PREDICTION OF HER2 STATUS IN BREAST CANCER DIRECTLY FROM HISTOPATHOLOGY SLIDES USING DEEP LEARNING

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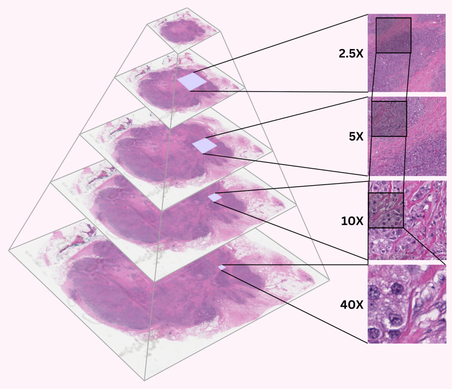
Introduction

- **Human epidermal growth factor 2** (HER2) is an oncogene that has an important role in cell growth and differentiation [1]
- Amplification of the HER2 gene is associated with aggressive tumour growth and poor prognosis [2]
- HER2+ cancer accounts for **20-25%** of all breast cancers [1]
- Standard breast cancer treatments are dependent on various biomarkers including HER2 status [3]
- HER2 testing is routinely applied to invasive breast cancer cases and serves as the primary biomarker for HER2-targeted therapies [4]
- Standard testing methods include immunohistochemistry (IHC), with equivocal cases confirmed by fluorescence in situ hybridisation (FISH) [5]
- These **molecular assays** are time-consuming, cause tissue damage, are expensive and not available in many countries; results can also vary across laboratories due to preparation protocols and pathologist subjectivity [6]
- The use of inexpensive, **widely available** H&E slides can decrease costs and accelerate biomarker detection, reducing time to treatment decisions
- Changes at the molecular level can bring about phenotypic changes in tumour cells as well as their microenvironment [7]
- **Can molecular features of cancer be inferred from morphological features in H&E images alone?**

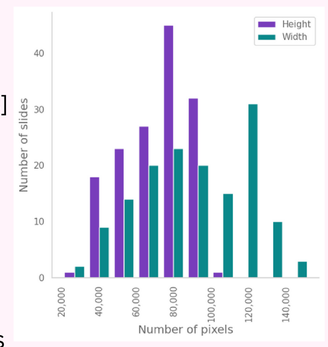
Digital Slides

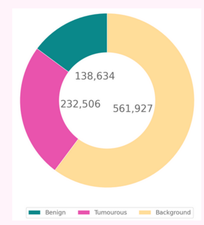
- Samples stained with **Haematoxylin and Eosin stain (H&E)**
- Typical pathology samples are digitised at a resolution of .25 microns/pixel, or 40X magnification ~ 10 GB uncompressed per 15mmx15mm sample
- Whole slide image (WSI) files are contained in an image pyramid
- Multiple images are stored at different resolutions

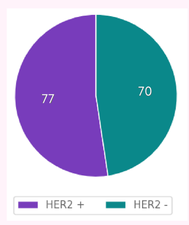


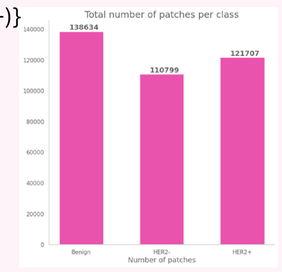
Dataset

- **147 TCGA-BRCA** whole slide images with available HER2 status were downloaded from the GDC portal [8]
- Annotated areas of invasive breast carcinoma were obtained from [9] through the TCIA platform [10]
- Average image dimensions at **10X** magnification: (89 9512, 71 082)
- 256x256 patches ~ 6348 per slide
- **364, 585** tissue patches with classes {benign, tumour (HER2-), tumour (HER2+)}



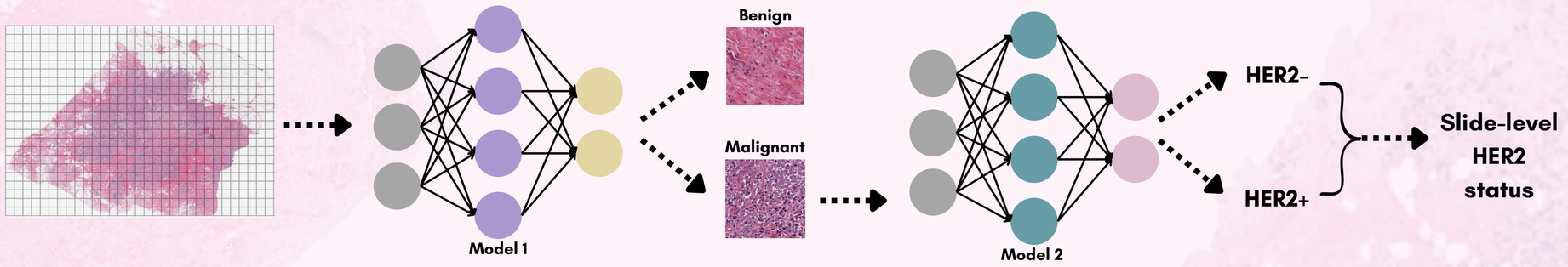






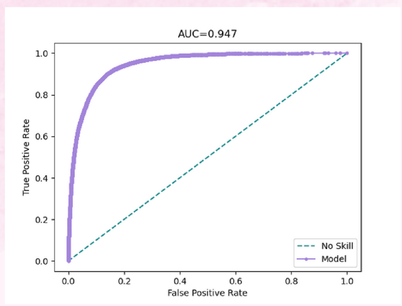
Methods

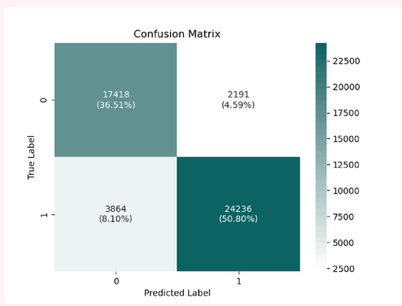
- Stage 1: 'Segmentation' model -> a 2-class patch classification problem
- Stage 2: Status prediction
- Background patches are ignored due to computational costs
- Implement **Inception-v3** (stage 1) and **InceptionResNet-v2** (stage 2) model architectures
- Patch-level output utilised to determine slide-level HER2 status



