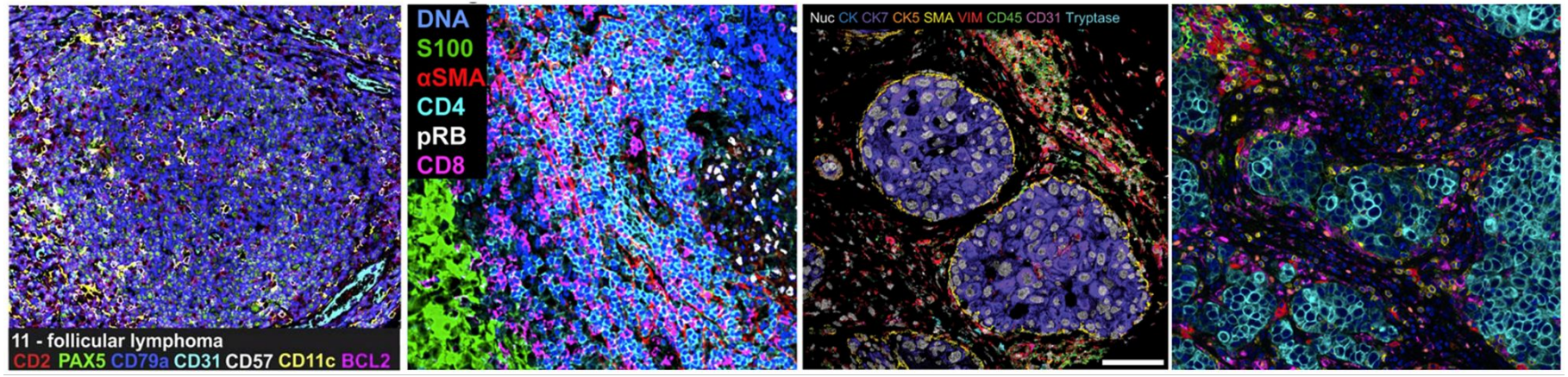
Using vision transformers to predict outcome in ductal carcinoma in situ (DCIS)

IMM310

Candace Liu, Eila Arich-Landkof, Joshua Gillard, Yury Goltsev, John Hickey

Background

- Multiplexed imaging techniques allow us to measure 40+ antibodies on the same tissue section
- MIBI, CODEX, IMC, CyCIF, etc.



CODEX CyCIF MIBI Vectra

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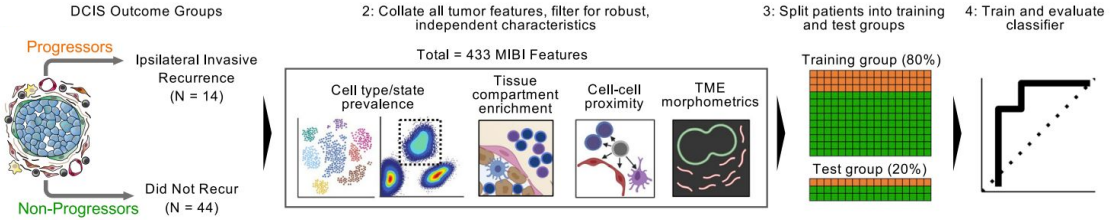
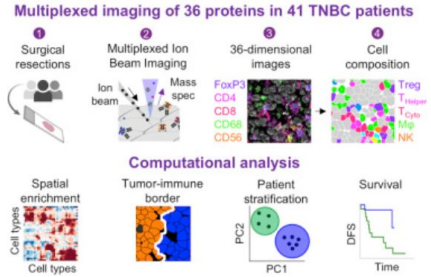
Risom et al., 2022



Keren et al., 2018



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- Can we skip this “feature extraction” step and use a transformer to predict the outcome variable?
    - Let the model tell us what the “interesting” features are

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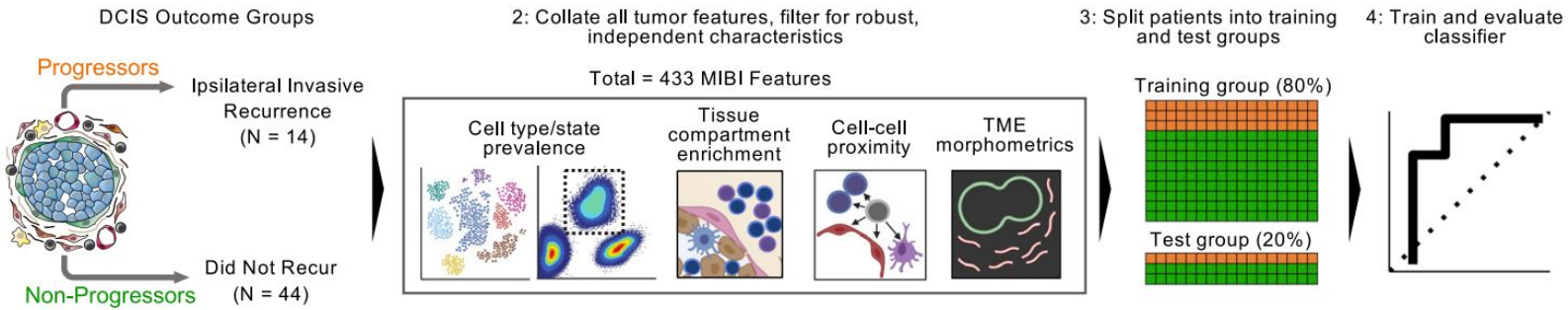

