Extending Unsupervised Neural Image Compression With Supervised Multitask Learning

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Erasmus MC Cancer Institute
Facebook AI Research

MIDL Montréal 2020

facebook artificial intelligence research

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Introduction to Histopathology Imaging

Surgery or Biopsy

Tissue Section

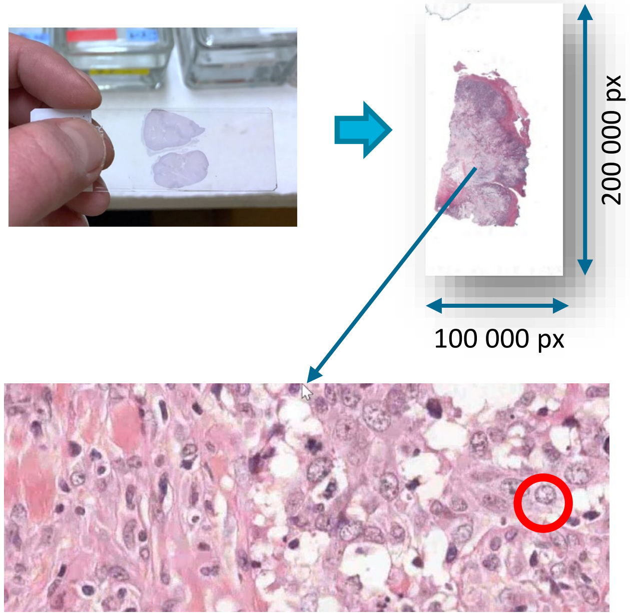
Digital Slide Scanner

Whole-Slide Image

Demo Whole-Slide Image

Image credits: pixabay.com, 3Dhistech.com

Digitized Histopathology Sections Are *Huuge*



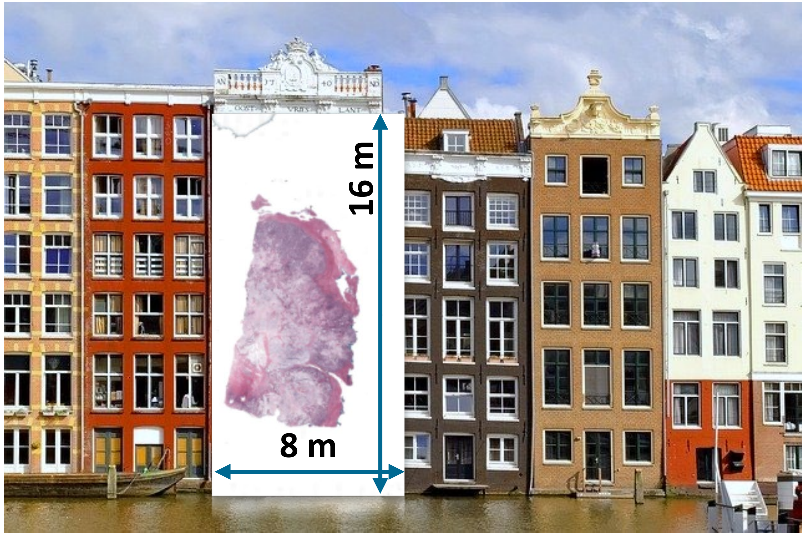


Image credits: pixabay.com, camelyon16.grand-challenge.org

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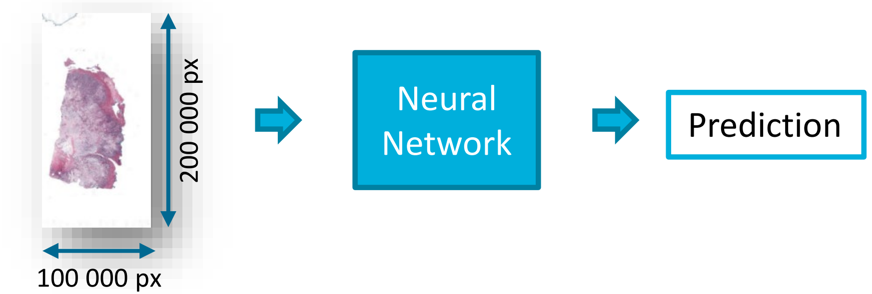
Problem Statement

- Task: classify patients based on histopathology imaging
  - **Input**: gigapixel RGB image
  - **Output**: patient label (survival, recurrence, response, -omics, biomarkers, etc.)



