Bioinformatics analysis of morphological differences in tissue images of Hodgkin lymphoma patients regarding new and recurrent cases

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Hodgkin lymphoma (HL) is a cancerous disease which has a different outcome in early relapses compared to primary cases [1]. Bioinformatic analysis can provide insight into the morphological differences of cells and nuclei between new and recurrent HL patients. In the present analysis, Whole Slide Images (WSI) of 29 primary and 30 recurrent HL tissue sections with fuchsine (binding to anti-CD30) and hematoxylin staining were used. We expanded the CD30+ cell detection pipeline by Haladik [2] with a nuclei segmentation [4] of the detected cells, investigated morphological features, e.g. cell and nuclei size, and explored graph features of interacting CD30+ cells [3] like transitivity in a set of sub-images with high-quality segmentation.

Introduction

Input data
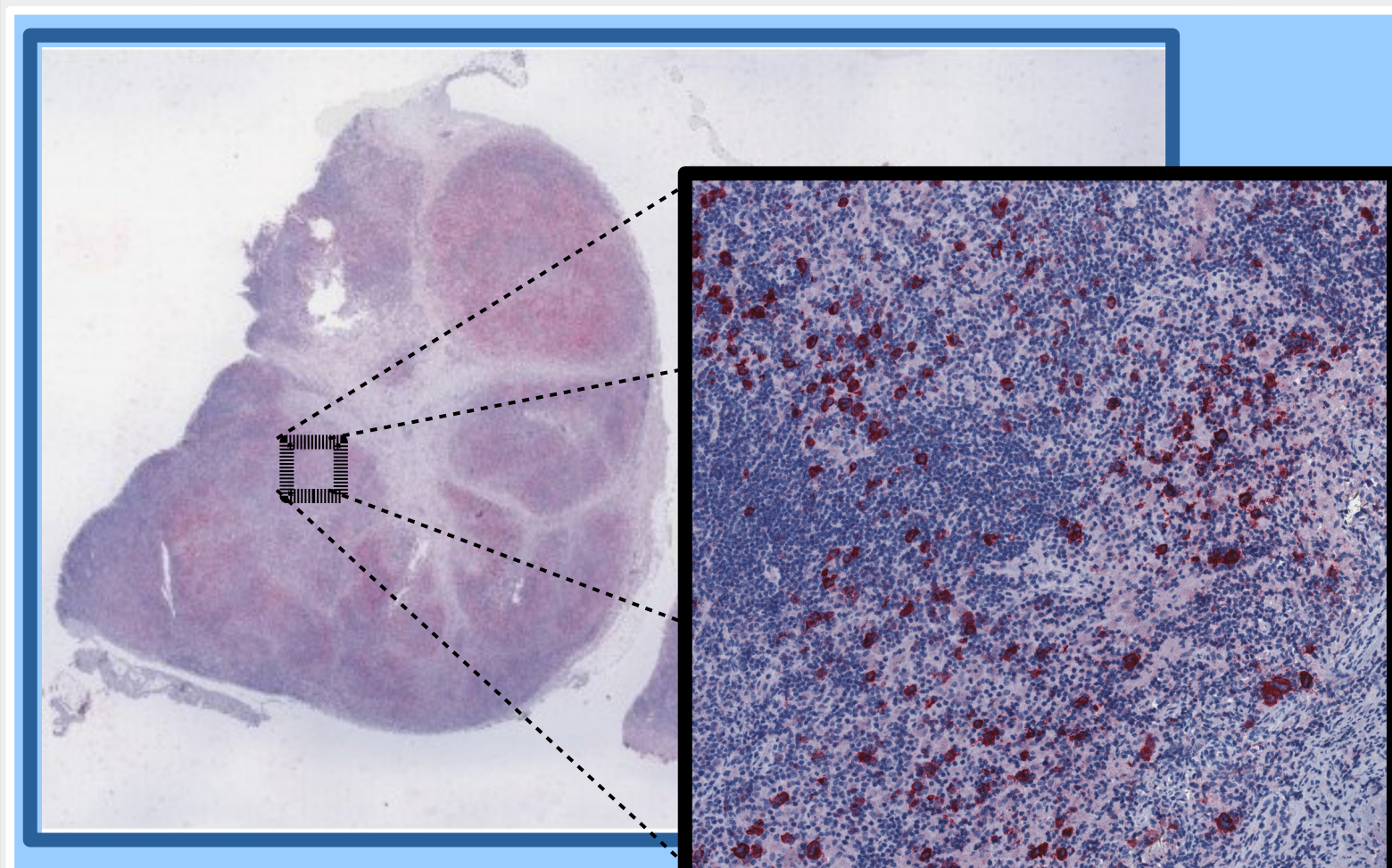
Immunohistologically stained tissue. Red stained cells are CD30+ cells, nuclei are colored in blue.