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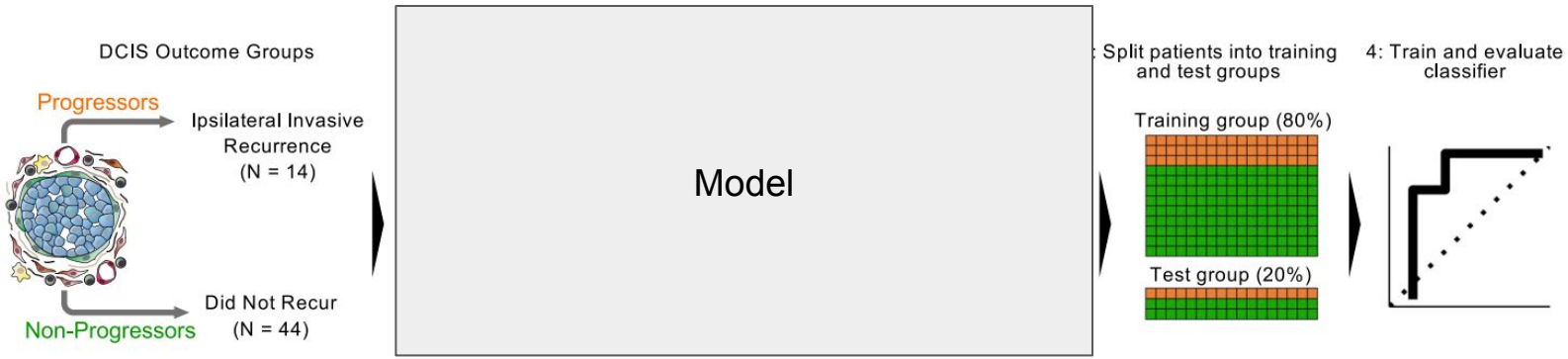
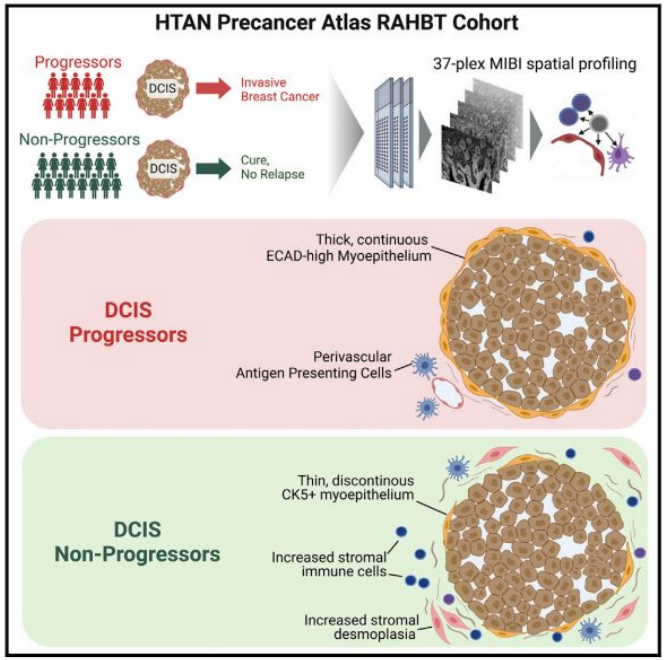


Cell

Transition to invasive breast cancer is associated with progressive changes in the structure and composition of tumor stroma

Graphical abstract



Authors

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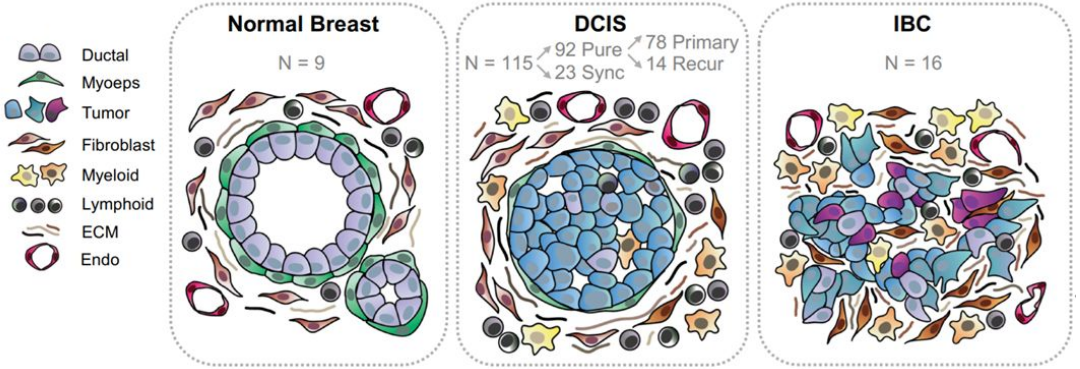
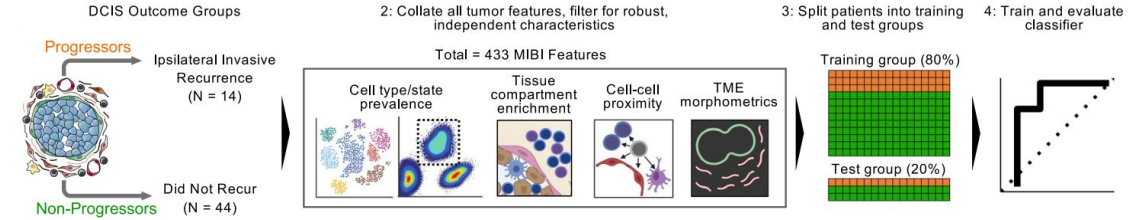
In brief

A spatial imaging atlas of patient-matched ductal carcinoma *in situ* and invasive breast cancer depicts coordinated changes in the tumor microenviroment associated with invasive relapse, suggesting a potential protective role of myoepithelial disruption against invasive progression.

