

URINARY TRACT OBSTRUCTION AND REDUCED NEPHRON NUMBER: ADAPTATION OF NEPHRONS FOLLOWED THROUGH ADULTHOOD IN A MOUSE MODEL

Maria SERGIO¹, C.I. GALATARREA², B.A. THORNILL², M.S. FORBES² and R.L. CHEVALIER²

¹Pediatric Surgery, Dipartimento Materno Infantile, Palermo, ITALY

² University of Virginia, Department of Pediatrics, Charlottesville, USA

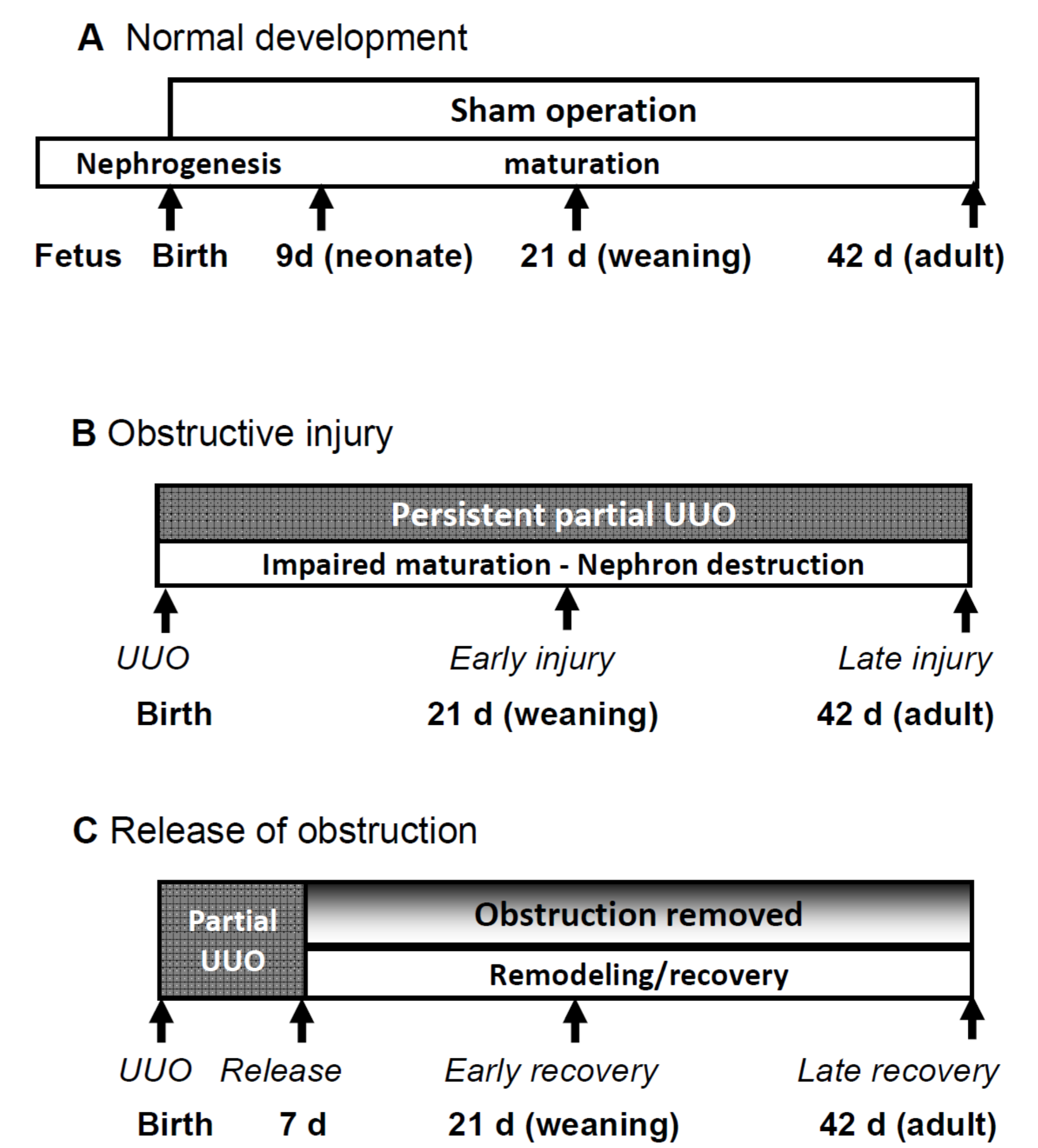
Introduction: Congenital urinary tract obstruction affects renal development and maturation, often leading to chronic kidney disease (CKD). Associated with CAKUT (congenital anomalies of kidneys and urinary tract), reduced nephron number (NN) at birth is an independent risk factor for adult CKD. (Luyckx VA et al. Lancet 2013; 382: 273).

