Microinvasive breast cancer: how to diagnose it, and results from the Sloane Project

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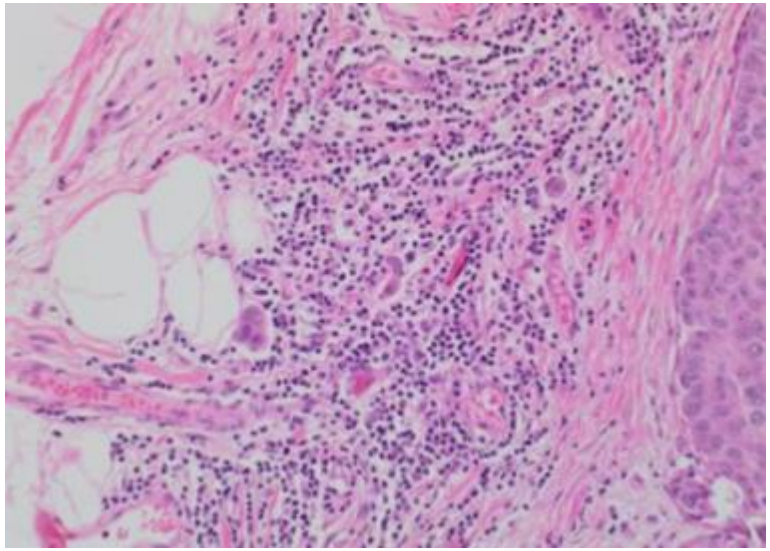
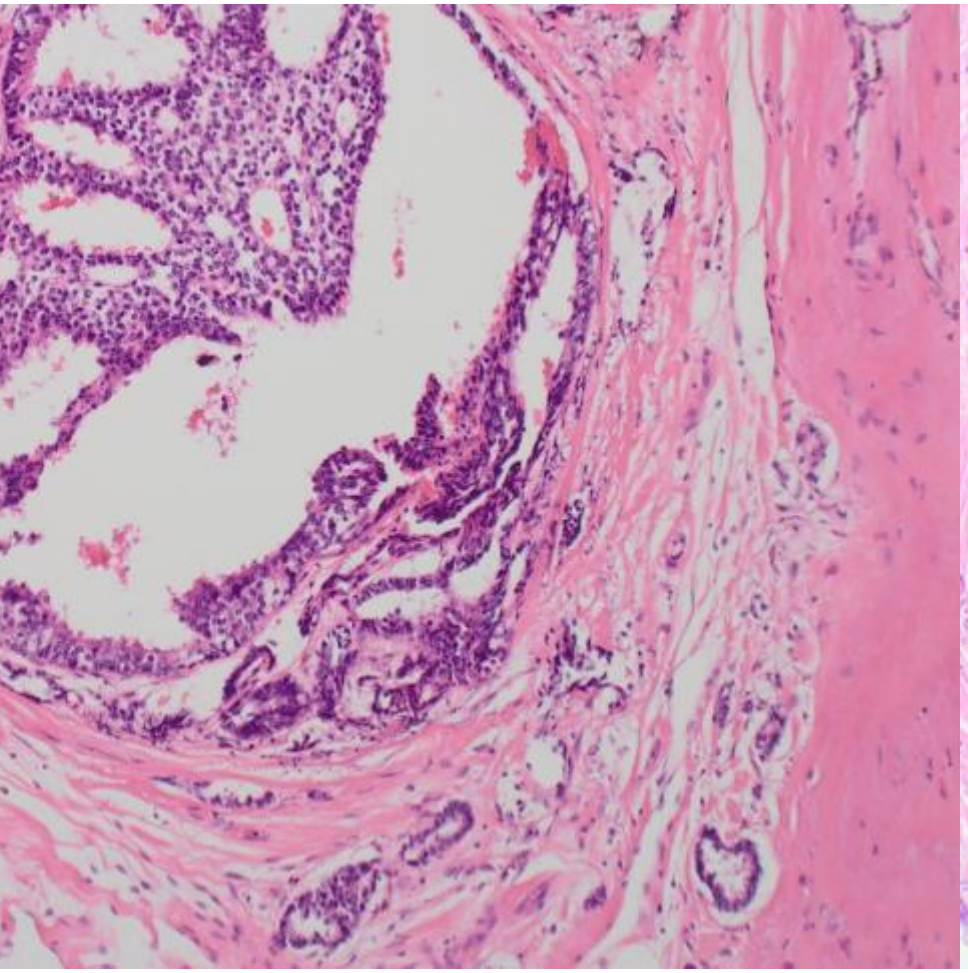
On behalf of the Sloane Project Steering Committee

What is microinvasion(MI)?

