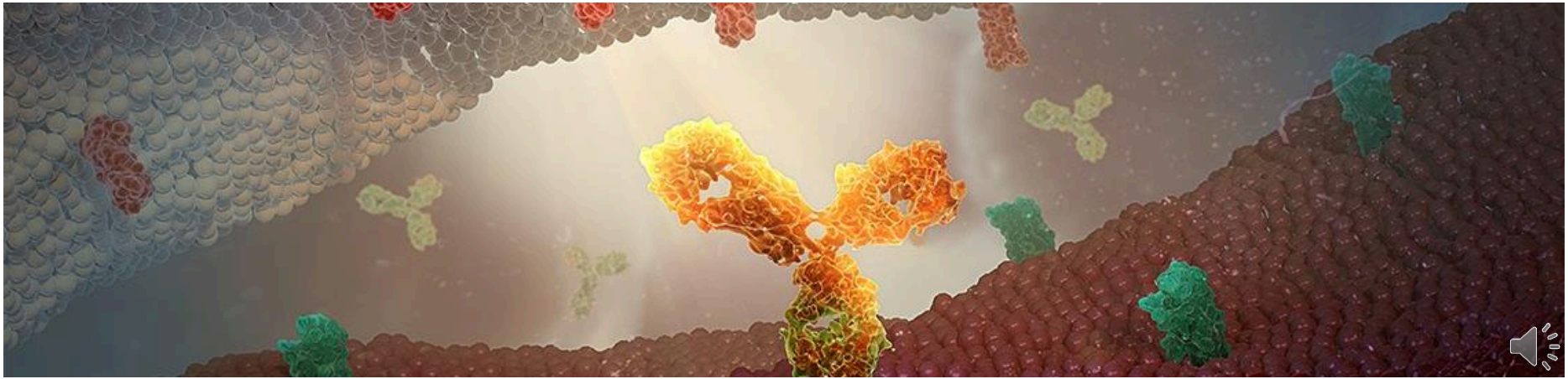
Breast cancer patient stratification using domain adaptation-based lymphocyte detection in HER2 stained tissue sections

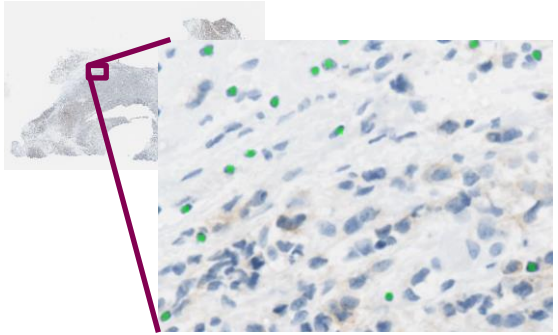
Ansh Kapil[1] , Armin Meier[1], Anatoliy Shumilov[1,] Susanne Haneder[1,] Helen Angell[2] and Günter Schmidt[1]
[1] AstraZeneca Computational Pathology, Munich, Germany
[2] AstraZeneca Translational Medicine, Cambridge, UK



Problem Statement and Motivation

Quantify tumor infiltrating lymphocyte (TIL) population on HER2 stained TNBC tissue sections and assess prognostic value of stromal TIL density as a biomarker

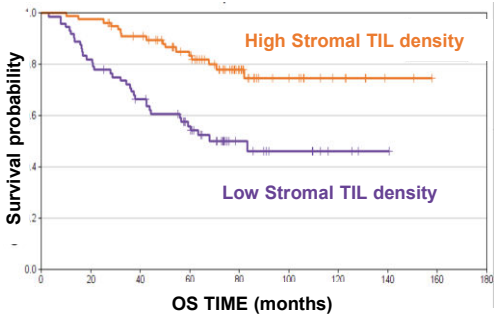
Image analysis



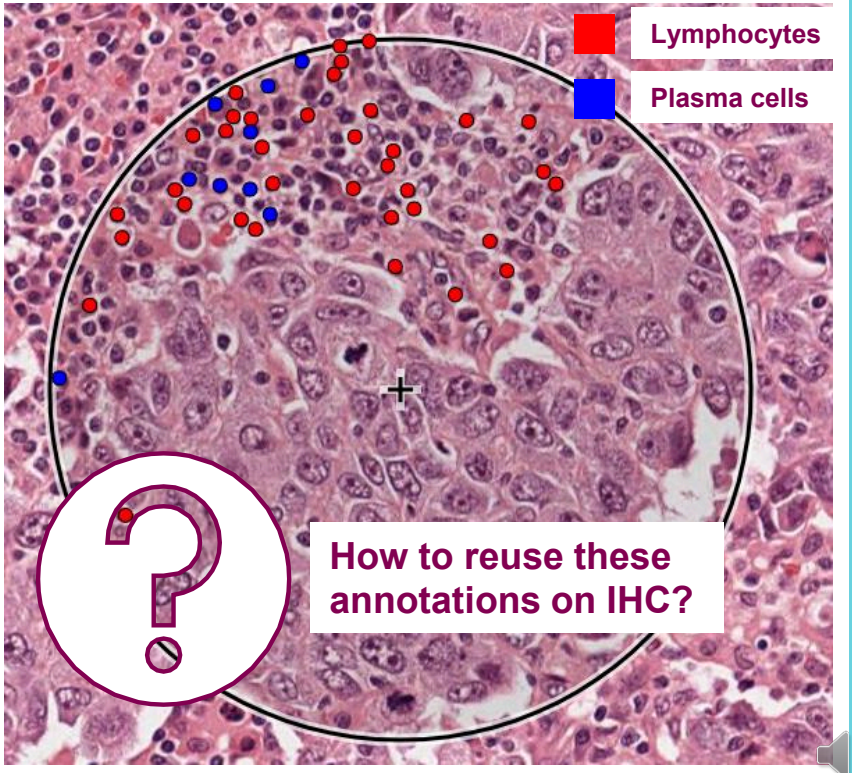
Detected tumor infiltrating lymphocytes (TILs)

TIL detection directly on IHC will allow us to do survival analysis using TIL features as well as spatial relationship analysis of TILs and HER2 positive tumor cells with single tissue section.

