

Ultrasound and 3D imaging characterisation of a rat model of polycystic kidney disease

Authors

Maria Ougaard, Trine Porsgaard, Louise Thisted, Jacob Skytte, Johanna Perens, Frederikke Sembach, Michael Christensen

Gubra, Hørsholm Kongevej 11B, Hørsholm, Denmark

Corresponding author

Michael Christensen - mch@gubra.dk

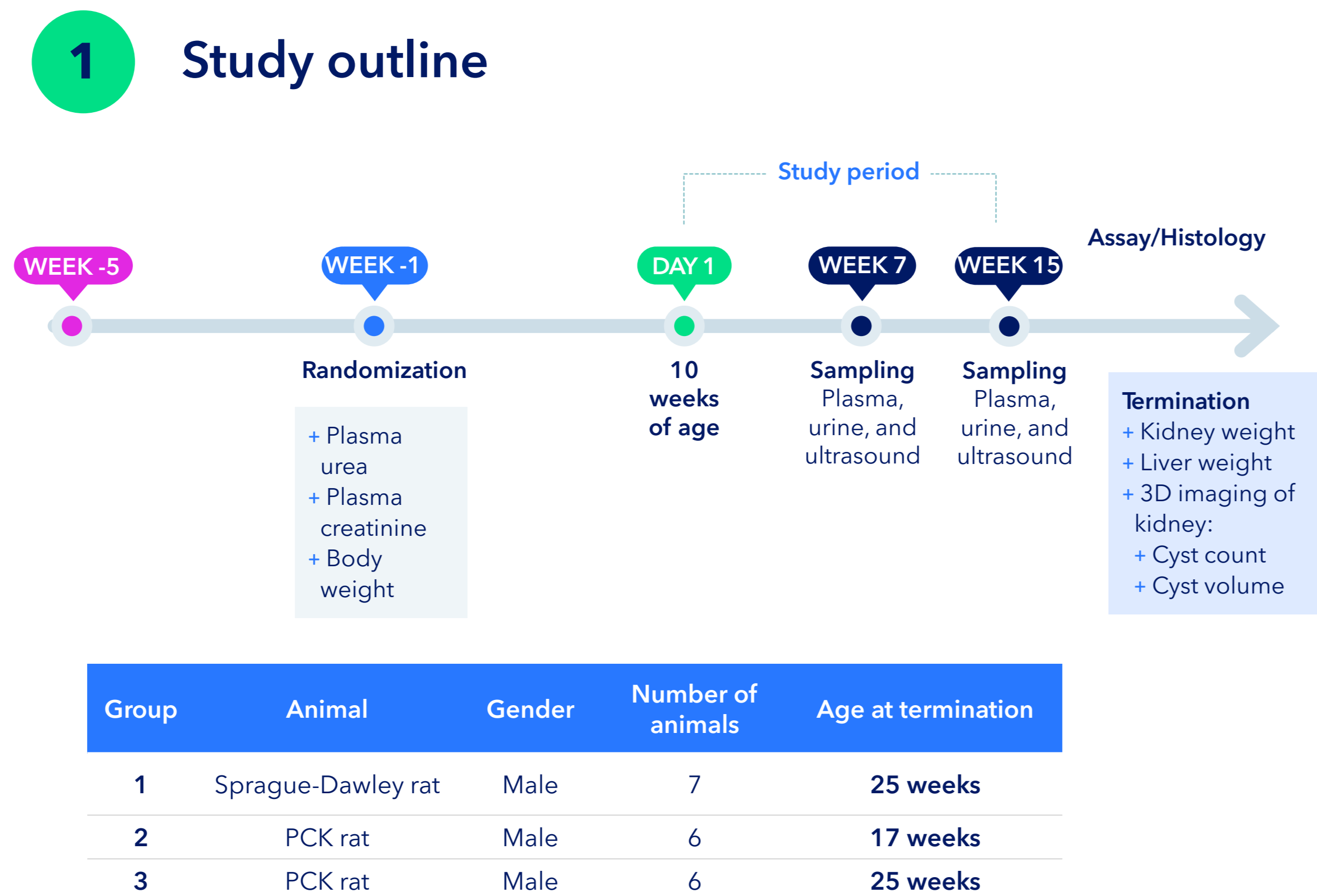
Background & Aim

Polycystic kidney disease (PKD) is a congenital fibrocystic disorder where cysts are forming within the kidney causing kidney enlargement and declining kidney function which can eventually lead to chronic kidney disease (CKD). Translational animal models can inform about potential clinical efficacy of novel drug candidates for PKD. The PCK rat is an established genetic model of PKD with natural history and renal histologic abnormalities that resemble the human disease.

