The Royal College of Pathologists
Pathology: the science behind the cure

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Can infrared fingerprints help personalise breast cancer care?

Artificial intelligence + FTIR spectroscopy for rapid prediction of HER2 status, treatment response and DCIS progression

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PATHOLOGY AT THE HEART: routine tissue contains a biochemical fingerprint that may support faster, lower-cost precision oncology. **Preliminary results are promising, not yet clinically validated.**

1 CLINICAL NEED & ORIGINALITY

Current pathways can be slow, costly or uncertain:

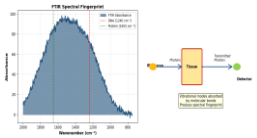
- HER2 IHC/ISH guides targeted therapy, but equivocal 2+ cases require reflex testing.
- Oncotype DX costs about £2,580 and may take around 2 weeks.
- DCIS progression risk remains difficult to predict, creating potential overtreatment.

2 RESEARCH QUESTIONS

Can infrared signatures:

- distinguish HER2 categories?
- predict complete vs incomplete neoadjuvant response?
- identify DCIS likely to progress or recur?
- reach clinically useful sensitivity and specificity?

3 WHY FTIR?



FTIR measures absorption by proteins, lipids, nucleic acids and carbohydrates. The resulting spectrum is a chemical "fingerprint" with no labels or stains.

ETHICS & TRANSPARENCY

Retrospective FFPE tissue; Liverpool University Biobank approval 24-07. Data are de-identified. No patient images or identifiers are shown. Preliminary research only; no clinical decisions should be based on these findings. Conflict of interest: LDIR technology is patent-pending.

4 TECHNICAL APPROACH



FFPE selection → adjacent H&E annotation → LUMOS II FTIR imaging → spectral preprocessing → metric analysis / neural network → biomarker panel.

RIGOUR & REPRODUCIBILITY

- Three sequential 5 µm sections; H&E on adjacent sections and FTIR on CaF_2 discs.
- 4000–750 cm^{-1} range, 4 cm^{-1} resolution, 8 co-additions.
- Rubber-band baseline correction, fingerprint-region truncation and vector normalisation.
- 60/20/20 split, neural-network optimisation and 10-fold cross-validation.
- Sensitivity, specificity, accuracy and ROC-AUC reported.

CRITICAL INTERPRETATION

Strengths

- Millions of spectra and compact, interpretable wavenumber panels.
- Direct link between histopathology regions and biochemical signatures.

Limitations

- Patient numbers remain small despite very large spectral datasets.
- Spectra from one patient are correlated, so patient-level validation is essential.
- HER2 2+ groups are biologically overlapping and heterogeneous.
- External, prospective validation and calibration are required before clinical use.

5 PRELIMINARY RESULTS

AUC 0.90

NEOADJUVANT RESPONSE
Pilot n=10 patients; 2.5M spectra
Sensitivity 82.9% | Specificity 81.2%
Accuracy 81.9% (estimated ±7%)

AUC 0.86

HER2 CLASSIFICATION
0+ vs 3+: 7 + 7 patients; ~3.5M spectra; 8 wavenumbers.
2+ FISH+ vs FISH−: ~5 + 5 patients; AUC ≈0.73, indicating a harder, overlapping distinction.

n 6

DCIS FEASIBILITY
8 candidate IR biomarkers.
Progression/recurrence: sensitivity 79%, specificity 77%.
Non-progressing DCIS: sensitivity 84%, specificity 75%.

6 IMPACT ON FUTURE PRACTICE

Next steps

1. Expand cohorts and lock analysis plans.
2. Validate by patient, site and scanner, not only by spectra.
3. Integrate RNA sequencing to explain the biology behind candidate wavenumbers.
4. Co-design a breast-specific LDIR Wand and map UKCA / CE-mark requirements.

Potential impact
A rapid, label-free triage or adjunct test could support earlier treatment decisions, reduce reliance on centralised assays and widen access in laboratories with limited molecular capacity.

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Selected references: Ingham et al., 2022, IOP SciNotes 3:034001 | Ellis et al., 2023, Analyst 148:1948–1953 | Bhargava, 2023, Annu Rev Anal Chem 16:205–230 | Rakha et al., 2015, J Clin Pathol 68:93–99 | Holt et al., 2024, Br J Cancer 130:1149–1156