Background


Ductal
Myoeps
Tumor
Fibroblast
Myeloid
Lymphoid
ECM
Endo
Normal Breast
N = 9
DCIS
N = 115
92 Pure
23 Sync
78 Primary
14 Recur
IBC
N = 16


DCIS Outcome Groups
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Ipsilateral Invasive Recurrence (N = 14)
Did Not Recur (N = 44)
Non-Progressors
2: Collate all tumor features, filter for robust, independent characteristics
Total = 433 MIBI Features
Cell type/state prevalence
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3: Split patients into training and test groups
Training group (80%)
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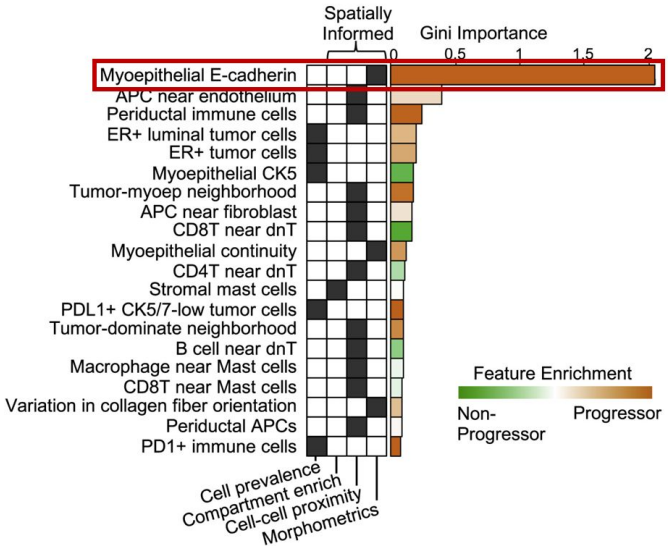
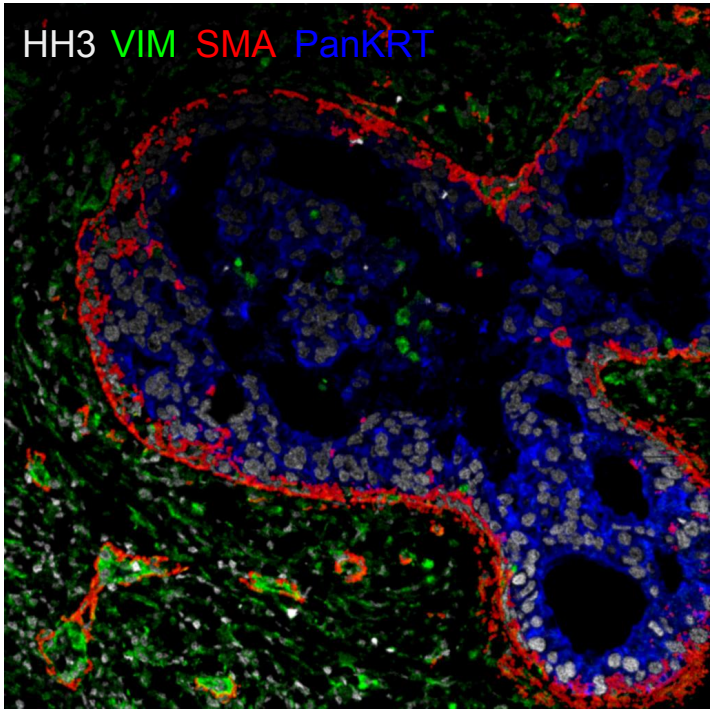
4: Train and evaluate classifier


Spatially Informed
Gini Importance
0
0.5
1
1.5
2
Myoepithelial E-cadherin
APC near endothelium
Periductal immune cells
ER+ luminal tumor cells
ER+ tumor cells
Myoepithelial CK5
Tumor-myoep neighborhood
APC near fibroblast
CD8T near dnT
Myoepithelial continuity
CD4T near dnT
Stromal mast cells
PDL1+ CK5/7-low tumor cells
Tumor-dominate neighborhood
B cell near dnT
Macrophage near Mast cells
CD8T near Mast cells
Variation in collagen fiber orientation
Periductal APCs
PD1+ immune cells
Cell prevalence
Compartment enrich
Cell-cell proximity
Morphometrics
Feature Enrichment
Non-Progressor
Progressor

