

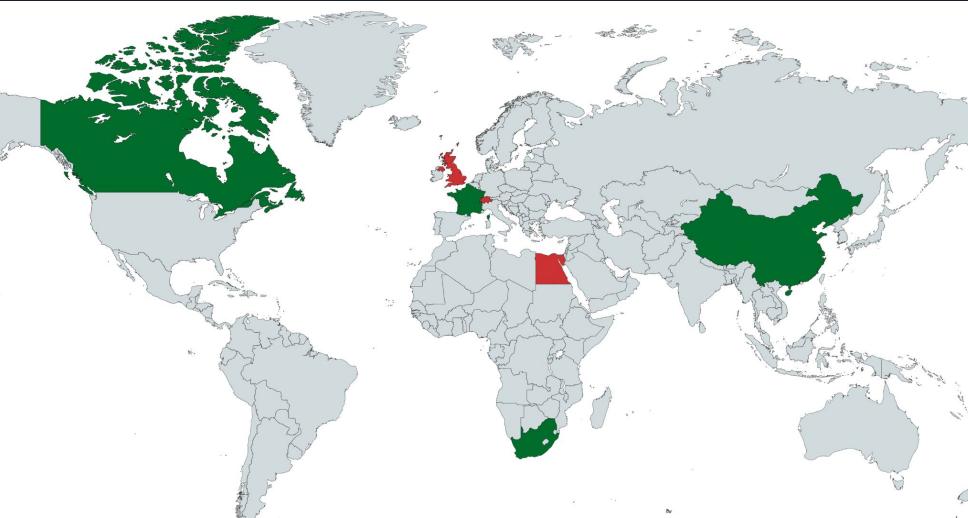


ORLIAn presents: Eln-Al-ny

Modeling pathology data to predict cancer survival

What is ORLIAn?

Wide range of skills from data science to biological science. 2 data scientists, 1 biologist



Project set up to tackle Challenge 1, made of international volunteers, spanning across different time zones!

I played in all the countries where the core contributors are from, so they named it after me





How did we approach this challenge?

Literature review
for ideas

Evaluation using Feature Selection (Leave-One-Out) and Feature Importance (XGBoost) methods, while checking with medical literature for sanity checks to get our answer

November

Initial experiments suggested metadata and image data alone wasn't sufficient.

December

Develop model, training for all the data (full network), optimize for performance against Test Macro

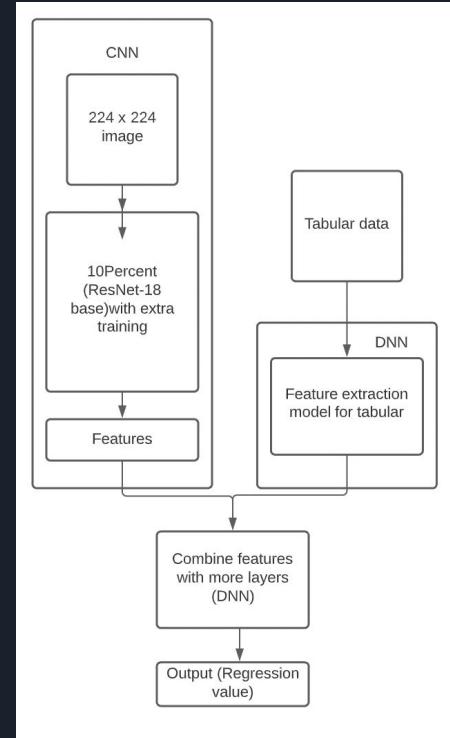
January

What did we deliver?

1. Trained the EI-nAI-ny model using a novel approach: self supervised contrastive learning pretrained [1] model, with both convolutional and tabular DL elements combined into one element. This is then visualized using GRAD-CAM
 - a. Trained using K-Folds Cross Validation
 - b. Purpose is to overlay heat-maps over TIFFs to see which layer's it best represents
2. Conducted analysis of the TIFF files by our team's biological expertise

[1] Using TenPercent as a foundation- ([Self supervised learning for digital histopathology](#))

Basically, we used another model which identifies lung, breast cancer etc. as a starting point, made it look at ENT images using the dataset (training) and adapted it to work on the task (figuring OS from the images)

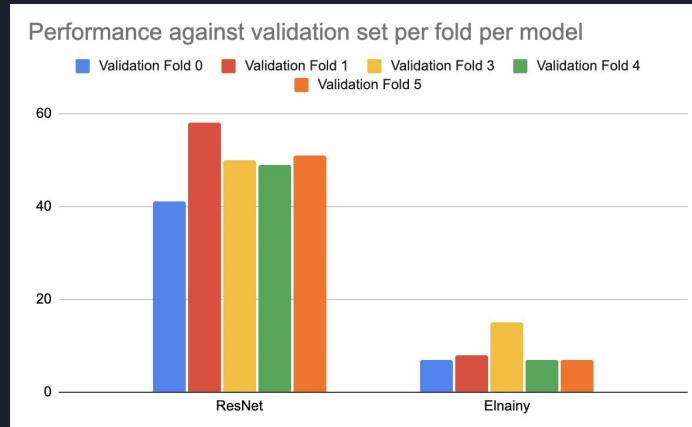


How did we do?