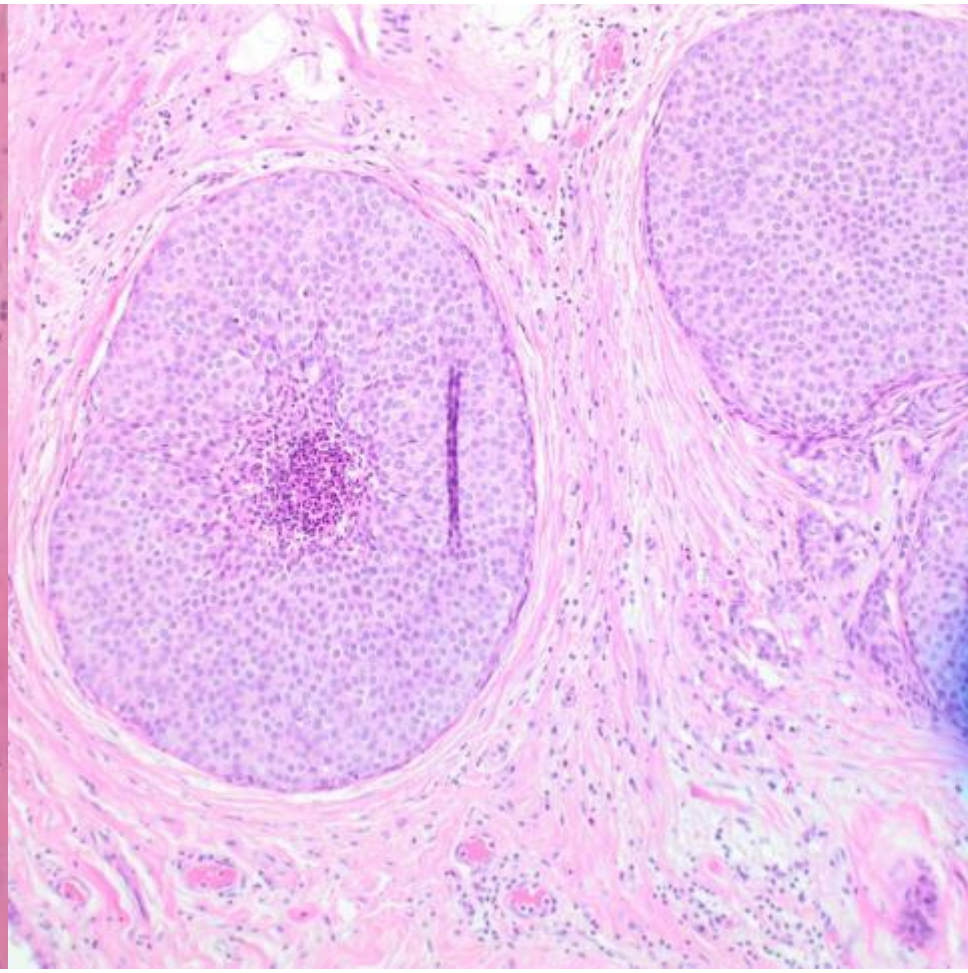
- Current definition: one or more small invasive foci ≤ 1mm.
- Infiltration outside specialised stroma dropped
- Mostly seen in association with high grade DCIS.
- On core biopsy: B5a
- On excision: pT1mic



