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A full pipeline to analyse lung histopathology images

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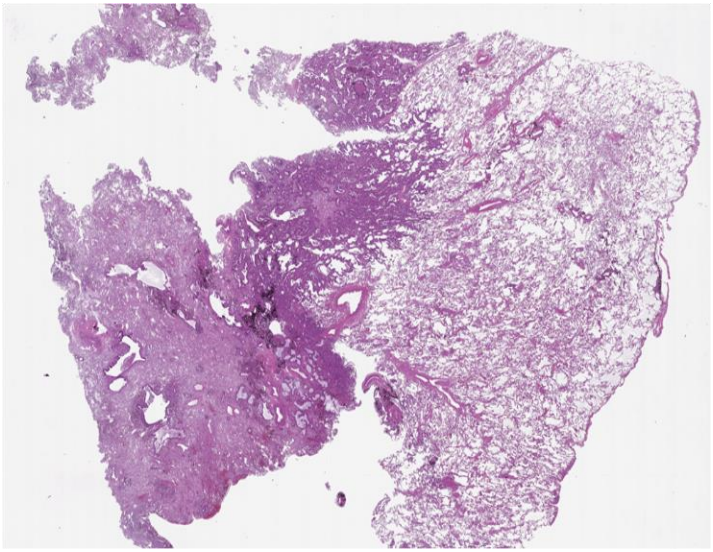

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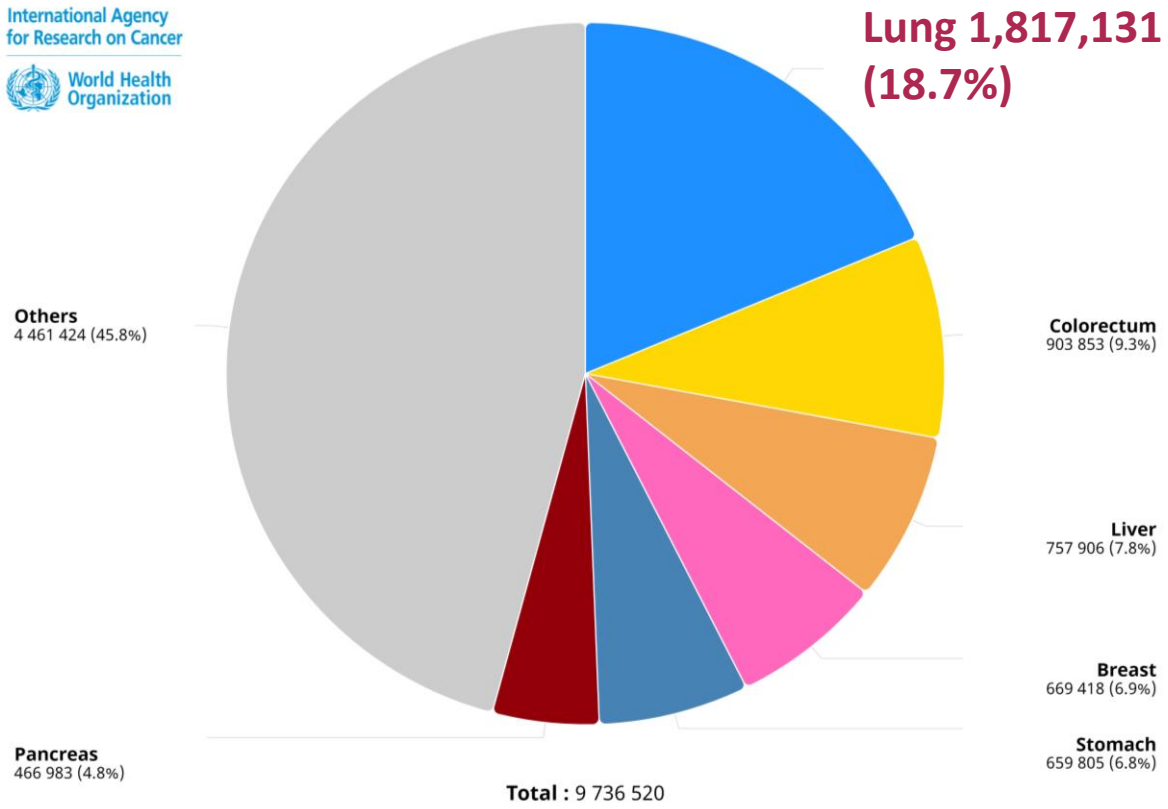
Funded by the European Union