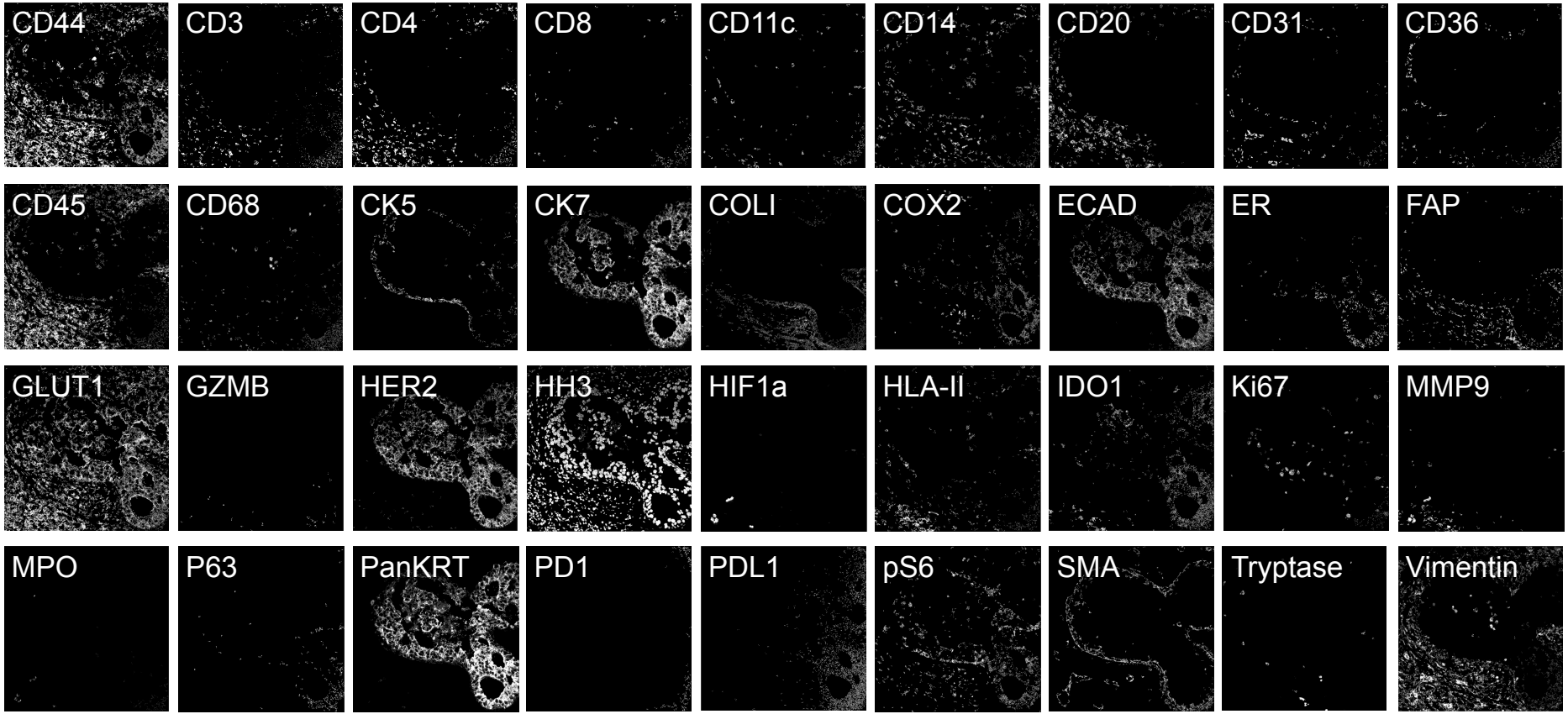
Dataset details

- 58 primary DCIS samples
  - 44 non-progressors, 14 progressors
- Imaged 41 proteins per sample using MIBI-TOF
- **Goal**: stratify non-progressors and progressors using MIBI-TOF images