We aimed to examine the behavior of nephrons in adult mice with reduced NN subjected to partial unilateral ureteral obstruction (UUO).

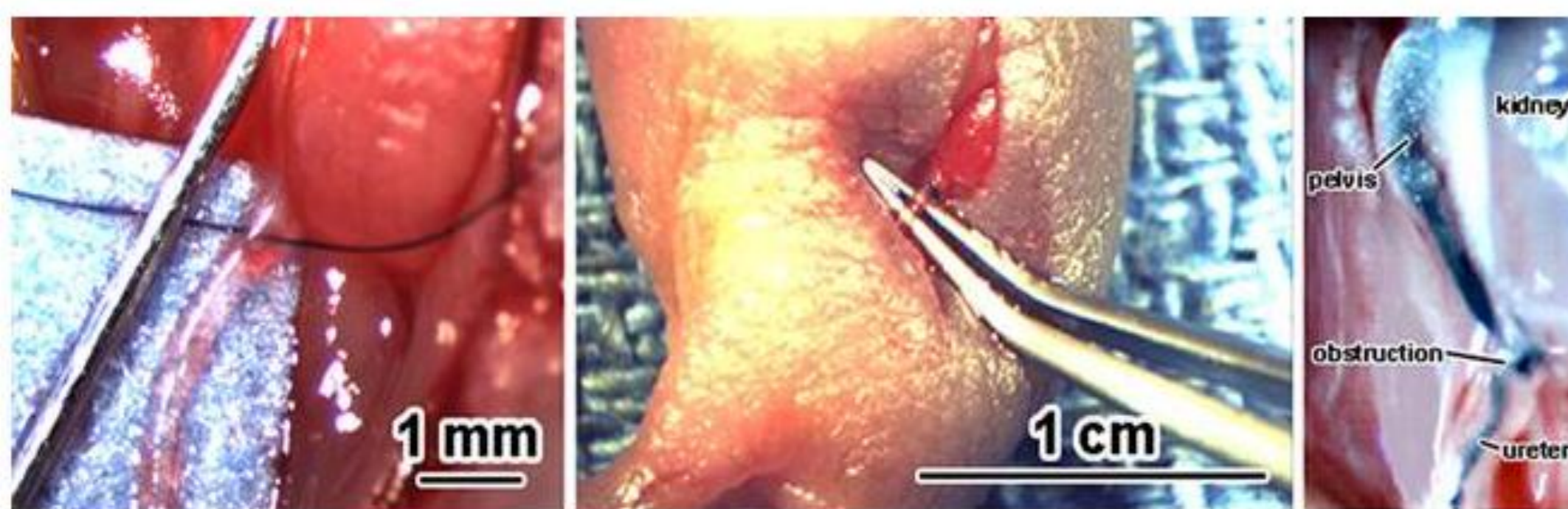
Methods: Wild-type (WT) and Os/+ mice (with 50% fewer nephrons) were subjected to sham operation or partial UUO in the first 2 days of life. Additional mice underwent release of UUO at 7 days. All kidneys were harvested at 3 weeks (weaning) or 6 weeks (adulthood). Parameters evaluated by histomorphometry were: glomerular number and area, glomerulotubular junction integrity, proximal tubular volume fraction, and interstitial fibrosis.