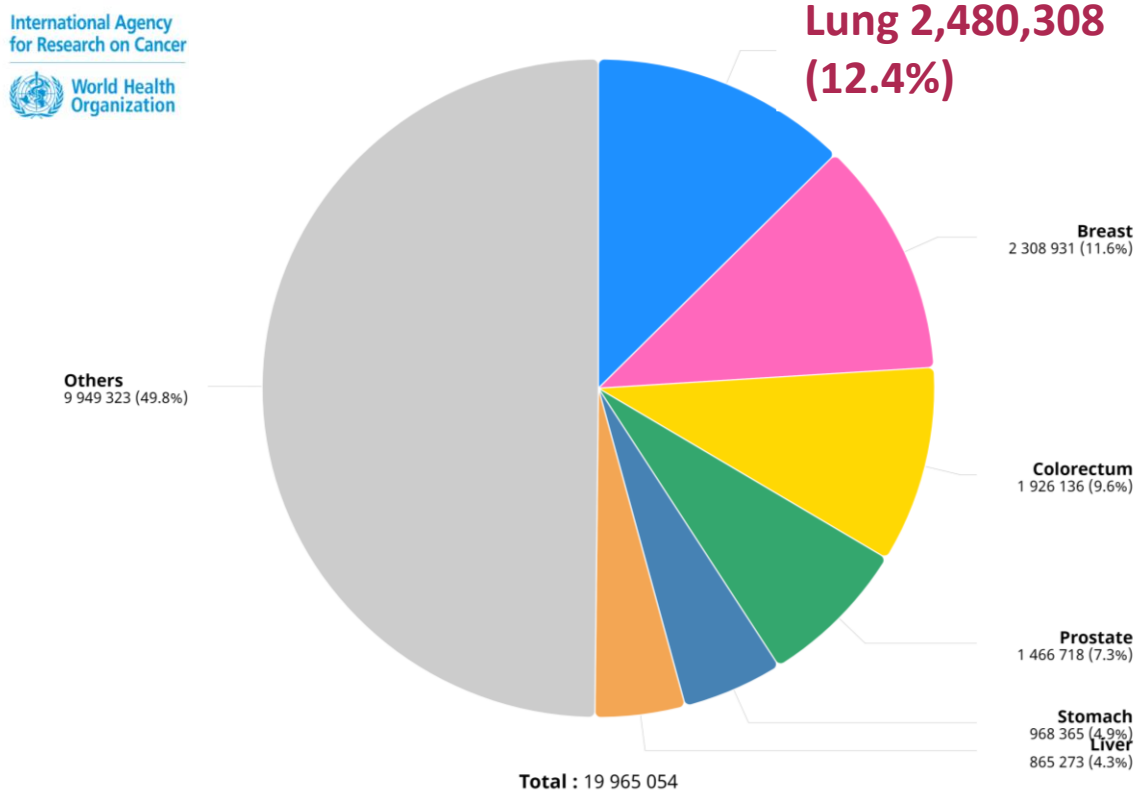
Background

- **Lung cancer** has **high mortality** and incidence

Absolute numbers, **Mortality**, Both sexes, in 2022.