The present study aimed to characterize disease progression in the PCK rat model.

Methods

10 weeks-old male PCK rats (PCK/CrljCrl-Pkhd1pck/Crl) were from Charles River Laboratories. Male Sprague-Dawley rats served as healthy controls. Body weight was measured bi-weekly. Plasma urea/creatinine, urine albumin/creatinine and right kidney size/volume (ultrasound imaging) was assessed. Upon termination at 17 and 25 weeks of age, kidney and liver weight was obtained, and right whole-kidney cyst morphometrics was performed using quantitative light sheet 3D imaging.



2 Terminal body, kidney and liver weight

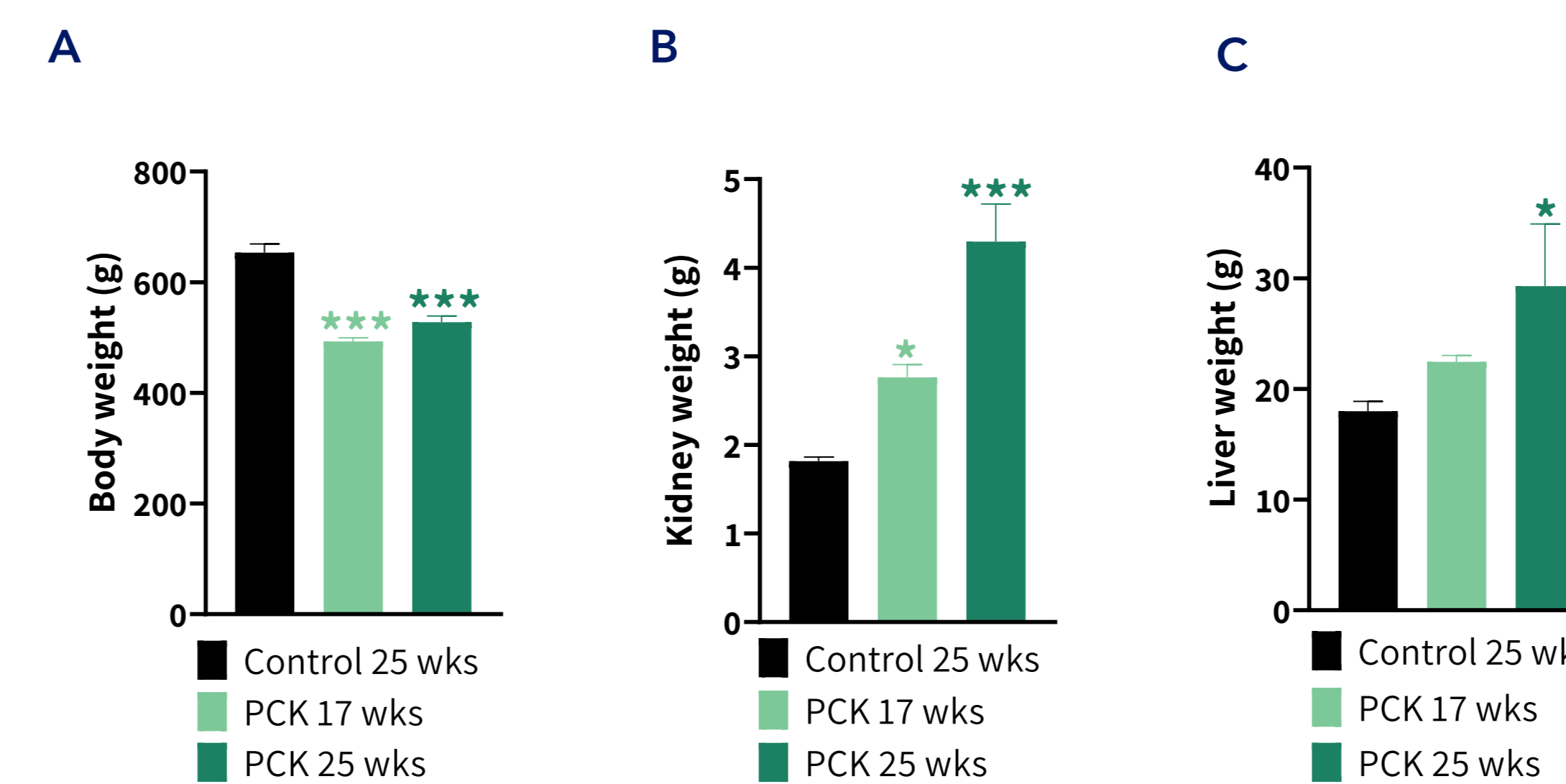


