Supplemental Material

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Supplemental Methods

Annotations

Each cell and each capillary were annotated separately. Annotations for the cells were made on what appeared for the pathologists to be the outer surface of the cell membrane, equivalent to cytoplasmic labeling. We believe the margin of error can only be a few pixels. Object annotation was achieved through consensus among the kidney pathologists. The retained parietal epithelial cells were the ones lining Bowman's capsule and not located at the vascular or tubular pole. Objects marked as podocytes were the cells located on the outer side of the glomerular basement membrane. Cells annotated as endothelial were the ones lining the glomerular capillaries. Cells annotated as mesangial were the cells located within the glomerular basement membrane and exterior to the glomerular capillaries.

The glomeruli included in the Training, Testing, and Application cohorts had to be non-blurry, encompass the entire Bowman's capsule, and not be located at the biopsy edge.

Supplemental Table 1: Formulas

Parameters	Formula
Number of Object per Glomerulus	$\dfrac{Total\ Number\ of\ Objects}{Number\ of\ Glomeruli}$
Mean Objects' Area	$\dfrac{Total\ Area\ of\ Objects}{Number\ of\ Objects}$
Relative Area of Objects	$\dfrac{100\ \times\ Total\ Area\ of\ Objects}{Total\ Area\ of\ Glomeruli}$
Cell Density (1)	$\dfrac{1}{\beta}\ x\ \sqrt[2]{\dfrac{\left(\dfrac{Total\ Number\ of\ Cells}{Total\ Area\ of\ Glomeruli}\right)^3}{\dfrac{Total\ Area\ of\ Cells}{Total\ Area\ of\ Glomeruli}}}$ β=1.382 (shape coefficient for spheres)
Precision (2)	$\dfrac{items\ belonging\ to\ a\ class}{all\ of\ the\ items\ predicted\ to\ belong\ to\ a\ class}$
Recall (2)	$\dfrac{items\ predicted\ to\ belong\ to\ a\ class}{all\ of\ the\ items\ belonging\ to\ a\ class}$
F-score (2)	$2 \times \dfrac{Precision \times Recall}{Precision + Recall}$
Intersection Over Union (2)	$\dfrac{common\ area\ between\ the\ predicted\ and\ the\ annotated\ item}{(area\ of\ the\ predicted\ +\ annotated\ item\ -\ common\ area\ of\ the\ annotated\ and\ predicted)}$

Supplemental Table 2: Convolutional neural networks accuracy of transplant biopsies in the Test cohort

Objects	Number Of Objects	Precision[a]	Recall[b]	F-score[c]	Intersection Over Union[d]
Parietal Epithelial Cells	196	0.97	0.85	0.91	0.79
Podocytes	226	0.90	0.85	0.87	0.71
Mesangial Cells	305	0.94	0.87	0.91	0.74
Endothelial Cells	443	0.96	0.92	0.94	0.80
Capillaries	670	0.99	0.94	0.97	0.94

a Precision: percentage of items belonging to the interest class among items identified as belonging to the interest class

b Recall: percentage of items identified as belonging to the interest class among all items belonging to the interest class

c F-score: 2*(Precision*Recall)/(Precision+Recall)

d Intersection over union: (common area between the predicted and the annotated object)/(area of the predicted object 1 area of the annotated object - common area of the annotated and predicted object)