Results: In Os/+ mice, NN decreased further in the UUO kidney, and glomerular growth from 21 to 42 days of Os/+ mice was impaired, regardless of the release of UUO. Whereas UUO impaired maturation of the glomerulotubular junction and proximal tubular growth in all mice, release of obstruction preserved these in wild-type mice only. Interstitial collagen accumulated after 42 days of ipsilateral UUO, decreased following release of obstruction in wild-type, but not Os/+ mice.

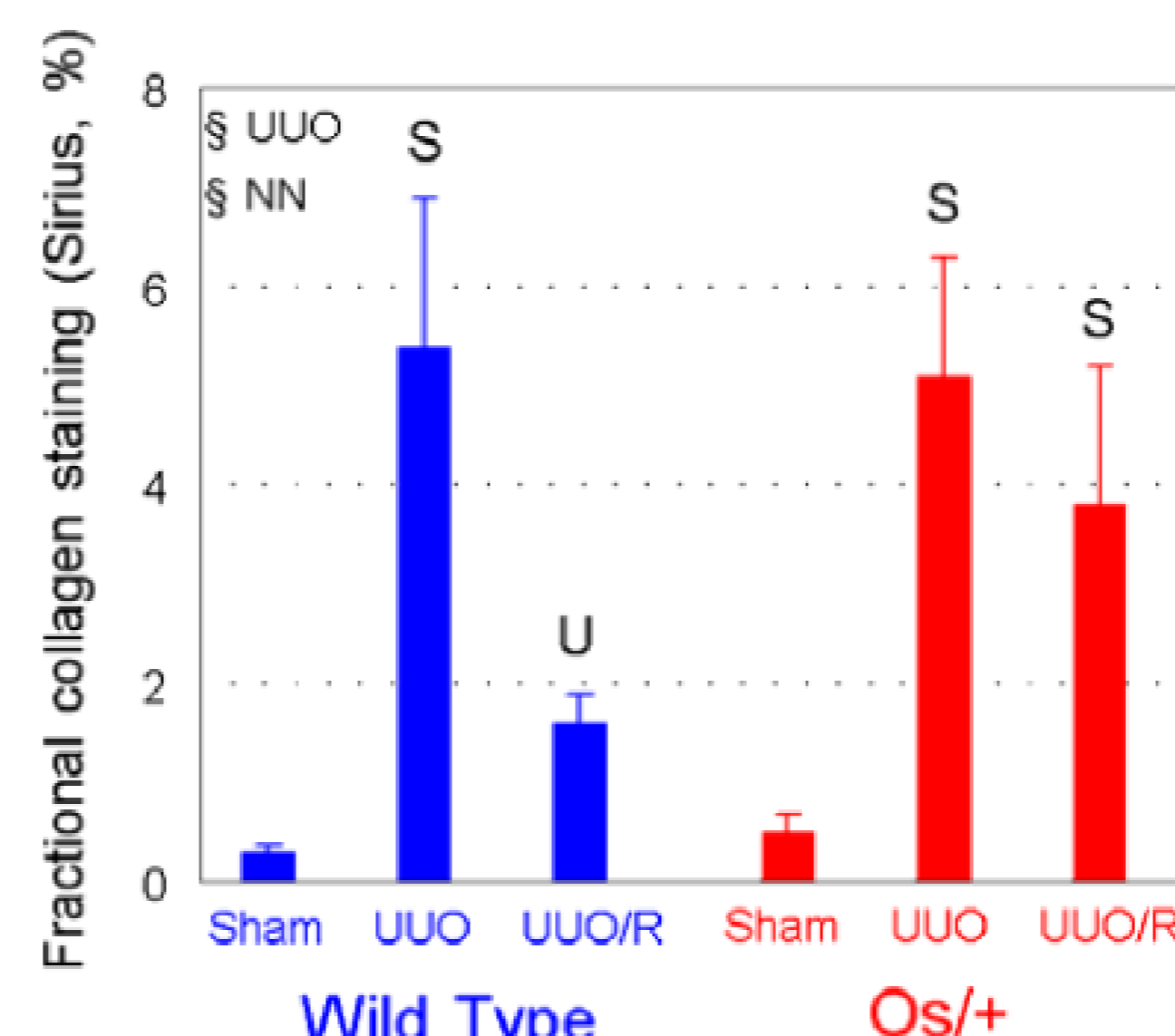
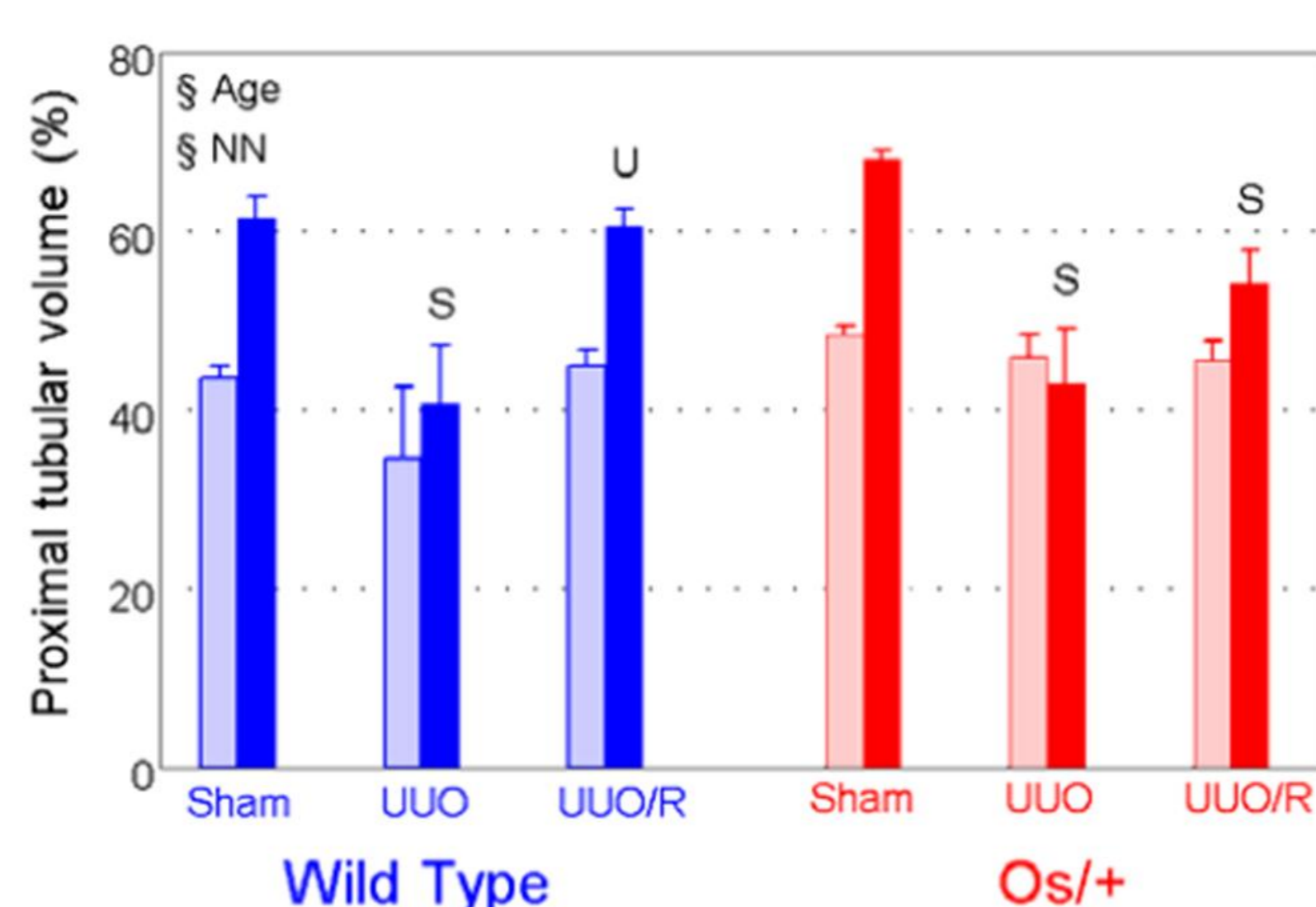
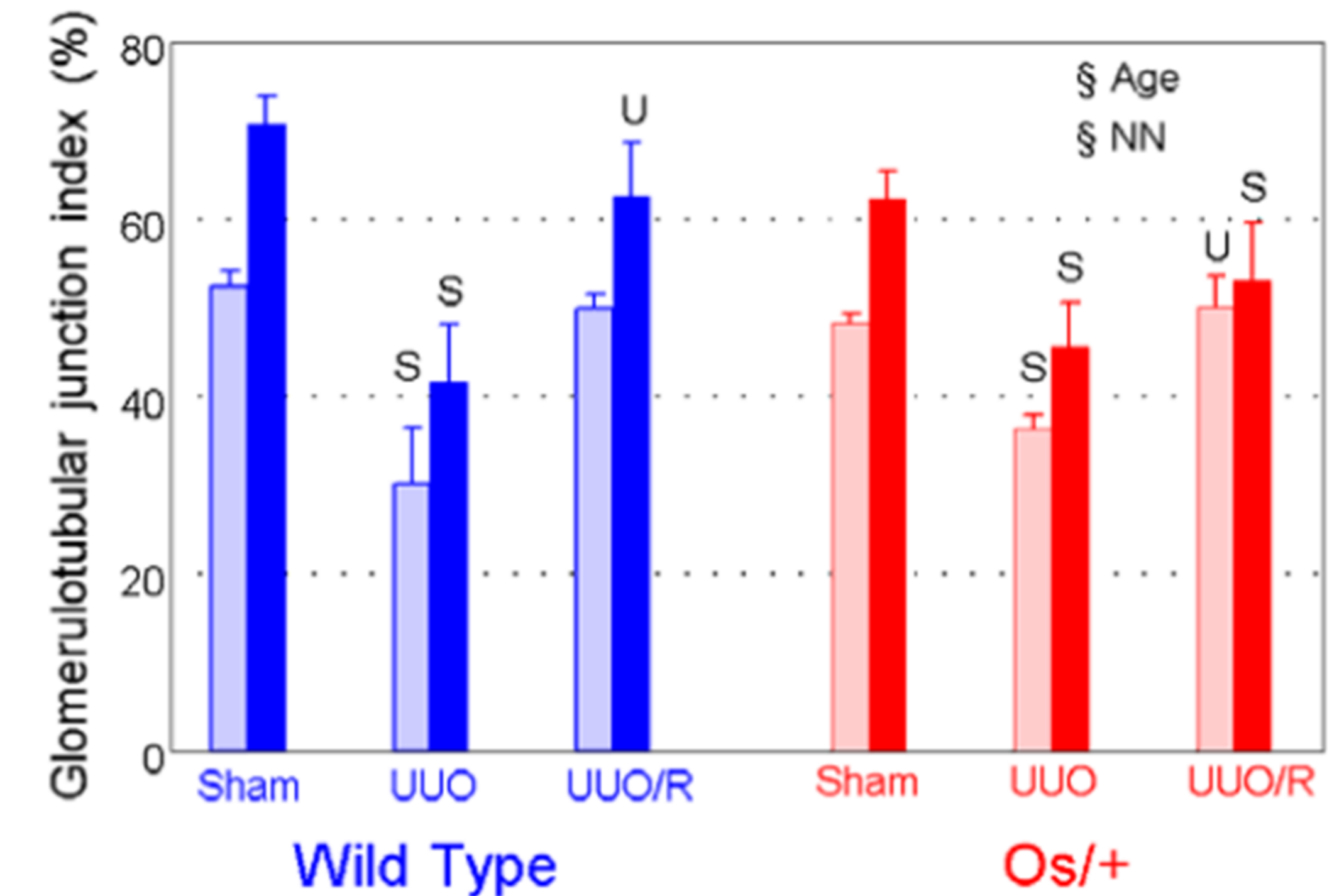
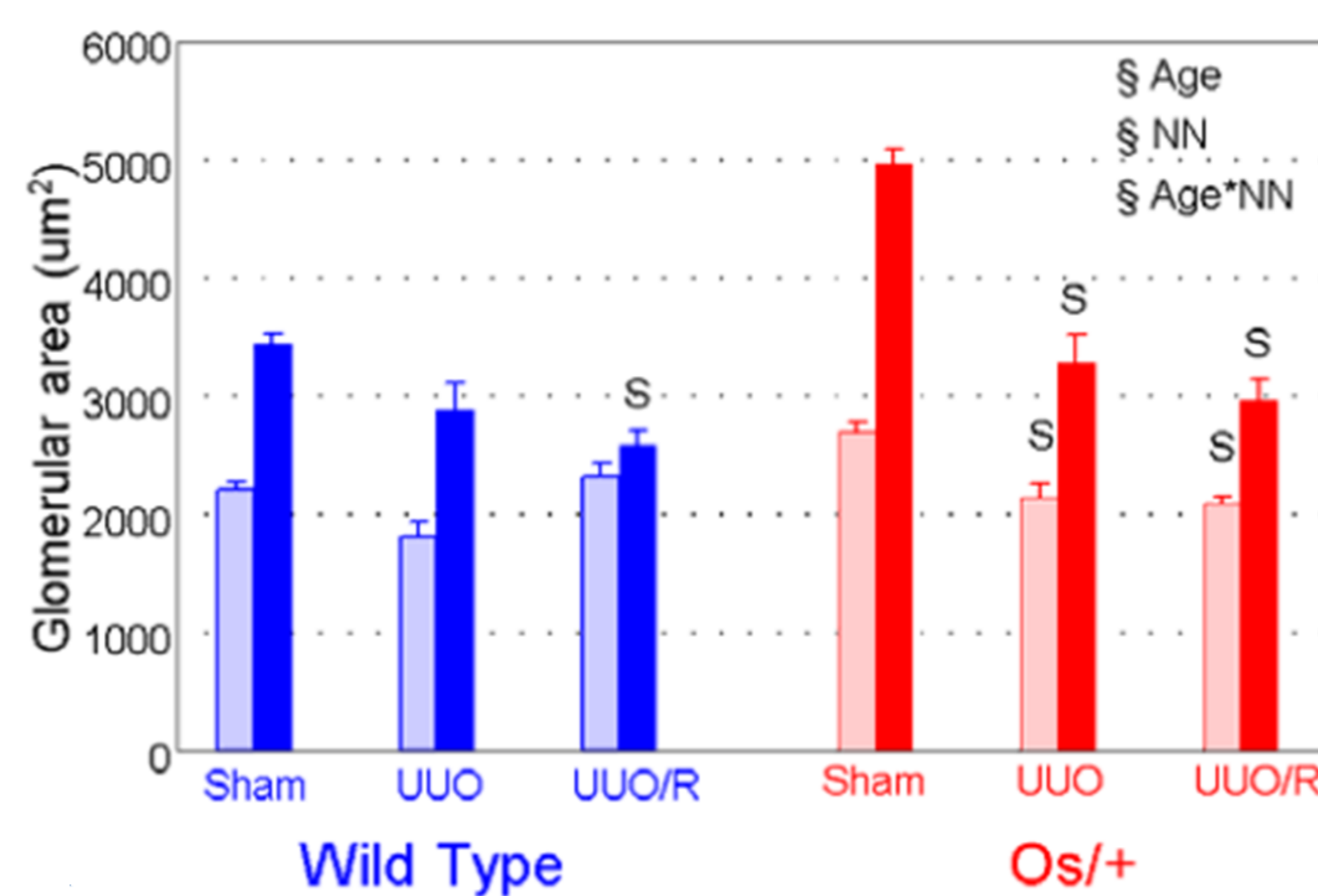
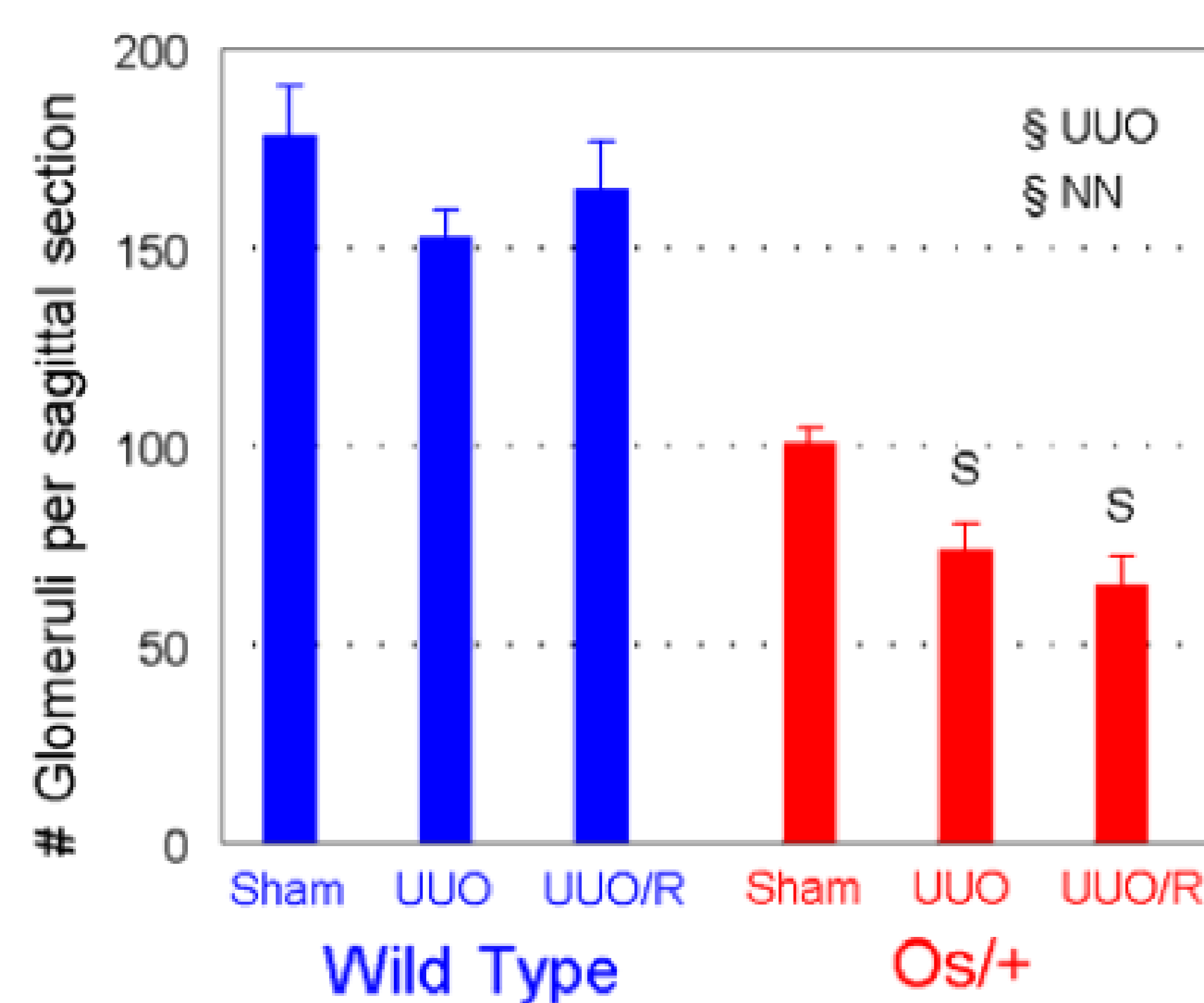
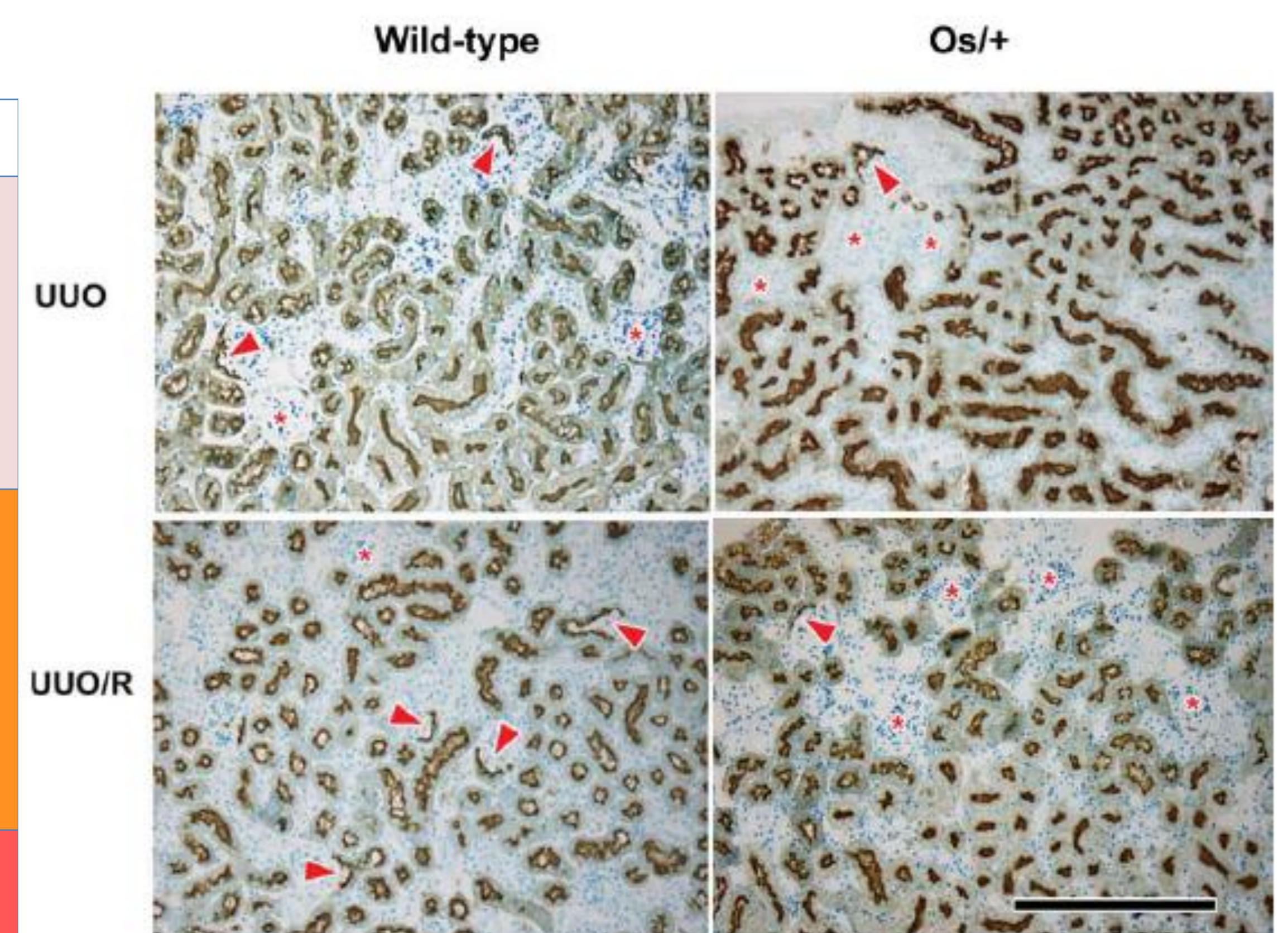
Conclusions: Suppression of nephron growth and maturation by UUO is more severe in mice with reduced NN, and release of obstruction is less effective in reversing obstructive renal injury. Children with prematurity and congenital urinary tract obstruction are at increased risk to develop CKD.



Surgical Creation of Partial Ureteral Obstruction In the Neonatal Mouse



Histomorphometry	
Glomerular number/section	PAS
Glomerular Area (μm ²)	
Intact glomerulo-tubular junction %	Lotus Tetragonolobus Lectin
Proximal tubular mass %	
Interstitial collagen %	Picosirius red



1-way ANOVA
S = p<0.05 vs. Sham
U = p<0.05 vs. UUO

§ = 2-way ANOVA
p<0.05 effect of Age, UUO, Nephron number (NN)