Figure 1. PCK rats demonstrate lowered body weight concomitant with progressively increased kidney and liver weight. (A) Terminal body weight. (B) Right kidney weight. (C) Liver weight. Mean + SEM. *p<0.05, ***p<0.001 compared to Control (Dunnett's test one-factor linear model).

3 Progressive kidney injury in PCK rats

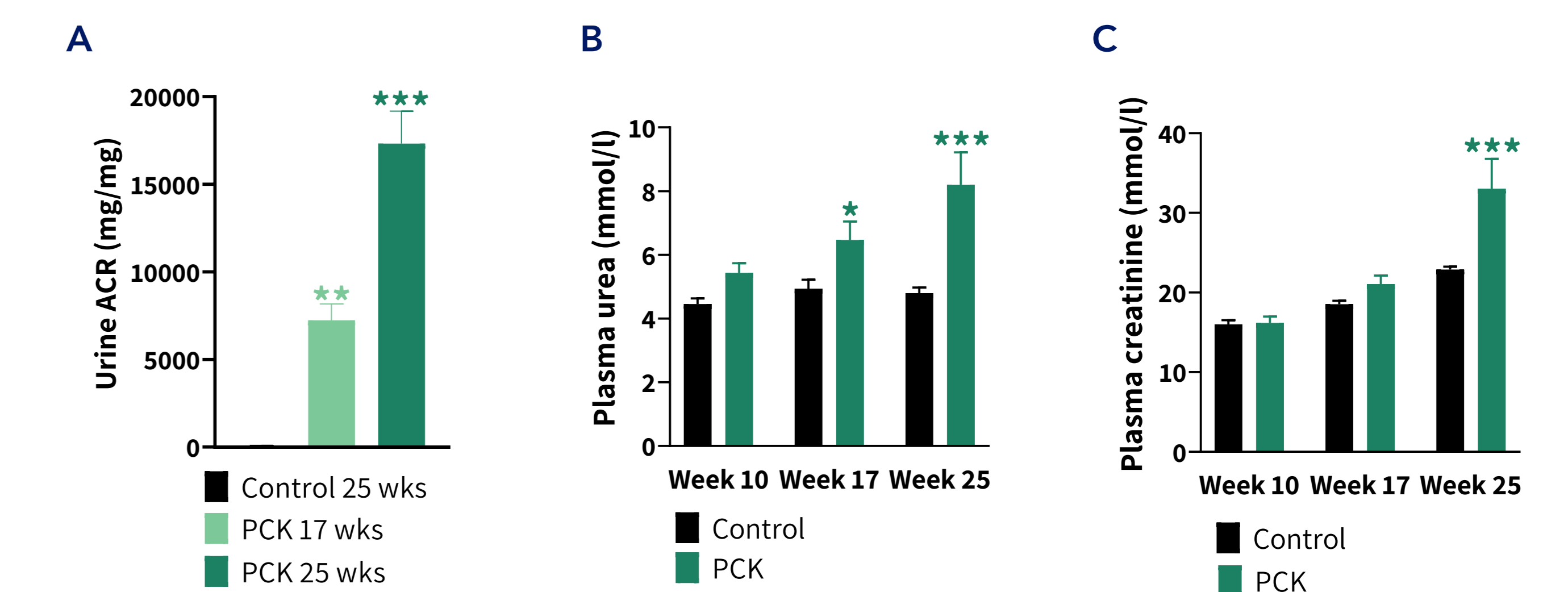


Figure 2. PCK rats show increased plasma and urine markers of kidney injury. (A) Urine albumin-to-creatinine ratio (ACR) at termination. (B) Plasma urea. (C) Plasma creatinine. Mean + SEM. *p<0.05, **p<0.01, ***p<0.001 compared to Control (Dunnett's test one-factor linear model).

