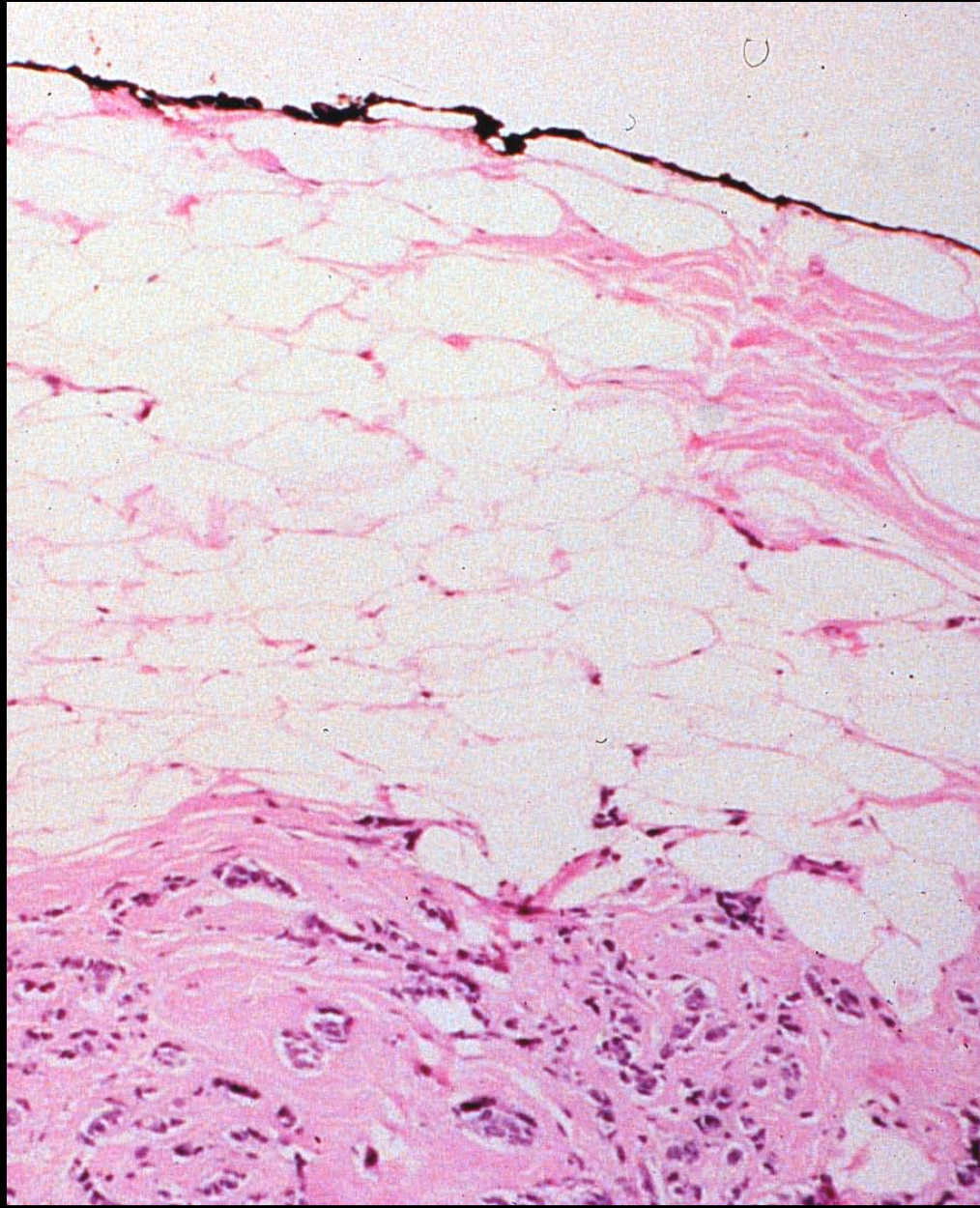
Cytologic Evaluation of Margins

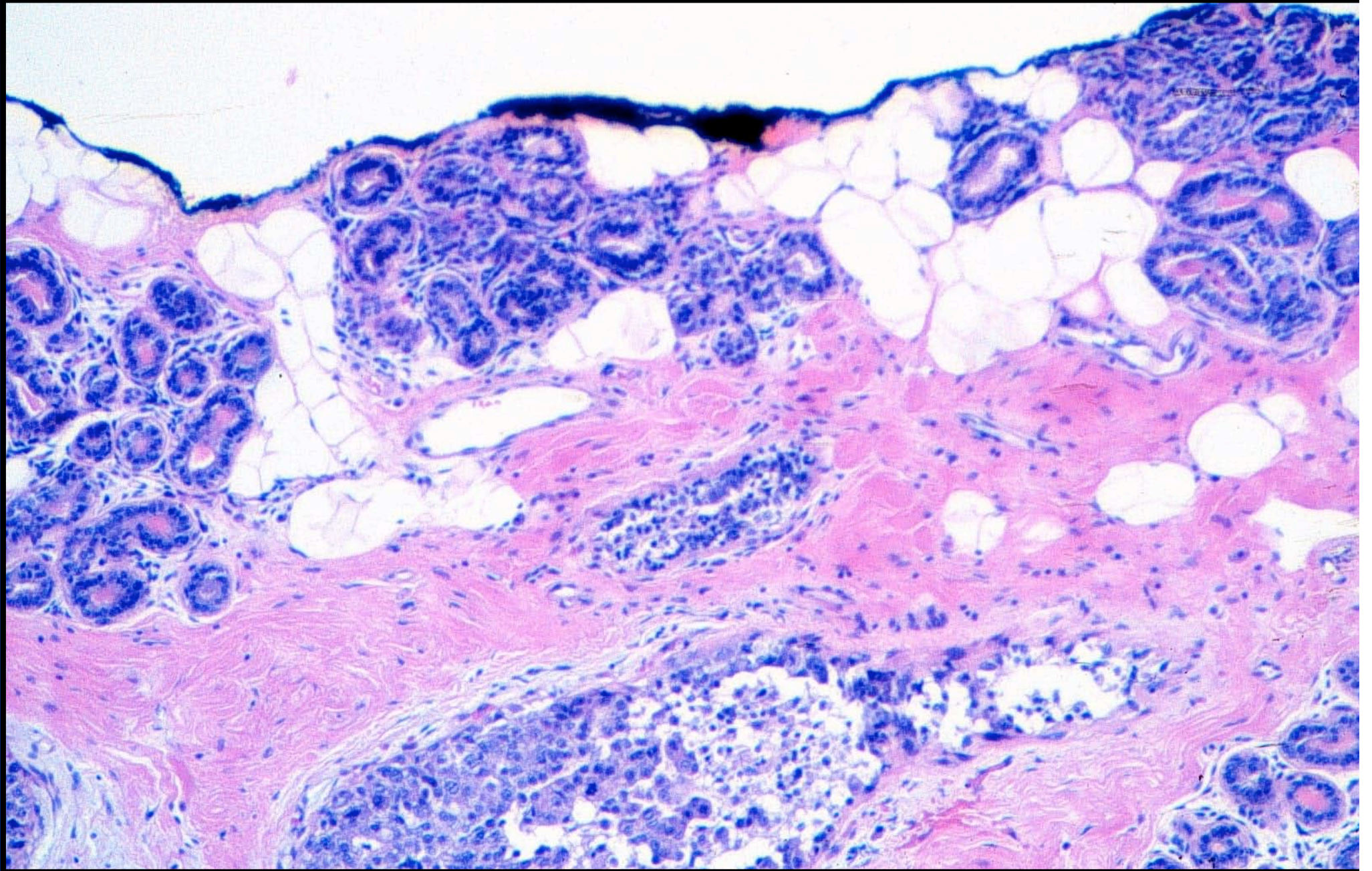
- Some studies have reported high sensitivity and specificity
- Requires expertise in breast cytopathology
- ? Wisdom of intraoperative evaluation of margins by either cytology or frozen section