WSIs of classical HL (cHL) with subtype nodular sclerosis (NScHL) and mixed cellularity (MCcHL) from primary and recurrent cases.

Data set:

- Primary (29 WSIs)
  - NScHL (24 of 29 WSIs)
  - MCcHL (5 of 29 WSIs)
- Recurrent (30 WSIs)
  - NScHL (25 of 30 WSIs)
  - MCcHL (5 of 30 WSIs)

Pipeline
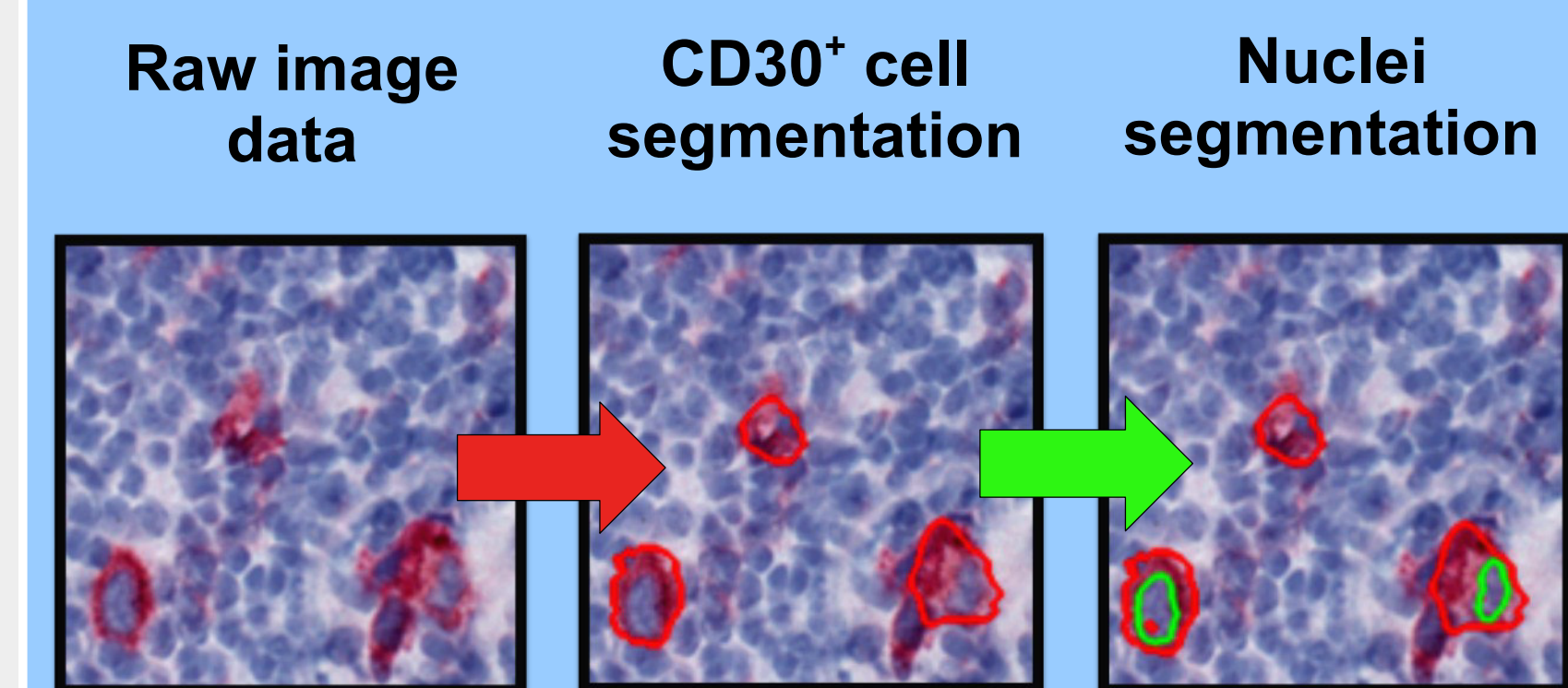
Workflow of the pipeline. Segmented CD30+ cell are red, segmented nuclei are green.