Best ever model against the Dataiku macro scored 0.829 (MAPE - mean absolute percentage error)

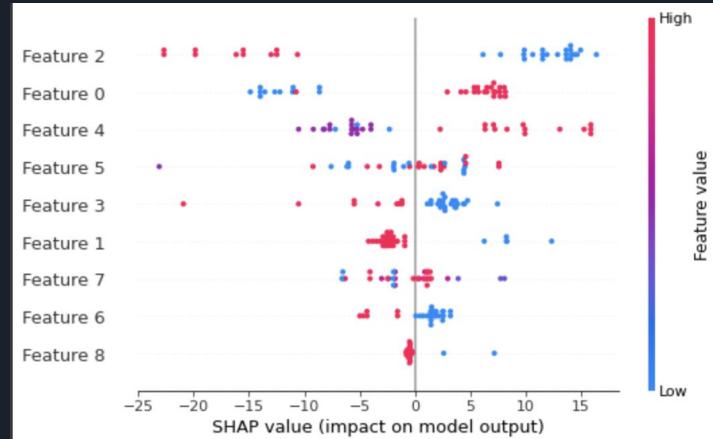
Current model against the Dataiku macro scored 5.77 (MAPE)

EIn-AI-ny outperforms against its original ResNet-18 model (just the vanilla regressor version, fixed weights) significantly. We used MAE (mean absolute error) during validation evaluation in each fold.



Best ever is better than your current?

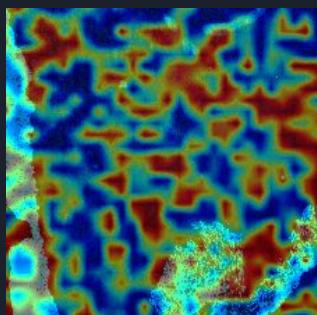
- Experiments suggested decisions coming primarily from tabular data
- Turns out, our engineered features really help it out! (Feature 2)
- Image data wasn't able to learn too well on its own
- XGBoost with just tabular scored 8.40696 on its validation set (MAE)
- We fixed this exploit by removing the offending features and training again



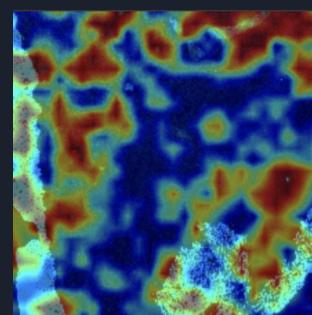
Experiment: Just tabular suggesting feature importance



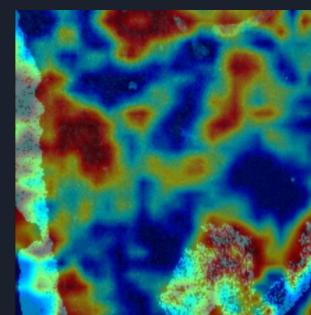
Far better at grasping
microenvironmental
information