- Constraints:
  - Single-GPU during training and testing
  - No pixel-level task associated with patient label
  - Limited number of patients (<1000 images)

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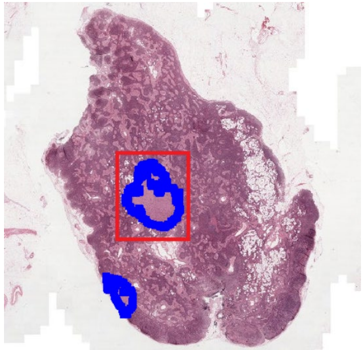
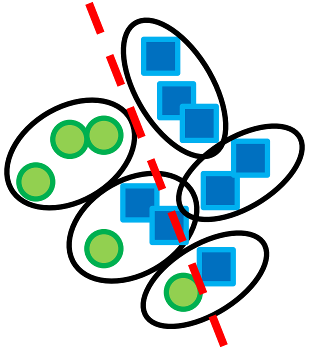
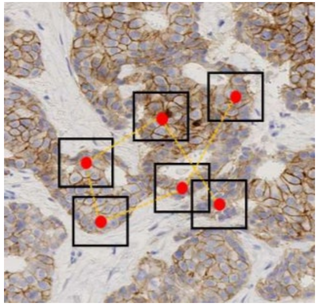
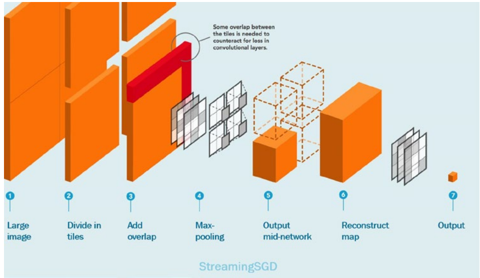
Prior Work









Pixel annotations
Requires proxy task
Requires annotations

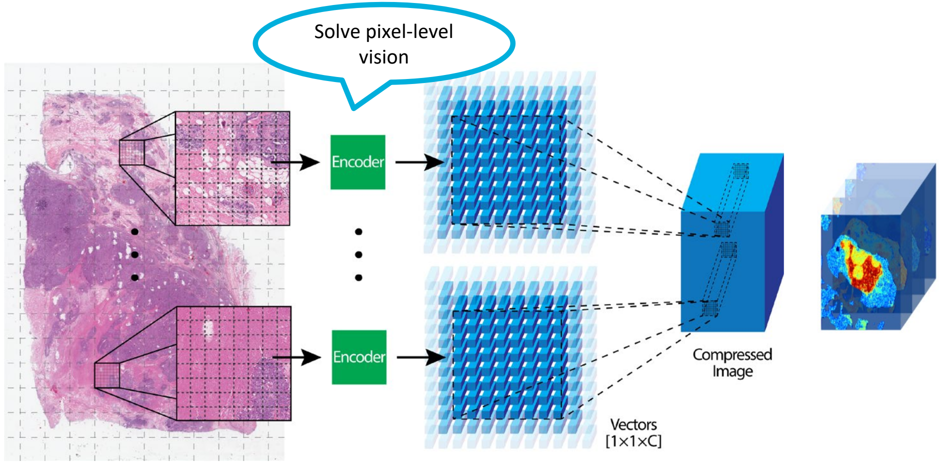
Multiple Instance Learning
Does not exploit relations among instances

Reinforcement learning
Unstable training
Unexplored areas

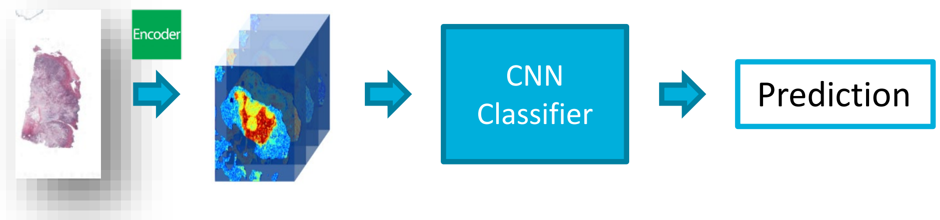
Memory Efficient Training
Overfitting due to lack of training samples

Image credits: camelyon16.grand-challenge.org
Qaiser, Talha, et al. "Learning where to see: A novel attention model for automated immunohistochemical scoring." TMI 2019.
Pinckaers, Hans, et al. "Streaming convolutional neural networks for end-to-end learning with multi-megapixel images." Arxiv 2019.