Supplemental Table 3: Donors and Recipients Data in the Application cohort

Data	Donors (N=154)	Recipients (N=154)
Age (year)	56±17	55±13
Male sex	80 (52)	96 (62)
Hypertension	46 (30)	140 (93)
Diabetes	15 (10)	34 (22)
Body Mass Index (kg/m^2)	26±5	25±5
Serum Creatinine level at donation (mg/dL)	0.9±0.3	-
eGFR at donation (mL/min/1.73m^2)	83±28	-
Proteinuria at Donation (g/day)	0.5±0.3	-
Antithymocyte globulin at induction	-	31 (20)
Basiliximab at induction	-	123 (80)
Tacrolimus	-	153 (99)
Mycophenolate mofetil	-	153 (99)
Corticosteroids	-	154 (100)
Delayed Graft Function	-	16 (10)
Initial Hospital Duration (days)	-	13±8
Serum Creatinine level at hospital discharge (mg/dL)	-	1.9±1.0
eGFR at hospital discharge (mL/min/1.73m^2)	-	43±22
Proteinuria at hospital discharge (g/day)	-	0.6±0.3
Serum Creatinine level at biopsy (mg/dL)	-	1.5±0.5
eGFR at biopsy (mL/min/1.73m^2)	-	53±20
Proteinuria at biopsy (g/day)	-	0.3±0.3
Donor Specific Antibodies before biopsy	-	5 (3)
BK virus replication before biopsy	-	30 (19)
Follow-up (months)	-	44±29
Serum Creatinine level at Follow-up (mg/dL)	-	1.6±1.1
eGFR at Follow-up	-	54±26
Proteinuria at Follow-up (g/day)	-	0.4±0.7
Rejection during Follow-up	-	7 (5)
Death	-	10 (6)
Dialysis at Follow-up	-	6 (4)
Initiation of dialysis, or a 30% decline in eGFR	-	25 (16)

Quantitative data are expressed as means±standard deviations, semi-quantitative data are expressed as numbers (percentages).

eGFR: evaluation of Glomerular Filtration Rate

Supplemental Table 4: Data associated with eGFR at biopsy

Factors	Univariate[a]		Multivariate[b]	
	r (95%CI)	*P* value	Beta (95%CI)	*P* value
Donor's data				
Donor's Age (per year)	-0.67 (-0.75; -0.56)	**< .001**	-0.68 (-0.80; -0.56)	**< .001**
Donor's Male sex	-0.34 (-0.48; -0.18)	**< .001**	-	-
Donor's Hypertension	-0.37 (-0.50; -0.21)	**< .001**	-	-
Donors' Diabetes mellitus	-0.19 (-0.35; -0.02)	**.027**	-	-
Donors' BMI (per kg/m^2)	-0.09 (-0,26; 0,08)	.269		
Recipient's data				-
Recipient's Age (per year)	-0.55 (-0.67; -0.43)	**< .001**	-	-
Recipient's sex	-0.02 (-0.19; 0.15)	.840	-	-
Recipient's Hypertension	-0.09 (-0.25; 0.09)	.312	-	-
Recipient's Diabetes mellitus	-0.24(-0.39; -0.07)	**.004**	-	-
Recipient's BMI (per kg/m^2)	-0.24(-0.39; -0.07)	**.005**		
Donor Specific Antibodies	0.04 (-0.12; -0.21)	.585		
BK virus blood replication at biopsy	0.04 (-0.13; -0.21)	.617		
Proteinuria after transplantation (per g/day)	0.06 (-0.12; 0.23)	.511	-	-
Predicted histological data				
Number of parietal epithelial cells per glomerulus	0,20 (0,03; 0.36)	**.016**	-	-
Relative parietal epithelial area (per %)	0.11 (-0.06; 0.27)	.191	-	-
Mean parietal epithelial cell area (per µm^2)	-0.38 (-0.52; -0.23)	**< .001**	-	-
Parietal epithelial density (per cell/mm^2)	0.29 (0.12; 0.44)	**< .001**	-	-
Number of podocytes per glomerulus	-0.04 (-0.21; 0.13)	.613	-	-
Mean podocyte area (per µm^2)	-0.13 (-0.30; 0.04)	.110	-	-
Relative podocyte area (per %)	0.01 (-0.16; 0.17)	.950	-	-
Podocyte density (per cell/mm^2)	0.09 (-0.07; 0.26)	.238	-	-
Number of endothelial cells per glomerulus	0.13 (-0.04; 0.30)	.114	-	-
Mean endothelial cell area (per µm^2)	0.05 (-0.12; 0.21)	.582	-	-
Relative endothelial area (per %)	0.19 (0.02; 0.34)	**.028**	-	-
Endothelial density (per cell/mm^2)	0.20 (0.03; 0.36)	**.017**	0.13 (0.06; 0.32)	**.040**
Number of mesangial cells per glomerulus	0.12 (-0.05; 0.29)	.140	-	-
Mean mesangial cell area (per µm^2)	-0.08 (-0,25; 0,09)	.343	-	-
Relative mesangial area (per %)	0.18 (0.01; 0.34)	**.030**	-	-
Mesangial density (per cell/mm^2)	0.22 (0.05; 0.37)	**.010**	-	-
Number of capillaries per glomerulus	-0.03 (-0.19; 0.14)	.768	-	-
Mean capillary area (per µm^2)	0.03 (-0.14; 0.19)	.718	-	-
Relative capillary area (per %)	0.16 (-0.01; 0.32)	.055	-	-
Banff score of protocol biopsies[c]				
t score	0.01 (-0.17; 0.17)	.999	-	-
ptc score	-0.12 (-0.28; 0.05)	.155	-	-
g score	-0.10 (-0.27; 0.07)	.218	-	-
mm score	-0.11 (-0.27; 0.06)	.206	-	-
cg score	-0.05 (-0.21; 0.12)	.552	-	-
i score	-0.07 (-0.24; 0.10)	.417	-	-
ah score	-0.14 (-0.30; 0.03)	.092		
IF/TA score	-0.21 (-0.37; -0.04)	**.011**	-	-
cv score	-0.30 (-0.44; -0.13)	**< .001**	-	-

