Deep Learning for Classification of Non-Small Cell Lung Cancer histologic subtypes

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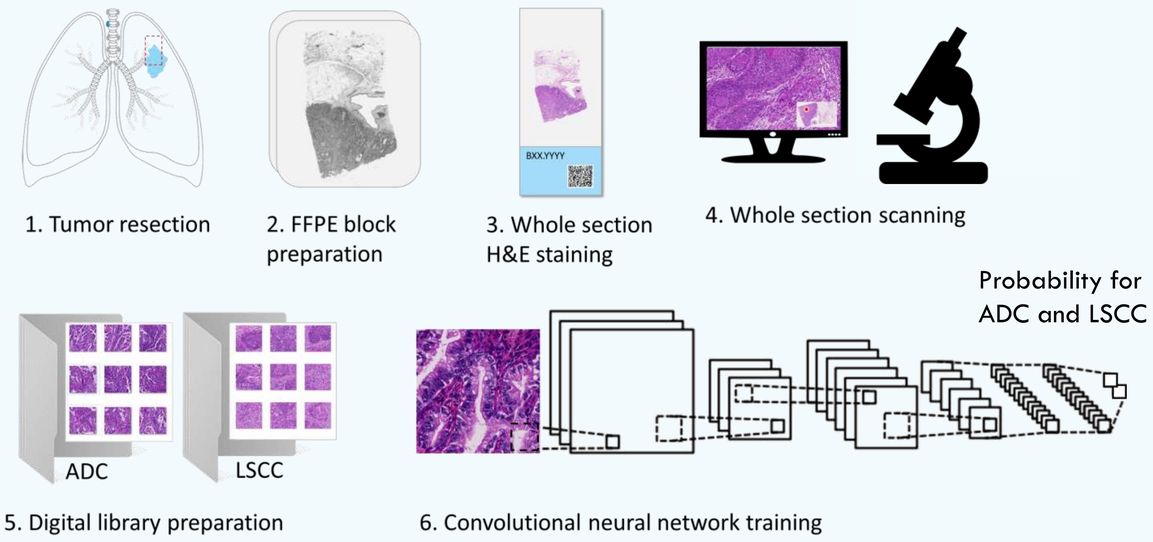
Motivation

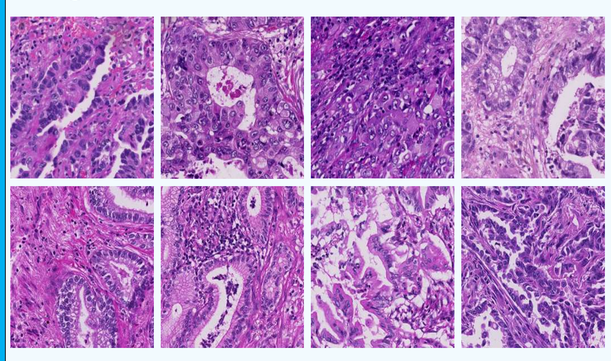
- Non-Small Cell Lung Cancer (NSCLC) is the main lung cancer type and comprises two main histologic classes: adenocarcinoma (ADC) and squamous cell carcinoma (LSCC).
- Tumor subtyping is routinely done by trained pathologists using conventional microscopy. Automated image analysis can potentially speed-up routine diagnostic.
- In clinical practice, histologic subtyping is an important factor for treatment decisions, as different therapies are proposed to non-squamous NSCLC.
- Deep learning methods have become increasingly popular in recent years, mostly because they can outperform traditional machine learning algorithms, without requiring extraction of handcrafted features.
- In this work we show the potential of deep learning with convolutional neural networks (CNN) in the classification of histologic images of lung cancer.

Sample preparation workflow

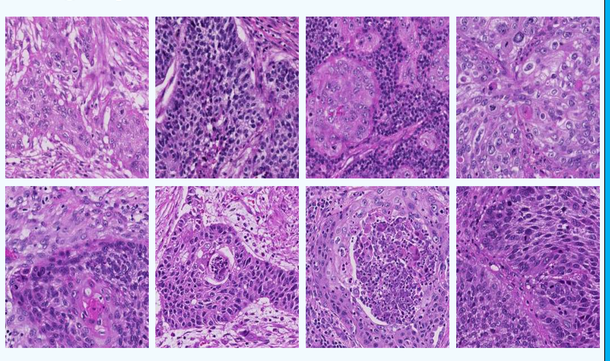


Legend: FFPE=Formalin-Fixed, Paraffin-Embedded (tissue); H&E=Hematoxylin and eosin stain