Methods

We measured different parameters for the morphology of cells and nuclei. The CD30+ cells were used to build a cell graph. Possible cell-cell interaction is represented as unit disk graph where two cells are connected if their Euclidean distance is less than 175 µm.
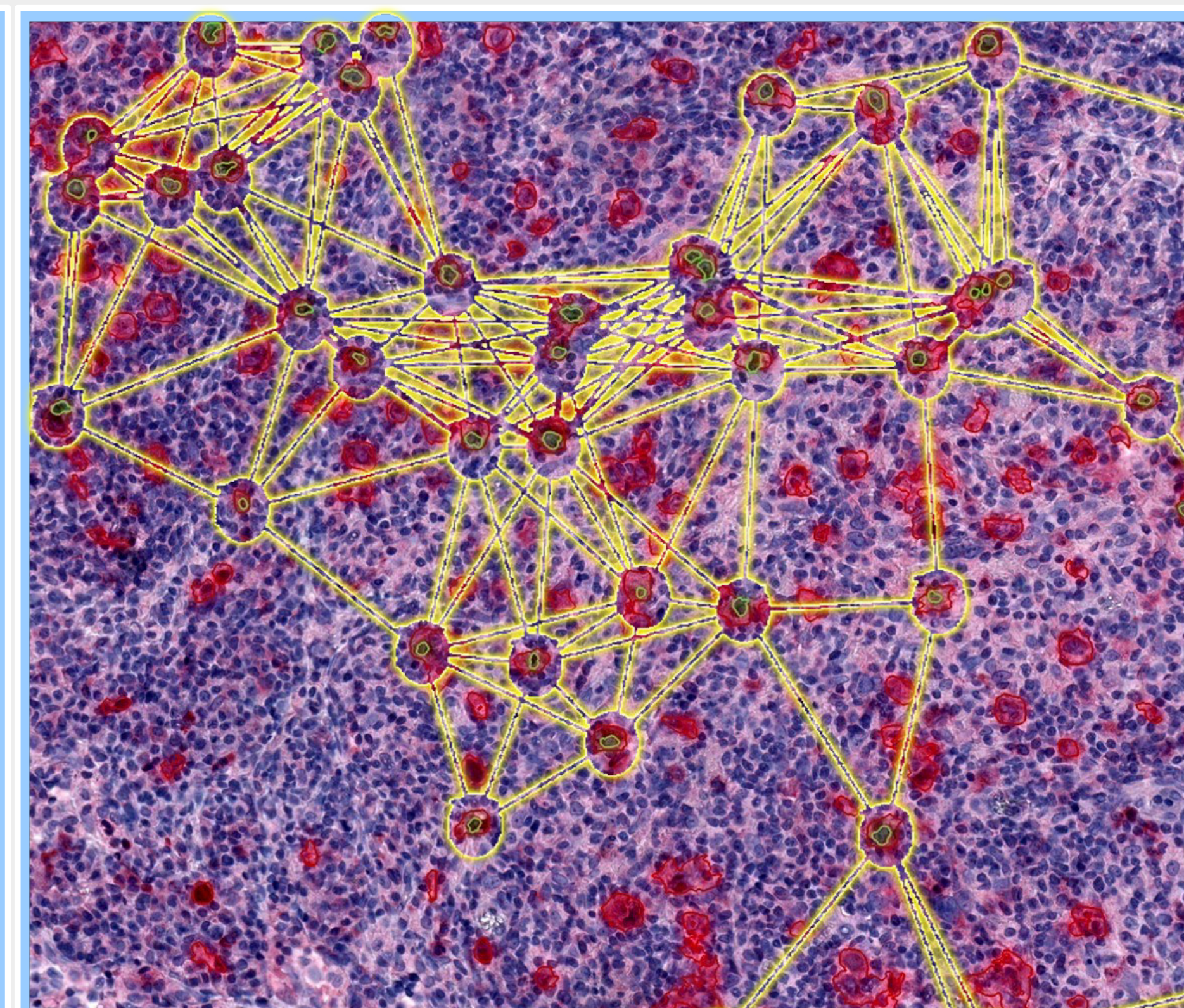
Investigated cell/nucleus properties

- Size
- Roundness
- Eccentricity
- Solidity
- Number of cells per image
- Number of nuclei per cell
- Number of nuclei per image