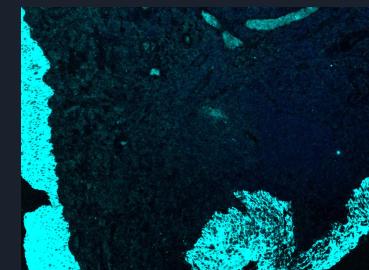
ResNet-18



TenPercent



EIn-Al-ny



Original image

Biological insights

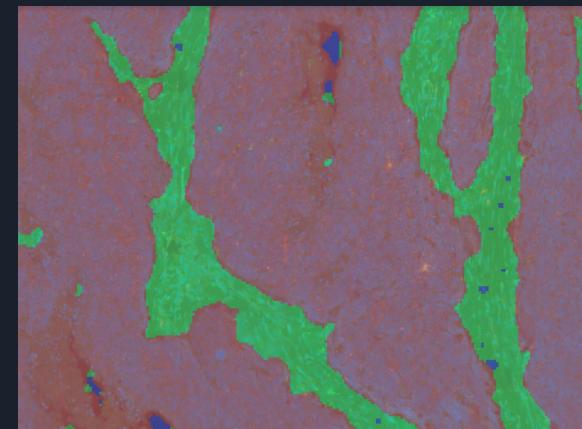
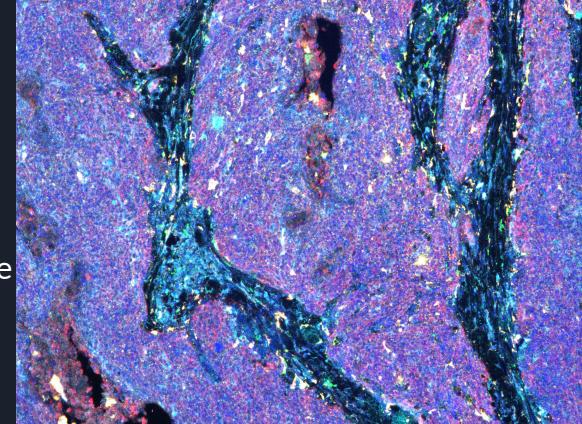
ORLIAn's expert biologist analysed the TIFF images in ImageJ, revealing complex arrangements of marker staining and inflammatory cells in both tumor and stromal compartments

Previous analyses* suggested in another tumor type, that cells expressing the surface protein PD-1 (programmed cell death 1), acting after activation of T-lymphocytes and persisting in the presence of stimuli, could diminish survival expectancy.

The histochemical stains likely highlight white blood cells (CD4 and CD8 T-lymphocytes, B-lymphocytes, macrophages, or natural killers (NK)), such that markers 1-6 can co-localise.

Whether this occurs in the tumor or the stroma probably determines OS.

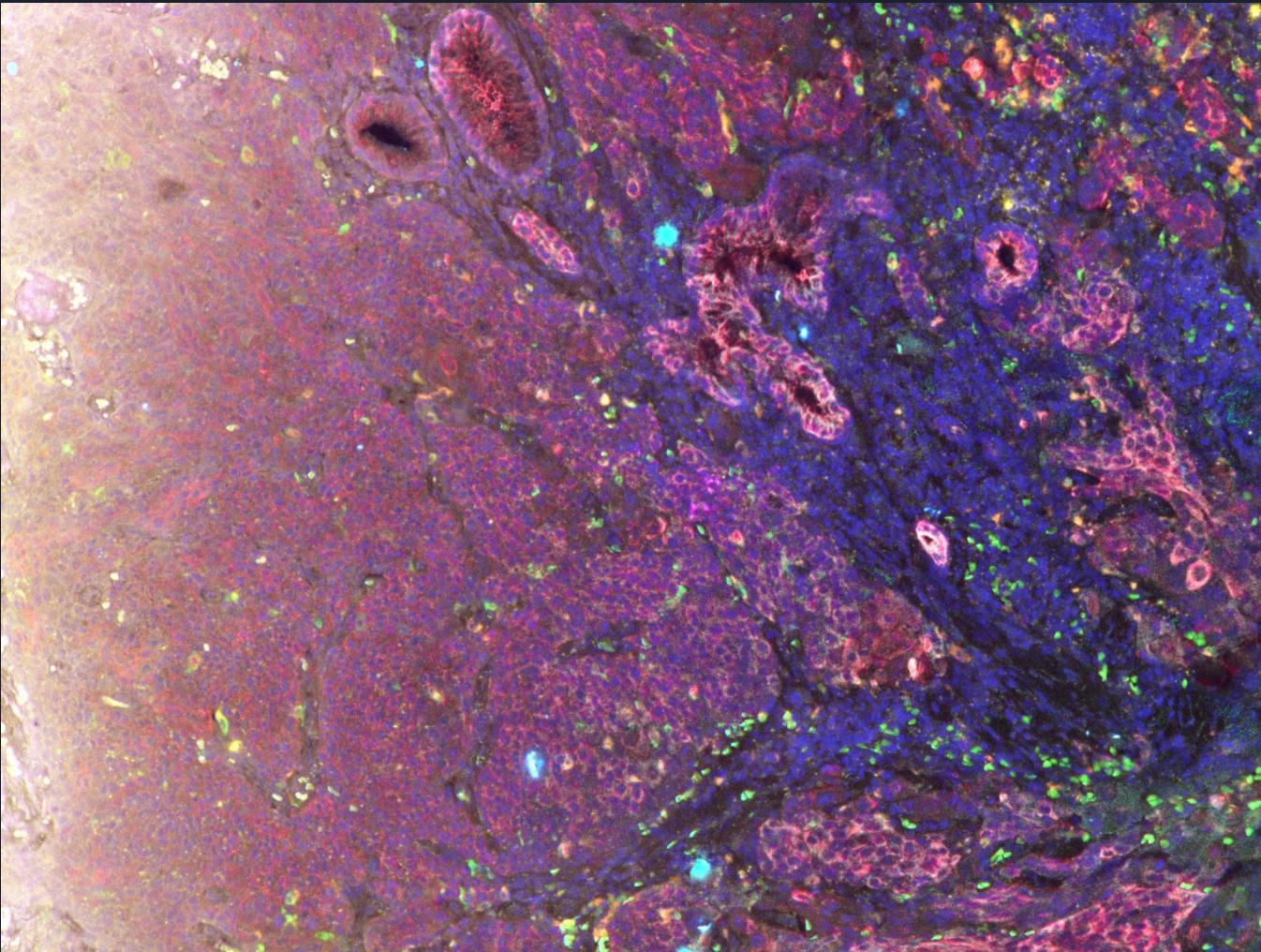
Overall levels of staining may even correlate with a poor prognosis.
Current work may thus be validated by our model.



