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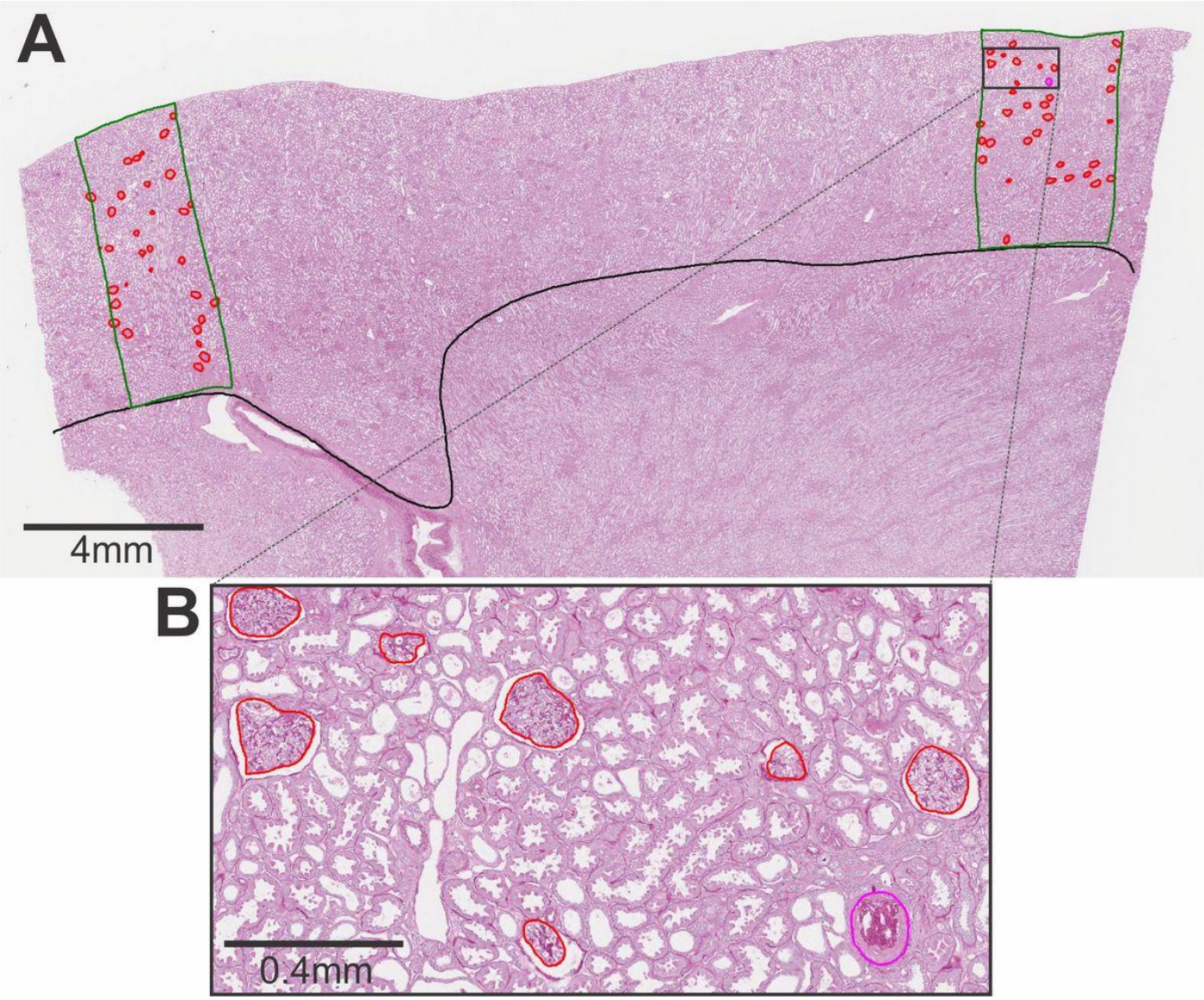
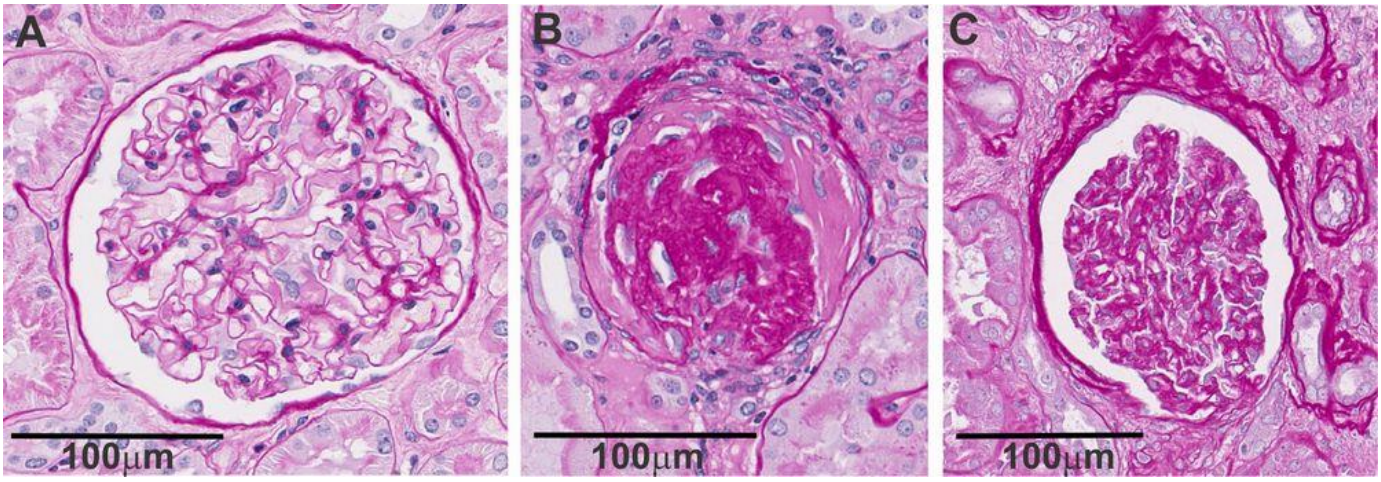