Proposed: Neural Image Compression



- ✓ Single-GPU
- ✓ No pixel-level association with label
- ✓ Limited number of patients
- ✓ Local and global context



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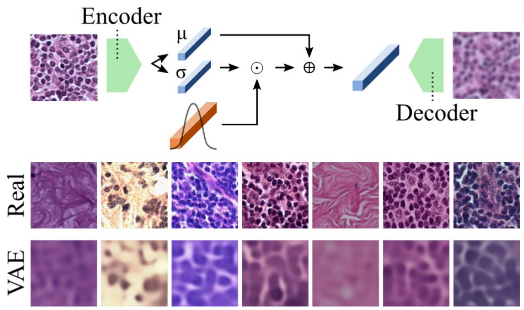
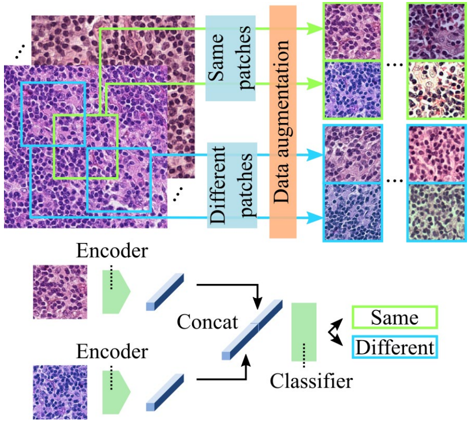
Previous Work: Unsupervised Encoder



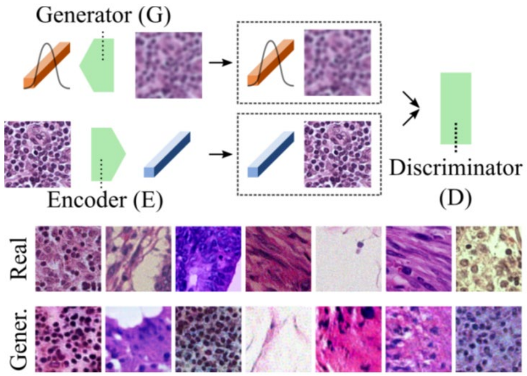
Variational autoencoder

$$\mathcal{V}_{\text{VAE}}(x,n,\theta_E,\theta_D) =$$
$$= \min_{E,D}\Big[\underbrace{(x - D(E(x,n)))^2}_{\text{Reconstruction error}} + \underbrace{\gamma(1+\log\sigma^2 - \mu^2 - \sigma^2)}_{\text{KL divergence}}\Big]$$



Contrastive learning

(self-supervised learning)

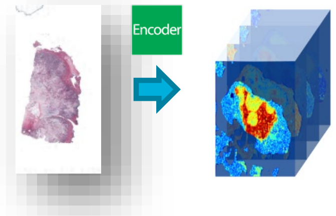


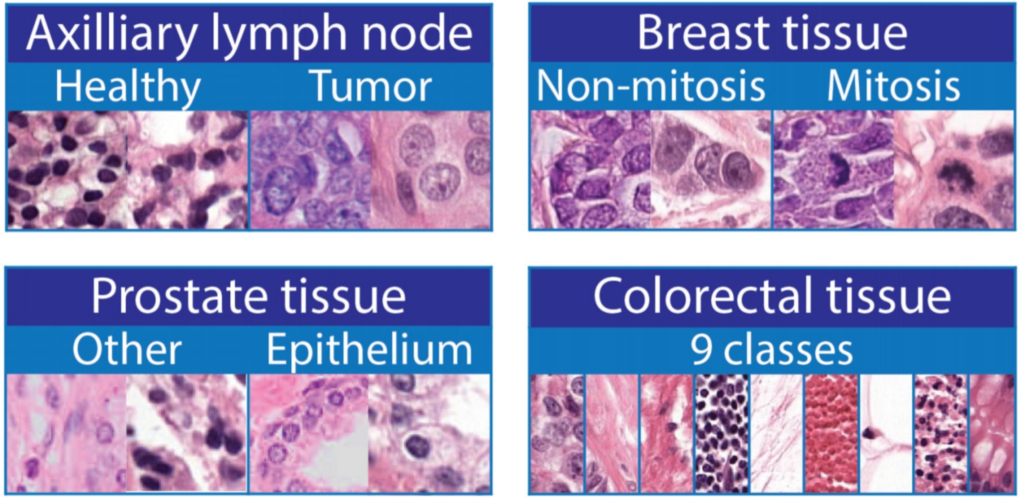
Bidirectional GAN

$$\mathcal{V}_{\text{BiGAN}}(x,z,\theta_G,\theta_E,\theta_D) =$$
$$= \min_{G,E}\max_{D}\Big[\log\big[D(x,\underbrace{E(x)}_{e})\big] + \log\big[1 - D(\underbrace{G(z)}_{x'}, z)\big]\Big]$$

Tellez, David, et al. "Neural Image Compression for Gigapixel Histopathology Image Analysis." TPAMI 2019.

