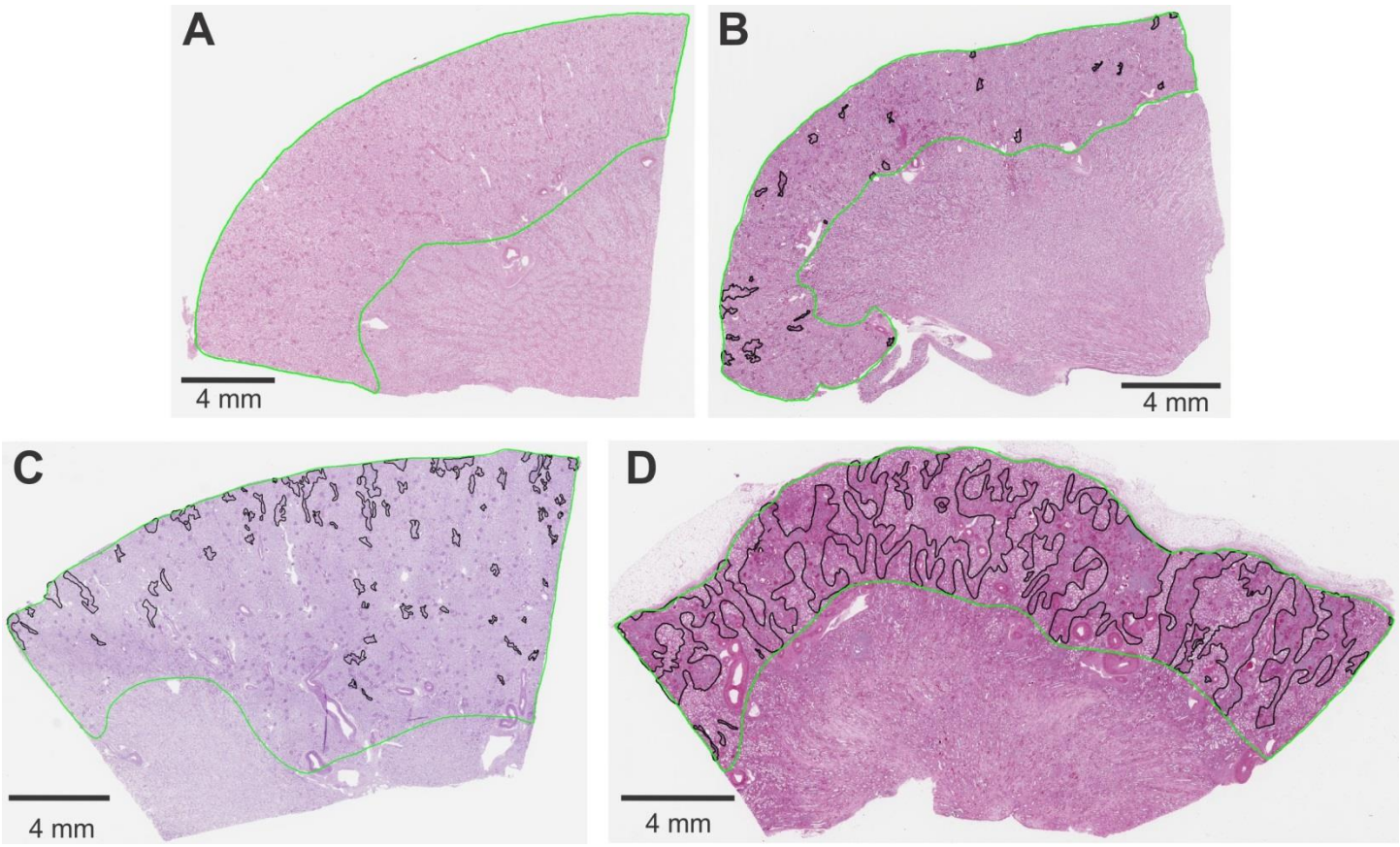