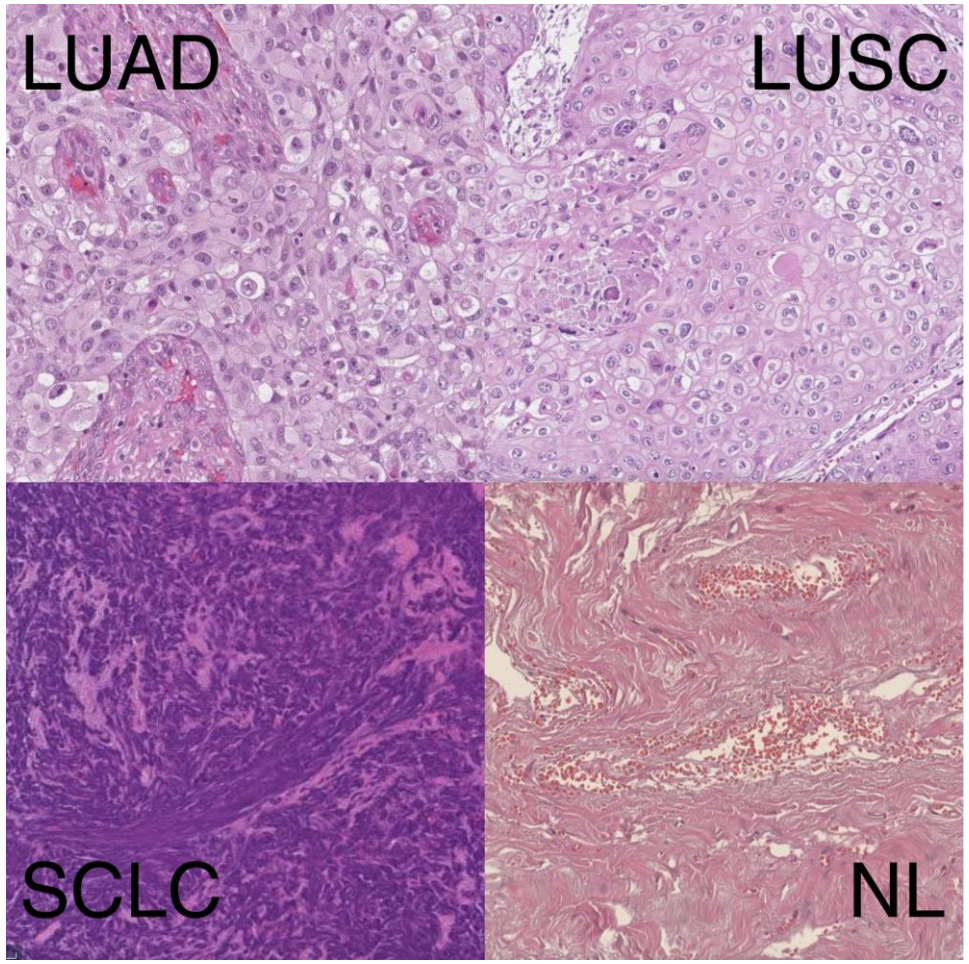


Absolute numbers, **Incidence**, Both sexes, in 2022.



Lung cancer subtypes

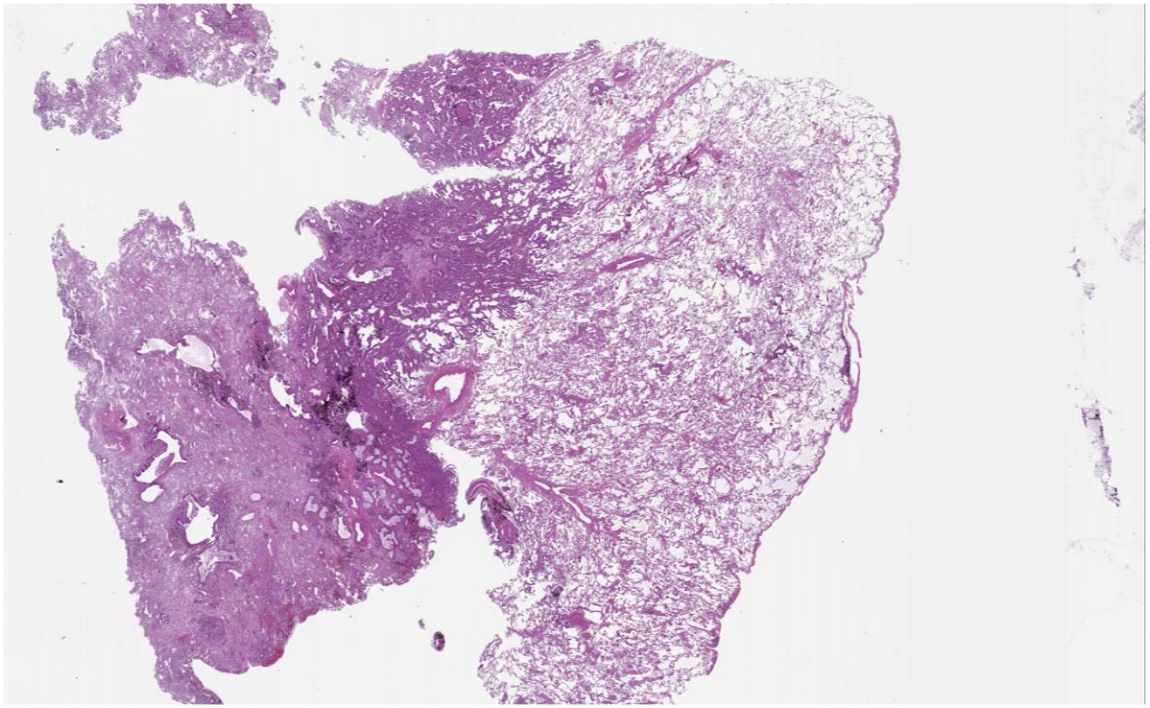
- Small-cell lung cancer (**SCLC**), 20%
- Non-small-cell lung cancer, 80%
  - Adenocarcinoma (**LUAD**), 50%
  - Squamous cell carcinoma (**LUSC**), 30%
  - Others, 20%
- Normal tissue (**NL**)
- Data are **heterogeneous**



Goldstraw, P., Ball, D., Jett, J.R., Le Chevalier, T., Lim, E., Nicholson, A.G., Shepherd, F.A., 2011. Non-small-cell lung cancer. The Lancet 378, 1727–1740.
Van Meerbeeck, J.P., Fennell, D.A., De Ruysscher, D.K., 2011. Small-cell lung cancer. The Lancet 378, 1741–1755.

