

Projects in the use of AI identification and quantification of breast tumour pathological features.

Supervisors:

Ciarán Eising (UL Electronic and Computer Engineering)

James Brown (UL Biological Sciences)

Máire Lavelle (University Hospital Limerick, Consultant Pathologist (Breast))

Number of projects sought: 2

Breast cancer affects 1 in 8 women in Ireland, and number affected is growing. The large number of cases puts a large burden the clinical system, particularly clinical pathologists responsible for confirming the presence of tumour cells in biopsy, and then categorising the breast tumour type. Current approaches to selecting the correct treatment regime for breast cancer require precise diagnostic stratification of patient tumours, which both predicts survival and informs tailored therapeutic strategies. This stratification is primarily based on manual interpretation of pathology slides from tumour biopsies- which is both time-consuming and has known interobserver variability (even by experienced trained clinical pathologists).

This pathological categorisation (counting the number of tumour cells present, quantifying specific staining patterns) is crucial for informing clinicians choice of treatment options and treatment regimes. While several key biomarkers used are relatively definitive, some are subjective and require interpretation by experienced pathological experts. Digitization in pathology facilitates computer-based image analysis solutions, which have the potential to provide a more objective and quantitative slide reviews. The aim of this project is to explore the ability of AI to define and quantify key clinically relevant pathological features in patient's tumour samples (such as objective quantification of current clinical biomarker intensity's such as Her2 staining, and improve cell counts, defining cell morphology, size, and spatial location).

The overall goal is to determine which breast tumours respond to Herceptin/trastuzumab. This is an antibody used to treat breast cancer, specifically for cancer that is HER2 receptor positive. This is important because it helps to determine whether the patient gets neoadjuvant chemotherapy i.e. chemo BEFORE surgery and dictates adjuvant chemo (chemo after surgery). Herceptin treatment is very expensive, so clinicians are judicious in prescribing it.

Project 1:

What we'd like AI to do with the Her2 immunohistochemistry is calculate the completeness of membrane staining, the intensity of staining and what percentage of the cells are staining. Then assign it a score 0, 1+, 2+ or 3+ (see the figures below - Fig 1).

Project 2:

What I'd like it to do with DDISH is count the black dots and red dots in 20 tumour cells and give the ratio (Fig 2 - 4).

Spectrum of HER2 positivity according to ASCO/CAP guidelines

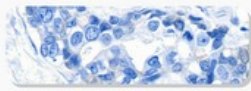
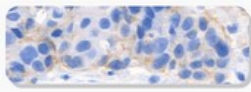
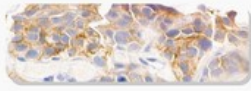
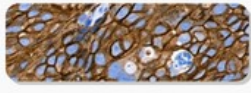
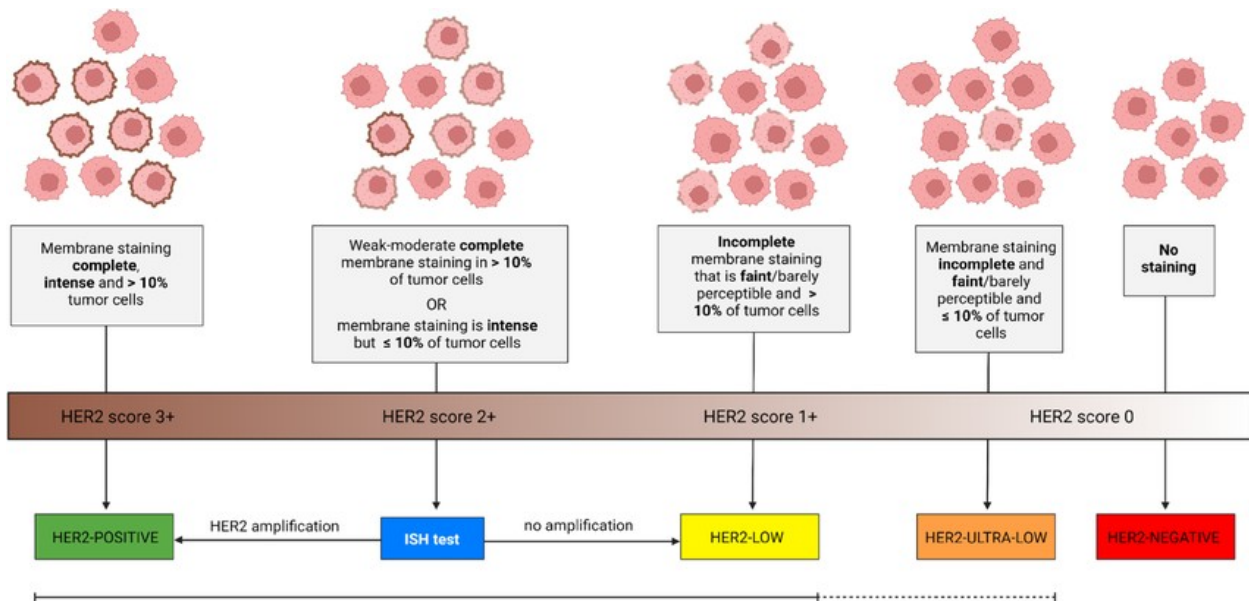
	IHC score	HER2 test interpretation	HER2 status	Spectrum of HER2 positivity
	0	No staining or incomplete and faint/barely perceptible membrane staining in $\leq 10\%$ of tumor cells	Negative	
	1+	Incomplete and faint/barely perceptible membrane staining in $>10\%$ of tumor cells	Low	
	2+	Weak-moderate complete membrane staining in $>10\%$ of tumor cells OR intense membrane staining in $\leq 10\%$ of tumor cells	ISH amplification?	
	3+	Complete and intense membrane staining in $>10\%$ of tumor cells	Positive	