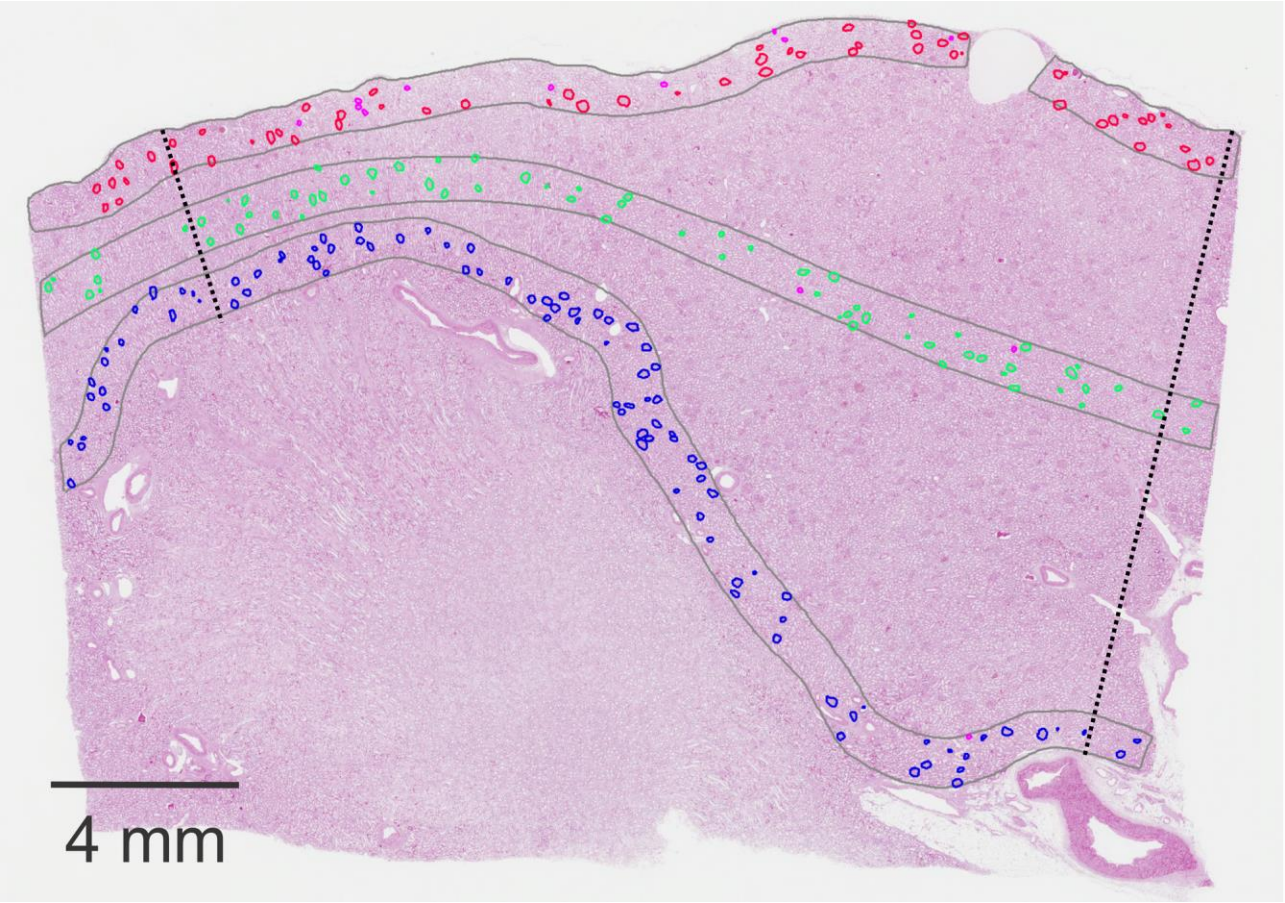
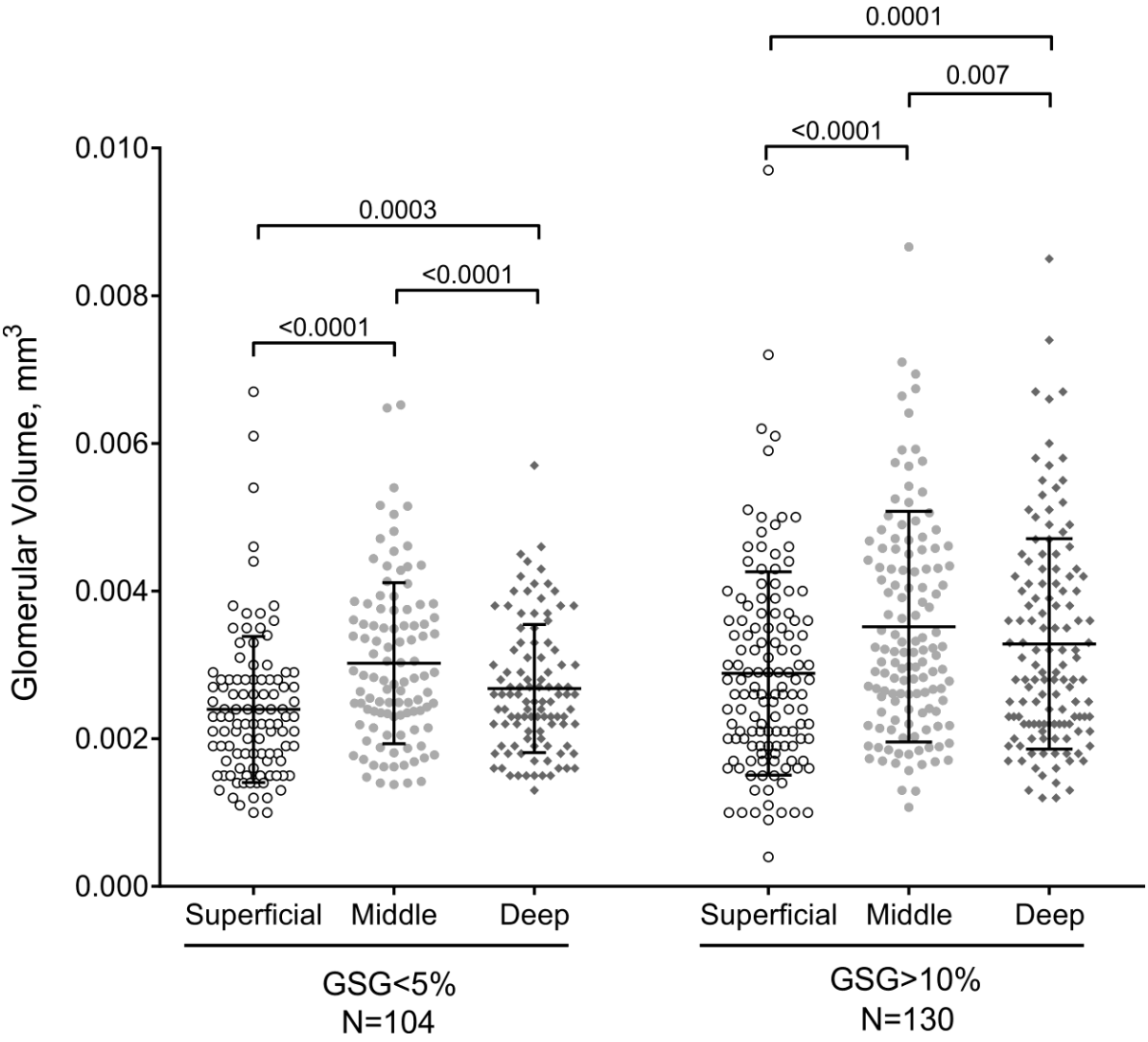
Table of Contents for Supplemental Material:



Supplemental Figure 1. Percent fibrosis area was calculated by dividing the sum of all IF/TA areas (black traces) with a biopsy cortex area (green trace). Examples of different degrees of fibrosis are shown: **A)** 0%, **B)** 2.2%, **C)** 5.3%, and **D)** 45%. All four images were taken at the same magnification.



Supplemental Figure 2. An example of a wedge section with asymmetric cortex thickness that allowed continuous demarcation of superficial, middle and deep regions, but not 2 additional regions (superficial/middle and middle/deep).



Supplemental Figure 3. Non-sclerotic glomerular volume in superficial, middle and deep regions in different subsets of patients with minimal or moderate to severe globally sclerotic glomeruli (GSG).

Glomeruli were consistently largest in middle region compared to superficial and deep regions among 104 patients with less than 5% glomerulosclerosis in all three regions, and among 130 patients with more than 10% glomerulosclerosis in all three regions. Data presented as mean ± standard deviation.

Supplemental Tables.

Supplemental Table 1. Number of patients and the mean number of non-sclerotic glomerular (NSG) profiles and globally-sclerotic glomerular (GSG) profiles per patient by each age group.

Age group	Number of patients	Number of NSG profiles in each region			Number of GSG profiles in each regions		
		Superficial	Middle	Deep	Superficial	Middle	Deep
20-29 years	3 (0.4%)	47.0 (22.6)	44.7 (26.5)	35.7 (21.2)	3.0 (2.0)	0.0 (0.0)	0.3 (0.6)
30-39 years	28 (3.4%)	44.2 (25.5)	44.0 (23.1)	37.2 (14.7)	6.0 (25.8)	1.6 (5.8)	1.6 (2.0)
40-49 years	72 (8.9%)	41.4 (20.7)	43.3 (19.9)	37.3 (17.3)	6.3 (16.9)	2.5 (5.6)	3.3 (3.5)
50-59 years	193 (23.7%)	43.0 (21.7)	44.2 (20.3)	37.1 (18.2)	5.7 (8.0)	1.9 (2.8)	3.6 (3.8)
60-69 years	241 (29.7%)	42.6 (25.2)	41.7 (19.3)	35.8 (15.6)	11.6 (18.9)	3.1 (4.5)	4.5 (4.7)
70-79 years	200 (24.6%)	39.0 (23.3)	40.3 (21.0)	36.6 (19.9)	14.8 (22.3)	4.1 (7.1)	4.5 (5.7)
80-91 years	75 (9.2%)	38.6 (19.0)	40.6 (16.9)	38.3 (17.4)	26.2 (27.6)	5.6 (5.0)	5.8 (4.7)

Data are presented as n (%), or Mean (SD).

Supplemental Table 2. Clinical characteristics and biopsy findings of patients with thin and thick cortex.

	Thin cortex (n=386)	Thick cortex (n=406)	P value
Demographic			
Age, y	66.8 (12.1)	61.3 (11.6)	<0.0001
Men, %	208 (53.9%)	300 (73.9%)	<0.0001
Height, cm	170.0 (10.0)	174.6 (9.4)	<0.0001
Race			0.09
White or unknown	372 (96.4%)	389 (95.8%)	
Black	8 (2.1%)	4 (9.9%)	
American Indian/Alaskan Native	1 (0.3%)	7 (1.7%)	
Other	5 (1.3%)	6 (1.5%)	
Risk factors			
Diabetes Mellitus, %	47 (12.2%)	66 (16.3%)	0.10
Hypertension, %	250 (64.8%)	249 (61.3%)	0.32
Body mass index, kg/m^2	29.0 (6.3)	31.1 (6.6)	<0.0001
Current smoker, %	41 (10.6%)	82 (20.2%)	0.0002
Tumor size, cm^3	100 (34-227)	101 (40-275)	0.31
Kidney function			
eGFR, ml/min/1.73 m^2	68.2 (20.8)	74.7 (17.4)	<0.0001
24-hour urine protein, mg†	715 (2626)	439 (1537)	0.23
Microstructural pathology			
Interstitial fibrosis area, %			
>10%	52 (13.5%)	35 (8.6%)	0.03
>25%	21 (5.4%)	17 (4.2%)	0.41
Artery luminal stenosis			
>50% (arteriosclerosis)	280 (72.5%)	260 (64.0%)	0.01

Data are presented as Mean (SD), n (%), or median (interquartile range). eGFR = estimated glomerular filtration rate. †24-hour urine protein estimates were available in 272 patients (70.5%) with thin and 294 patients with thick cortex (72.4%).