a Spearman correlation test

b After exclusion of non-significative and collinear variables, the backward multiple linear regression model included: Donor's age, sex, history of hypertension, diabetes, recipients' history of Diabetes, BMI, endothelial, parietal epithelial, and mesangial densities, mean parietal epithelial cell area, IF/TA and cv scores.

c Banff score elements as previously published (3)

P-values of the factors statistically associated with the eGFR are bolded.

eGFR: evaluation of Glomerular Filtration Rate, CI: Confidence Interval, BMI: Body Mass Index, IF/TA : interstitial fibrosis/ tubular atrophy
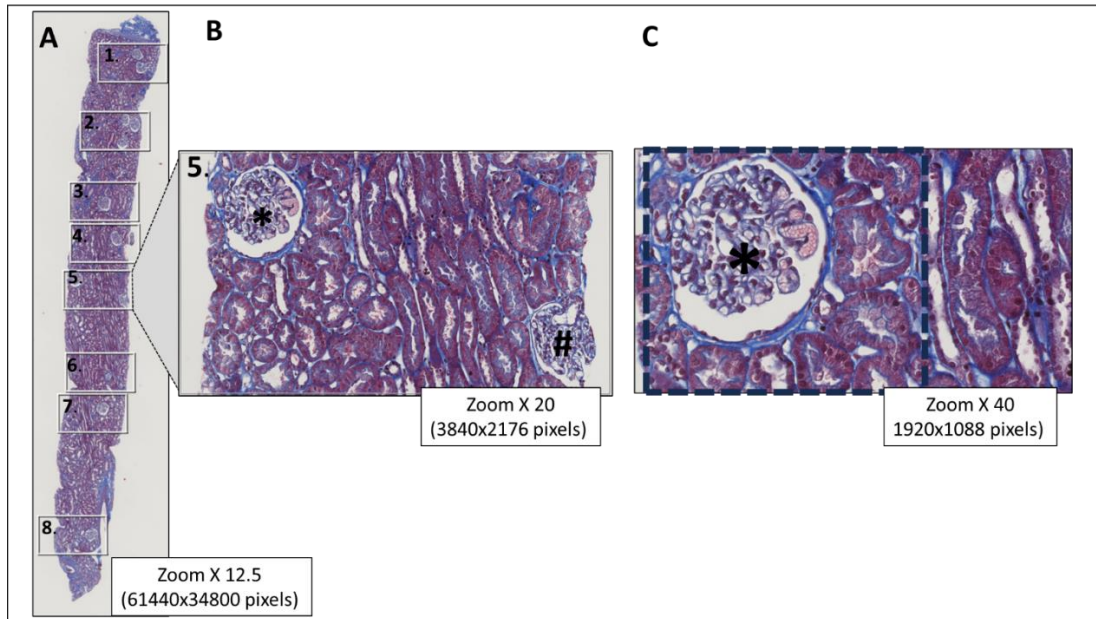
Supplemental Table 5: Data associated with neural networks predictions