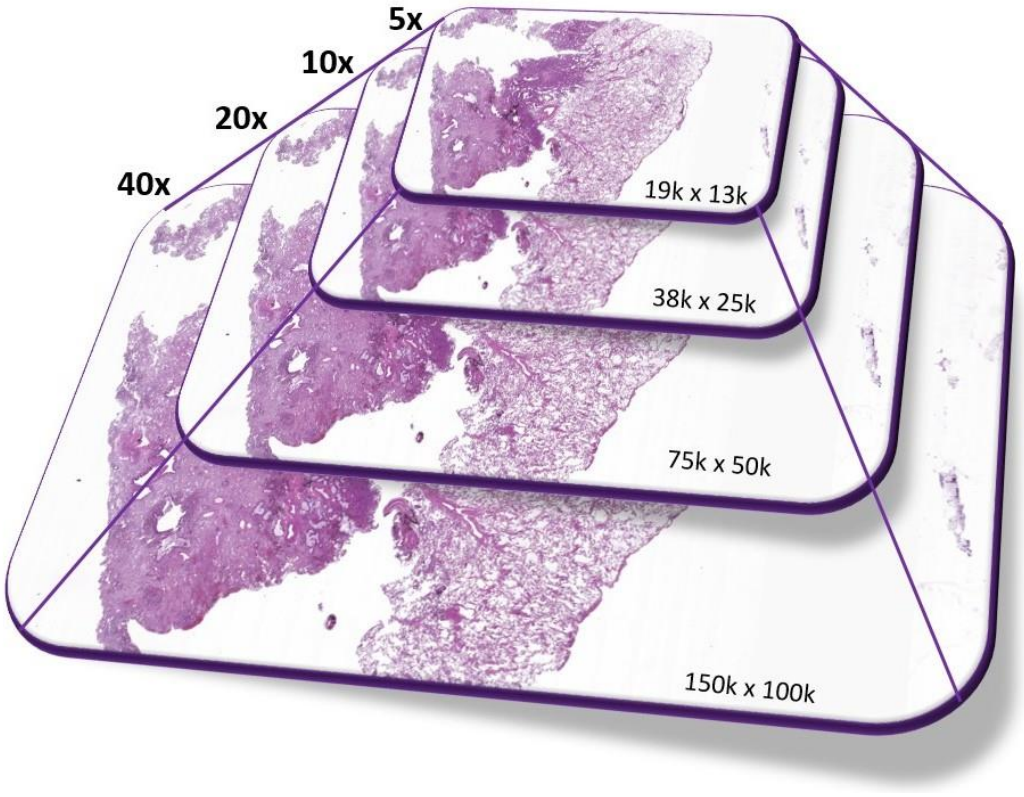
Histopathology

- **Microscopic images** of the tissues
- **Gold standard** to **diagnose** cancer
- **Identify** which **cancer subtype**
- **Experts** are needed



Digital pathology

- **Whole Slide Image** (WSI) is a **digitized slide** scanned at high-resolution
- **Multi-scale** format
- **Gigapixel** images
- **SOTA** based on **Deep Learning**



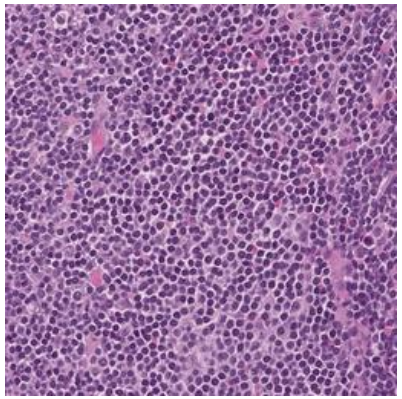
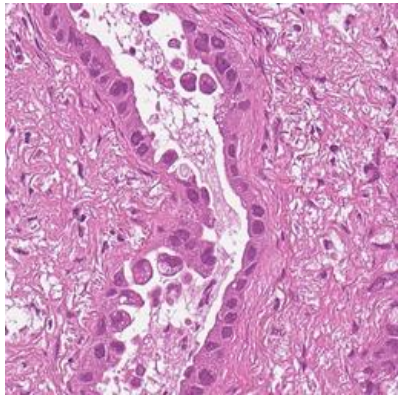
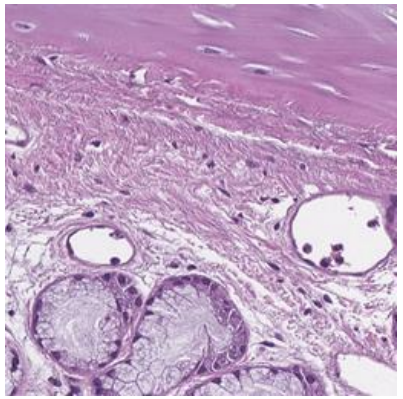
Marini, N., Otalora, S., Podareanu, D., van Rijthoven, M., van der Laak, J., Ciompi, F., Muller, H., Atzori, M., 2021a. Multi scale tools: a python library to exploit multi-scale whole slide images. Frontiers in Computer Science 3, 684521.