Proposal: Supervised Encoder





Pixel-level annotations unrelated to patient label

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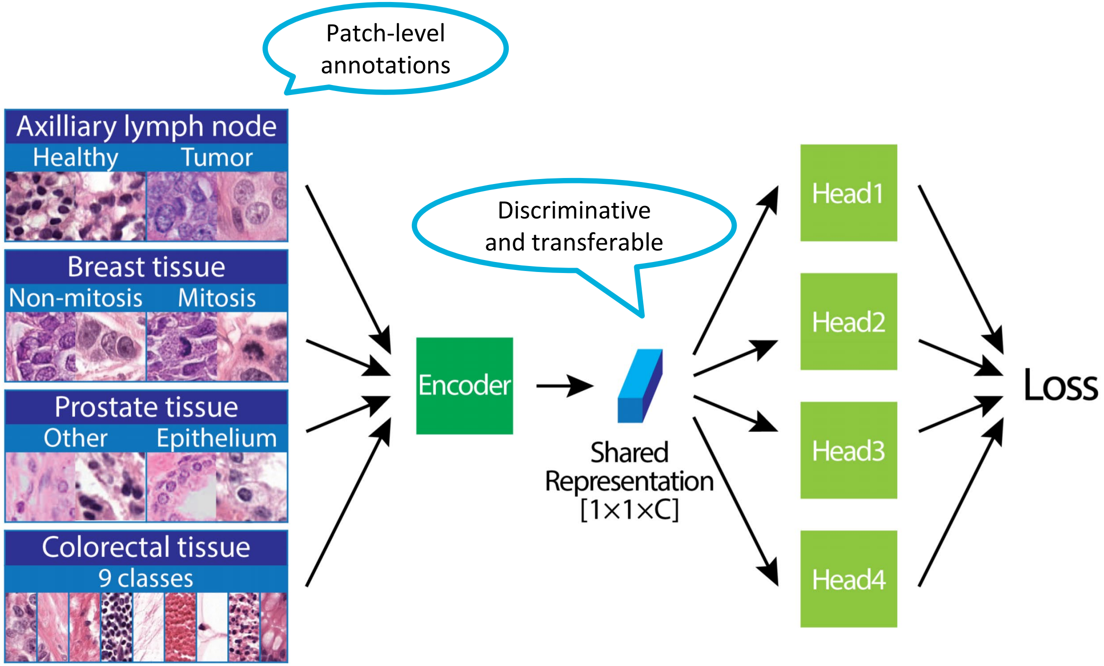
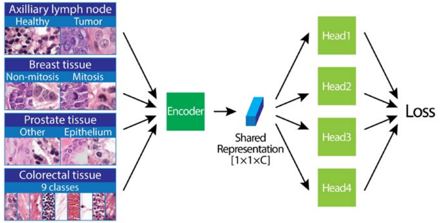
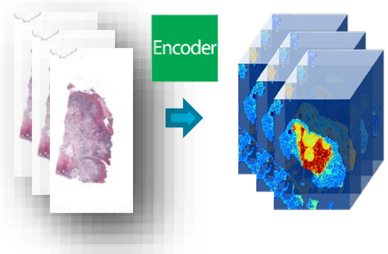
Supervised Multi-Task Learning



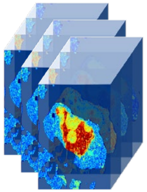
Neural Image Compression with Multi-Task Encoder



1. Train Encoder with Multi-Task Learning



2. Compress All Whole-Slide Images



CNN Classifier

Patient Prediction

3. Train Model at Patient Level

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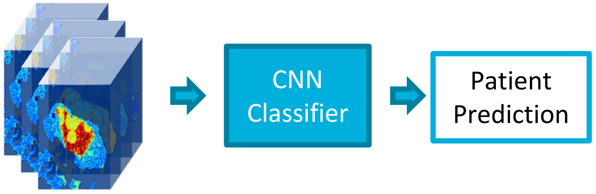
Experimental Results on TUPAC