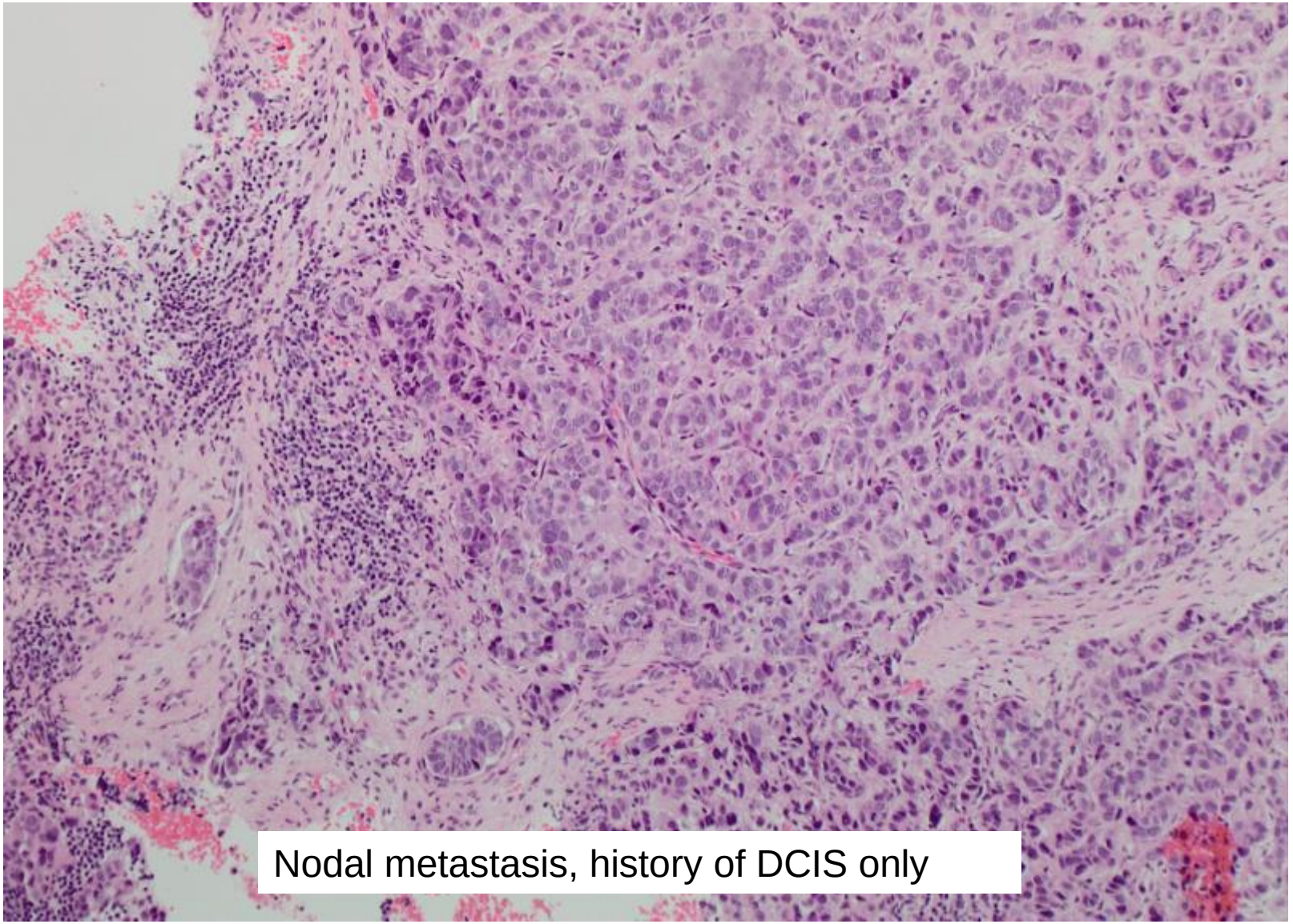
Non high grade DCIS

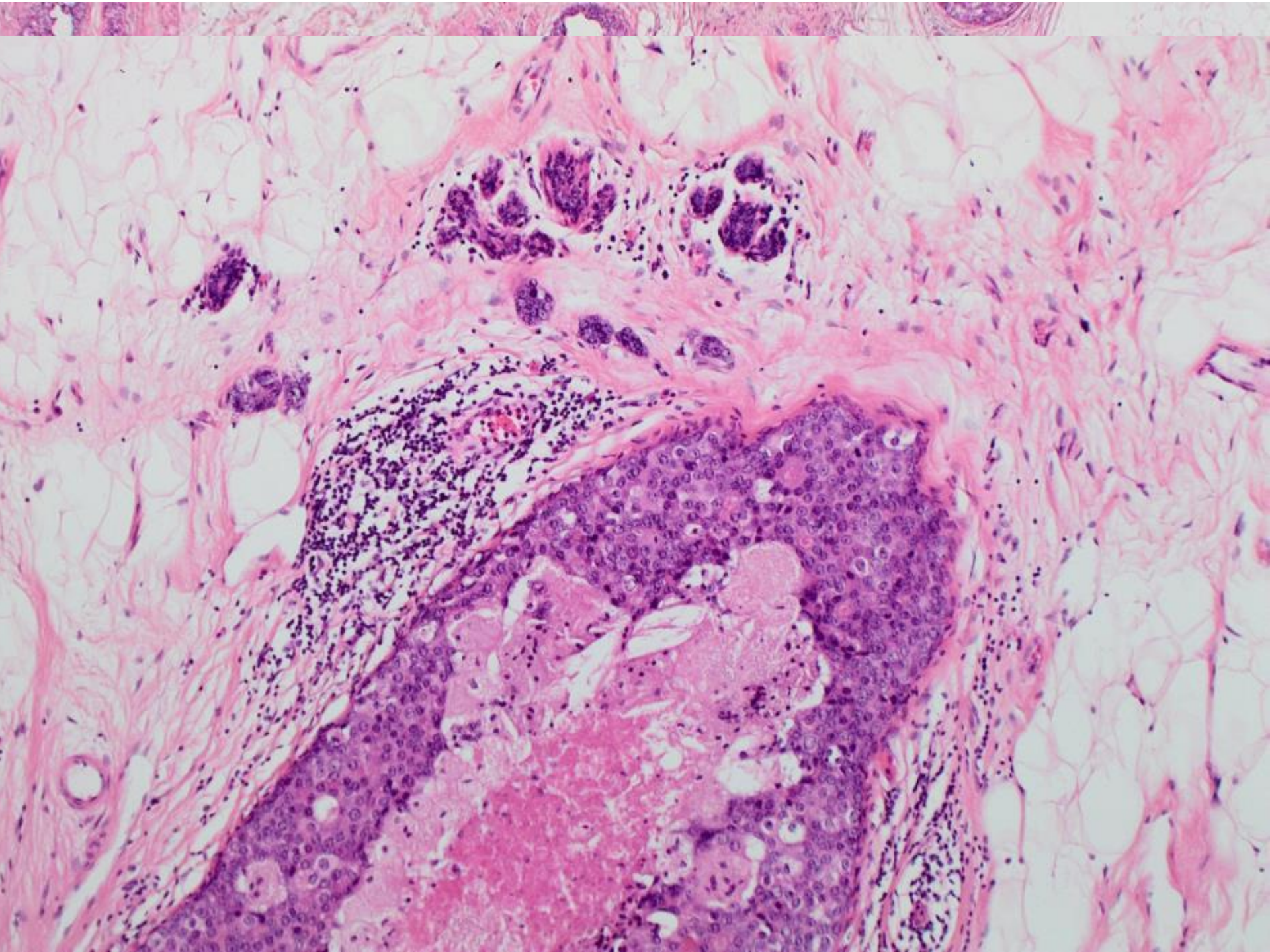


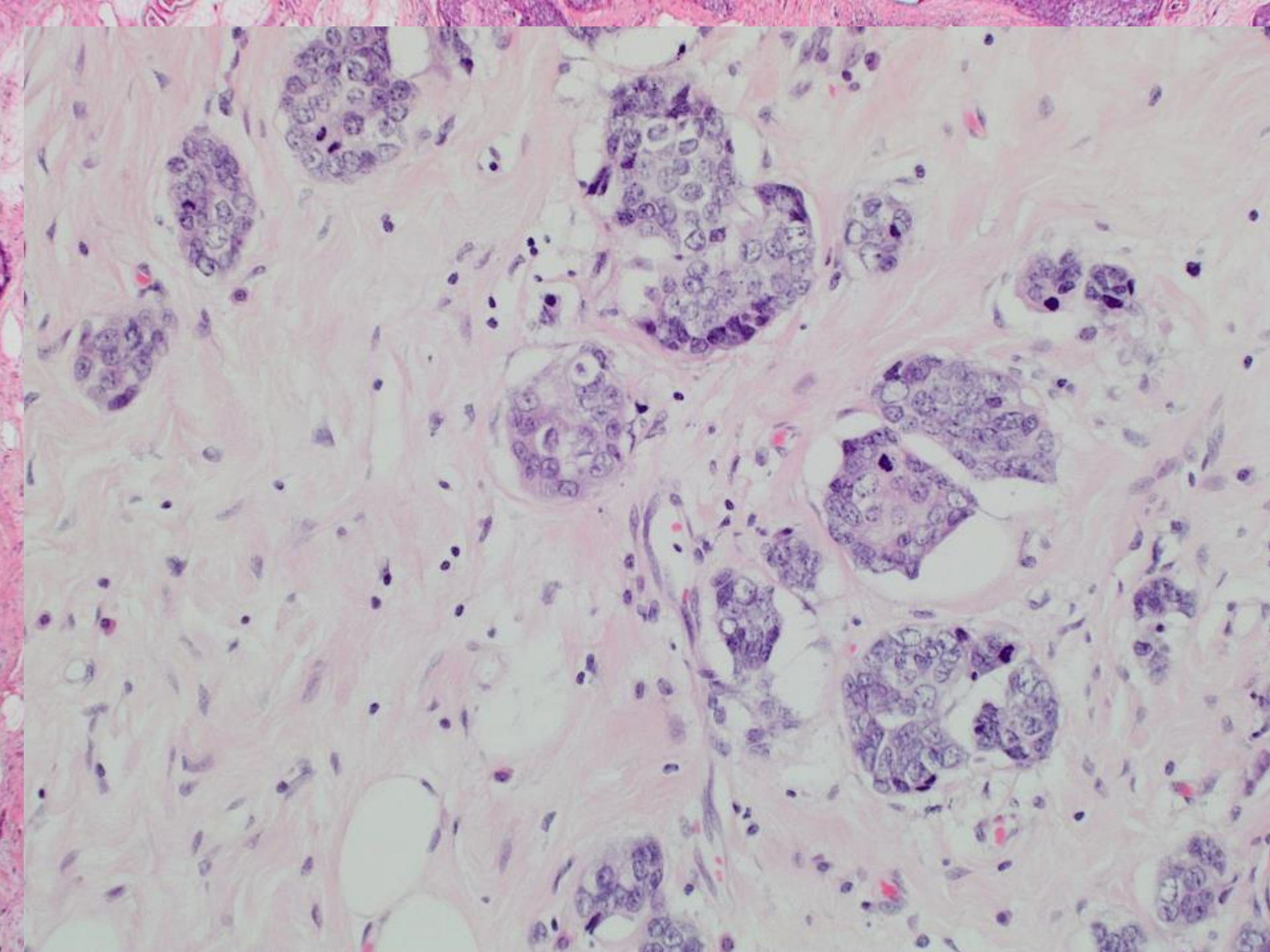
Florid LCIS



Focal lesion- can be missed





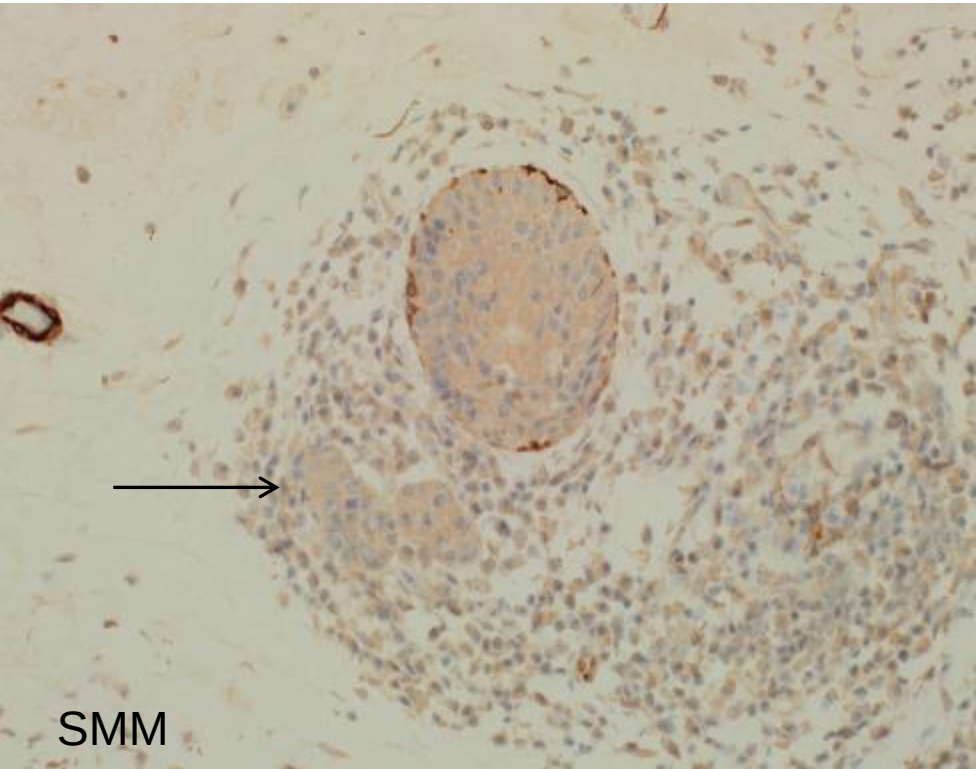


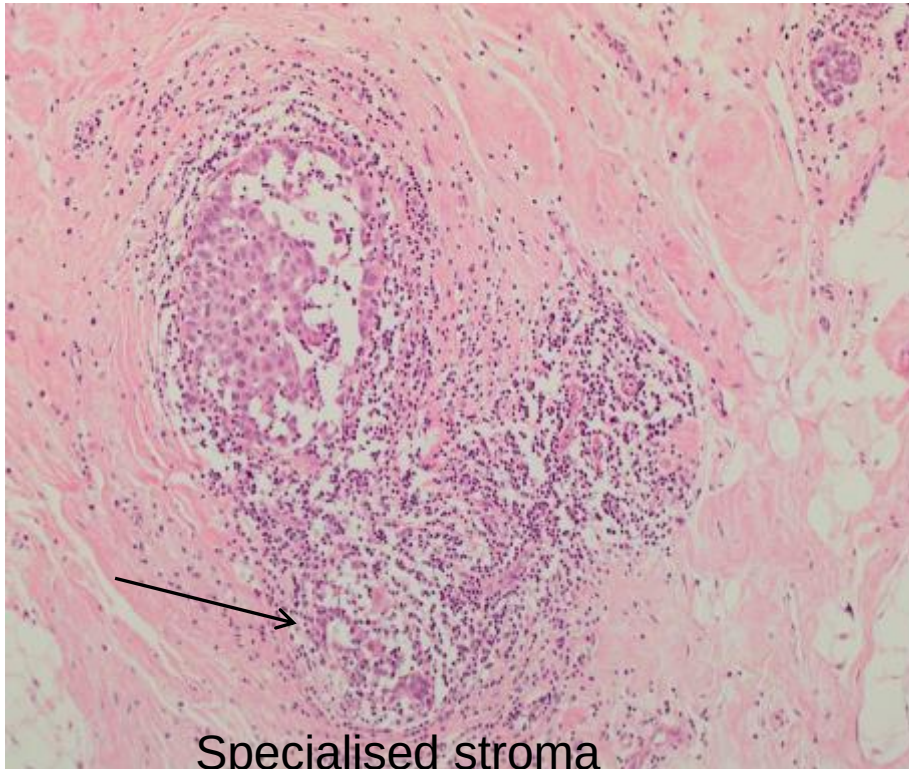
Evolution of Definition

- 1982: First definition of <1mm : Lagios
- 1989: focal microinvasion below the basement membrane in one