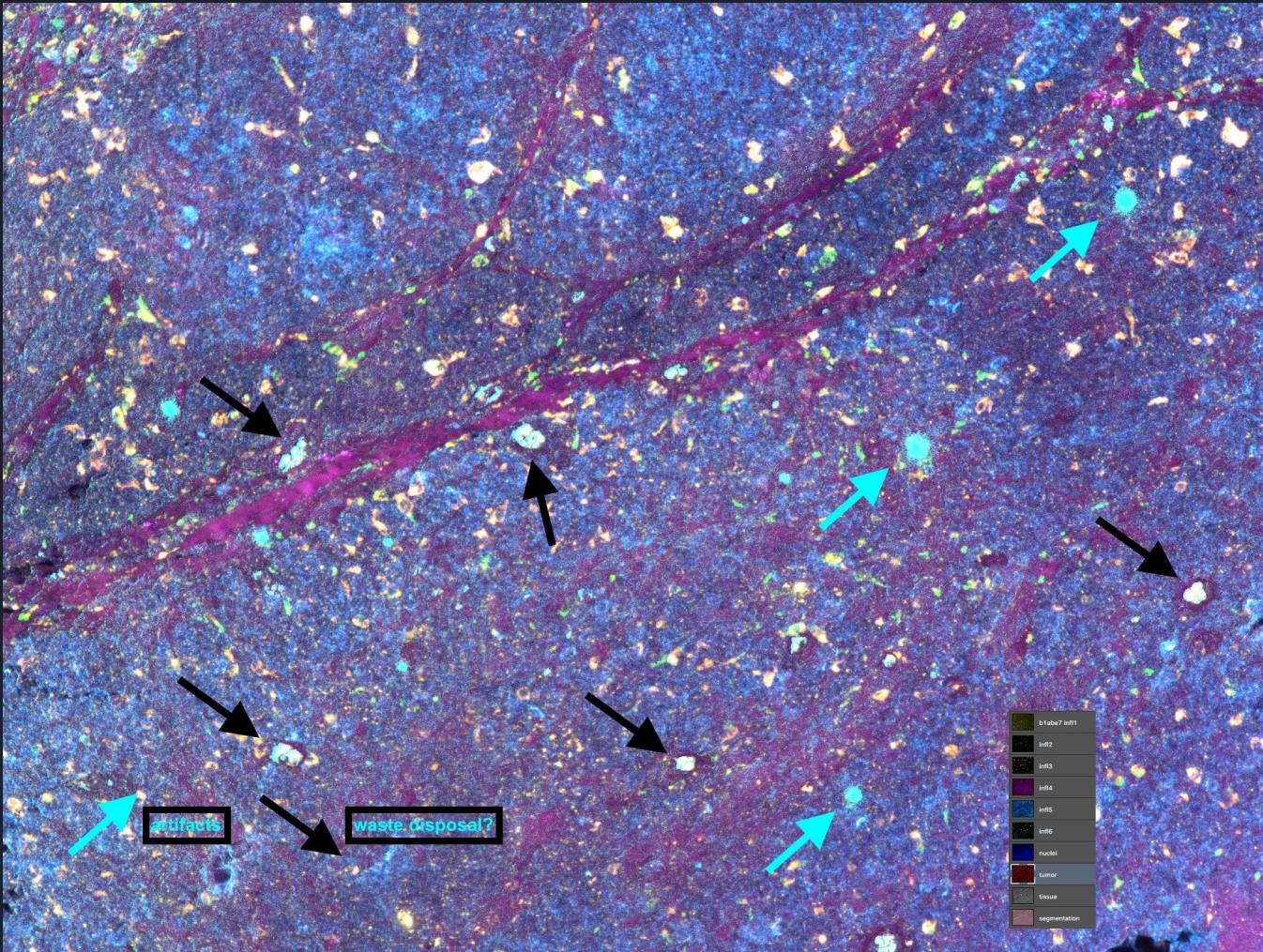
*DOI: 10.1007/s12105-020-01147-x

More detail on these insights can be found [here](#)

