Pathology & Histology

Analysis Report

Meridian Pathology Institute • Department of Anatomical Pathology

MPI-2024-0847
Reported: 14 November 2024
Received: 11 November 2024
Biopsy • Surgical Specimen

Patient & Clinical Information

Patient Name
Margaret L. Harrington

Date of Birth
03 April 1962 (Age: 62)

Patient ID
PT-#H-883421

Gender
Female

Referring Physician
Dr. Thomas A. Wentworth, MD

Institution
Synapse General Hospital, Ward 7-B

Clinical Indication
Right breast mass, suspicious on imaging; BI-RADS 4C

Specimen Type
Core needle biopsy × 4 cores, right breast (2:00 position)

Gross Description
Four tan-white cylindrical cores, each approx. 12 mm in length and 1.5 mm in diameter, submitted in entirety in one block.

Clinical History
Palpable lump noted 6 weeks prior; no prior breast biopsies; family history of breast carcinoma (maternal aunt).

Gross Examination

Specimen Condition
Received fresh, immediately fixed in 10% neutral buffered formalin

Dimensions
Aggregate tissue: 4.8 cm × 0.15 cm

Colour / Texture
Tan-white, firm; no haemorrhage or necrosis on gross inspection

Cassettes Submitted
1 cassette (A1) – all cores in toto

Fixation Time
6–8 hours (ASCO/CAP compliant)

Processing & Staining

Tissue Processing
Standard overnight automated processor; paraffin embedded

Sectioning
5 µm sections, 3 levels

Routine Stain
Haematoxylin & Eosin (H&E)

Special Stains
Periodic Acid–Schiff (PAS); Masson Trichrome

Immunohistochemistry Panel
ER, PR, HER2, Ki-67, CK5/6, p63, CD44

Microscopic Findings

Architectural Pattern

The cores show infiltration by a malignant epithelial proliferation arranged predominantly in irregular solid nests and single-file cords (*Indian-file pattern*) traversing a desmoplastic stroma. Focal gland formation is present, accounting for approximately 10–15% of the tumour volume. No evidence of lobular in situ carcinoma is identified in the adjacent tissue.

Cytological Features

- Tumour cells are large with moderate-to-abundant eosinophilic cytoplasm and markedly pleomorphic nuclei (nuclear grade 3).
- Nuclear:cytoplasmic ratio is high; prominent macronucleoli present in the majority of cells.
- Mitotic figures: 12 per 10 high-power fields (HPF), including atypical forms.
- Intracytoplasmic lumina (ICL) focally present; mucin-positive on PAS stain.

Stromal Characteristics

Moderate desmoplastic stroma; scattered lymphocytic infiltrate (TIL score ≈ 15%). Masson Trichrome highlights an increase in collagen deposition around tumour nests. No vascular or lymphatic invasion identified on H&E or D2-40 staining.

Associated Findings

Adjacent non-neoplastic breast tissue demonstrates columnar cell change with atypia (flat epithelial atypia, FEA). Microcalcifications are present in association with both the tumour nests and the benign lobules.

Immunohistochemistry Results

Marker	Result	Score / Extent	Clone	Interpretation
ER (Oestrogen R.)	✓ **Positive**	Allred 7/8 (90%, 3+)	SP1	Strong nuclear positivity
PR (Progesterone R.)	✓ **Positive**	Allred 6/8 (60%, 3+)	1E2	Moderate nuclear positivity
HER2 (c-erbB2)	⊗ Negative	Score 1+	4B5	Incomplete faint membrane staining
Ki-67 (MIB-1)	! Elevated	28% of nuclei	30-9	High proliferative index
CK5/6	⊗ Negative	0%	D5/16B4	No basal phenotype
p63	⊗ Negative	0%	4A4	No myoepithelial layer
CD44	✓ Positive	40% (2+)	IM7	Focal expression

Note: HER2 FISH reflex testing recommended per ASCO/CAP 2023 guidelines (Score 1+ borderline). All controls performed satisfactorily. Automated staining platform: Meridian Benchmark ULTRA.

Histological Grading — Nottingham (Elston–Ellis)

Parameter	Score	Maximum	Comment
Tubule Formation	3	3	<10% tubule formation
Nuclear Pleomorphism	3	3	Marked vesicular nuclei with prominent nucleoli
Mitotic Count	3	3	12 mitoses / 10 HPF (field diameter 0.44 mm)
Total Score	**9/9**	**9**	**Grade 3 (Poorly Differentiated)**

Grading performed on H&E-stained sections at 400× magnification (Olympus BX53 with calibrated eyepiece reticule).

Special Stain Summary

Stain	Findings
PAS (Periodic Acid–Schiff)	Focal positivity in ICL
Masson Trichrome	Desmoplastic stroma
Alcian Blue (pH 2.5)	Focal mucin pools
Reticulin	Disrupted framework

Measurements & Quantitative Data

Parameter	Value
Tumour extent (cores)	3 of 4 cores positive
Max. linear extent	9.2 mm
Percentage core involved	65%
TIL Score	≈ 15%
Microcalcifications	Present

Differential Diagnosis Considered

[1] **Invasive Ductal Carcinoma NST, Grade 3** **FAVOURED** — Supported by solid/cord growth pattern, nuclear grade 3, desmoplastic stroma, ER/PR positivity, and absence of myoepithelial cells (p63, CK5/6 negative).

[2] **Invasive Lobular Carcinoma** — Excluded — Indian-file pattern was initially considered; however, E-cadherin staining (performed reflexly) shows preserved membranous positivity, excluding lobular phenotype.