Problems with Microscopic Margin Evaluation

- Ink runs
- Anatomy of ductal system
- No uniform sampling method; sampling error
- No uniform definitions of “positive” and “negative” margins







Reporting of Margin Status

- **Tumor on ink = positive margin**
 - Report for both invasive cancer and DCIS
 - Extent of involvement
 - Specify margin(s) involved (if specimen oriented)
- **Tumor not on ink**
 - Report closest distance to margin for both invasive cancer and DCIS
 - Specify closest margin(s) (if specimen oriented)

Clinical Implications

- Margin status is best viewed as a way to estimate the likelihood of residual disease
- Despite limitations, margin status generally considered to be the most important determinant of local recurrence in patients treated with breast conserving therapy

Microscopic Margins and Local Recurrence: Invasive Cancer

(studies with \geq 8yr results)

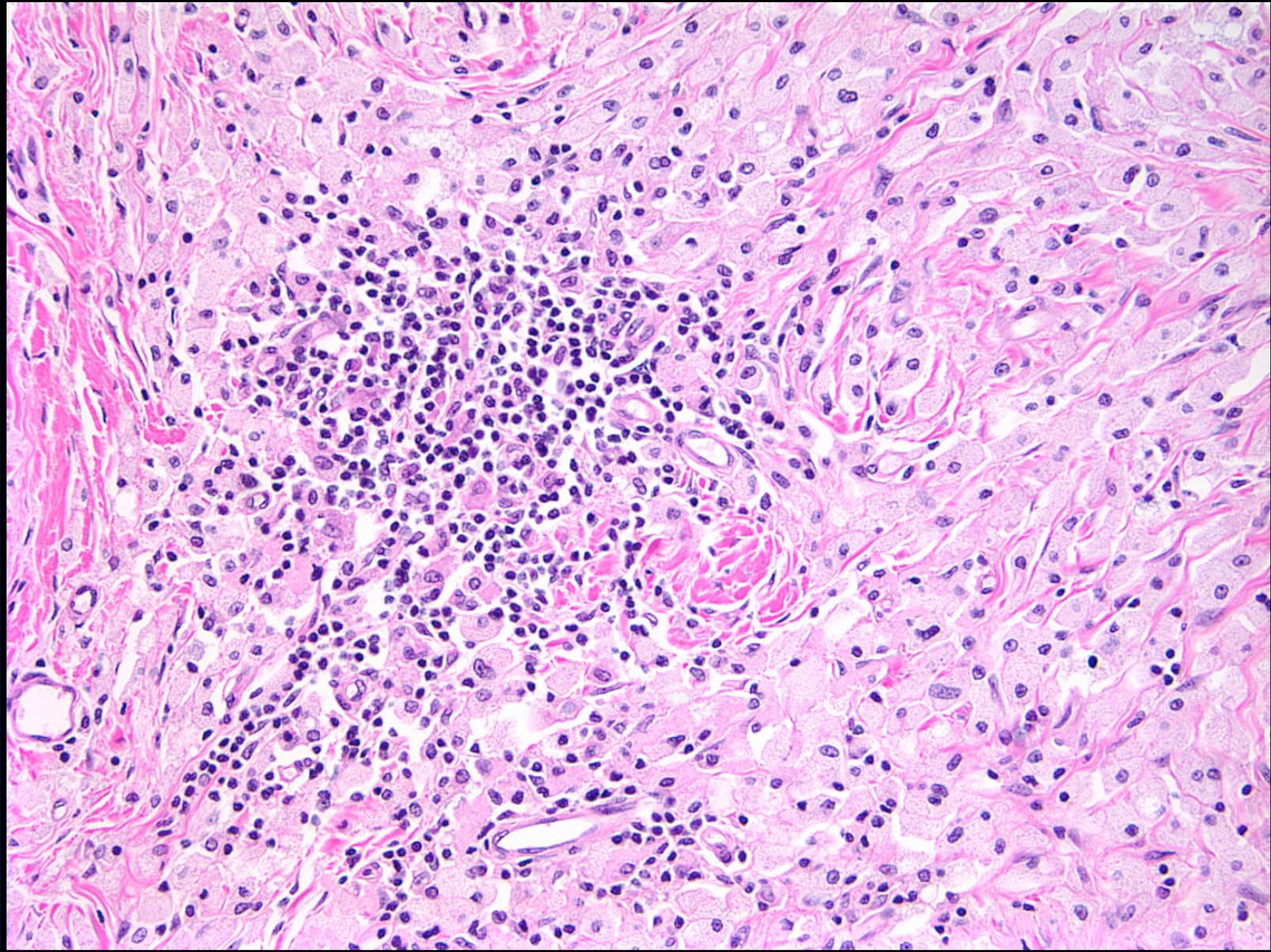
Study	# pts (f/u)	LR with + margins	LR with - margins
Park	533 (8 yr crude)	18%	7%
Van Dongen	431 (8 yr act)	20%	9%
Peterson	1021 (8 yr act)	10%	8%
Kini	400 (10 yr act)	17%	6%
Mansfield	704 (10 yr act)	16%	8%
Smitt	303 (10 yr act)	22%	2%
Freedman	1262 (10 yr act)	14%	7%
Wazer	494 (12 yr act)	16%	7%