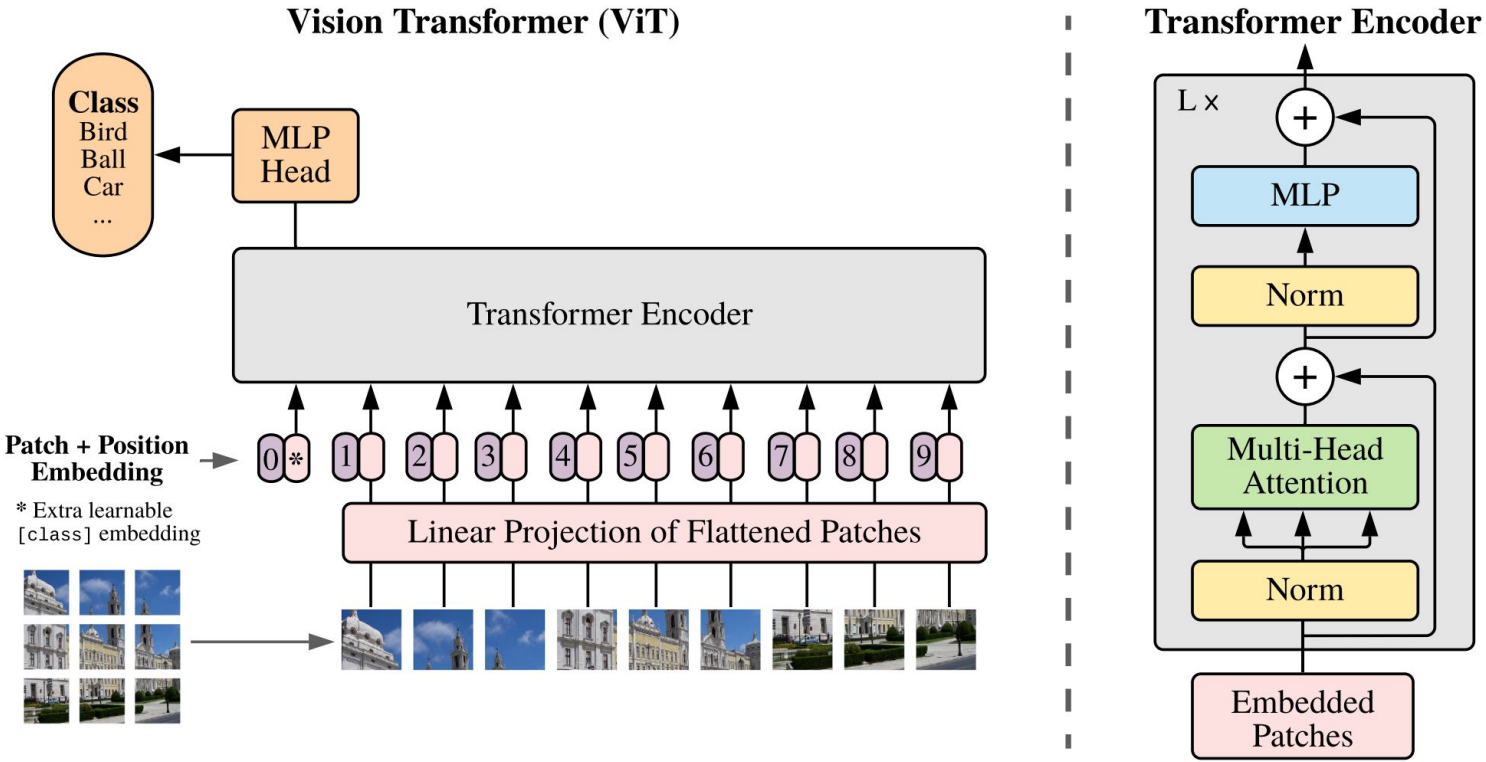
41-plex MIBI images



41-plex MIBI images



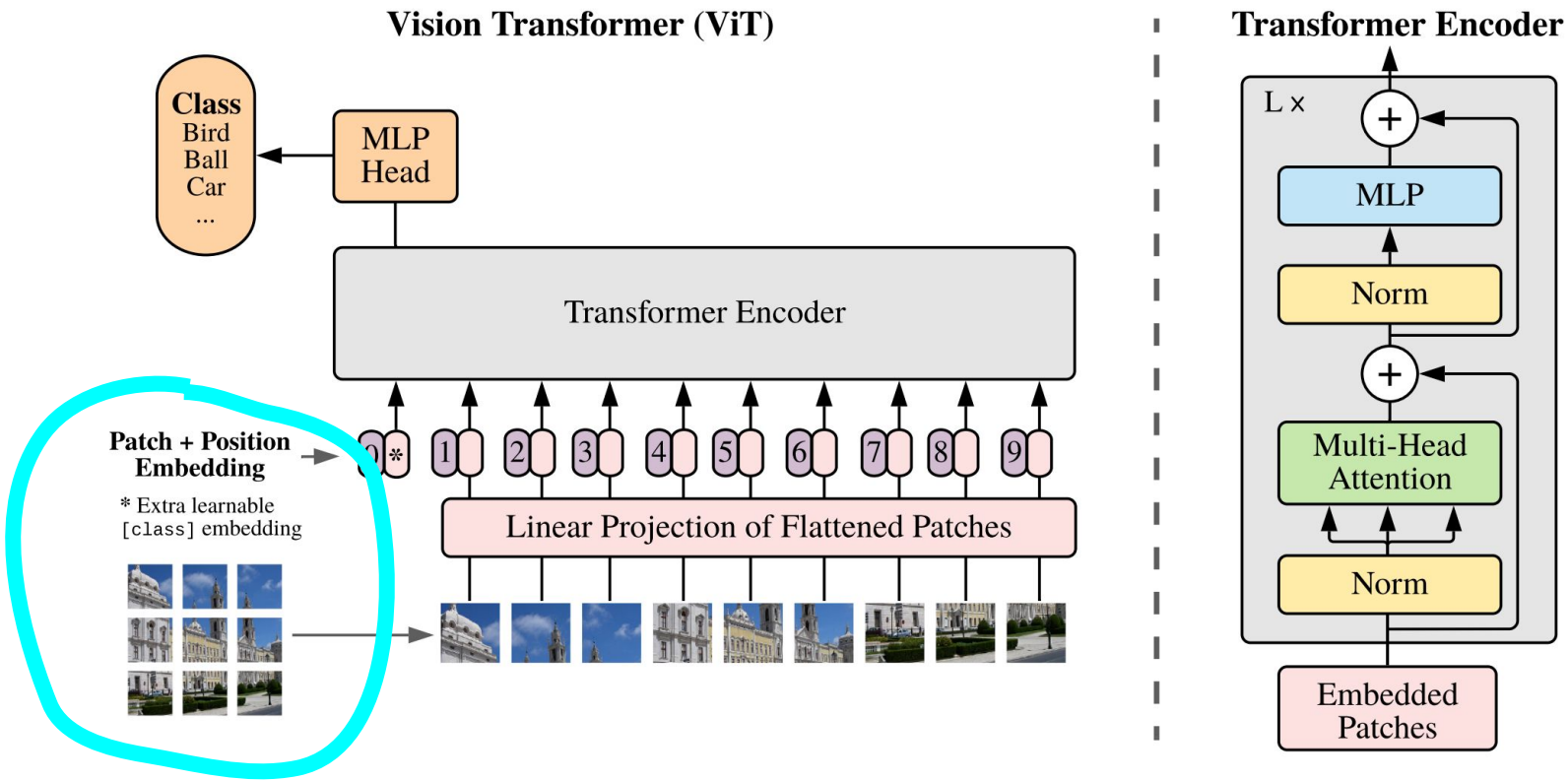
Vision transformer (ViT)