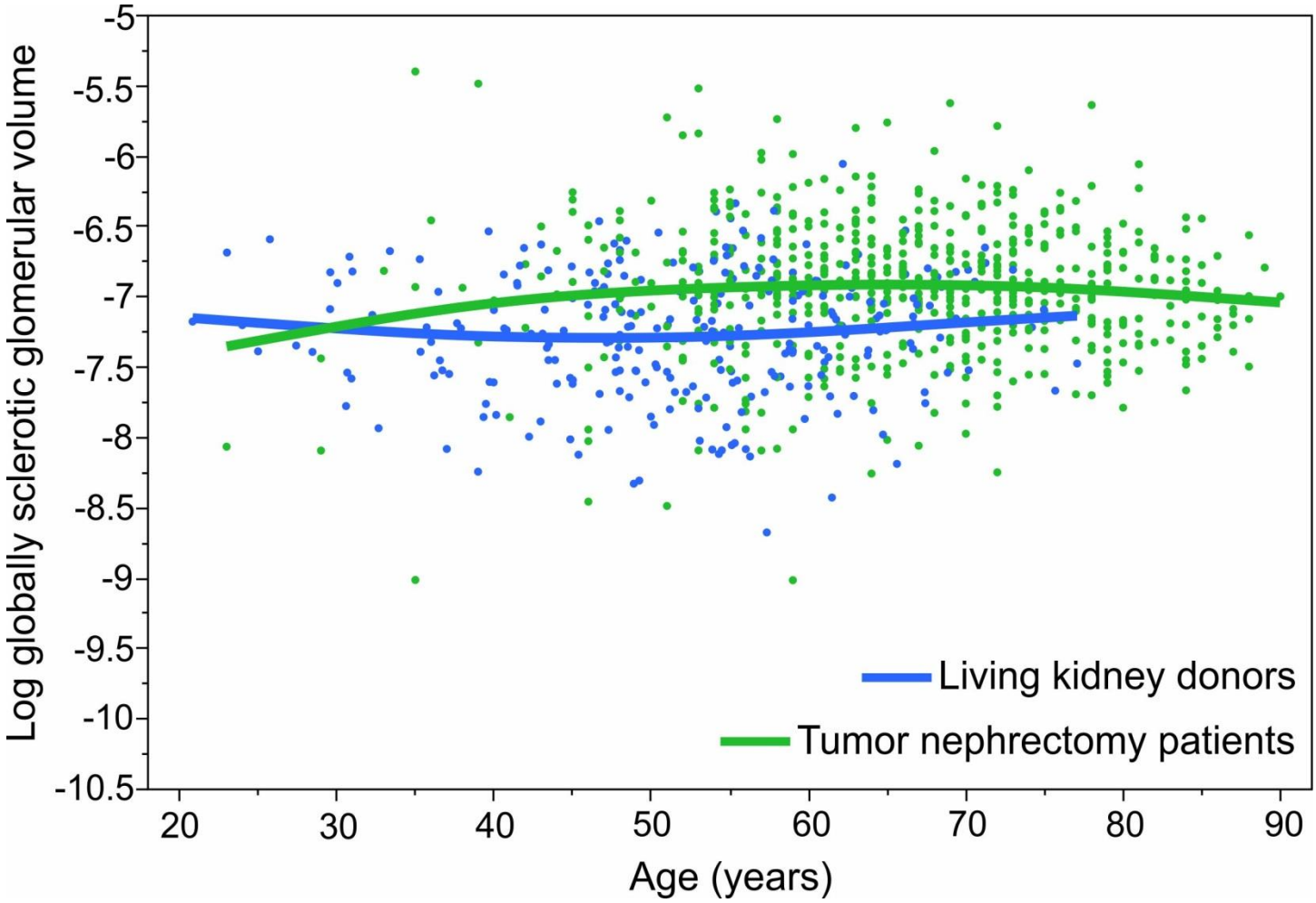