Investigated graph properties
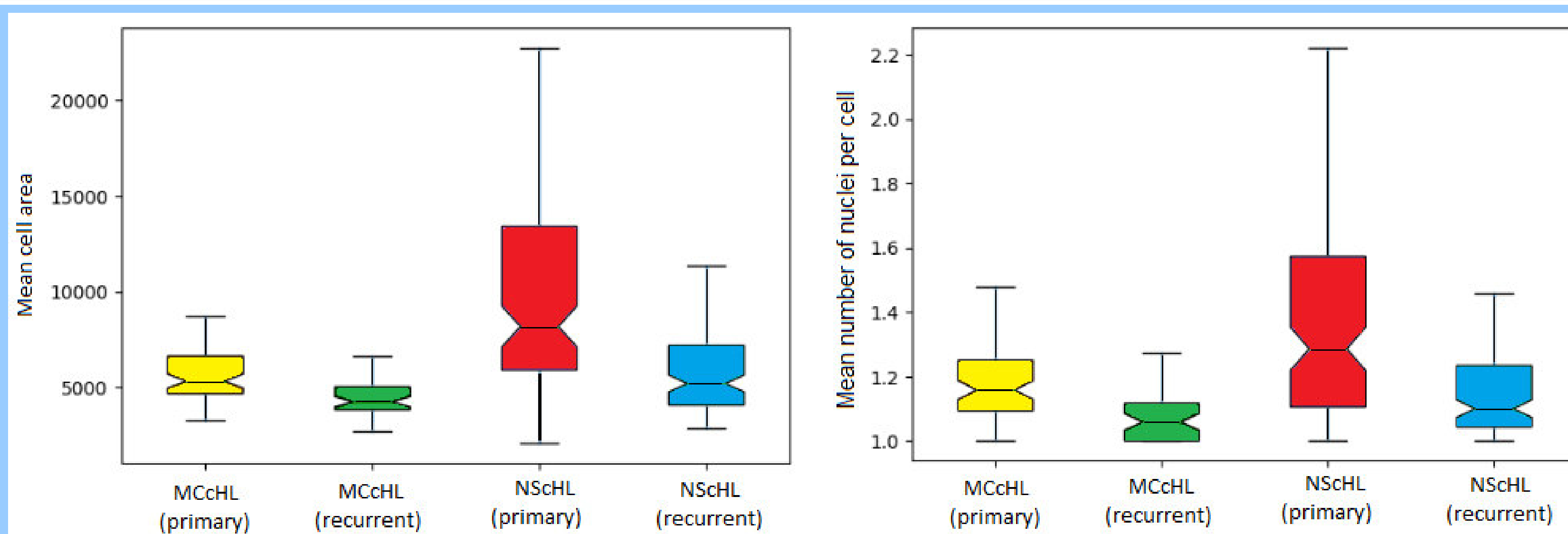
- Density
- Transitivity
- Clustering Coefficient
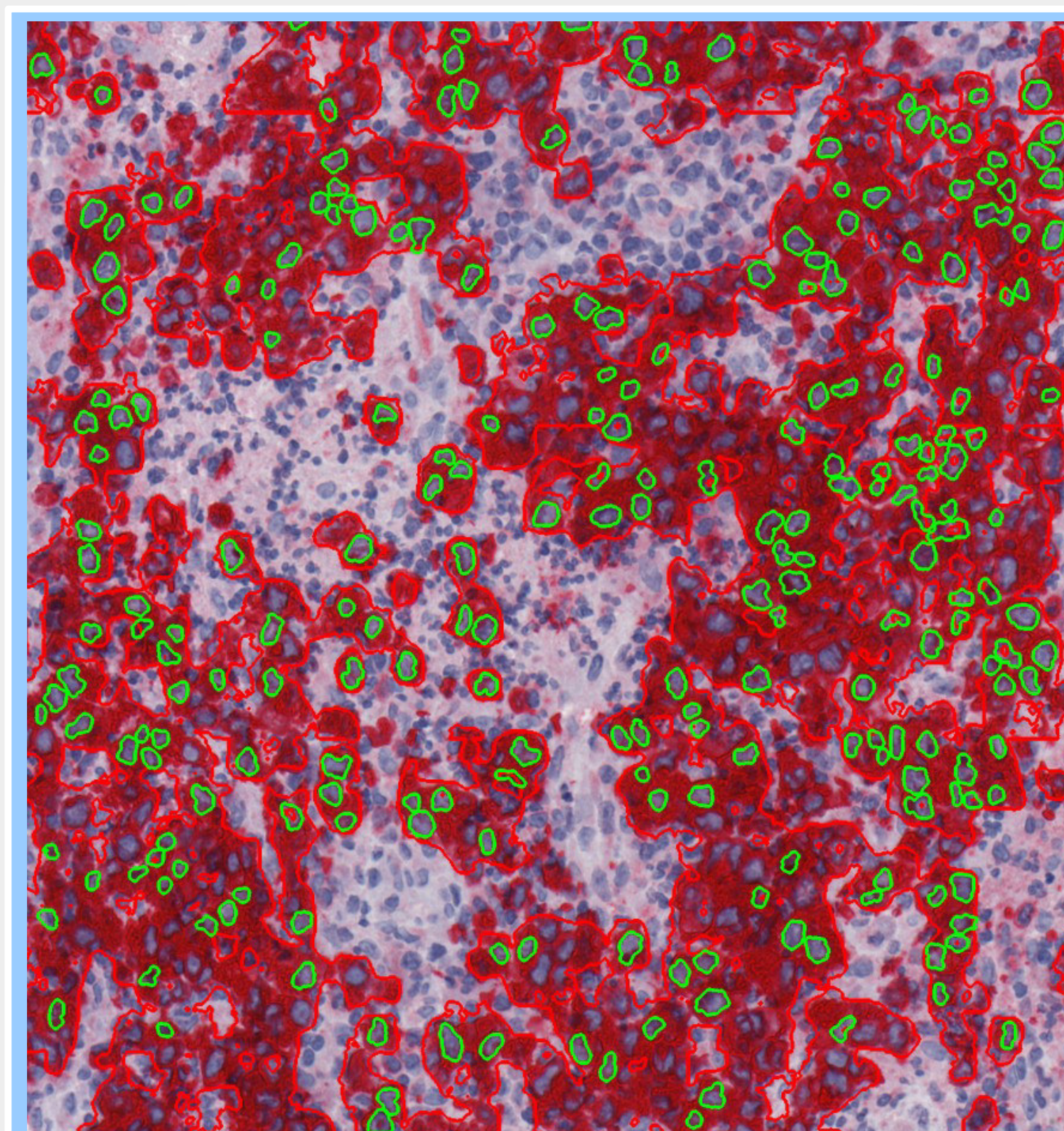
CD30-antibody and hematoxylin-stained tissue section with segmented CD30+ cells (red) and segmented nuclei (green)