or several individual ducts, but in not more than 10% of the surface of the histological sections examined. Patchevsky et al.
- 1992: single focus of invasive carcinoma ≤2mm, or up to three foci of invasion each not more than 1mm in greatest dimension, Silver & Tavassoli.
- 1992: The maximal extent of invasion is not more than 2mm or comprising <10% of the tumour, with 90% of DCIS. Solin et al.

- **1990: National Coordinating Group:** One or more microscopic foci of possible invasion not >1mm in greatest dimension

- **1995 National Coordinating Group:** outside specialised stroma





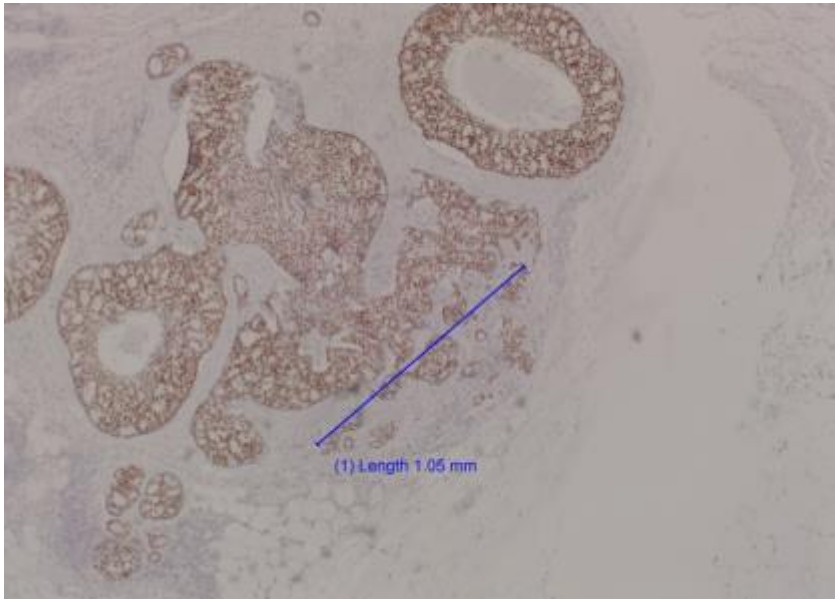
- **1997 AJCC:** the extension of cancer cells beyond the basement membrane into the adjacent tissues with no focus more than 0.1cm in greatest dimension (pT1mic). Sobin &Wittekind.