Lung adenocarcinoma

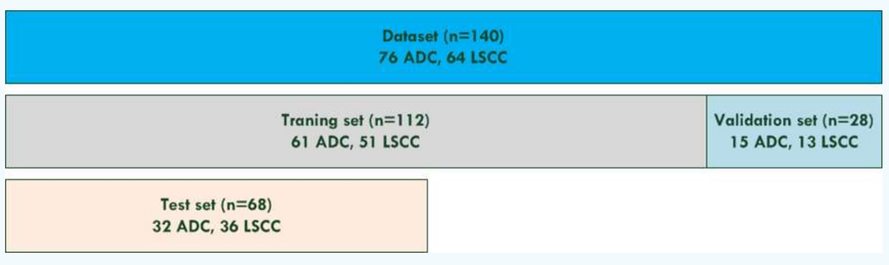


Lung squamous cell carcinoma



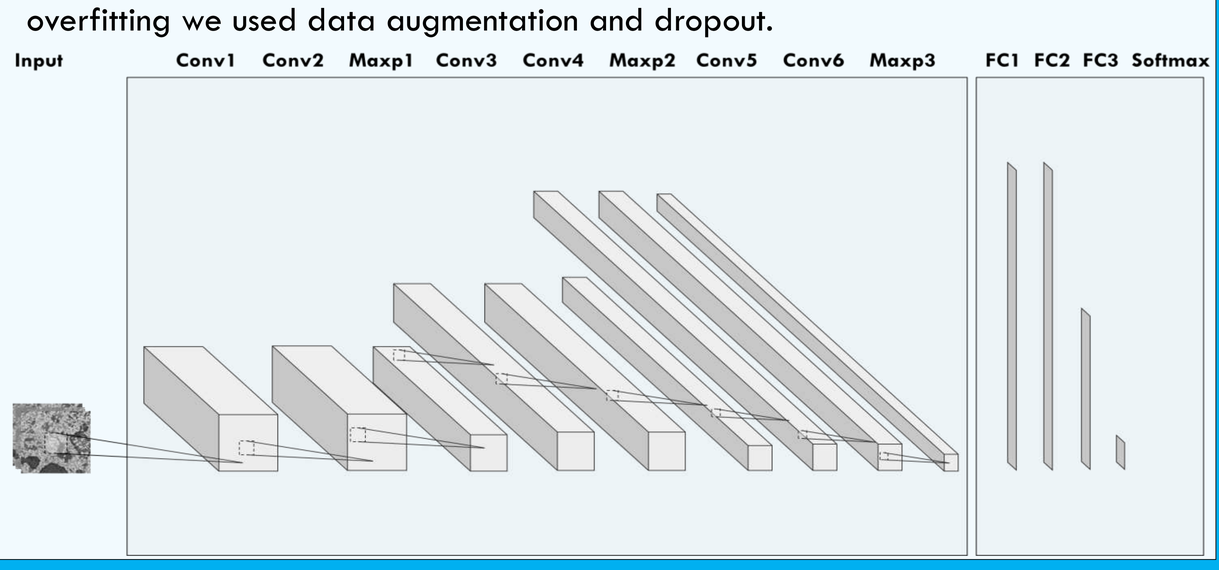
Examples of NSCLCs, stained by Hematoxylin and eosin (H&E)

Data and Network architecture

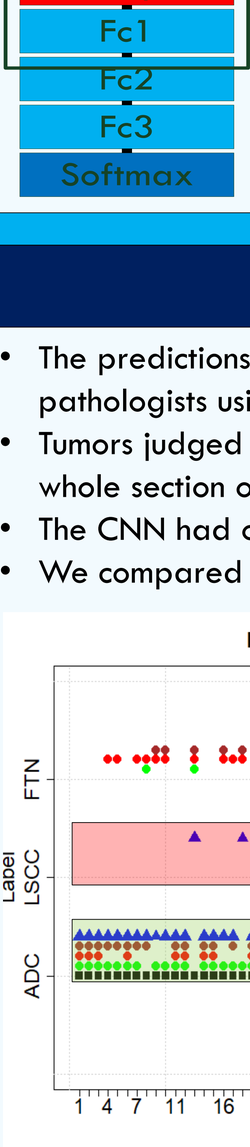


Original	**(256x256x3)**
Input	**(128x128x3)**
Conv1	**(128x128x32)**
Conv2	**(128x128x32)**
Maxp1	**(64x64x32)**
Conv3	**(64x64x64)**
Conv4	**(64x64x64)**
Maxp2	**(32x32x64)**
Conv5	**(32x32x128)**
Conv6	**(32x32x128)**
Maxp3	**(16x16x128)**
FC1	**(200)**
FC2	**(200)**
FC3	**(50)**
Softmax	**(2)**