Supplemental Table 3. Multivariable-adjusted association of clinical characteristics with glomerular volume in three mid-cortical regions among 406 patients with thick cortex.

	Glomerular Volume						
	Superficial/Middle region		Middle region		Middle/Deep region		
Clinical characteristic	**% Diff.**	**P Value**	**% Diff.**	**P Value**	**% Diff.**	**P Value**	**Test for interaction**
Age per 10 years	0.1%	0.92	-0.6%	0.67	-2.5%	0.09	**0.04**
Male sex	10.3%	0.06	7.0%	0.19	11.4%	0.05	0.37
Height, per SD	2.7%	0.25	3.1%	0.18	0.8%	0.76	0.33
Body mass index, per SD	**11.1%**	**<0.0001**	**9.1%**	**<0.0001**	**6.7%**	**0.0003**	**0.002**
Hypertension	6.5%	0.05	6.6%	0.05	**7.8%**	**0.03**	0.85
Diabetes	5.9%	0.27	8.0%	0.11	10.1%	0.06	0.54
eGFR, per SD	-0.1%	0.98	-1.9%	0.35	-1.9%	0.36	0.46
24-hr urine protein per doubling, mg	**4.3%**	**0.0004**	**2.8%**	**0.008**	**3.8%**	**0.001**	0.17
Tumor volume per doubling	**1.5%**	**0.03**	0.8%	0.15	0.9%	0.14	0.40
Current smoker	**15.1%**	**0.0003**	**11.9%**	**0.004**	8.3%	0.06	0.09

eGFR = estimated glomerular filtration rate. Bold text denotes significant P value (<0.05).

Supplemental Table 4. Multivariable-adjusted association of clinical characteristics with level increase in percentage globally sclerotic glomeruli (%GSG) category in three mid-cortical regions among 406 patients with thick cortex.

	%GSG category (0-3)						
	Superficial/Middle region		Middle region		Middle/Deep region		
Clinical characteristic	**OR (95% CI)**	**P Value**	**OR (95% CI)**	**P Value**	**OR (95% CI)**	**P Value**	**Test for interaction**
Age per 10 years	**1.59 (1.15-2.19)**	**0.005**	1.24 (0.92-1.85)	0.20	1.26 (0.91-1.74)	0.16	0.22
Male sex	1.03 (0.41-2.62)	0.95	1.49 (0.60-4.42)	0.42	0.50 (0.15-1.66)	0.26	0.23
Height, per SD	1.02 (0.65-1.59)	0.95	0.71 (0.45-1.11)	0.15	1.16 (0.68-1.99)	0.58	0.26
Body mass index, per SD	1.13 (0.84-1.53)	0.42	1.03 (0.75-1.53)	0.87	1.01 (0.66-1.55)	0.95	0.82
Hypertension	1.08 (0.58-2.02)	0.80	**2.27 (1.07-4.85)**	**0.03**	1.75 (0.74-4.16)	0.21	0.15
Diabetes	1.79 (0.93-3.47)	0.08	**2.37 (1.09-5.14)**	**0.03**	1.87 (0.81-4.33)	0.14	0.73
eGFR, per SD	**0.42 (0.27-0.64)**	**<0.0001**	**0.36 (0.22-0.57)**	**<0.0001**	**0.42 (0.27-0.66)**	**0.0001**	0.72
24-hr urine protein per doubling, mg	1.06 (0.87-1.28)	0.58	1.22 (0.98-1.53)	0.08	**1.36 (1.11-1.66)**	**0.003**	0.07
Tumor volume per doubling	0.87 (0.75-1.00)	0.05	**0.87 (0.76-0.99)**	**0.04**	**0.85 (0.74-0.98)**	**0.02**	0.97
Current smoker	**1.92 (1.04-3.57)**	**0.04**	1.37 (0.63-2.96)	0.43	1.09 (0.39-3.08)	0.87	0.55