- If multiple, use largest only.

Microinvasion unanswered questions

- Management issues:
  - Is it in situ or invasive disease?
  - Should SLNB be routinely performed?
  - Is it associated with adverse outcome?
  - What parameters predict outcome?

- Pathology issues:
  - Definition
  - Incidence
  - Consistency of reporting
  - Measurement of multiple foci
  - Reporting on core biopsy (suspected/definite)



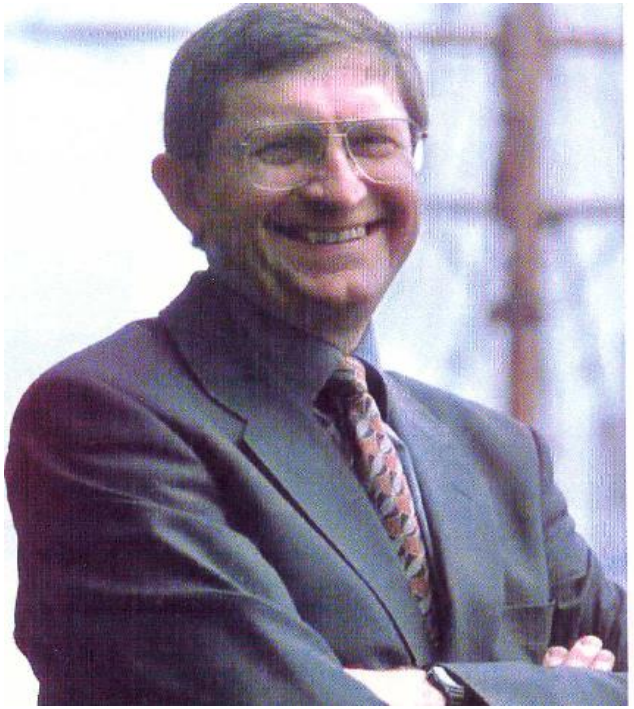
The Sloane Project
Understanding non-invasive breast disease

NHS

NHS Prospective Cohort Study of Screen-Detected Non-invasive Neoplasias

Aims

- To improve knowledge about the **diagnosis**, treatment and clinical outcomes of screen detected DCIS/atypical hyperplasia
- Identify imaging and **pathology features**
- Identify variations in **diagnostic** and therapeutic (surgery, radiotherapy, endocrine therapy) practice



Prof John Sloane
University of Liverpool
Born April 14 1946;
died May 10 2000

Methods

- Multi-disciplinary data collection forms: Radiology, Pathology, Treatment, Radiotherapy **01 April 2003 to 31 March 2012 (phase 1)**