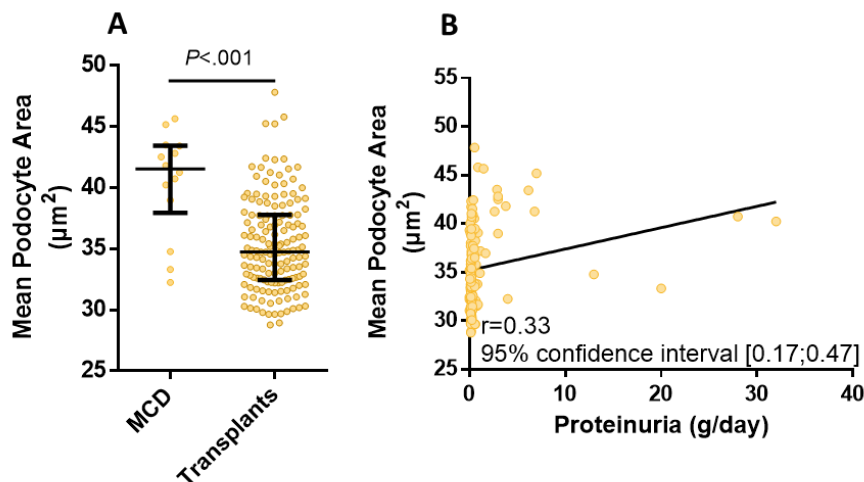| Data	Mean parietal epithelial cell area (μm²) r= (95% CI)	Parietal epithelial density (cell/mm²) r= (95% CI)	Mean podocyte area r= (95% CI)	Podocyte density (cell/mm²) r= (95% CI)	Mean endothelial cell area (μm²) r= (95% CI)	Endothelial density (cell/mm²) r= (95% CI)	Mean mesangial cell area (μm²) r= (95% CI)	Mesangial density (cell/mm²) r= (95% CI)	Relative capillary area (%) r= (95% CI)
Donor's data									
Donor's Age (year)	**0.38 (0.23; 0.51)**	**-0.22 (-0.37; -0.05)**	0.09 (-0.07; 0.25)	-0.06 (-0.22; 0.10)	-0.13 (-0.29; 0.03)	**-0.17 (-0.33; -0.01)**	0.04 (-0.12; 0.20)	**-0.18 (-0.34; -0.02)**	**-0.32 (-0.46; -0.17)**
Donor's sex	-0.07 (-0.23; 0.10)	**0.29 (0.14; 0.43)**	-0.02 (-0.19; 0.14)	0.02 (-0.15; 0.17)	0.03 (-0.13; 0.19)	**0.21 (0.05; 0.36)**	0.07 (-0.10; 0.23)	0.11 (-0.05; 0.27)	**0.17 (0.01; 0.32)**
Donor's Hypertension	**0.38 (0.23; 0.51)**	-0.15 (-0.30; 0.01)	**0.25 (0.09; 0.40)**	**-0.16 (-0.32; 0.00)**	0.00 (-0.16; 0.16)	-0.15 (-0.31; 0.01)	0.04 (-0.13; 0.20)	-0.09 (-0.25; 0.08)	**-0.27 (-0.41; -0.12)**
Donors' Diabetes	**0.21 (0.04; 0.36)**	**-0.22 (-0.37; -0.06)**	**0.22 (0.06; 0.37)**	**-0.20 (-0.36; -0.04)**	-0.01 (-0.17; 0.15)	0.03 (-0.14; 0.19)	0.05 (-0.12; 0.21)	0.00 (-0.16; 0.16)	0.04 (-0.12; 0.21)
Donors' BMI (kg/m²)	0.10 (-0.06; 0.26)	-0.09 (-0.25; 0.08)	**0.22 (0.05; 0.37)**	**-0.22 (-0.37; -0.06)**	-0.05 (-0.21; 0.11)	0.07 (-0.09; 0.23)	-0.02 (-0.18; 0.15)	0.08 (-0.09; 0.24)	-0.04 (-0.20; 0.13)
Recipient's data									
Recipient's Age (year)	**0.28 (0.11; 0.42)**	-0.20 (-0.35; 0.04)	0.13 (-0.03; 0.29)	-0.09 (-0.25; 0.08)	-0.14 (-0.30; 0.02)	-0.02 (-0.19; 0.14)	-0.04 (-0.19; 0.13)	-0.11 (-0.26; 0.06)	**-0.28 (-0.42; -0.12)**