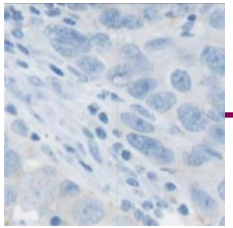
Survival analysis



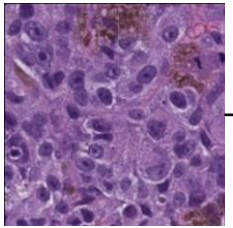
Annotations available only on H&E
How to reuse them on HER2 IHC?



Method – CycleGAN with adaptive instance normalization*



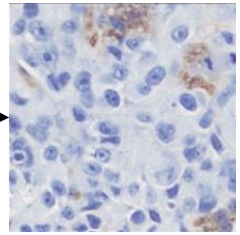
Style image from HER2 domain



Real image from H&E domain

Style Encoder

Generator



H&E image transformed to HER2 domain

Scale vector

Shift vector

$$\mathrm{AdaIN}(x, y) = \sigma(y)\left(\frac{x - \mu(x)}{\sigma(x)}\right) + \mu(y)$$

Instance Norm

Huang et al 2017: Arbitrary Style Transfer in Real-time with Adaptive Instance Normalization

Normal Residual block

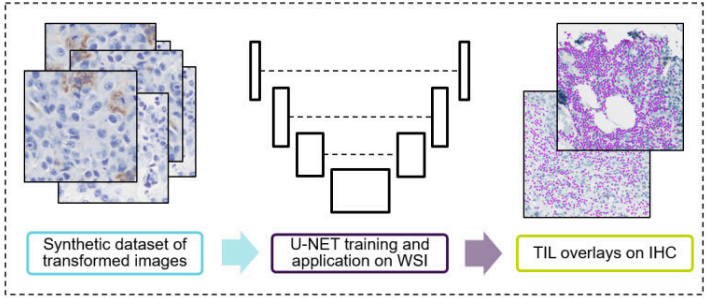
Residual block with adaptive instance normalization

Adaptive instance normalization enables realistic style transfer

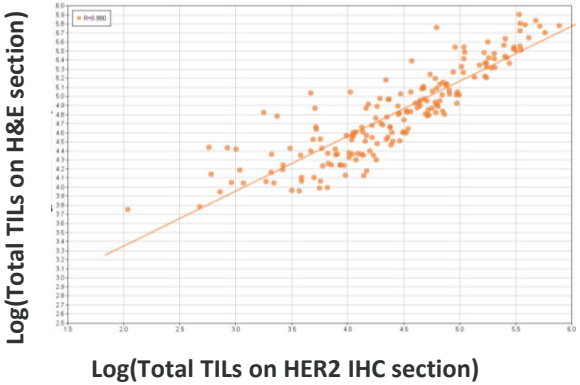
*Full architecture not shown for time concerns. Please follow the original CycleGAN paper here.

Results – Analytical and clinical validation

Model training and Analytical Validation



Strong correlation of TIL counts on H&E and HER2 sections from the same tissue block



Test results against pathologist annotations

F1 D=10px	0.68
SCC	0.93
Total ROIs	38
Total Cells	3144

UNet: Ronnenberger et al. 2015

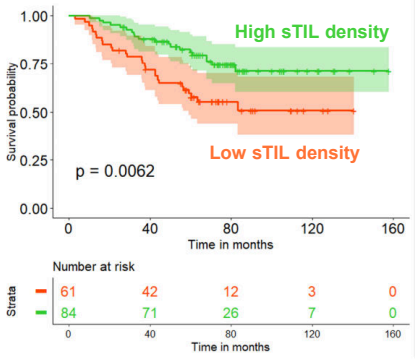
ROI: Regions of interest

SCC: Spearman correlation coefficient

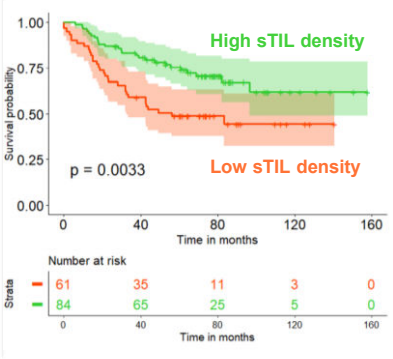
Clinical validation on a TNBC cohort* (N=145)

Using stromal TIL (sTIL) density as a biomarker, we get significant stratification for both OS and PFS.

Overall survival



Progression free survival



- Results are 2-fold cross-validated*.
- The cohort is NOT treated for IO therapies, only with Standard of care (Chemo/radio therapy).

* If we optimize sTIL density cutoff for best log-rank p-value for OS/PFS, the cutoff is 752 sTILs/mm^2