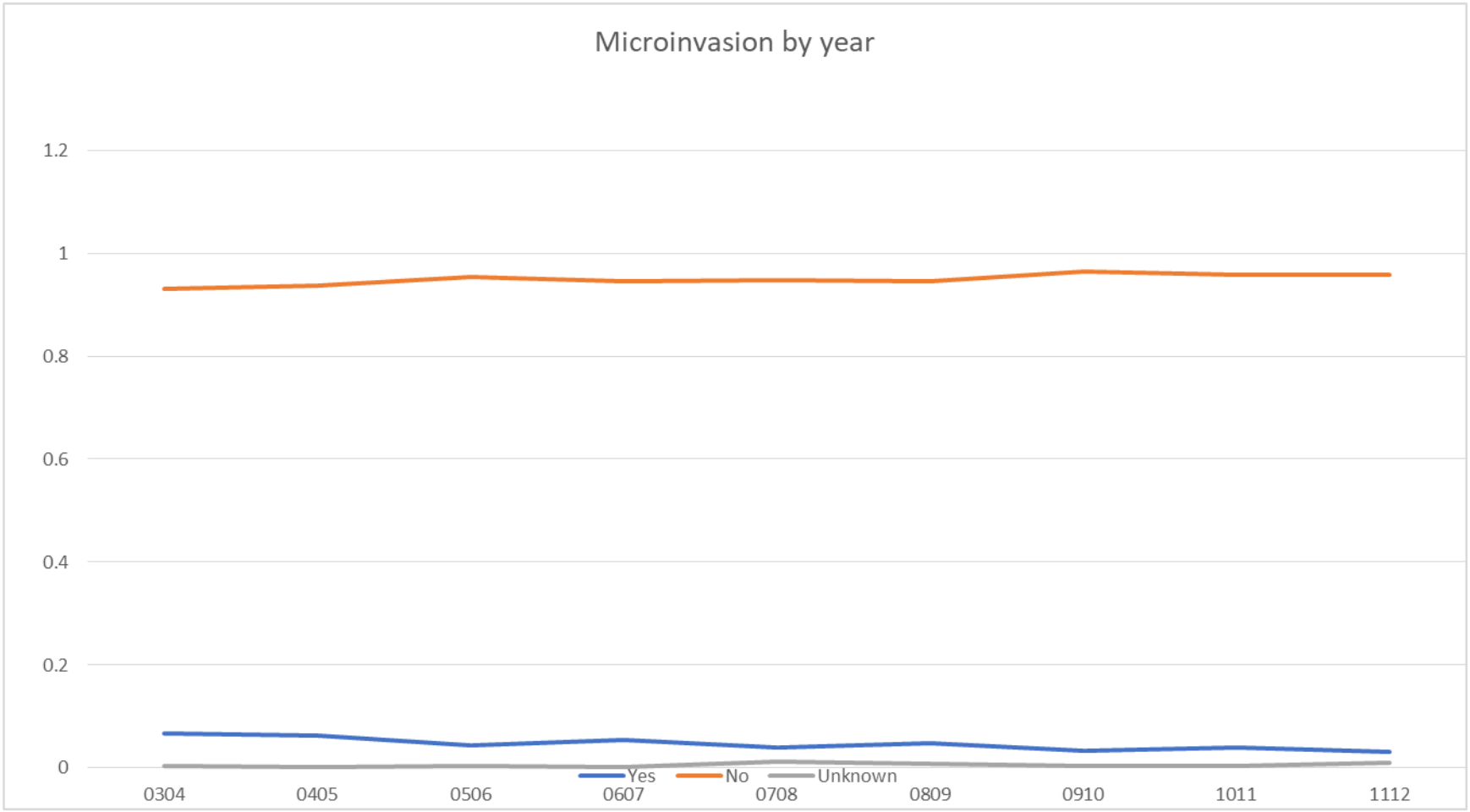
- Pathology: adherence to NHSBSP guidelines and Sloane Pathology protocol, EQA participation.

- Subsequent events: ipsilateral/contralateral DCIS and/or invasive disease and distant metastasis, 6 months or more following DCIS diagnosis

Results

- Total:11,285 DCIS patients diagnosed in the UK, microinvasion was reported in 521 (4.6%).

- The frequency of reported microinvasion varied considerably among screening units (0-25%).



Overall reporting decreased from 7% in 2003/04 to 3% in 2011/12.

Pathological Associations

- High grade DCIS (5.9% of 7182 cases) compared to 2.9% of intermediate grade and <1% of low grade DCIS.

- Larger DCIS size 2.2% of DCIS <10mm, 3.9% of DCIS 10-20mm, 5.8% of DCIS 20-30mm, 5.2% of DCIS 30-40mm and 8.0% of DCIS >40mm

- Comedo necrosis and solid, cribriform DCIS, flat architecture

Management

- MI more frequent in patients who underwent mastectomy (6.9%) than in those who had breast conserving surgery (BCS) (3.6%; $p<0.001$).

- Axillary nodal surgery was more commonly performed for microinvasion (60.4% vs 30.3%) including for patients undergoing BCS (43.4% vs 8.5% of all patients with BCS) $p<0.001$.

- Patients with MI who underwent BCS were also more likely to receive radiotherapy ($p<0.001$).

- There was no significant association between the presence or absence of MI and margin status or width in BCS.

Nodal metastasis

- Low rate, not significantly different between those with (0.4%) and without (0.1%) microinvasion, p=0.27.