Recipient's sex	**0.29 (0.14; 0.43)**	-0.05 (-0.21; 0.12)	**0.19 (0.03; 0.34)**	**-0.18 (-0.34; -0.02)**	0.06 (-0.10; 0.22)	**-0.16 (-0.31; 0.00)**	0.10 (-0.06; 0.26)	-0.05 (-0.21; 0.11)	-0.05 (-0.21; 0.12)
Recipient's Hypertension	0.05 (-0.12; 0.23)	-0.04 (-0.20; 0.13)	0.01 (-0.16; 0.17)	-0.02 (-0.18; 0.15)	0.08 (-0.08; 0.25)	0.03 (-0.13; 0.19)	0.09 (-0.08; 0.25)	0.06 (-0.11; 0.22)	-0.10 (-0.26; 0.07)
Recipient's Diabetes	0.10 (-0.07; 0.26)	-0.13 (-0.29; 0.03)	**0.19 (0.06; 0.37)**	-0.09 (-0.25; 0.07)	-0.11 (-0.27; 0.05)	-0.02 (-0.18; 0.15)	-0.09 (-0.25; 0.08)	0.01 (-0.15; 0.18)	-0.15 (-0.30; 0.02)
Recipient's BMI (kg/m²)	-0.02 (-0.14; 0.19)	-0.06 (-0.22; 0.10)	0.03 (-0.13; 0.19)	-0.07 (-0.23; 0.09)	-0.10 (-0.26; 0.06)	-0.01 (-0.17; 0.16)	-0.12 (-0.15; 0.19)	-0.01 (-0.17; 0.15)	**-0.17 (-0.32; 0.00)**
Predicted data									
Mean epithelial cell area (μm²)	-	**-0.26 (-0.40; -0.10)**	**0.34 (0.19; 0.48)**	**-0.38 (-0.51; -0.23)**	**0.16 (0.00; 0.32)**	**-0.26 (-0.41; -0.10)**	**0.29 (0.14; 0.43)**	**-0.19 (-0.34; -0.03)**	**-0.28 (-0.42; -0.12)**
Relative epithelial area (%)	0.13 (-0.03; 0.29)	**0.90 (0.87; 0.93)**	**-0.18 (-0.34; -0.02)**	**0.47 (0.33; 0.58)**	-0.03 (-0.19; 0.14)	0.12 (-0.04; 0.28)	0.04 (-0.11; 0.21)	**0.17 (0.01; 0.32)**	-0.13 (-0.28; 0.03)
Epithelial density (cell/mm²)	**-0.26 (-0.40; -0.10)**	-	**-0.30 (-0.44; -0.14)**	**0.59 (0.47; 0.69)**	-0.09 (-0.25; 0.08)	**0.22 (0.06; 0.37)**	-0.07 (-0.23; 0.09)	**0.26 (0.10; 0.41)**	-0.03 (-0.19; 0.13)
Mean podocyte area (μm²)	**0.34 (0.19; 0.48)**	**-0.30 (-0.44; -0.14)**	-	**-0.46 (-0.59; -0.33)**	**0.25 (0.09; 0.39)**	-0.09 (-0.25; 0.07)	0.02 (-0.14; 0.19)	0.05 (-0.11; 0.22)	**-0.19 (-0.34; -0.03)**
Relative podocyte area (%)	-0.22 (-0.37; -0.06)	**0.45 (0.31; 0.57)**	0.05 (-0.11; 0.21)	**0.83 (0.77; 0.87)**	0.00 (-0.16; 0.16)	0.09 (-0.07; 0.25)	**-0.19 (-0.34; -0.02)**	-0.01 (-0.17; 0.15)	0.00 (-0.16; 0.16)