Data representation

- **Pre-training**
  - Transfer learning

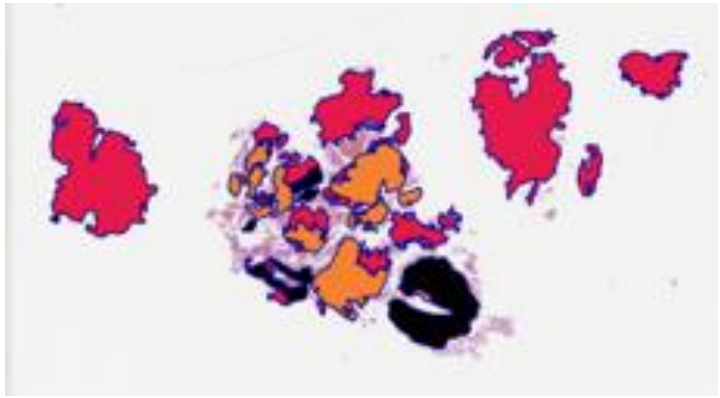
IMAGENET

  - Self-supervised learning

Annotations

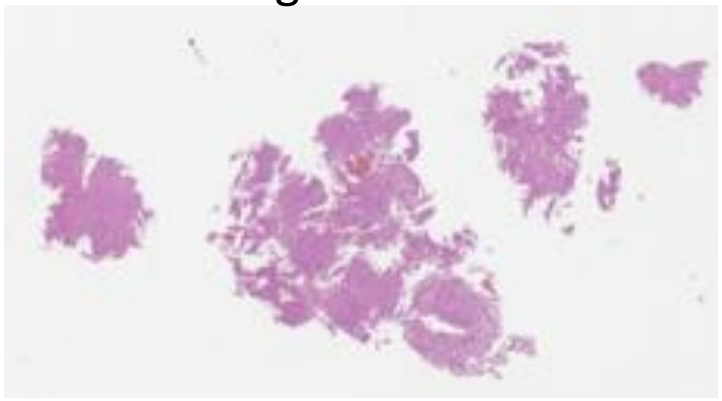
- **Training**
  - **Local Annotations**
    - Fully-supervised learning



- Label at **pixel-level**
- **Costly** to collect
- Highest performance

Label: Lung Adenocarcinoma

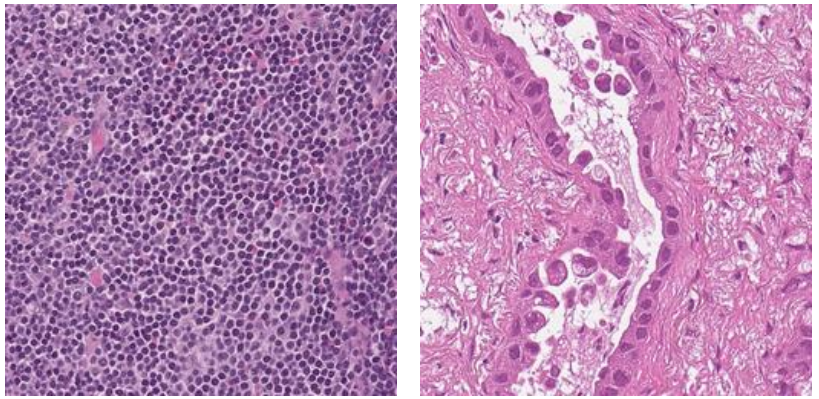
  - **Global Annotations**
    - Weakly-supervised learning



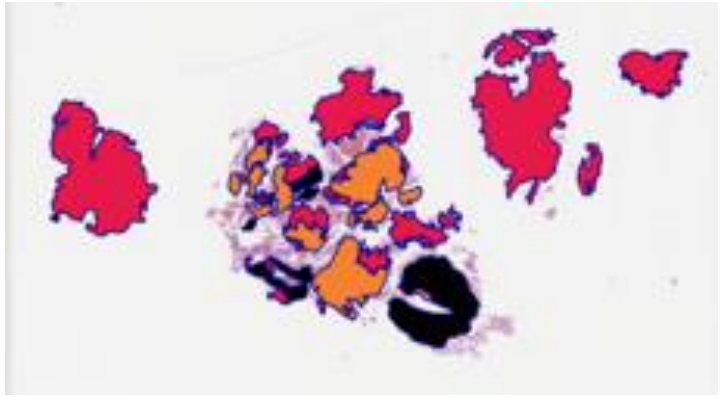
- Label at **WSI-level**
- **Cheaper** to collect

Motivation

- Representation from natural images may not be that effective for medical data



- Hard to collect large **locally-annotated datasets**



Objective

Develop a **fully automatic pipeline** for **WSI cancer subtype classification** using **self-supervision** and **weakly-supervised learning**