- Breast tissue
- 500 training images
- Label: **speed of tumor proliferation** from molecular profiling (float [-1, +1])
- Additional: 300 test images with labels known by organizers only

PAM50 Tumor Profiling Test

Image credits: tupac.tue-image.nl

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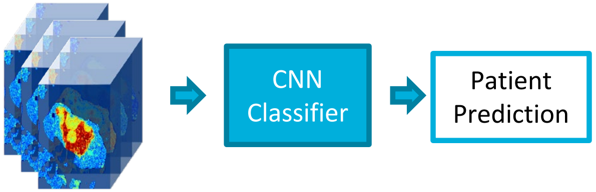
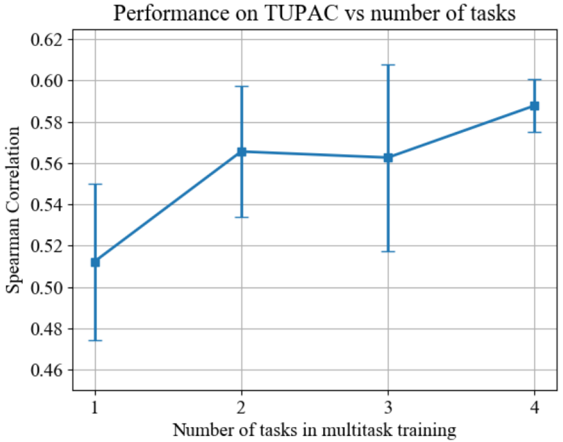
Experimental Results on TUPAC



Method	Training set	External test set
NIC unsupervised (Tellez et al., 2019)	0.522	0.558 [0.5191, 0.5962]
Streaming CNNs (Pinckaers et al., 2019)	-	0.570
TUPAC16 winner (Veta et al., 2019)	-	0.617
NIC multitask (proposed)	0.620	**0.632 [0.5966, 0.6641]**

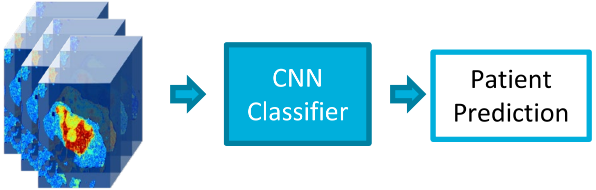
Predicting tumor proliferation speed

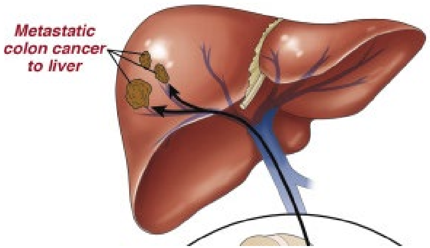


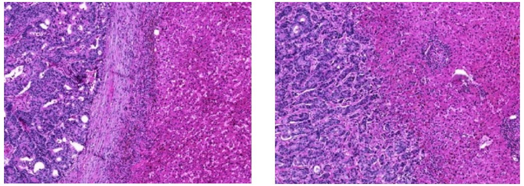
Main results:

- **State-of-the-art result** and first place in challenge leaderboard
- Validates the use of **supervised multitask learning** for gigapixel image-level prediction
- Performance increases with the number of **tasks used to train the encoder**

Experimental Results on Liver

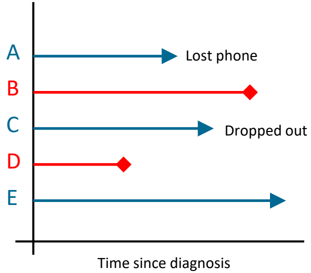






Growth Pattern

- Liver metastasis of colon cancer
- 1500 training images
- Label 1: **type of growth pattern** (binary classification)
- Label 2: patient outcome (**overall survival**)



Overall Survival

Image credit:
Zarour, Luai, et al. "Colorectal cancer liver metastasis: evolving paradigms and future directions." Cellular and molecular gastroenterology and hepatology 2017.
Höppener, Diederik, et al. "Enrichment of the tumour immune microenvironment in patients with desmoplastic colorectal liver metastasis." British Journal of Cancer 2020.