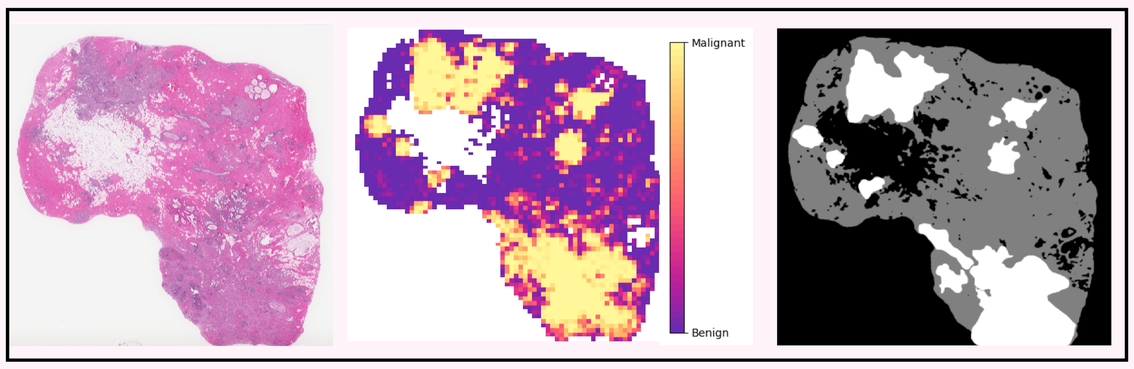
Results

Stage 1

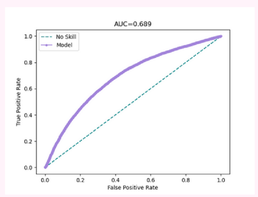




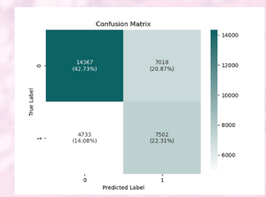
CLASS	Precision	Recall	F1-score
0: Benign	0.82	0.89	0.85
1: Malignant	0.92	0.86	0.89



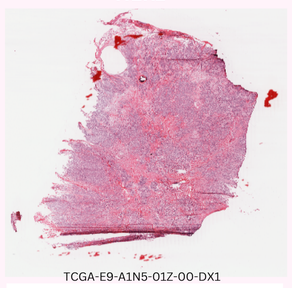
Stage 2 - initial results



CLASS	Precision	Recall	F1-score
0: HER2-	0.76	0.67	0.71
1: HER2+	0.52	0.61	0.56

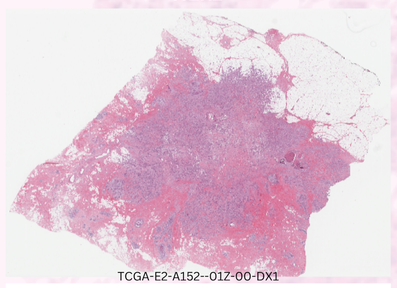


HER2 -

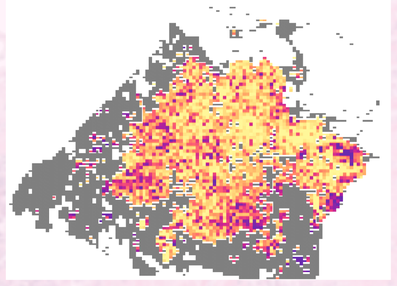


TCGA-E9-A1N5-01Z-00-DX1

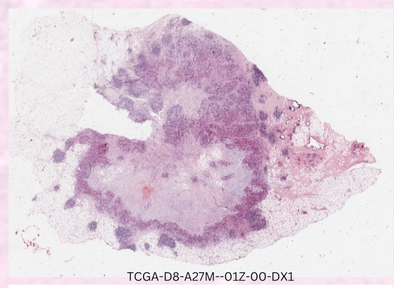
HER2+



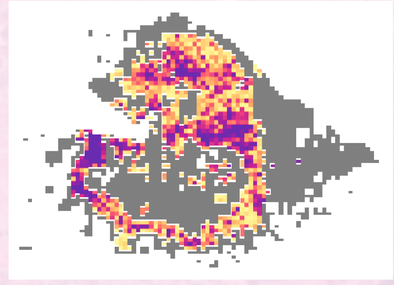
TCGA-E2-A152--01Z-00-DX1



HER2-



TCGA-D8-A27M--01Z-00-DX1



HER2- HER2+

Next steps...

- Cross validation for both models
- Report AUC confidence intervals via bootstrapping
- Further stage 2 model training for improved results
- Calculate slide-level HER2 status from patch-level predictions
- Test models on independent dataset
- Investigate saliency maps using SmoothGrad for stage 2 model interpretability

References

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