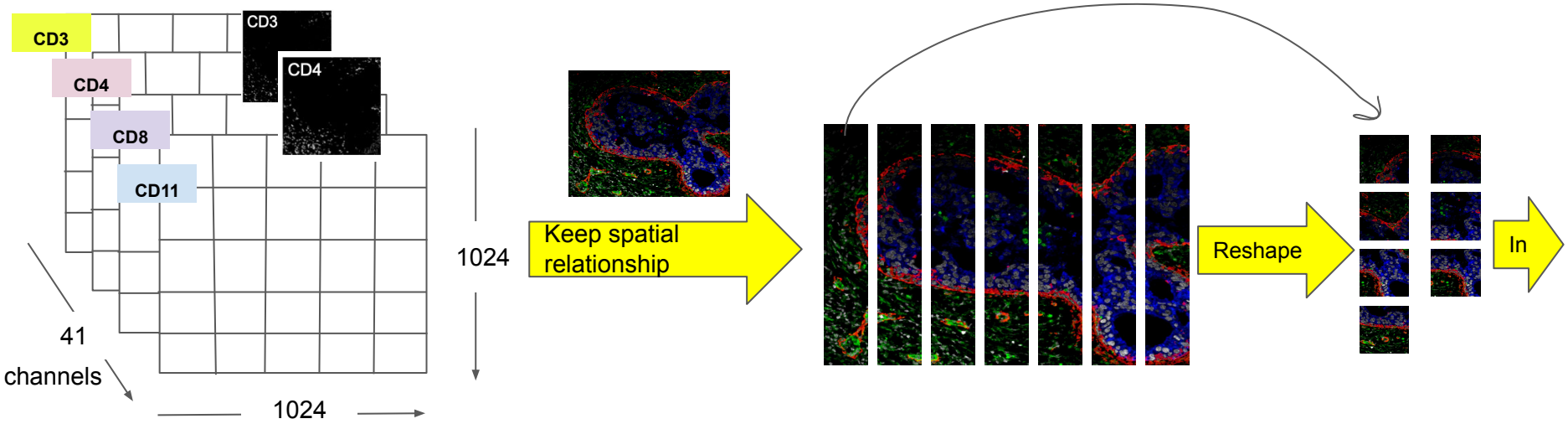
The ViT model details

- Pretrained model: 'google/vit-base-patch16-224-in21k'
  - patch16 => Patches the input images to 16x16
  - 224 => Requires images with dimensions 224x244x3 as input
  - in => Trained on ImageNet dataset
  - 21k => Train on over 21,000 classes (21,834 classes)

Vision transformer (ViT)



Data preprocessing Vision Transformers ViT



Data challenges:

- Spatial dependencies
- Unusual format on input data. 41 channels that need to be collapse
- Large “black” spaces
- Imbalance

Preprocess step 1:

- Collapse data vertically
- Vectorization (for each column, for all rows x channels)
- Remove all 0’z vectors

Addressed the challenges while keeping the spatial relationship

Preprocess step 2:

- Reshape to RGB
- Prepare input for the model (224x224x3)

Data preprocessing output

```
1  ds
```

```
{'train': Dataset({
    features: ['image_path', 'labels', 'pil_image'],
    num_rows: 30519
}),
'test': Dataset({
    features: ['image_path', 'labels', 'pil_image'],
    num_rows: 6542
}),
'validation': Dataset({
    features: ['image_path', 'labels', 'pil_image'],
    num_rows: 6539
})}
```

Training 1 - parameters & loss

```
lr = 5e-3
num_train_epochs = 50
batch_size = 16
early_stopping_callback = EarlyStoppingCallback(early_stopping_patience=5)
```

```
inputs = feature_extractor([Image.open(x) for x in example_batch['image_path']],
                           do_normalize=do_normalize,
                           do_rescale=do_rescale,
                           do_resize=do_resize,
                           augmentation_fn=augmentation_
                           return_tensors='pt')
```

```
  warnings.warn(
```

[8286/9540
4.34/50]

Epoch	Training Loss	Validation Loss	Accuracy
1	0.637200	0.633217	0.671509
2	0.632100	0.627364	0.671509
3	0.628800	0.624400	0.671509
4	0.626000	0.622007	0.671509

Training 2 - parameters & loss

```
inputs = feature_extractor([Image.open(x) for x in example_batch['image_path']],
                           do_normalize=do_normalize,
                           do_rescale=do_rescale,
                           do_resize=do_resize,
                           augmentation_fn=augmentation_fn,
                           return_tensors='pt')
```

```
 8 lr = 5e-2
 9 num_train_epochs = 50
10 batch_size = 8
11 # early_stopping_callback = Early
```

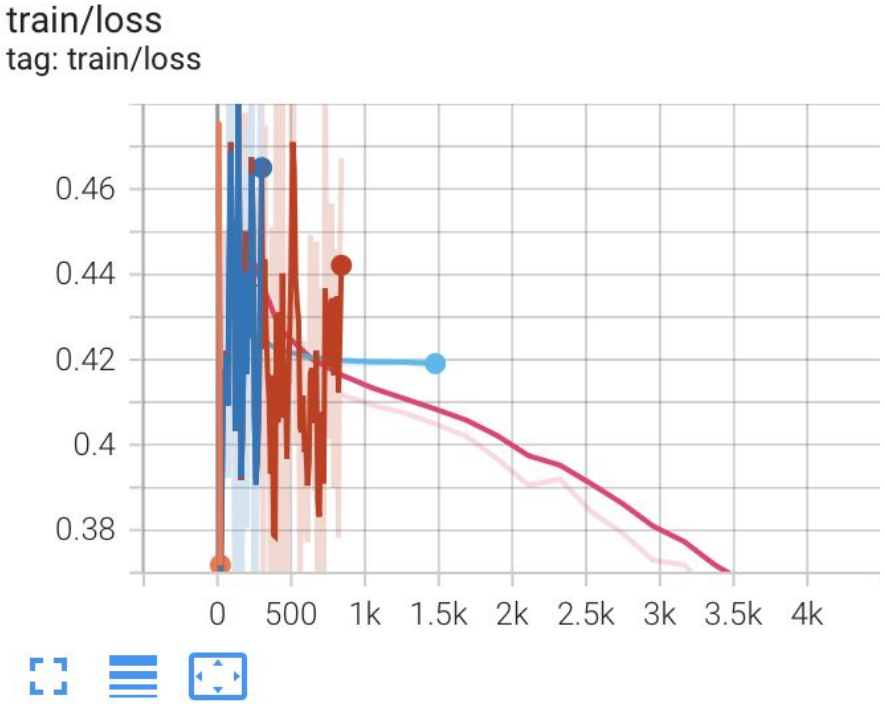
```
1 train_results = trainer.train()
2
```

```
/usr/local/lib/python3.10/dist-packages/transformers/optimiza
  warnings.warn(
[ 201/191000 1:43:10 < 1648:50:2
```