“Close” Margins and Local Recurrence

Study	# pts (f/u)	LR with + margins	LR with Close margins	LR with - margins
Borger	1026 (5 yr act)	16%	6%	2%
Park	533 (8 yr crude)	14%	7%	7%
Freedman	1262 (10 yr act)	12%	14%	7%
Smitt	303 (10 yr act)	22%	16%	2%
Wazer	498 (10 yr act)	15%	2%	2%

Neoadjuvant Treated Excision Specimens

- Pathologist needs to identify residual tumor
- Size/extent of tumor may be reported as
 - Largest contiguous focus of residual carcinoma
 - Number of residual foci over the extent of the tumor bed
- Margin status
 - Presence of invasive, in situ and tumor bed at the margin



From Schnitt and Collins, Biopsy Interpretation of the Breast, LWW, 2008

Margins and Local Recurrence: 2008

- **Vast majority of patients with invasive breast cancer and DCIS treated with breast conserving therapy will have negative margins by routine pathologic examination**
- **Patients with negative margins still develop local recurrences**
- **Therefore, identification of risk factors for local recurrence in patients with negative margins now of particular clinical interest and importance**

Risk Factors for Local Recurrence in Patients with Negative Margins

- **Intrinsic limitations of margin assessment**
- **Extent of surgical resection**
- **Amount of carcinoma close to margin**
- **Newer techniques:**
 - **Biomarkers**
 - **Molecular/genetic analysis**
 - **Newer imaging modalities**

Molecular/Genetic Approaches

- **Have been used to analyze histologically normal breast tissue adjacent to carcinomas**
- **Some histologically normal TDLUs contain cells with genetic abnormalities**
- **What is normal?**

Clinical Implications

- **AI/LOH in normal breast tissue may define a region at increased risk for development of breast cancer/local tumor recurrence**
- **Could this account for local recurrences among patients with histologically negative margins?**