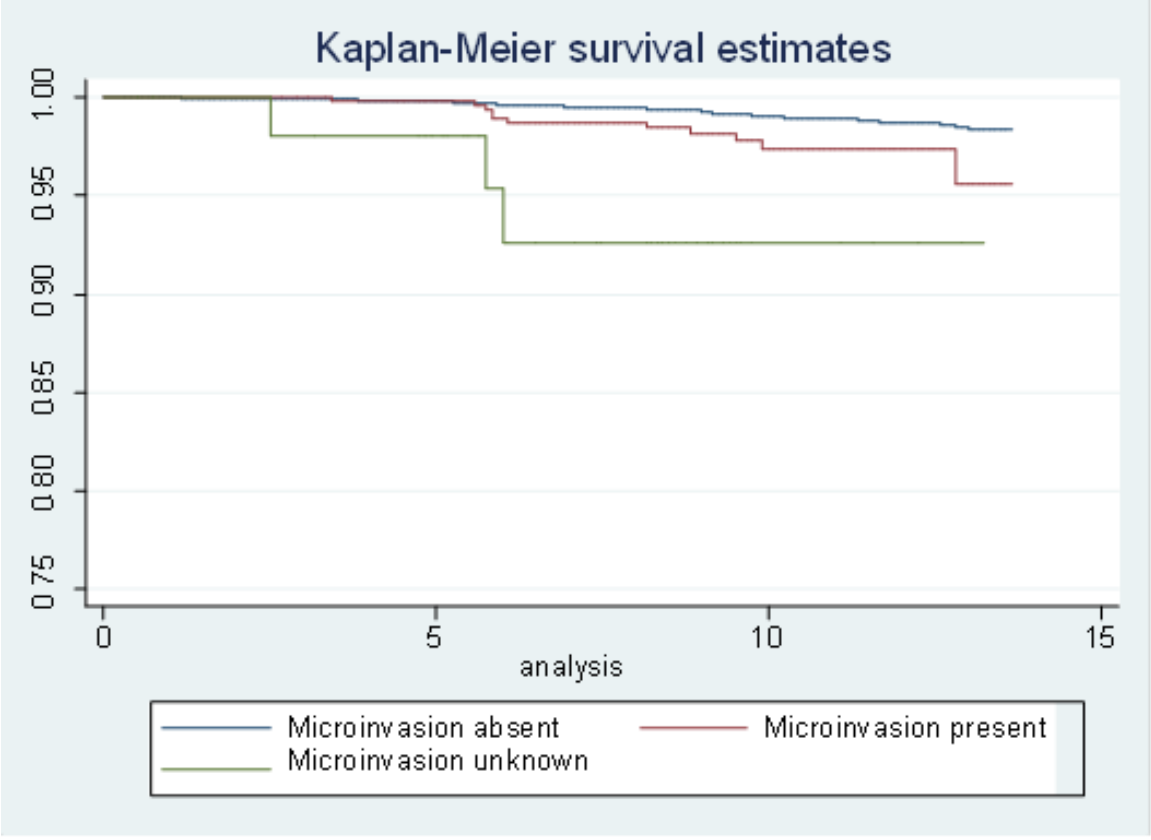
Patient outcome

- Median follow-up of 9 years (England).
- Low subsequent events rate: recurrent DCIS 2.3% and invasive carcinoma 4.2%.
- This was not statistically significant from DCIS without MI.

Breast cancer mortality

- *Significantly **higher** in women whose tumours showed microinvasion (2.1%) compared with those without it (0.8%; p=0.005).*

P =0.0049, excluding patients with unknown microinvasion status



- All subsequent ipsilateral DCIS events in patients with microinvasion were of high grade.

- The majority (71.4%) of subsequent ipsilateral invasive carcinomas were of grade 3 compared with only 30.4% of grade 3 carcinomas in patients with DCIS without microinvasion (p=0.02).

- No effect of DCIS size on frequency of recurrences or outcome.

Discussion

- Incidence (4.6%) is consistent with the reported literature.
- 5-10% of DCIS cases (Adamovich and Simmons 2003).
- 3.2% in SEER data (Champion et al. 2019).
- Variation among units warrants further investigation (EQA scheme).

Mortality: SEER Registry data

- 161,394 women with pure DCIS and 13,489 with DCIS & MI, their 20-year *breast cancer-specific mortality rate* was 3.8% and 6.9% respectively.

- Similar to small invasive carcinoma of up to 1cm (6.8%) but lower that for women with invasive carcinoma of 1.1-2.0 cm in size (12.1%).

- *Prognosis of DCIS with microinvasion is similar to that of small invasive carcinoma and worse than that of pure DCIS.* Sopik et al 2018

Axillary staging: No agreement

- Dutch study: recommended lymph node sampling in high grade DCIS, intermediate grade DCIS with comedo necrosis and cases with microinvasion (van la Parra et al. 2008).

- Memorial Sloan : Axillary staging performed in 77% of suspected and 94% of definite MI respectively ($p<0.001$). Upgraded to invasion on surgical excision 28% and 35% respectively.

- Meta analysis (2959 patients,23 studies): significant heterogeneity, 2% rate of nodal metastasis but no significant increase in clinically significant metastasis.

- Survival rates very similar to pure DCIS. Focality showed significant group differences

- Axillary staging unlikely to change management (mostly diagnosed on excision), MDT approach to tailor management is more preferable

Choi et al. 2021

Factors associated with poor outcome

- Large DCIS size
- Comedo necrosis
- Number of MI foci: ≥3 significantly associated with nodal positivity (p=0.03) and disease relapse (p=0.05). Zhang et al. 2020)
- Higher immune densities:CD4, FOXP3, CD163 Chen et al. 2021

Strengths

- Large well characterised cohort
- All screen detected lesions
- Comprehensive, robust MDT data including pathology
- Long follow up
- Validated outcome data
- Ability to assess trends over time

Limitations

- No data on whether MI was diagnosed on core or excision
- No info on number of MI foci or receptor status of DCIS
- MI definition changed over the years

Conclusions

- MI most commonly identified within high-grade DCIS and in larger DCIS lesions, and with comedo necrosis.

- Its pathological reporting decreased over a 10-year period.

- Patients with DCIS plus microinvasion were more likely to have undergone mastectomy, axillary node surgery and to receive radiotherapy after BCS.

- Subsequent events are few and prognosis good overall.

- The mortality associated with DCIS & microinvasion is, however, highly significantly higher than that for pure DCIS.

- Data supports managing MI similar to small invasive cancer.

MI Pathological Reporting

- DCIS parameters.
- Presence/absence of microinvasion.
- If multiple: do not add up, use largest
- Multiple foci of microinvasion should be noted and/or quantified
- Recommended: levels to assess the largest size.
- Foci are too small for adequate ER/PR/HER2 assessment.

The Current Sloane Steering Group

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This work uses data provided by patients and collected by the NHS as part of their care and support. **We thank all patients and all breast units who have participated in the Sloane Project Audit.**

Thank you for listening.