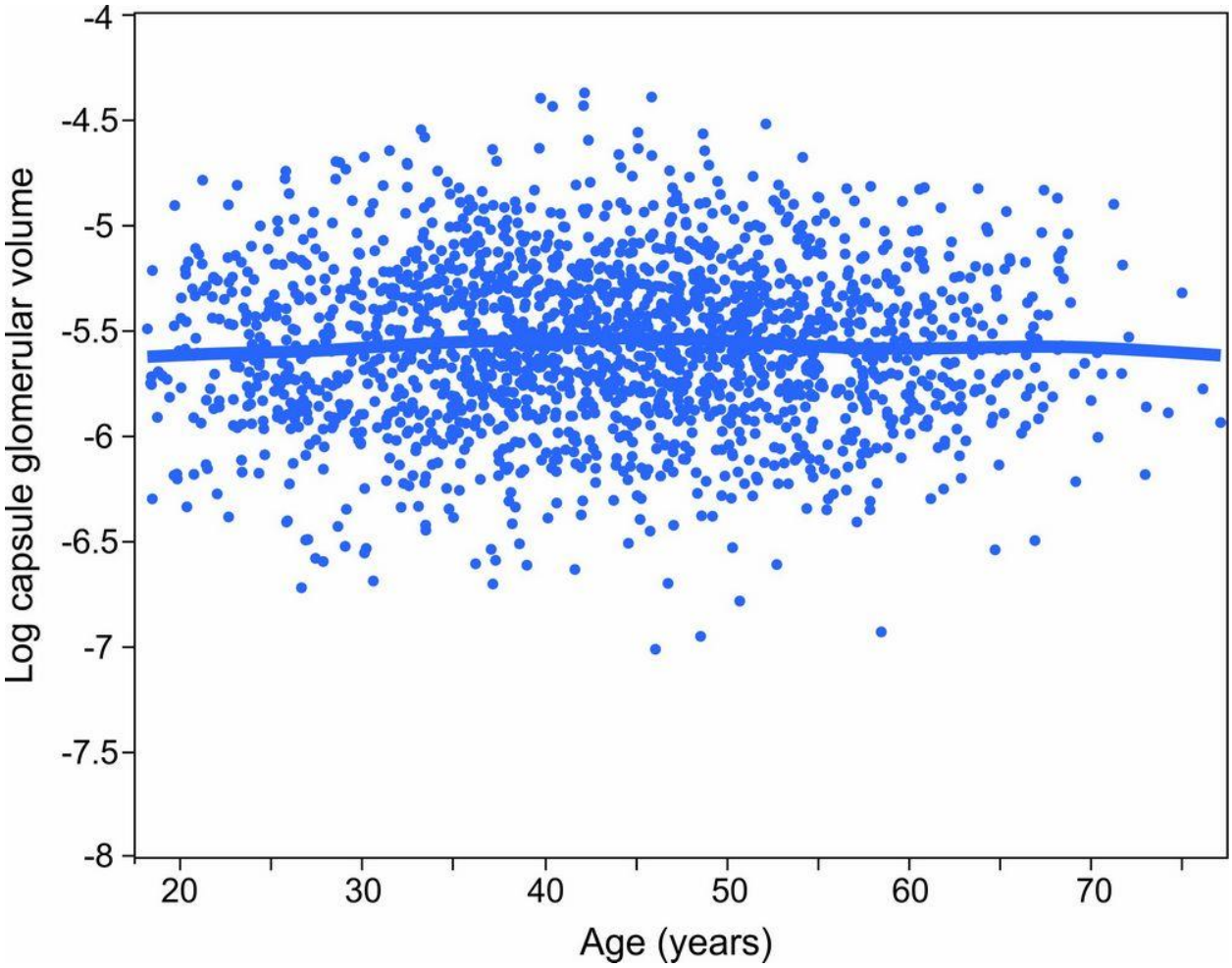
Supplemental Figure 1. A) Representative section of nephrectomy wedge biopsy section showing two cortical regions (dark green traces) at opposite ends, used to obtain glomerular measurements. Juxtamedullary junction is shown in black trace. **B**) A magnified view shows several non-sclerotic glomeruli (red traces) and one globally sclerosed glomerulus (pink trace).