4 Kidney enlargement in PCK rats - ultrasound imaging

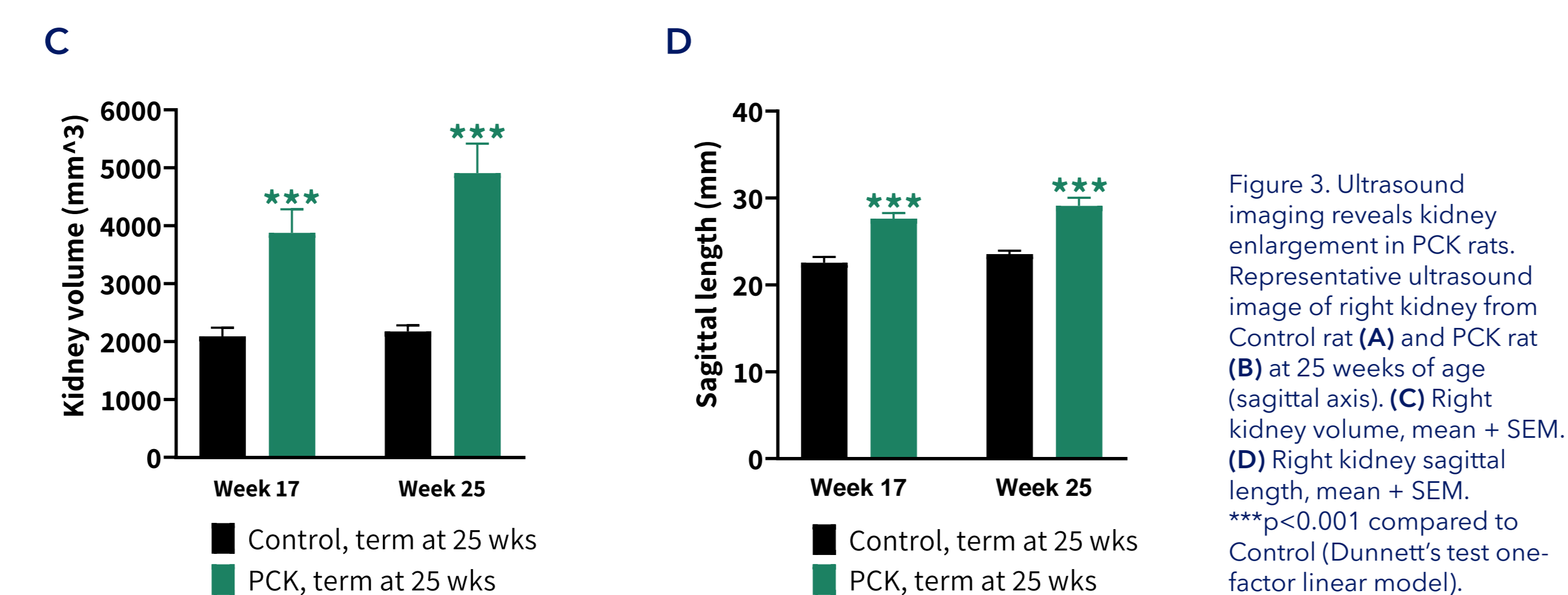
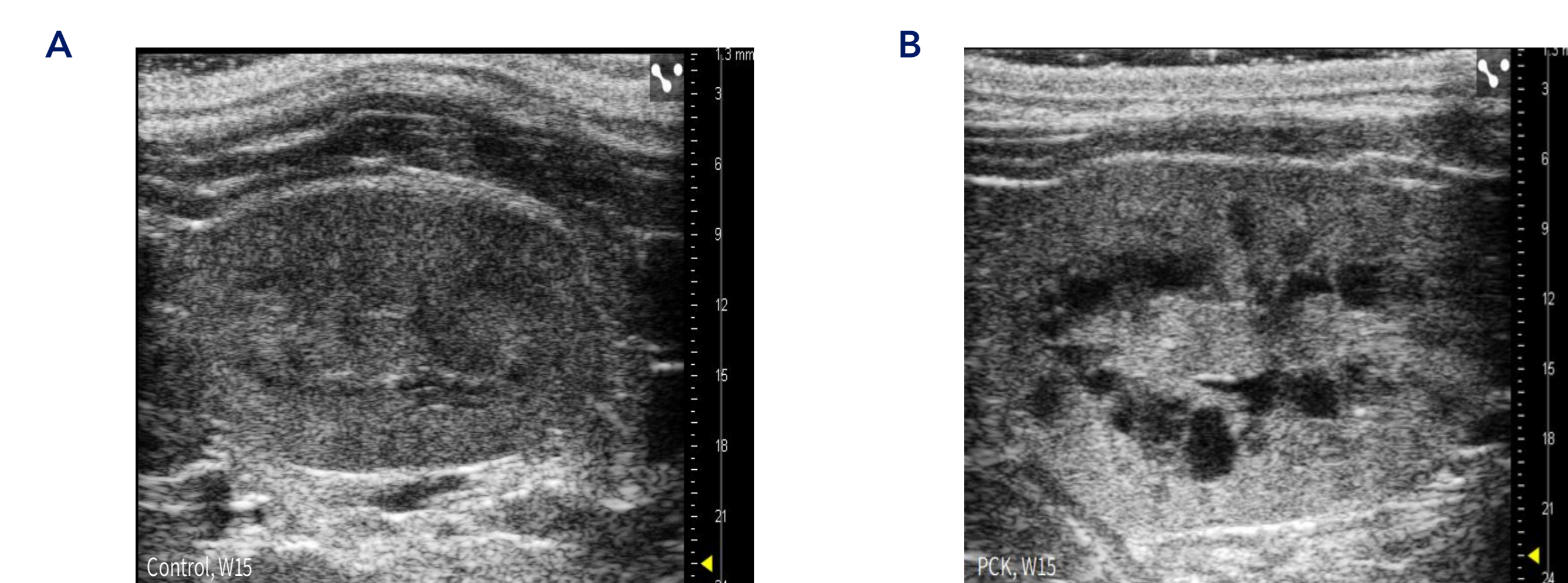