Figure 1 Spectrum of HER2 positivity according to ASCO/CAP guidelines



Potentially expanded spectrum of HER2 positivity
Figure 2 Her2 IMMUNOHISTOCHEMISTRY in diagrammatic form

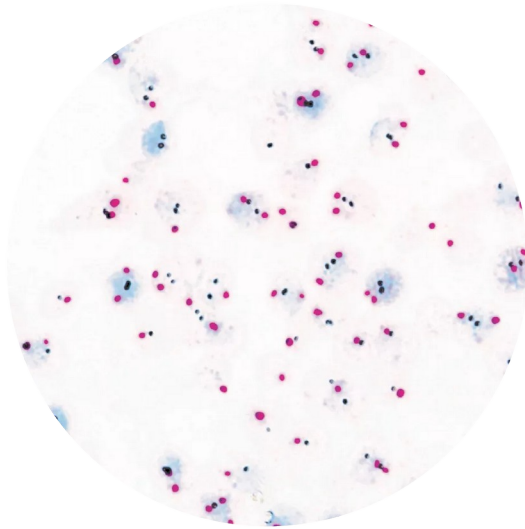


Figure 3 DDISH NON-AMPLIFIED. On average each cell has approx. 2 black dots (Her2 gene) and 2 red dots (Chromosome 17 gene)

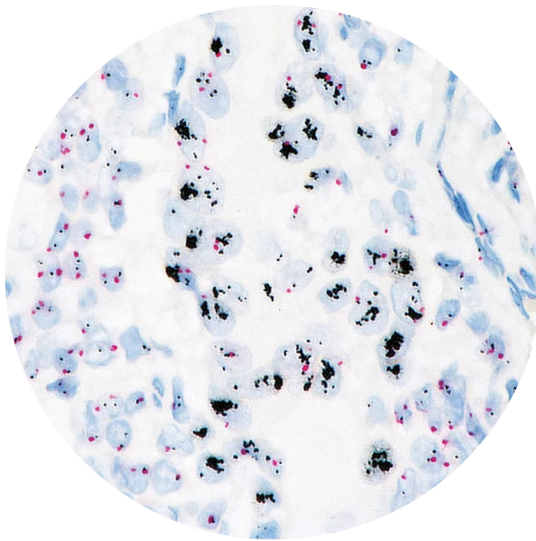


Figure 4 DDISH AMPLIFIED: the tumour cells on average have MANY more black dots than red dots