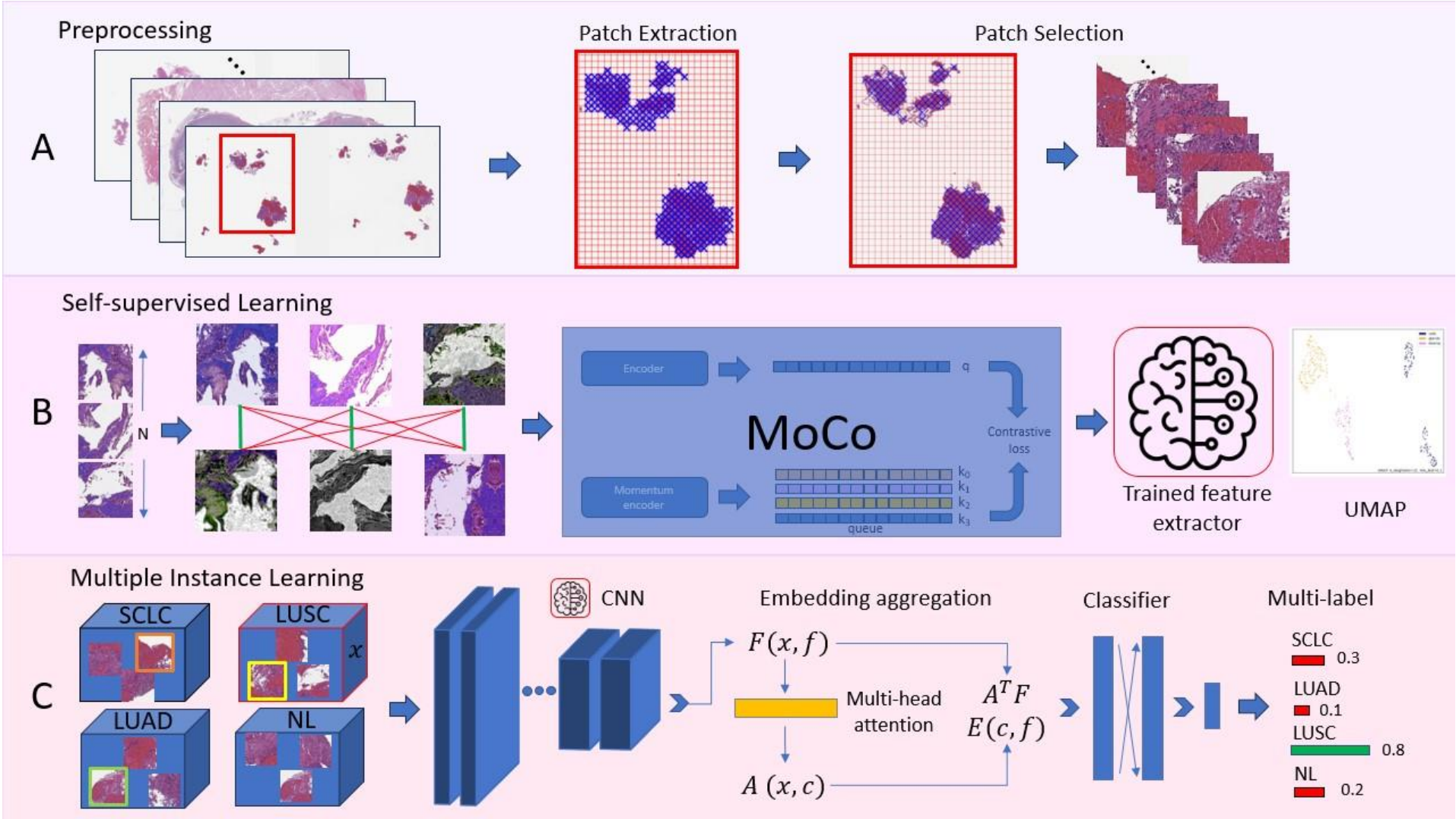
Datasets

- Data are **Multi-label**

Source	SCLC	LUAD	LUSC	Normal	Total labels	Total images
Training dataset from two different private datasets:						
AOEC	53	601	353	237	1,244	1,225
RUMC	0	297	205	499	1,001	1,001
Total	53	898	558	736	2,245	2,226
Testing private datastets:						
AOEC	17	16	9	14	46	46
RUMC	0	29	18	45	92	92
Total	17	45	27	59	138	138
Testing public dataset:						
TCGA	0	530	506	0	1,036	1,036

Albertina, B.,et al.. The cancer genome atlas lung adenocarcinoma collection (tcga-luad).
Kirk, S et al.. The cancer genome atlas lung squamous cell carcinoma collection (tcga-lusc).

Pipeline



He, K., Fan, H., Wu, Y., Xie, S., Girshick, R., 2020. Momentum contrast for unsupervised visual representation learning, in: Proceedings of the IEEE/CVF conference on computer vision and pattern recognition, pp. 9729–9738.

Chen, X., Fan, H., Girshick, R., He, K., 2020b. Improved baselines with momentum contrastive learning. arXiv preprint arXiv:2003.04297.

Ilse, M., Tomczak, J., Welling, M., 2018. Attention-based deep multiple instance learning, in: International conference on machine learning, PMLR. pp. 2127–2136.

