

Standardized Assessment of Digital Renal Biopsy Whole Slide Images

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Background: Evaluating kidney biopsies on digital whole-slide-images rather than conventional slides enables permanent identification of all glomeruli and application of a standardized scoring system to each single glomerulus. Within EURenOmics this approach is being used to analyze kidney biopsies from children with steroid resistant nephrotic syndrome.

As part of the INTERNATIONAL digital nephropATHology network (INTEGRATE) we have adopted and slightly modified a scoring system developed by the NEPTUNE study group, who have recently reported on the reproducibility of this descriptor based scoring system¹.

Conclusion: Digital annotation identifies significantly more glomeruli than conventional evaluation.

The application of a descriptor-based scoring system yields more reproducible results for less detailed descriptors and those that are already part of an established classification systems such as tip-lesions.

Methods: 180 kidney biopsies (652 deidentified glass slides) from children with steroid-resistant nephrotic syndrome from 13 centers (7 countries) of the PodoNet registry have been scanned at 40-fold mag. by a Hamamatsu Nanozoomer.

Glomeruli were identified and given a unique number even if present on several sections (see figure 1)

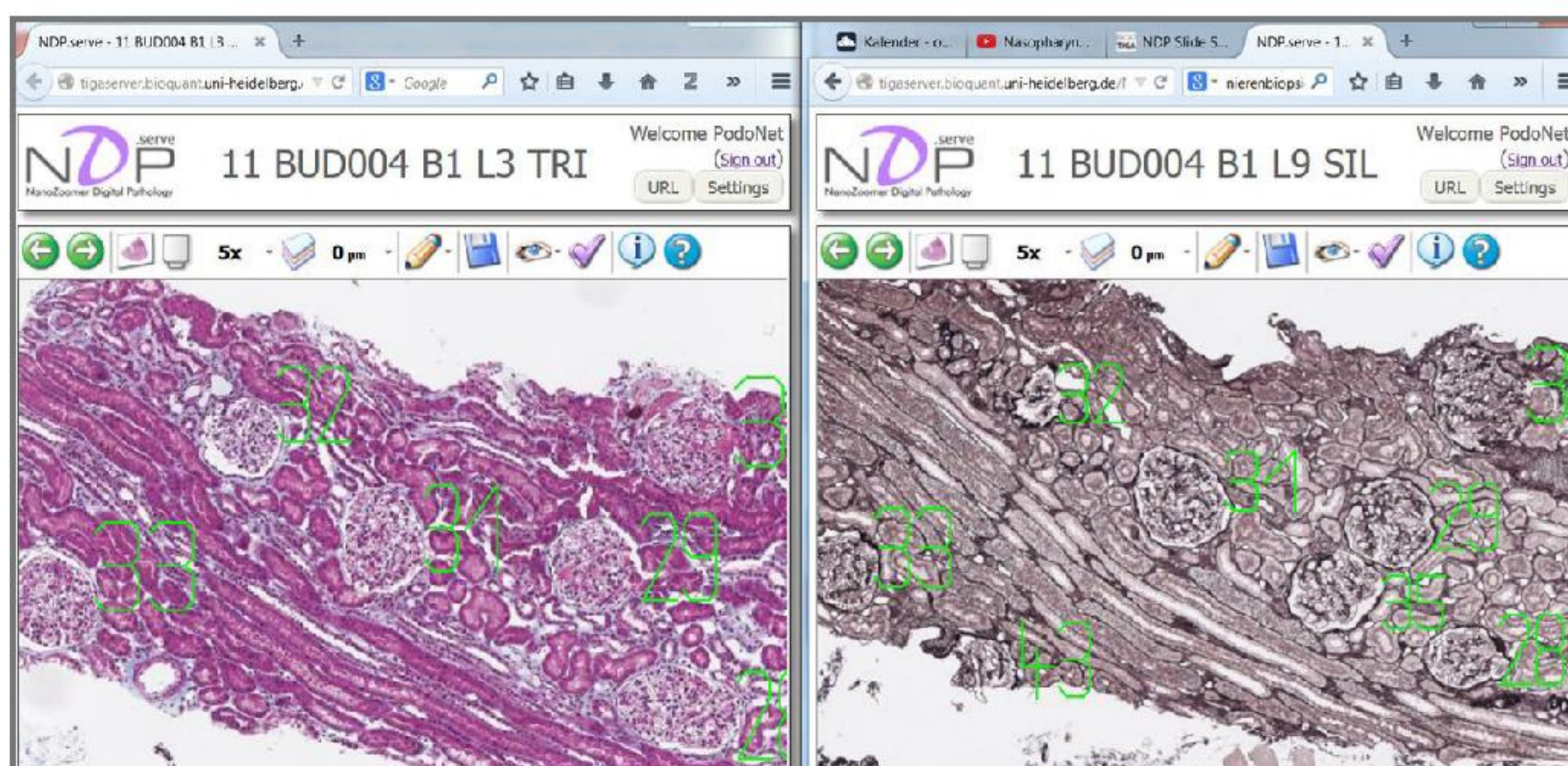


Figure 1: Screenshot of annotated glomeruli in parallel levels of one biopsy (synchronized pictures)

Results 1: Glomerular count

Digital annotation found over 70% more glomeruli than were given in the original reports (see table 1).

The number of additional glomeruli correlated to the number of slides that was available for digital annotation ($r=0.70$, $p<0.001$).

	No of Glomeruli	Range
Digital Annotation	38 ± 34	1-190
Original Pathology Report	22 ± 15	2-86
Difference	16 ± 31	$p<0.001$

Table 1: Number of glomeruli found by digital annotation vs given in original pathology reports in $n=126$ kidney biopsies

Results 2: Reproducibility

313 Glomeruli were scored by 2 blinded pathologists.

Clusters of glomerular descriptors	Kappa
Global obliteration	0.51
Segmental obliteration	0.13
Collapse (segmental and global)	0.75
Tip lesions (cellular and sclerosing)	0.67

Table 2: Fleiss kappa for reproducibility per glomeruli for 4 clusters of descriptors

Kappa coefficients of inter-rater reproducibility varied widely between the 51 detailed glomerular descriptors, and were generally improved by clustering into groups.

94 Glomeruli from biopsies with FSGS (focal segmental glomerulosclerosis)

	Kappa
All epithelial cell (podocyte) abnormalities	0.64
Epithelial cell hypertrophy (segmental and global)	0.61
Epithelial cell hyperplasia (segmental and global)	0.05
Segmental epithelial cell hypertrophy / hyperplasia	0.08
Global epithelial cell hypertrophy / hyperplasia	0.52

were scored by 3 blinded pathologists, with most reproducible detection of epithelial cell (podocyte) hypertrophy and global epithelial cell changes (table 3).

Table 3: Fleiss kappa for epithelial cell descriptors

References

1 Reproducibility of the NEPTUNE descriptor-based scoring system on whole-slide images and histologic and ultrastructural digital images. Barisoni L, Troost JP, Nast C, Bagnasco S, Avila-Casado C, Hodgin J, Palmer M, Rosenberg A, Gasim A, Liensziewski C, Merlino L, Chien HP, Chang A, Meehan SM, Gaut J, Song P, Holzman L, Gibson D, Kretzler M, Gillespie BW, Hewitt SM. Mod Pathol. 2016 Apr 22 [Epub ahead of print]