Podocyte density (cell/mm²)	**-0.38 (-0.51; -0.23)**	**0.59 (0.47; 0.69)**	**-0.46 (-0.59; -0.33)**	-	-0.15 (-0.31; 0.01)	0.16 (-0.01; 0.31)	**-0.18 (-0.33; -0.02)**	-0.01 (-0.17; 0.15)	0.11 (-0.05; 0.27)
Mean endothelial cell area (μm²)	**0.16 (0.00; 0.32)**	-0.09 (-0.25; 0.08)	**0.25 (0.09; 0.39)**	-0.15 (-0.31; 0.01)	-	-0.11 (-0.27; 0.05)	**0.55 (0.43; 0.65)**	-0.03 (-0.19; 0.14)	0.15 (-0.01; 0.31)
Relative endothelial area (%)	**-0.19 (-0.35; -0.03)**	0.18 (0.02; 0.33)	-0.01 (-0.17; 0.15)	0.09 (-0.07; 0.26)	**0.18 (0.01; 0.33)**	**0.95 (0.93; 0.96)**	0.00 (-0.16; 0.16)	**0.23 (0.07; 0.38)**	**0.21 (0.05; 0.36)**
Endothelial density (cell/mm²)	**-0.26 (-0.41; -0.10)**	**0.22 (0.06; 0.37)**	-0.09 (-0.25; 0.07)	0.16 (-0.01; 0.31)	-0.11 (-0.27; 0.05)	-	-0.16 (-0.31; 0.01)	**0.24 (0.08; 0.38)**	0.18 (0.02; 0.34)
Mean mesangial cell area (μm²)	**0.29 (0.14; 0.43)**	-0.07 (-0.23; 0.09)	0.02 (-0.14; 0.19)	**-0.18 (-0.33; -0.02)**	**0.55 (0.43; 0.65)**	-0.16 (-0.31; 0.01)	-	-0.13 (-0.29; 0.03)	0.15 (-0.01; 0.31)
Relative mesangial area	-0.10 (-0.25; 0.06)	**0.21 (0.05; 0.36)**	0.04 (-0.12; 0.21)	-0.09 (-0.25; 0.07)	**0.18 (0.02; 0.33)**	0.16 (-0.01; 0.31)	0.25 (0.09; 0.40)	**0.91 (0.87; 0.93)**	-0.08 (-0.24; 0.08)
Mesangial density (cell/mm²)	**-0.19 (-0.34; -0.03)**	**0.26 (0.10; 0.41)**	0.05 (-0.11; 0.22)	-0.01 (-0.17; 0.15)	-0.03 (-0.19; 0.14)	**0.24 (0.08; 0.38)**	-0.13 (-0.29; 0.03)	-	**-0.16 (-0.32; 0.00)**
Mean capillary area (μm²)	-0.02 (-0.18; 0.15)	**-0.26 (-0.41; -0.10)**	0.08 (-0.08; 0.24)	-0.12 (-0.27; 0.05)	**0.34 (0.19; 0.48)**	-0.04 (-0.20; 0.12)	**0.21 (0.04; 0.36)**	**-0.49 (-0.61; -0.36)**	**0.60 (0.49; 0.70)**
Relative capillary area (%)	**-0.28 (-0.42; -0.12)**	-0.03 (-0.19; 0.13)	**-0.19 (-0.34; -0.03)**	0.11 (-0.05; 0.27)	0.15 (-0.01; 0.31)	0.18 (0.02; 0.34)	0.15 (-0.01; 0.31)	**-0.16 (-0.32; 0.00)**	-
