



Updates in renal pathology

Hyeon Joo Jeong

Department of Pathology, Yonsei University College of Medicine, Seoul, Republic of Korea

Our understanding on the pathophysiology of glomerular diseases has largely relied on meticulous evaluation and strategic approaches to renal biopsy material using light microscopy (LM), immunofluorescence (IF), and electron microscopy (EM). Glomerular morphology has been categorized based on injury patterns indicated by changes in glomerular cellularity and cell types, and abnormal loop changes under LM, after which several primary glomerular diseases have been named, such as focal segmental glomerulosclerosis and diffuse proliferative or mesangioproliferative glomerulonephritis. Subtyping of glomerular morphology has been used as a therapeutic guide or prognostic parameter of immunoglobulin A (IgA) nephropathy, lupus nephritis, and antineutrophil cytoplasmic antibody-associated glomerulonephritis. IF can be used to identify IgA nephropathy and C3 glomerulopathy regardless glomerular histology, meanwhile diffuse glomerular basement membrane (GBM) thinning on EM characterizes thin GBM nephropathy. Recently, immunohistochemistry, mass spectrometry, and next-generation sequencing techniques have been included in the diagnosis of fibrillary glomerulonephritis, typing of amyloid fibrils, and exploring the etiology of hereditary nephropathy, respectively. We admit that correlations between renal morphology and clinical findings continue to fall short of our expectations, and we hope that further investigations into glomerular morphology and the discovery of new diagnostic/research

tools will narrow this gap.

This special issue of *Kidney Research and Clinical Practice* focuses on two selected topics, an update on lupus nephritis (glomerular morphology) and a three-dimensional EM technique (new diagnostic/research tool).

The first World Health Organization (WHO) classification of lupus nephritis was formulated in 1974, and modified in 1982, yet the benefit of renal biopsy in the prediction of renal outcomes and as a prognostic indicator remains an issue [1]. The 2003 International Society of Nephrology (ISN)/Renal Pathology Society (RPS) classification was another modified WHO system, which was more complex than the previous systems, did not reach a consensus among renal pathologists, and did not significantly improve clinicopathological correlation [1–3]. The modified ISN/RPS classification was proposed in 2018, of which classes were simplified and histologic indices were added [4]. Choi et al. [5] reviewed the 2018 ISN/RPS classification, especially the activity and chronicity indices, which were modified from the National Institutes of Health-sponsored 1983 classification, and the clinical significance of these histologic indices.

Conventional transmission EM (TEM) is useful for identifying glomerular cellular and GBM alterations, but is limited in viewing the whole scope of changes due to its two-dimensional nature. To overcome this limitation, Honda et al. [6] introduced several three-dimensional EM tech-

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Correspondence: Hyeon Joo Jeong

Department of Pathology, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea.

E-mail: jeong10@yuhs.ac

ORCID: <https://orcid.org/0000-0002-9695-1227>

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nologies—three-dimensional EM, correlative light and EM, low vacuum SEM, and scanning TEM—and demonstrated possible clinical applications in select glomerular diseases [7–12]. These techniques are fascinating in that glomerular podocytes and GBM can be observed three-dimensionally in frozen or formalin-fixed paraffin-embedded sections, and that the area of interest on LM and IF can be correlated with ultrastructural features.

I hope the concise, well-summarized reviews of lupus nephritis and EM methods in this special issue will contribute up-to-date information and knowledge that can be used in future patient management and research on glomerulonephritis.

Conflicts of interest

The author has no conflicts of interest to declare.

ORCID

Hyeon Joo Jeong, <https://orcid.org/0000-0002-9695-1227>

References

1. Wilhelmus S, Alpers CE, Cook HT, et al. the revisited classification of GN in SLE at 10 years: time to re-evaluate histopathologic lesions. *J Am Soc Nephrol* 2015;26:2938–2946.
2. Weening JJ, D'Agati VD, Schwartz MM, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. *J Am Soc Nephrol* 2004;15:241–250.
3. Weening JJ, D'Agati VD, Schwartz MM, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. *Kidney Int* 2004;65:521–530.
4. Bajema IM, Wilhelmus S, Alpers CE, et al. Revision of the International Society of Nephrology/Renal Pathology Society classification for lupus nephritis: clarification of definitions, and modified National Institutes of Health activity and chronicity indices. *Kidney Int* 2018;93:789–796.
5. Choi SE, Fogo AB, Lim BJ. Histologic evaluation of activity and chronicity of lupus nephritis and its clinical significance. *Kidney Res Clin Pract* 2023;42:166–173.
6. Honda K, Takaki T, Kang D. Recent advances in electron microscopy for the diagnosis and research of glomerular diseases. *Kidney Res Clin Pract* 2023;42:155–165.
7. Titze B, Genoud C. Volume scanning electron microscopy for imaging biological ultrastructure. *Biol Cell* 2016;108:307–323.
8. Briggman KL, Bock DD. Volume electron microscopy for neuronal circuit reconstruction. *Curr Opin Neurobiol* 2012;22:154–161.
9. Sjollem KA, Schnell U, Kuipers J, Kalicharan R, Giepmans BN. Correlated light microscopy and electron microscopy. *Methods Cell Biol* 2012;111:157–173.
10. Kubota Y, Sohn J, Kawaguchi Y. Large volume electron microscopy and neural microcircuit analysis. *Front Neural Circuits* 2018;12:98.
11. Inaga S, Kato M, Hirashima S, et al. Rapid three-dimensional analysis of renal biopsy sections by low vacuum scanning electron microscopy. *Arch Histol Cytol* 2010;73:113–125.
12. Aoyama K, Takagi T, Hirase A, Miyazawa A. STEM tomography for thick biological specimens. *Ultramicroscopy* 2008;109:70–80.