ORIGINAL ARTICLE

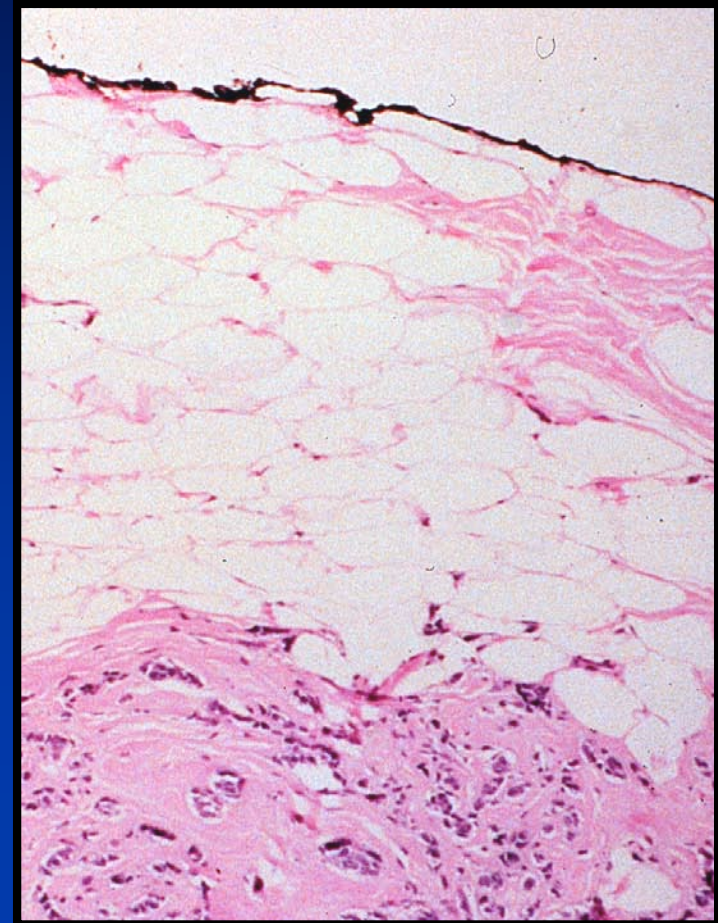
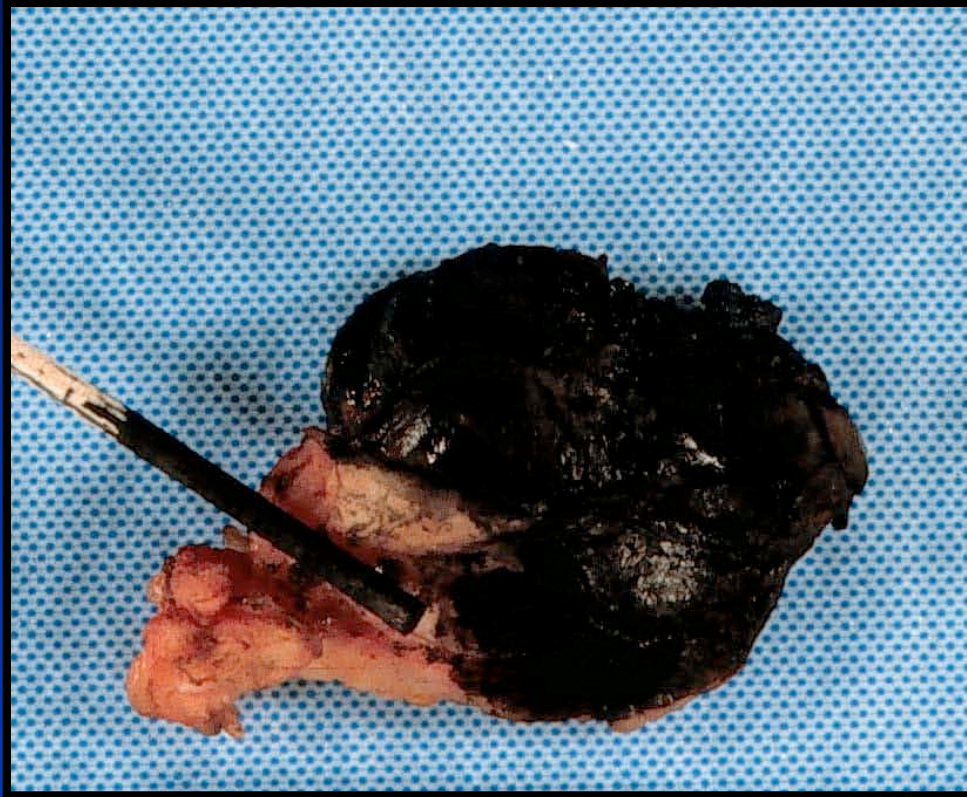
Gene Expression in Fixed Tissues and Outcome in Hepatocellular Carcinoma