OR = Odds Ratio; eGFR = estimated glomerular filtration rate. Bold text denotes significant P value (<0.05).

Supplemental Table 5. Unadjusted associations of non-sclerotic glomerular volume in three cortical regions with biopsy pathology.

	Glomerular Volume						
	Superficial region		Middle region		Deep region		
Biopsy pathology	**% Diff.**	**P Value**	**% Diff.**	**P Value**	**% Diff.**	**P Value**	**Test for interaction**
Interstitial Fibrosis>10%	**-10.6%**	**0.04**	-4.5%	0.38	-0.9%	0.86	0.05
Interstitial Fibrosis >25%	**-15.1%**	**0.03**	**-18.0%**	**0.004**	**-17.6%**	**0.001**	0.49
Arteriosclerosis (>50% stenosis)	-3.3%	0.25	-0.9%	0.72	-0.3%	0.92	0.35
Superficial GSG >10%	1.0%	0.71	2.0%	0.44	4.2%	0.11	0.37
Middle GSG >10%	**9.0%**	**0.02**	4.9%	0.16	**11.5%**	**0.001**	**0.01**
Deep GSG >10%	**8.0%**	**0.008**	**6.6%**	**0.02**	**10.6%**	**0.0002**	0.15
Superficial GSG >25%	-0.4%	0.91	2.6%	0.42	**6.5%**	**0.04**	**0.04**
Middle GSG >25%	**23.8%**	**0.02**	**17.9%**	**0.04**	**24.2%**	**0.004**	0.43
Deep GSG >25%	**21.2%**	**0.006**	**23.3%**	**0.0001**	**22.1%**	**0.0003**	0.90
Superficial Ischemic NSG > 5%	0.8%	0.79	**6.7%**	**0.01**	**9.7%**	**0.0006**	**0.0003**
Middle Ischemic NSG > 5%	7.0%	0.07	**9.1%**	**0.006**	**11.1%**	**0.0008**	0.43
Deep Ischemic NSG > 5%	**6.2%**	**0.03**	**9.0%**	**0.001**	**6.0%**	**0.03**	0.23

NSG = non-sclerotic glomeruli; GSG = globally sclerotic glomeruli. Bold text denotes significant P value (<0.05).

Supplemental Table 6. Unadjusted associations of non-ischemic glomerular volumes in three cortical regions with biopsy pathology.

	Glomerular Volume						
	Superficial region		Middle region		Deep region		
Biopsy pathology	**% Diff.**	**P Value**	**% Diff.**	**P Value**	**% Diff.**	**P Value**	**Test for interaction**
Superficial GSG >10%	3.2%	0.28	4.5%	0.09	5.4%	0.05	0.66
Middle GSG >10%	**10.9%**	**0.01**	**9.0%**	**0.01**	**12.4%**	**0.0007**	0.40
Deep GSG >10%	**10.3%**	**0.001**	**8.6%**	**0.003**	**11.7%**	**<0.0001**	0.32
Superficial GSG >25%	1.5%	0.70	5.6%	0.11	**7.2%**	**0.03**	0.18
Middle GSG >25%	**30.2%**	**0.007**	**26.8%**	**0.006**	**24.9%**	**0.009**	0.89
Deep GSG >25%	**26.3%**	**0.002**	**31.6%**	**<0.0001**	**24.3%**	**0.0003**	0.42

GSG = globally sclerotic glomeruli. Bold text denotes significant P value (<0.05).