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Automatic segmentation of histopathological slides from renal allograft biopsies using artificial intelligence

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Objective: Histopathological analysis of renal biopsies depends on the identification and assessment of specific histological structures. Both in research and routine diagnostics, this analysis can be time-consuming and suffer from observer variability. Recently, it has been shown that the combination of high resolution whole slide imaging (WSI) and artificial intelligence yields powerful new avenues for tissue section analysis. This study aims to develop an algorithm based on a specific type of artificial intelligence (a convolutional neural network; CNN) to fully automatically segment structures in cortical fragments of renal allograft biopsies. Automated segmentation of renal tissue allows an unbiased, reproducible computation of morphological characteristics of important structures. This in turn can be used as support in diagnostic quantitative measure-based decisions as for instance is employed in the Banff-classification.

Methods: The neural network was trained using a set of Periodic acid-Schiff (PAS) stained slides (n=26) of renal allograft biopsies. WSIs were produced using a 3DHISTECH Pannoramic 250 Flash II digital slide scanner with a 20x objective lens. We used a U-net architecture CNN, which has been proven to be specifically useful in biomedical image segmentation tasks. Training was based on exhaustive annotations in one to two randomly selected rectangular areas per WSI (size approximately 3000 x 4000 pixels; comparable to one 200x microscopic field of view). A total of nine classes were annotated: *Glomeruli*, *Sclerotic glomeruli*, *Proximal tubuli*, *Distal tubuli*, *Atrophic tubuli*, *Undefined tubuli*, *Arteries*, *Capsule* and *Interstitium.* All annotations were revised by a pathology resident (JK), under consultation of an experienced nephropathologist (ES). Our CNN was evaluated using the Dice coefficient for each individual class. This coefficient expresses the quality of the segmentation on a scale ranging from 0-1, taking into account both recall and precision. Because of the limited amount of annotations for certain classes, cross-validation was applied.

Results: We found the following Dice coefficients for the different histological segments: *Glomeruli*: 0.89, *Sclerotic glomeruli*: 0.43, *Proximal tubuli*: 0.88, *Distal tubuli*: 0.77, *Atrophic tubuli*: 0.32, *Undefined tubuli*: 0.11, *Arteries*: 0.71, *Capsule*: 0.47 and *Interstitium*: 0.85.

Conclusion: This study shows that segmentation of WSIs of PAS-stained renal allograft biopsies using a CNN is feasible. Segmentation of several important classes (*Glomeruli*, *Interstitium*, *Arteries*, *Proximal-*, and *Distal tubuli*) was highly accurate. CNNs learn from being exposed to many example images. The most probable reason for the lower performance for the other classes are the relatively low number of annotated regions for these classes, combined with a high level of variability inherently present in these tissue structures. To our knowledge, this is the first time artificial intelligence is being deployed in a nine-class segmentation task in the field of kidney transplant histopathology. Results of this study show the promising potential of CNNs in obtaining quantitative, spatial and morphometric information from renal tissue in an objective, reproducible, high-scale fashion supporting diagnostic decisions based on quantitative measures.