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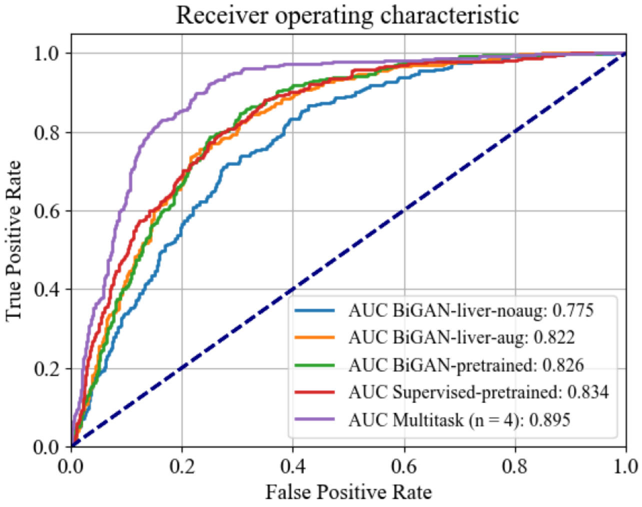
Experimental Results on Liver (growth)



Predicting desmoplastic histopathological growth pattern

Main results:

- Validates the use of supervised multitask learning for gigapixel image-level prediction
- Heavy **color augmentation** improves performance
- Supervision **with 1 task** is similar to unsupervised
- **Multitask supervision** provided the best result

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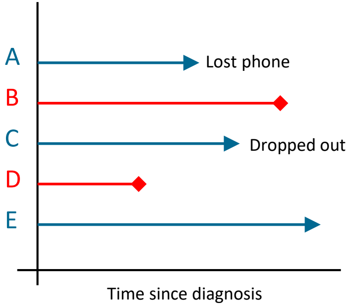
Experimental Results on Liver (survival)

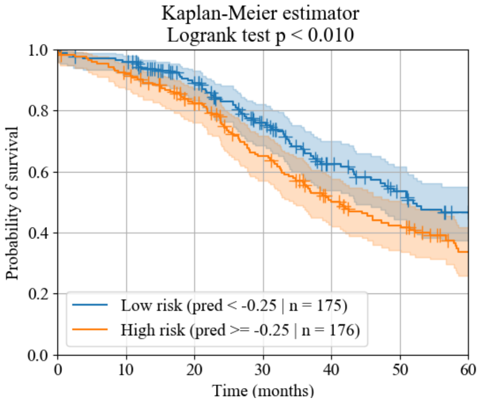


$$\hat{\theta} = \arg\max \log \prod_{i \in D} \frac{\exp f(x_i, \theta)}{\sum_{j \in R_i} \exp f(x_j, \theta)} =$$

$$= \arg\max \sum_{i \in D} \left(f(x_i, \theta) - \log \sum_{j \in R_i} \exp f(x_j, \theta) \right)$$

D: dead patients; R_i: set of patients that survived longer than patient i

Sort patients by risk of death



Learning from overall survival

Main result:

- The proposed method can **learn directly from patient outcome** data (without human annotations)

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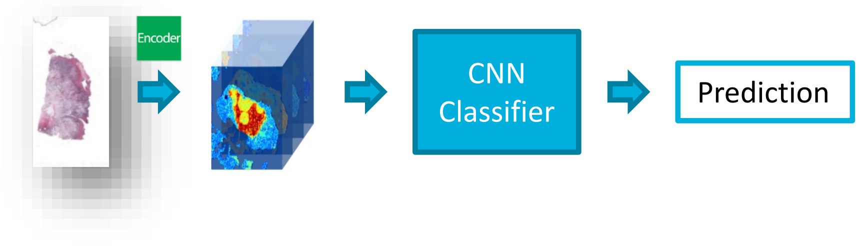
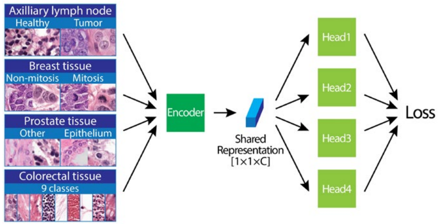
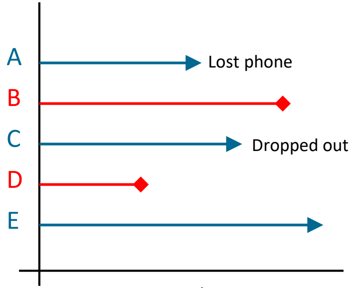
Take-Home Messages





Multi-task learning improves **patient-level classification** (even unseen organs)



Predicts patient risk using **outcome label data** (biomarker discovery)

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Thank You
Questions?

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