Step	Training Loss	Validation Loss	Accuracy
50	0.729300	0.708615	0.328491
100	0.631600	0.638786	0.671509
150	0.686900	0.643059	0.671509
200	0.829300	0.642763	0.671509

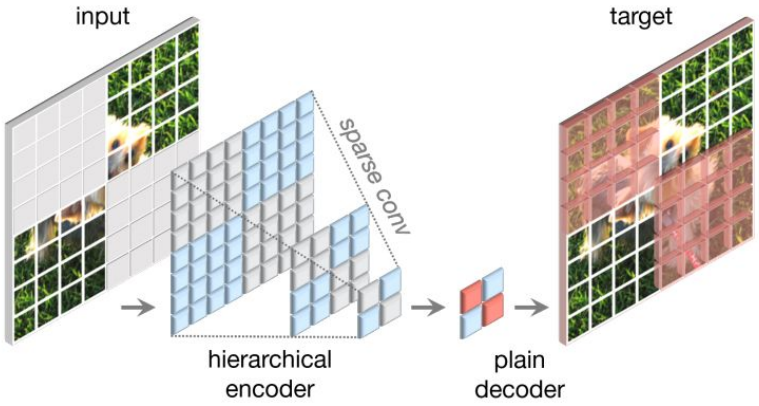
Multiple executions view & insights

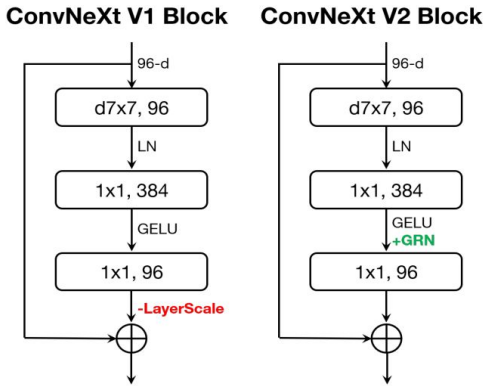
- It is possible to predict progression from the images
- More work need to be done
  - Additional images and execution tuning will be required to make it clinically relevant
- Code for all steps is public: https://github.com/ort-eila/csiseminar



ConvNeXt V2

- Convolutional model inspired by the design of vision transformers
- Successor of ConvNeXt
- Fully convolutional masked autoencoder framework and a new Global Response Normalization (GRN) layer





Preprocessing

- Similar for ViT, but did not reshape to 3 channels - altered the first layer to accept 41 channels
- Model_checkpoint = "facebook/convnextv2-tiny-1k-224"
- Normalized using mean and standard deviation for each channel across all images

Downloaded model:

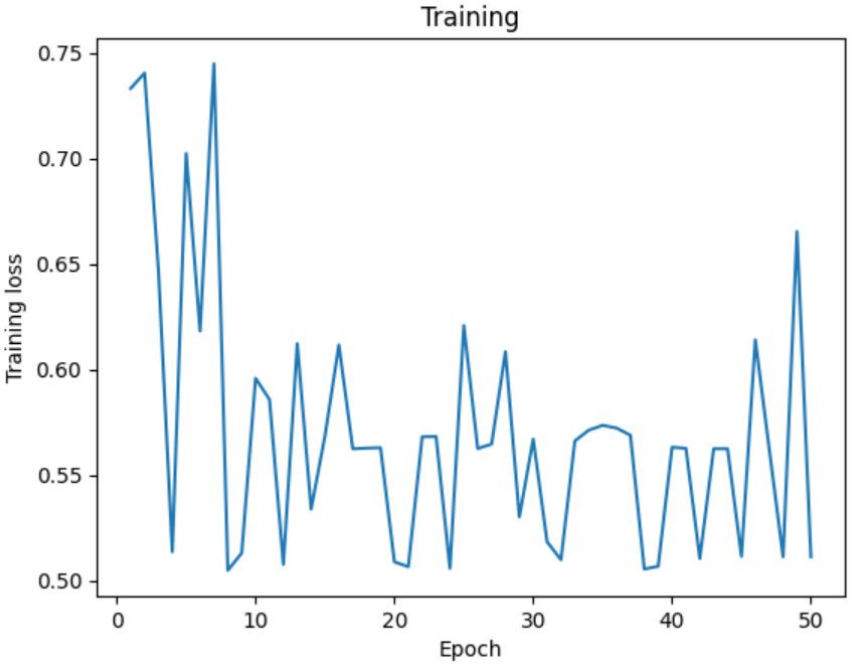
```
ConvNextV2ForImageClassification(
  (convnextv2): ConvNextV2Model(
    (embeddings): ConvNextV2Embeddings(
      (patch_embeddings): Conv2d(3, 96, kernel_size=(4, 4), stride=(4, 4))
      (layernorm): ConvNextV2LayerNorm()
    )
```