OS13



OS72



Putting it all together:

When determining a statistical link between the presence of one or more markers, in the tumor, in the stroma or in the microenvironment as a whole and better overall survival...

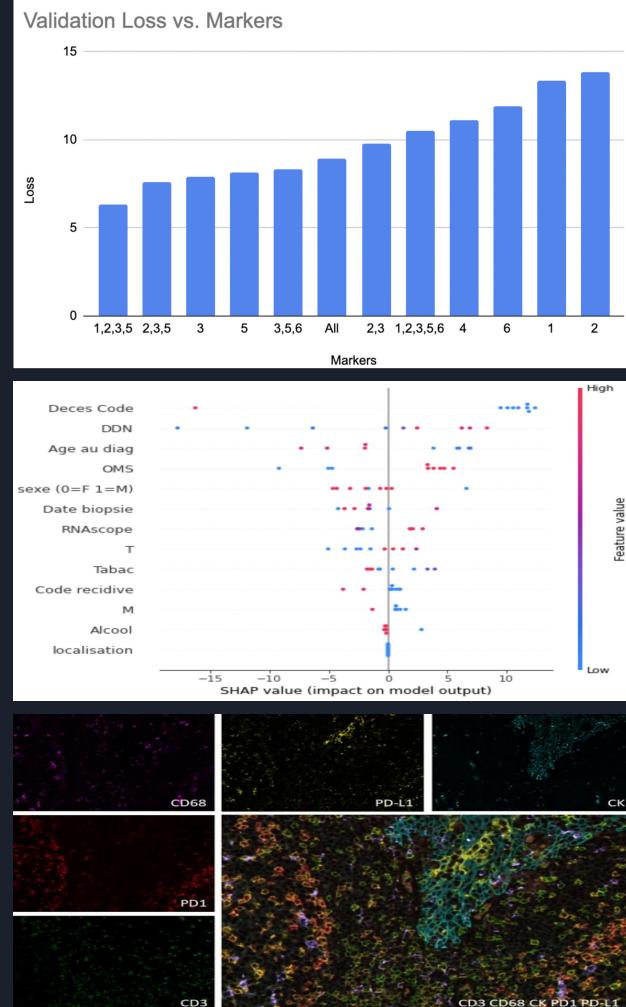
We find that a combination of Markers 3 (Layer 5), 2 (Layer 1) and 5 (Layer 4) and Marker 1 (Layer 8) to be strong indicators for better overall survival

With the corresponding importance individually being: 5 & 3 > 1 & 2 > 6 & 4

In terms of tabular data, we also find that the **whether they died or not (obviously), age of the patient, their gender and severity of condition (OMS)** is a strong indicator on OS

We believe these findings match with the literature available (example: [The Microenvironment of Head and Neck Cancers: Papillomavirus Involvement and Potential Impact of Immunomodulatory Treatments](#))

- We believe if big clumps of marker + staining are in the tumour, without DNA, this may be good for survival
- If 5 or 6 is in the tumour, this results in a lower OS
 - 5 could be the exhausted cells and 6 the





What are the next steps?

As a proof of concept, we believe we have shown that not only can pathology sections be learned by machines, but also that histologically pretrained models can potentially improve analyses. We would like to:

- Apply more rigorous statistical testing with more data to test insights
- Investigate the scans the model have produced further and to a higher degree of accuracy, with 'OS from diagnosis time perhaps a useful modification.
- Test use of GAN architectures to initially train the model on the segmentation image, before any further analysis of each patients' data stack.
- Obtain more extensive validated data-set as this was the largest constraint
- Refine model architecture to optimize for both performance and explainability
 - For example, using something similar to XCaps
(<https://github.com/lalonderodney/X-Caps>)



Retrospective

Insights

1. There is a need for better histological pre-trained models to provide a foundation for these kind of tasks.
2. Imaging from the model can be helpful and useful!

Constraints

1. Small dataset really hampered training
2. Resources and time was hard to find
3. Some of the layers have artefacts impacting performance of the model