[3] **Metaplastic Carcinoma** — Excluded — No squamous or mesenchymal differentiation identified; CK5/6 and p63 negative.

[4] **Phyllodes Tumour (malignant)** — Excluded — No biphasic architecture; stromal overgrowth absent; epithelial nature confirmed by IHC.

Surrogate Molecular Subtype

Based on IHC profile (St. Gallen 2023 consensus):

Luminal B (HER2-negative)

ER:	Positive ($\geq 1\%$)
PR:	Positive ($\geq 20\%$)
HER2:	Negative
Ki-67:	High ($\geq 20\%$)

Oncotype DX / Prosigna testing may be considered per MDT guidelines.

Critical / Actionable Findings

- **Malignancy confirmed** — Immediate MDT referral required.
- **Ki-67 28%** — Indicates high proliferative activity; discuss adjuvant chemotherapy with oncology team.
- **HER2 Score 1+** — FISH reflex testing ordered (specimen block A1 forwarded to Vertex Molecular Diagnostics Laboratory).
- **FEA in adjacent tissue** — Bilateral surveillance imaging recommended.

Referring clinician notified by telephone: 14 Nov 2024, 09:47 hrs.

FINAL DIAGNOSIS

Site: Right breast, 2:00 position — core needle biopsy

Diagnosis:

INVASIVE BREAST CARCINOMA OF NO SPECIAL TYPE (NST)
Nottingham Grade 3 (Score 9/9)
ER: Positive (Allred 7/8) | PR: Positive (Allred 6/8) | HER2: 1+ (FISH pending) | Ki-67: 28%

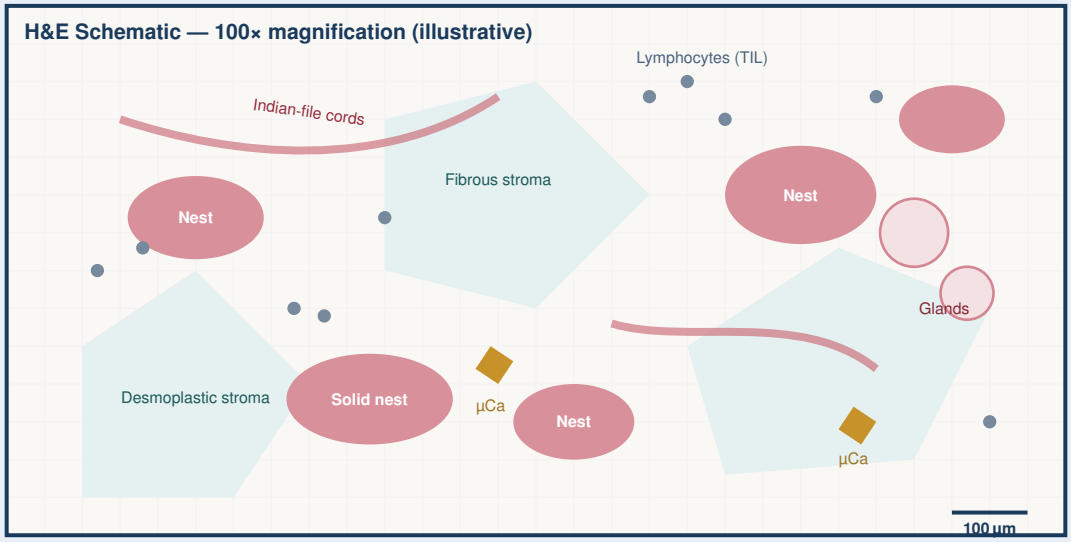
Associated Findings:

Flat Epithelial Atypia (FEA) in adjacent non-neoplastic breast tissue
Microcalcifications present

Staging Correlate (pathological biopsy):

pTx (size not assessable on core biopsy) N0 M0 per AJCC 8th Ed.
Final staging to be assigned post-excision.

Schematic Representation of Microscopic Architecture



Clinical Correlations & Pathologist Recommendations

1. Surgical Management

Surgical excision with sentinel lymph node biopsy is recommended. Wide local excision (breast-conserving surgery) vs. mastectomy to be determined by the MDT following MRI staging. Clip marker placed at biopsy site for surgical localisation.

2. Systemic Therapy Consideration

Luminal B (HER2-negative) subtype with Ki-67 of 28% and Grade 3 morphology warrants discussion of adjuvant chemotherapy in addition to standard endocrine therapy (aromatase inhibitor recommended given post-menopausal status).

3. Genomic Testing

Oncotype DX Recurrence Score or Prosigna (PAM50) testing may refine chemotherapy decision-making in this pN0 setting (per NICE DG34 guidance).

4. HER2 FISH Reflex

HER2 FISH has been requested reflexly. Results expected within 5 business days. Block A1 retained at Meridian Pathology Institute for FISH and future ancillary studies.

5. Surveillance of Contralateral Breast

FEA identified in adjacent tissue and family history of breast carcinoma indicate annual bilateral MRI surveillance per Apex Breast Imaging Network protocol.

Quality Assurance

Slide review:	Dr. Clara S. Okafor, MD
Second opinion:	Dr. James Whitfield, FRCPath
QA status:	Passed
EQA scheme:	Nimbus Pathology EQA 2024
Turnaround:	3 calendar days

Pathologist Authorisation

Reporting Pathologist:	Dr. Clara S. Okafor, MD
Qualification:	MBBCh, FRCPath, PhD
Date Authorised:	14 November 2024
Digital Signature:	`[Digitally signed -- MPI]`
Report Status:	**FINAL**