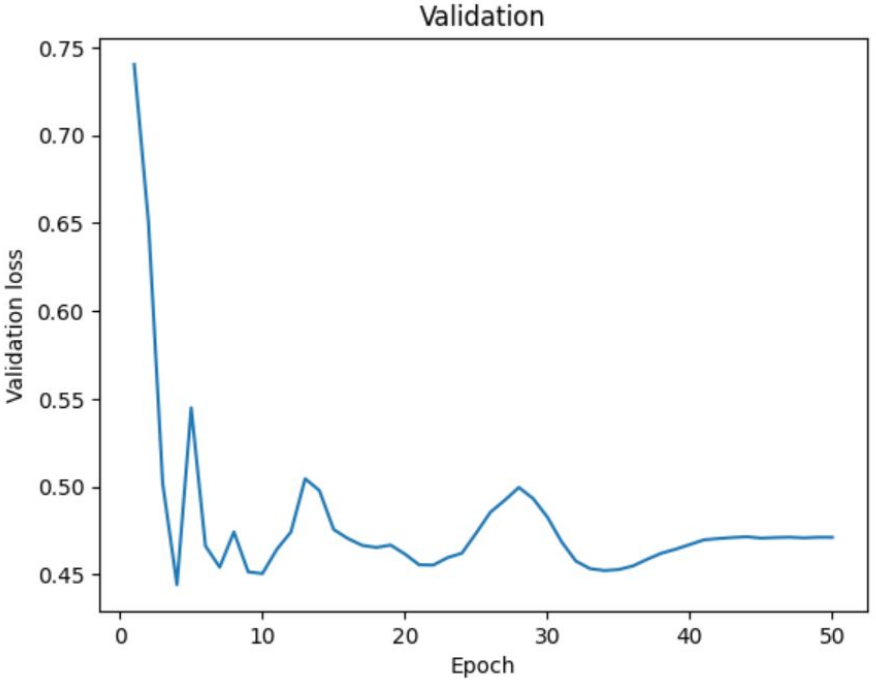
Changed to:

```
ConvNextV2ForImageClassification(
  (convnextv2): ConvNextV2Model(
    (embeddings): ConvNextV2Embeddings(
      (patch_embeddings): Conv2d(41, 96, kernel_size=(4, 4), stride=(4, 4))
      (layernorm): ConvNextV2LayerNorm()
    )
```

```
train_transforms = Compose(
        [
            ToTensor(),
            normalize,
            RandomResizedCrop(crop_size),
            RandomHorizontalFlip(),
        ]
    )
```

Results (kind of)





Validation accuracy = 0.8333

Future directions

- More work to be done
- Acquire more samples
- Data augmentation
- Pre-train or fine-tune the model using multiplexed images from other technologies and disease states so the model can learn what these images look like
- Try different model architectures
  - ImageGPT
  - Swin Transformer
  - Pyramid Vision Transformer
  - Many more…
- Encouraging results!

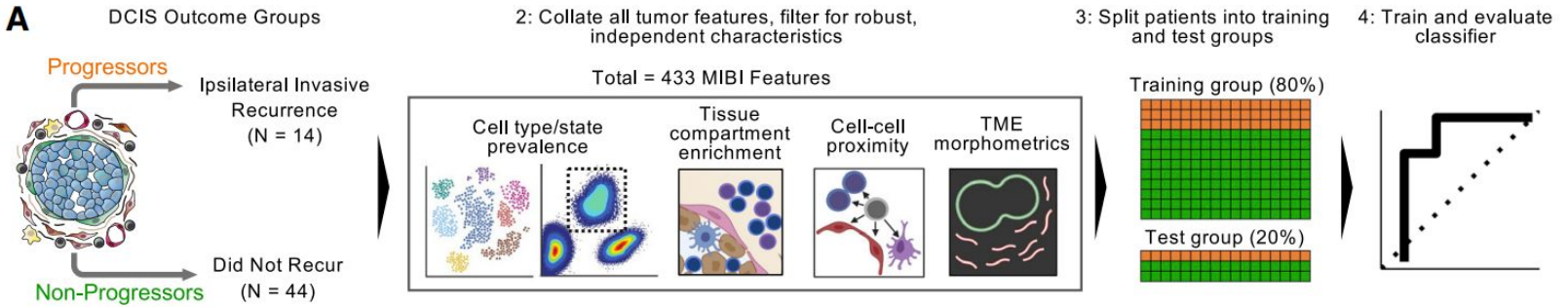
Challenges

- Most pre-trained image classification models expect inputs with 3 channels (RGB)
  - Had to adapt existing models to accept 41 channels
- Small sample size

Future options

- Data augmentation
- Use other MIBI images of other types of patients to help with variety of the data and
  - Can be also helpful with non-progressors by reasoning the progressors.

a)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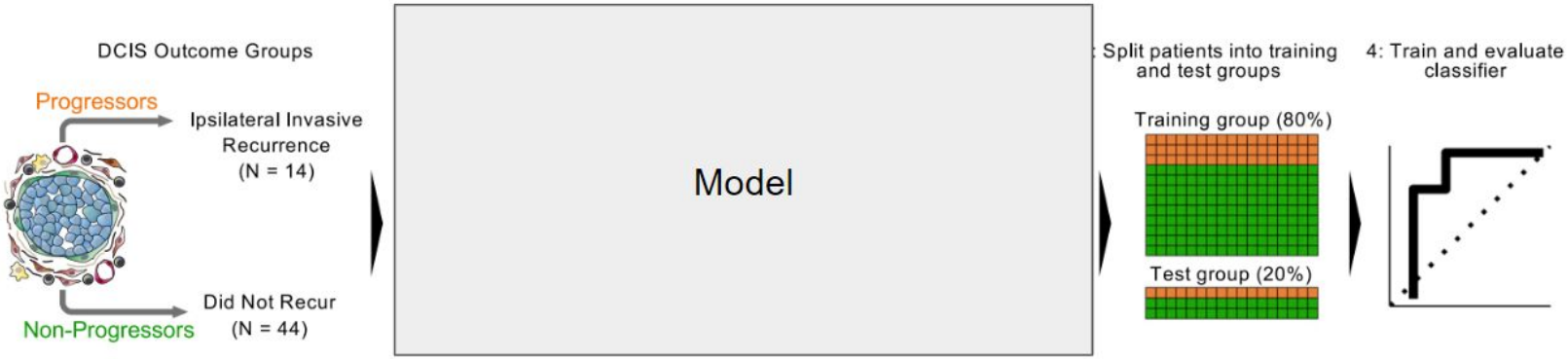
b)


DCIS Outcome Groups
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Model
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4: Train and evaluate classifier