Figure 3. Ultrasound imaging reveals kidney enlargement in PCK rats. Representative ultrasound image of right kidney from Control rat (A) and PCK rat (B) at 25 weeks of age (sagittal axis). (C) Right kidney volume, mean + SEM. (D) Right kidney sagittal length, mean + SEM. ***p<0.001 compared to Control (Dunnett's test one-factor linear model).

5 Progressive cystic enlargement in PCK rats-Light sheet imaging

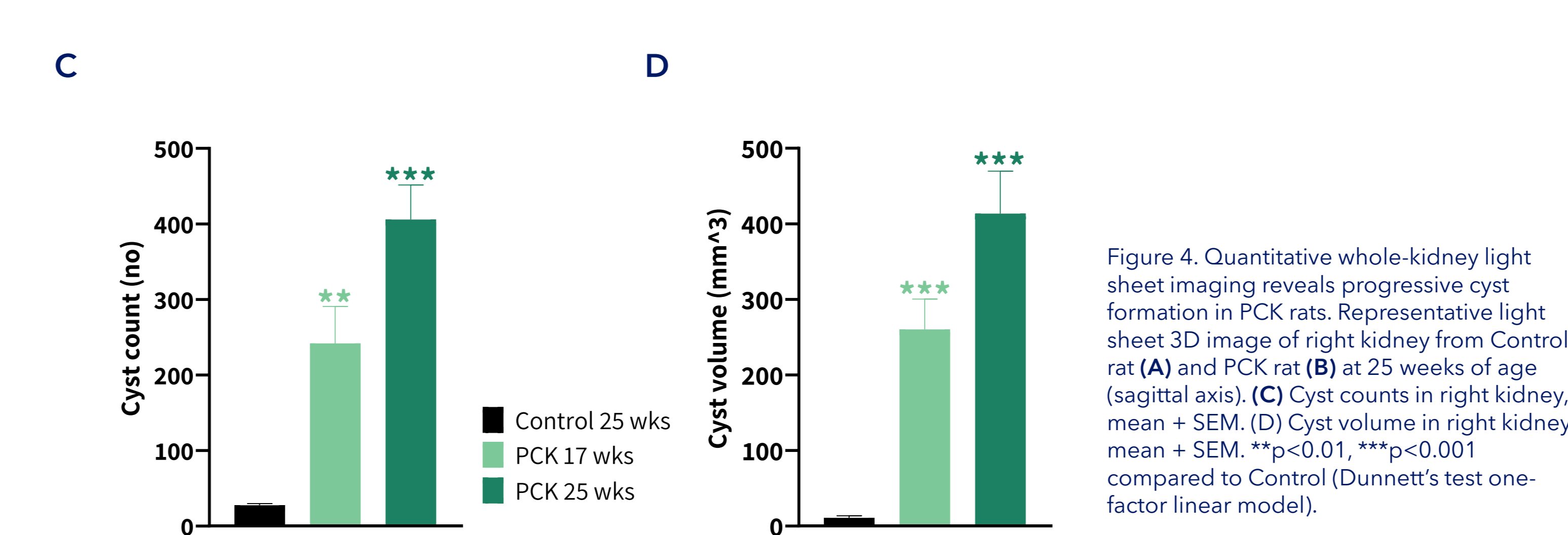
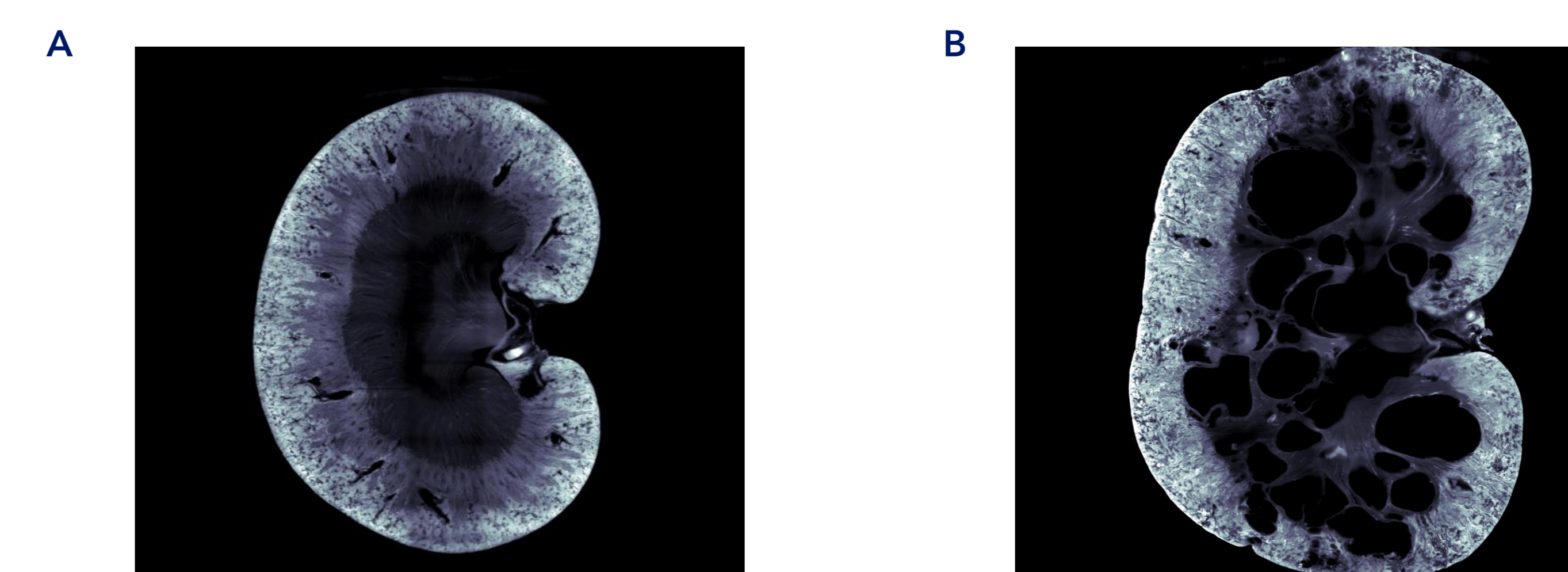


Figure 4. Quantitative whole-kidney light sheet imaging reveals progressive cyst formation in PCK rats. Representative light sheet 3D image of right kidney from Control rat (A) and PCK rat (B) at 25 weeks of age (sagittal axis). (C) Cyst counts in right kidney, mean + SEM. (D) Cyst volume in right kidney, mean + SEM. **p<0.01, ***p<0.001 compared to Control (Dunnett's test one-factor linear model).

Conclusion

- + The PCK rat shows progressive kidney injury and enlarged kidneys
- + The PCK rat shows marked and progressive renal cyst formation
- + Combined ultrasound and light sheet imaging is advantageous for quantitative analysis of whole-kidney pathology in the PCK rat.

The PCK rat model is a translational preclinical model suitable for testing novel drug therapies for PCK.

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