Yujin Hoshida, M.D., Ph.D., Augusto Villanueva, M.D., Masahiro Kobayashi, M.D., Judit Peix, A.S., Derek Y. Chiang, Ph.D., Amy Camargo, B.A., Supriya Gupta, B.S., Jamie Moore, M.A., B.S., Matthew J. Wrobel, M.S., Jim Lerner, B.S., Michael Reich, B.S., Jennifer A. Chan, M.D., Jonathan N. Glickman, M.D., Ph.D., Kenji Ikeda, M.D., Masaji Hashimoto, M.D., Goro Watanabe, M.D., Maria G. Daidone, Ph.D., Sasan Roayaie, M.D., Myron Schwartz, M.D., Swan Thung, M.D., Helga B. Salvesen, M.D., Ph.D., Stacey Gabriel, Ph.D., Vincenzo Mazzaferro, M.D., Jordi Bruix, M.D., Scott L. Friedman, M.D., Hiromitsu Kumada, M.D., Josep M. Llovet, M.D., and Todd R. Golub, M.D.

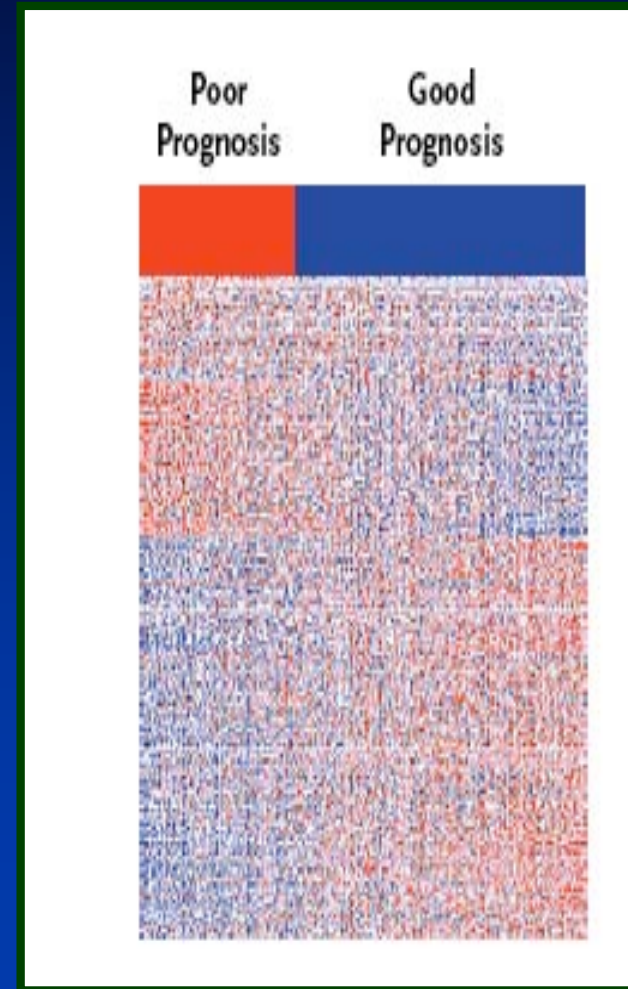
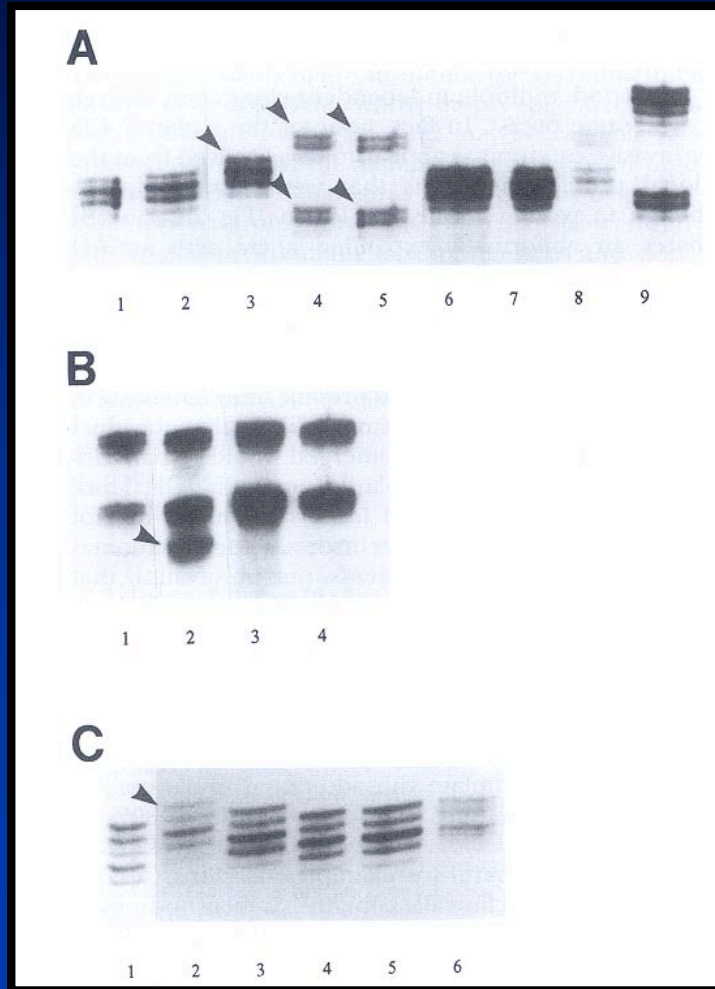
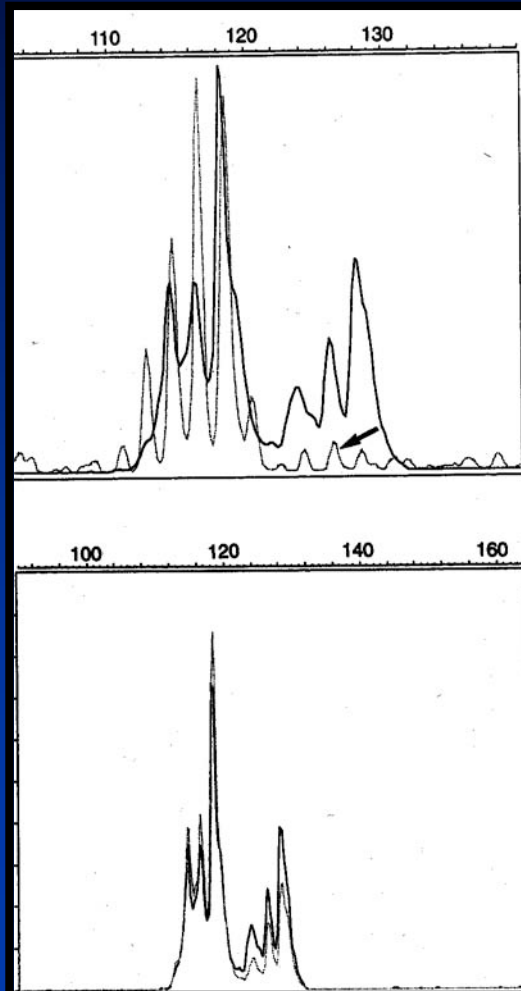
CONCLUSIONS

We have demonstrated the feasibility of genomewide expression profiling of formalin-fixed, paraffin-embedded tissues and have shown that a reproducible gene-expression signature correlated with survival is present in liver tissue adjacent to the tumor in patients with hepatocellular carcinoma.

Assessing Adequacy of Excision: The Present



Assessing Adequacy of Excision: The Future?



Conclusions

- **Adequate excision is the most important way to maximize local control in patients treated with breast conserving therapy**
- **Assessing microscopic margins of excision is imperfect, but is a clinically useful means to help guide the extent of conservative surgery and estimate the risk of local recurrence**

Conclusions

- **In current clinical practice, most patients have negative margins; identification of risk factors for local recurrence in this group should be an important goal of clinical research**
- **Role of molecular/genetic markers and newer imaging modalities to assess adequacy of excision and risk of local recurrence is an area of active investigation**

- **Margin status**
- **Other pathologic factors**

Clinical Factors

**Local
Recurrence**

Extent of Surgery

**Cosmetic
Outcome**

**Mammographic
Findings**