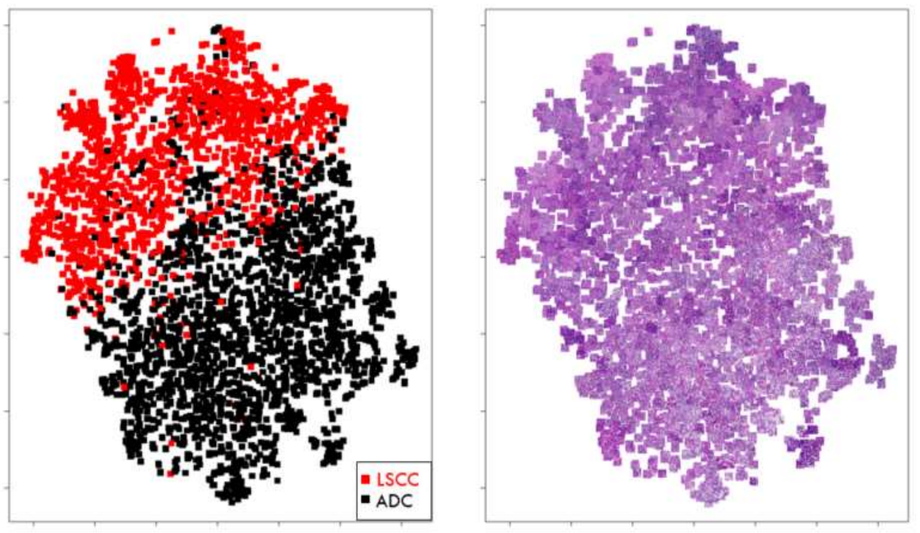
- We developed and trained a CNN to differentiate ADC from LSCC. Patients were split into a training and validation set. Each patient contains 50 histologic images.
- The performances of the CNN were evaluated on the test set and are compared with the results of three experienced pathologists.
- We merged the 50 predictions for each patient via majority vote to a final prediction with a confidence score.
- As activation function ReLu was used, and to prevent overfitting we used data augmentation and dropout.



Unsupervised tsne visualization



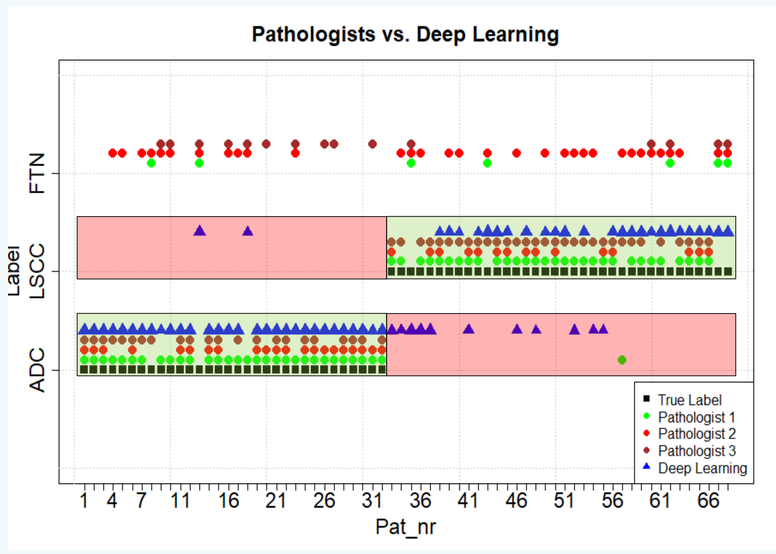
- A pretrained VGG16 network, trained on ImageNet data, was used as a feature extractor for the histological images.
- 4096 features of the third last layer ("Fc1") before the activation function were extracted for each image.
- Here we show results of a 2D tsne representation of all images in the training set. If you take a close look, you see that similar images are close to each other.



- There is a very good separation between ADC and LSCC. The labels were only used to color the tsne plot, this is a completely unsupervised approach.

Results

- The predictions of our network were compared to the predictions of three pathologists using the same image set.
- Tumors judged too difficult to evaluate by the pathologists, without access to the whole section or additional staining, were scored as FTN (further tests needed).
- The CNN had only two choices: ADC or LSCC.
- We compared the number of evaluated patients with the accuracy on those.



Deep Learning			
	#evaluated	**%**	**Acc.**
Cs>0.5	**68 / 68**	**100%**	**80.8%**
Cs>0.6	**60 / 68**	**88.2%**	**86.6%**
Cs>0.7	**58 / 68**	**85.3%**	**87.9%**
Cs>0.8	**43 / 68**	**63.2%**	**93.0%**

Cs: Confidence score

Pathologists			
	#evaluated	**%**	**Acc.**
patho 1	**61 / 68**	**89.7%**	**98.4%**
patho 2	**36 / 68**	**52.9%**	**100.0%**
patho 3	**53 / 68**	**77.9%**	**100.0%**

Conclusion / Outlook

- In this work we showed the potential of CNNs in that routine classification tasks with accuracies almost approaching those from trained pathologist with years of experience.
- The performances of the network could be improved by increasing the training set, or using images with different magnifications.
- Further improvements can be expected by choosing other network architecture or using batch normalization layers. In addition, dropout in the forward pass could also be used to get a confidence score for every image.
- An important future step includes classification visualization, to understand which parts of the image contribute to the class decision.

References

- Single-Cell Phenotype Classification Using Deep Convolutional Neural Networks (Oliver Dürr, Beate Sick, 2016)
- Very Deep Convolutional Networks for Large-Scale Image Recognition (Karen Simonyan, Andrew Zisserman, 2015)
- Visualizing Data using t-SNE (Laurens van der Maaten, Geoffrey Hinton, 2008)