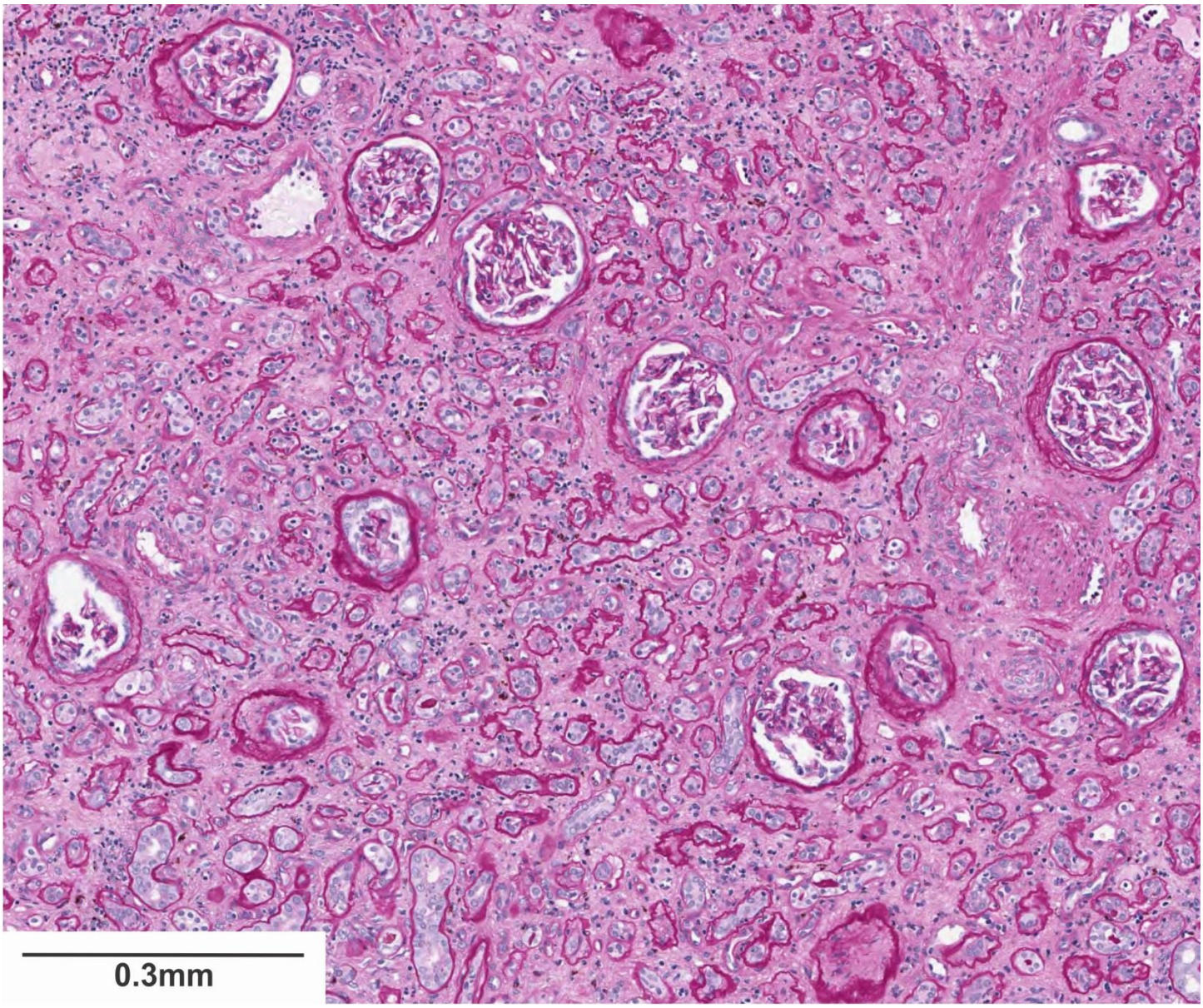
Supplemental Figure 2. Examples of (**A**) non-ischemic-appearing non-sclerotic glomerulus, (**B**) globally sclerotic glomerulus and (**C**) ischemic-appearing non-sclerotic glomerulus.