Results

- Test on the private AOEC and RUMC datasets

Pre-training	AUC SCLC	AUC LUAD	AUC LUSC	AUC Normal	micro-AUC	weighted f1-score
Train on AOEC and RUMC:						
Self-supervised	0.8825 ± 0.0712	0.7457 ± 0.0267	0.8428 ± 0.0171	0.8468 ± 0.0	**0.8558 ± 0.0051**	**0.6537 ± 0.0237**

Results

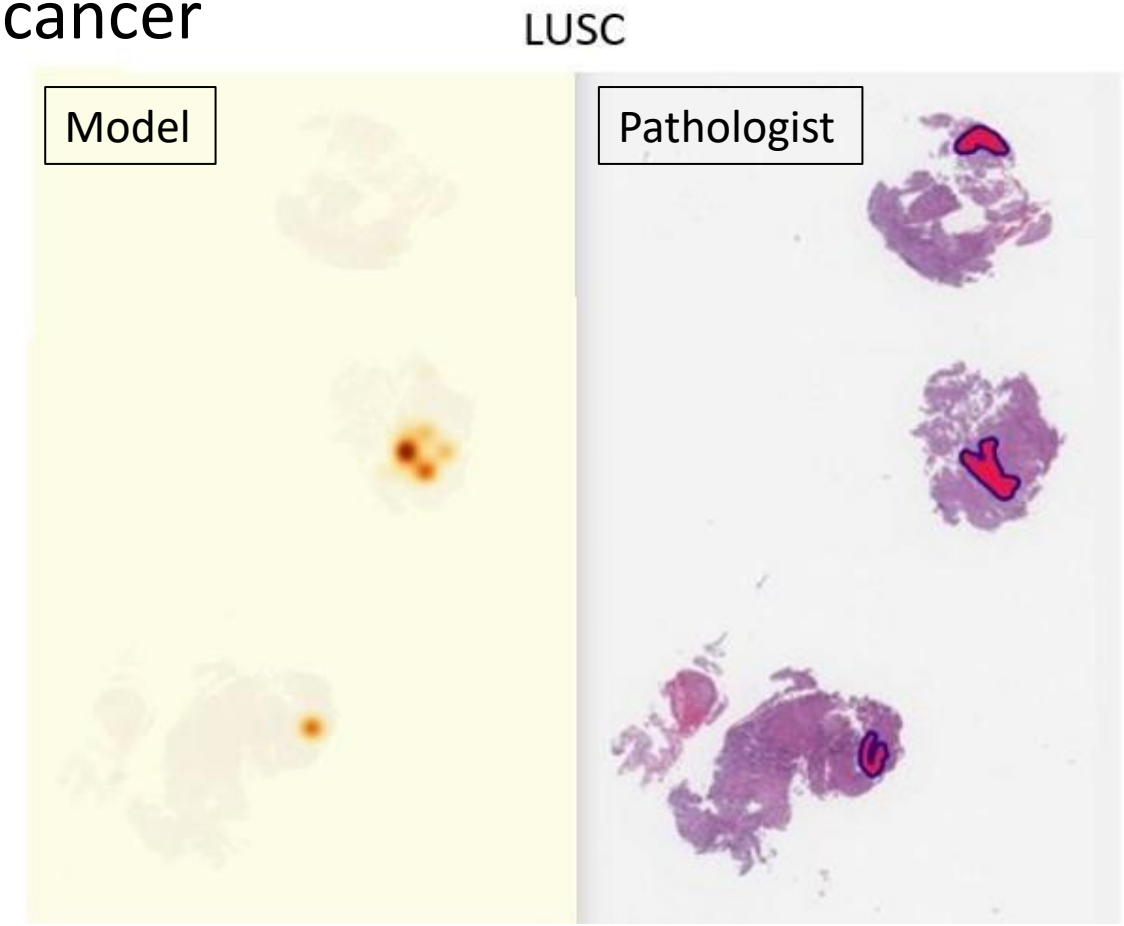
- Test on the public TCGA dataset
  - Capability of **generalize** on public data

Pre-training	micro-AUC	weighted f1-score
Test on TCGA:		
Train on AOEC and RUMC:		
Self-supervised	**0.9433 ± 0.0198**	**0.7726 ± 0.0438**

Albertina, B.,et al.. The cancer genome atlas lung adenocarcinoma collection (tcga-luad).
Kirk, S et al.. The cancer genome atlas lung squamous cell carcinoma collection (tcga-lusc).