Cell graph (yellow) with CD30+ cells as vertices and possible cell-cell interaction (distance less than 175 µm) as edges.
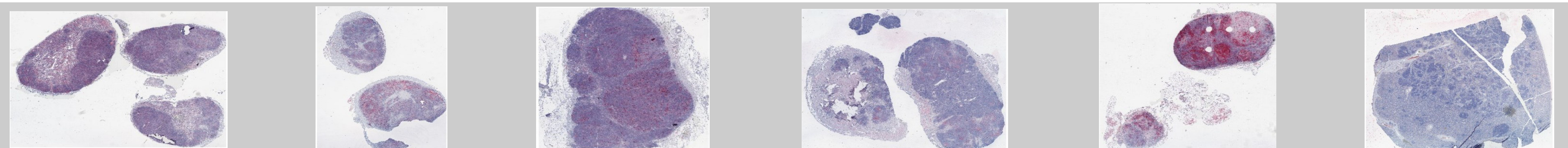
Results

Examples of measured features in primary and recurrent cases of mixed cellularity (MCcHL) and nodular sclerosis (NScHL) classical HL without outliers. Hodgkin/Reed-Sternberg (HRS) cells are characteristic of HL with large and multinucleated appearance. The mean cell area (left part) and mean number of nuclei per cell (right part) show smaller cells with less nuclei for recurrent cases in both subtypes.

Minimal differences were observed by comparing all CD30+ cells or their nuclei.

The average results per sub-image showed differences on a local scale:

The average cell area and the average number of nuclei per cells shows significantly lower results in recurrent cases in comparison to primary cases for the subtypes MCcHL and NScCHL (Gini index: 26-52%, corrected p-value < 0.01).

Outlook

Analysis of images from specific disease stages and exploration of the intercorrelations of the morphological characteristics between primary and recurrent cases would further validate the results of this study.

References

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[4] Yaniv, Z., Lowekamp, B. C., Johnson, H.J., & Beare, R. (2018). SimpleITK Image-Analysis Notebooks: a Collaborative Environment for Education and Reproducible Research, *J Digit Imaging, 31(3): 290-303.*

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