Supplemental Figure 3. Globally sclerotic glomerular (GSG) volume in living kidney donors and patients with renal tumor does not increase with age. The volume of globally sclerosed glomeruli from cohorts of living kidney donors and tumor nephrectomy patients with at least 2 GSG profiles was log transformed and plotted with age. Smoother spline fit is shown; by linear regression, GSG volume did not change with age, in either living kidney donors (1.3% per 10 years, p=0.58) or patients with renal tumor (0.5% per 10 years, p=0.78).



Supplemental Figure 4. The volume of non-sclerotic glomerular (NSG) capsules does not increase with age in living kidney donors. A volume of NSG from the cohort of living kidney donors was log transformed and plotted with age. No change in the volume was observed by linear regression (0.4% per 10 years, p=0.63).



Supplemental Figure 5. Representative image of interstitial fibrosis and tubular atrophy with ischemic appearing NSG. The NSG surrounded by interstitial fibrosis show various degrees of Bowman's capsule thickening and wrinkling (deflation) of the glomerular capillary tufts.

Supplemental Table 1. Characteristics associated with non-sclerotic glomerular tuft volume in living kidney donors compared to patients with renal tumor in analysis limited to persons with at least 10 glomeruli on biopsy.

	Unadjusted				
	Kidney donors (N=1965)		Patients with tumor (N=780)		
Characteristics	**% Diff.**	**P Value**	**% Diff.**	**P Value**	**Test for interaction**
Age per 10 years (up to age 75 years)	-0.1%	0.88	-1.6%	0.24	0.32
Age per 10 years (>75 years) *	-		**-21.1%**	**0.009**	-
Male	**14.3%**	**<0.0001**	**19.3%**	**<0.0001**	0.17
Height per SD	**6.4%**	**<0.0001**	**7.6%**	**<0.0001**	0.45
BMI per SD	**11.1%**	**<0.0001**	**9.3%**	**<0.0001**	0.22
Hypertension	**6.4%**	**0.03**	**10.7%**	**0.0002**	0.30
Diabetes	-		**22.6%**	**<0.0001**	-
eGFR per SD	-0.8%	0.40	0.7%	0.58	0.34
Family history of end stage renal disease	**8.5%**	**<0.0001**	-		-
24hr Urine Protein per doubling, mg †	**2.8%**	**<0.0001**	**4.1%**	**<0.0001**	0.21
Tumor volume per doubling	-		0.9%	0.11	-

* Because of the older than 75 years (N=2), analysis was not performed for the donors.

† Total N does not add up to 1965 or 780 due to missing data (N=1614 for donors, N=545 for patients with renal tumor).

Supplemental Table 2. In the donors, associations with non-sclerotic glomerular (NSG) tuft volume were similar to association with NSG capsule volume.

	Unadjusted			
	NSG Tuft Volume (N=1868)*		NSG Capsule Volume (N=1868)*	
Characteristics	**% Diff.**	**P Value**	**% Diff.**	**P Value**
Age per 10 years	-0.1%	0.86	0.4%	0.63
Male	**14.4%**	**<0.0001**	**11.7%**	**<0.0001**
Height per SD	**6.5%**	**<0.0001**	**5.6%**	**<0.0001**
BMI per SD	**11.0%**	**<0.0001**	**11.1%**	**<0.0001**
Hypertension	**11.5%**	**0.0002**	**12.3%**	**<0.0001**
eGFR per SD	-0.9%	0.40	-1.9%	0.08
Family history of end stage renal disease	**6.8%**	**0.0002**	**6.2%**	**0.0007**
24hr Urine Protein per doubling, mg†	**2.8%**	**<0.0001**	**3.1%**	**<0.0001**

SD = Standard Deviation: 9.6cm for height, 5.3 kg/m^2 for BMI, and 19.5 ml/min for eGFR.

*Analysis limited to the first 1868 kidney donor biopsies scanned into images. Further NSG capsules were not annotated when it became evident that there were no substantive differences in associations with NSG tuft volume compared to with NSG capsule volume.

†Urine protein sample size was smaller due to missing data (N=1555)

Supplemental Table 3. Characteristics associated with non-sclerotic glomerular tuft volume in living kidney donors across three sites. MCR=Mayo Clinic Rochester, MCA=Mayo Clinic Arizona, CC=Cleveland Clinic

	Unadjusted						Test for site interaction
	MCR (N=1832)		MCA (N=318)		CC (N=303)		
Characteristics	**% Diff.**	**P Value**	**% Diff.**	**P Value**	**% Diff.**	**P Value**	
Age per 10 years (up to age 75 years)	-1.2%	0.11	1.6%	0.32	-0.1%	0.95	0.29
Male	**14.6%**	**<0.0001**	6.6%	0.12	**15.6%**	**0.0007**	0.25
Height per SD	**5.6%**	**<0.0001**	3.7%	0.07	**9.2%**	**<0.0001**	0.19
BMI per SD	**10.5%**	**<0.0001**	**7.2%**	**0.003**	**6.8%**	**0.02**	0.28
Hypertension	**5.8%**	**0.04**	1.4%	0.87	5.1%	0.68	0.90
eGFR per SD	1.6%	0.15	0.0%	0.98	0.1%	0.98	0.78
Family history of end stage renal disease	**9.7%**	**<0.0001**	-2.0%	0.61	5.9%	0.18	**0.04**
24hr Urine Protein per doubling, mg *	1.2%	0.30	**3.3%**	**0.04**	-		0.27

SD = Standard Deviation: 9.6cm for height, 5.3 kg/m^2 for BMI, and 19.5 ml/min for eGFR.