Results

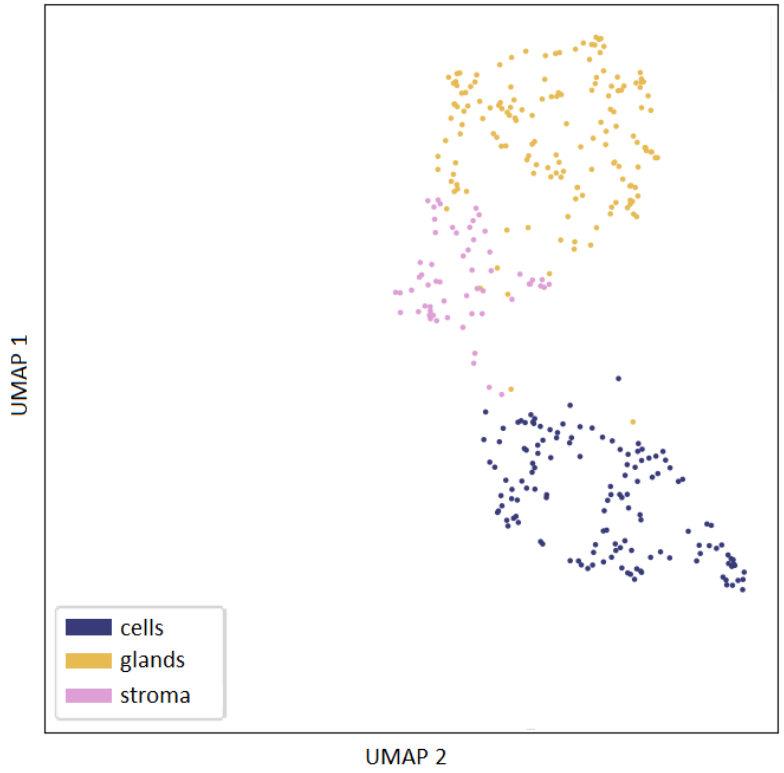
- **Heatmaps** can **help** pathologists **localizing** and **diagnosing** lung cancer



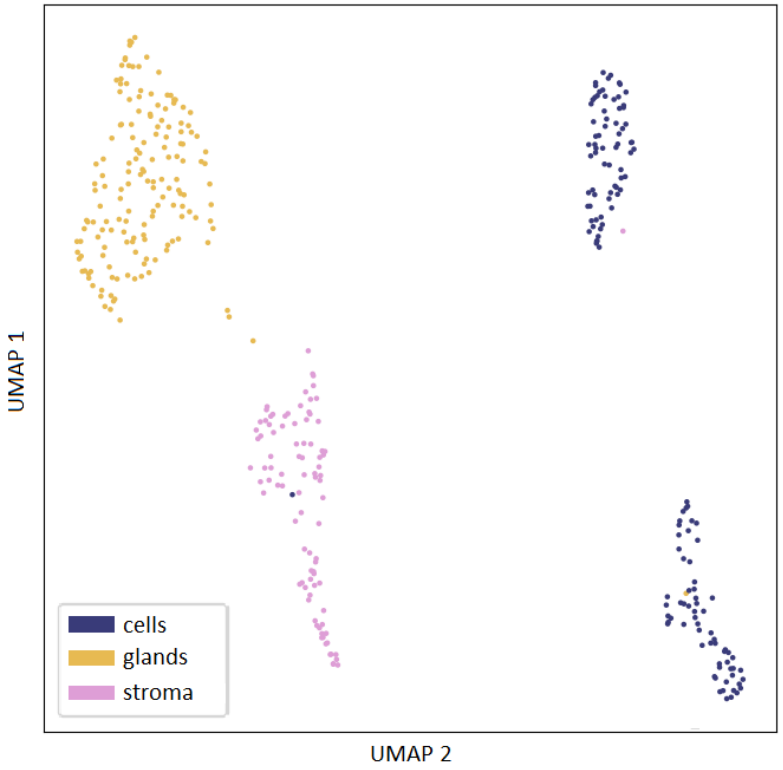
Discussion

- Differences on **Data representation**

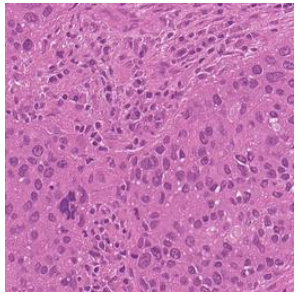
UMAP ImageNet



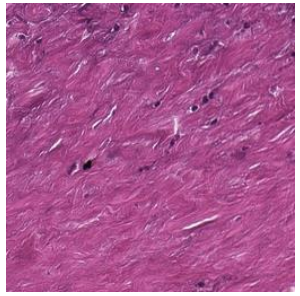
UMAP Self-supervised



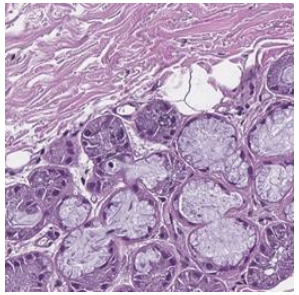
cells



stroma



glands



McInnes, L., Healy, J., Melville, J., 2018. Umap: Uniform manifold approximation and projection for dimension reduction. arXiv preprint arXiv:1802.03426 .

Conclusions

- A **fully automatic pipeline** to classify **4-class** lung cancer WSIs
- **Pre-training** with **self-supervision** for a better **data representation**
- **Weakly-supervised learning** enables **training** the model using only **global annotations**
- The model generates **accurate predictions** on the **TCGA** dataset showing its **generalization** capabilities
- **Heatmaps** a potential **tool** to **help pathologists** in the **localization** and **diagnosis** of lung cancer on WSI

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Hes·so VALAIS WALLIS

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