*****Data not available for Cleveland Clinic site.

Supplemental Table 4. The association of non-sclerotic glomerular (NSG) tuft volume with nephrosclerosis in both kidney donors and patients with renal tumor.

Biopsy finding	Kidney donors		Patients with tumor		Test for interaction
	% Diff.	P Value	% Diff.	P Value	
Ischemic-appearing NSG >5%					
Unadjusted	-1.9%	0.57	2.0%	0.56	0.42
Adjusted for clinical characteristics*	-6.8%	0.05	-4.2%	0.26	0.64
% GSG (11 to 25 % versus ≤10% of glomeruli)					
Unadjusted	0.2%	0.95	3.2%	0.28	0.45
Adjusted for clinical characteristics*	-1.6%	0.57	5.8%	0.11	0.25
% GSG (>25% versus ≤10% of glomeruli)					
Unadjusted	-5.1%	0.39	4.0%	0.41	0.24
Adjusted for clinical characteristics*	-1.6%	0.81	**13.1%**	**0.04**	0.19
Interstitial Fibrosis (11 to 25% versus ≤10% of cortex)					
Unadjusted	-2.5%	0.78	14.7%	0.08	0.18
Adjusted for clinical characteristics*	-8.5%	0.32	-7.5%	0.36	0.70
Interstitial Fibrosis (>25% versus ≤10% of cortex)					
Unadjusted	-	-	**-19.4%**	**0.0002**	-
Adjusted for clinical characteristics*	-	-	**-29.7%**	**<0.0001**	-
% Luminal stenosis (>50% of lumen)					
Unadjusted	1.7%	0.39	-1.1%	0.68	0.42
Adjusted for clinical characteristics*	2.8%	0.19	1.8%	0.59	0.50

* Clinical characteristics were age, sex, height, BMI, hypertension, diabetes, eGFR, family history of end-stage renal disease and 24h urine protein.

Supplemental Table 5. The association of globally sclerotic glomerular (GSG) volume with nephrosclerosis in both kidney donors and patients with renal tumor. Analysis was limited to kidney donors and patients with renal tumor with at least 2 GSG profiles to analyze.

Biopsy finding	Kidney donors		Patients with tumor		Test for interaction
	% Diff.	P Value	% Diff.	P Value	
Ischemic-appearing NSG (>5% of all NSG)					
Unadjusted	8.1%	0.37	**25.3%**	**<0.0001**	0.14
Adjusted for clinical characteristics*	3.2%	0.76	**15.1%**	**0.007**	0.24
% GSG (11 to 25 % versus ≤10% of glomeruli)					
Unadjusted	3.6%	0.56	**14.7%**	**0.0007**	0.17
Adjusted for clinical characteristics*	5.4%	0.45	**18.1%**	**0.0009**	0.08
%GSG (>25% versus ≤10% of glomeruli)					
Unadjusted	**19.9%**	**0.03**	**25.7%**	**0.0005**	0.67
Adjusted for clinical characteristics*	21.1%	0.09	**23.1%**	**0.02**	0.51
Interstitial Fibrosis (11 to 25% versus ≤10% of cortex)					
Unadjusted	32.4%	0.08	**22.3%**	**0.05**	0.78
Adjusted for clinical characteristics*	30.5%	0.08	-1.6%	0.90	0.35
Interstitial Fibrosis (>25% versus ≤10% of cortex)					
Unadjusted	-	-	**22.9%**	**0.009**	-
Adjusted for clinical characteristics*	-	-	0.4%	0.97	-
% Luminal stenosis (>50% of lumen)					
Unadjusted	4.3%	0.51	5.0%	0.24	0.93
Adjusted for clinical characteristics*	6.4%	0.40	4.2%	0.41	0.75

* Clinical characteristics were age, sex, height, BMI, hypertension, diabetes, eGFR, family history of end-stage renal disease and 24h urine protein.