Banff score[a]									
t score	-0.11 (-0.27; 0.05)	0.04 (-0.12; 0.20)	-0.02 (-0.18; 0.14)	0.11 (-0.05; 0.27)	0.04 (-0.13; 0.20)	0.14 (-0.02; 0.30)	-0.10 (-0.26; 0.06)	0.07 (-0.09; 0.23)	0.01 (-0.15; 0.17)
ptc score	**0.17 (0.00; 0.32)**	-0.05 (-0.21; 0.11)	0.01 (-0.15; 0.18)	-0.01 (-0.17; 0.15)	0.08 (-0.08; 0.24)	-0.15 (-0.31; 0.01)	0.09 (-0.08; 0.25)	0.01 (-0.15; 0.17)	-0.06 (-0.22; 0.10)
g score	-0.13 (-0.28; 0.04)	-0.14 (-0.30; 0.02)	0.00 (-0.16; 0.16)	0.00 (-0.16; 0.16)	-0.03 (-0.19; 0.13)	0.00 (-0.16; 0.16)	-0.12 (-0.27; 0.05)	0.02 (-0.14; 0.18)	0.08 (-0.09; 0.23)
mm score	0.13 (-0.03; 0.29)	0.03 (-0.13; 0.20)	0.10 (-0.07; 0.26)	-0.07 (-0.23; 0.09)	**-0.17 (-0.31; -0.01)**	-0.06 (-0.22; 0.10)	-0.07 (-0.23; 0.09)	**0.21 (0.05; 0.36)**	**-0.31 (-0.45; -0.15)**
cg score	-0.13 (-0.29; 0.03)	-0.01 (-0.17; 0.16)	-0.08 (-0.23; 0.09)	0.08 (-0.08; 0.24)	0.01 (-0.15; 0.17)	0.11 (-0.06; 0.27)	-0.10 (-0.26; 0.06)	0.08 (-0.17; 0.16)	0.13 (-0.04; 0.28)
i score	-0.01 (-0.17; 0.15)	0.01 (-0.15; 0.17)	-0.03 (-0.19; 0.13)	0.15 (-0.01; 0.31)	0.08 (-0.08; 0.24)	0.06 (-0.11; 0.22)	-0.03 (-0.20; 0.13)	-0.01 (-0.17; 0.16)	-0.02 (-0.18; 0.15)
ah score	**0.21 (0.05; 0.36)**	0.00 (-0.16; 0.16)	0.07 (-0.10; 0.23)	-0.11 (-0.27; 0.06)	-0.06 (-0.22; 0.10)	-0.14 (-0.29; 0.03)	0.04 (-0.13; 0.20)	-0.02 (-0.18; 0.14)	-0.02 (-0.18; 0.15)
IF/TA score	0.11 (-0.06; 0.27)	0.01 (-0.16; 0.17)	-0.07 (-0.23; 0.09)	0.02 (-0.15; 0.17)	-0.11 (-0.26; 0.06)	**-0.22 (-0.37; -0.06)**	-0.02 (-0.18; 0.14)	0.02 (-0.15; 0.18)	-0.11 (-0.27; 0.05)
cv score	0.15 (-0.02; 0.30)	**-0.18 (-0.33; -0.01)**	-0.02 (-0.18; 0.14)	**-0.21 (-0.36; -0.04)**	0.02 (-0.14; 0.19)	**-0.26 (-0.41; -0.10)**	0.12 (-0.05; 0.28)	-0.11 (-0.26; 0.06)	-0.06 (-0.24; 0.08)

a Banff score elements as previously published (3)

Spearman correlation test, Significant values are bolded.
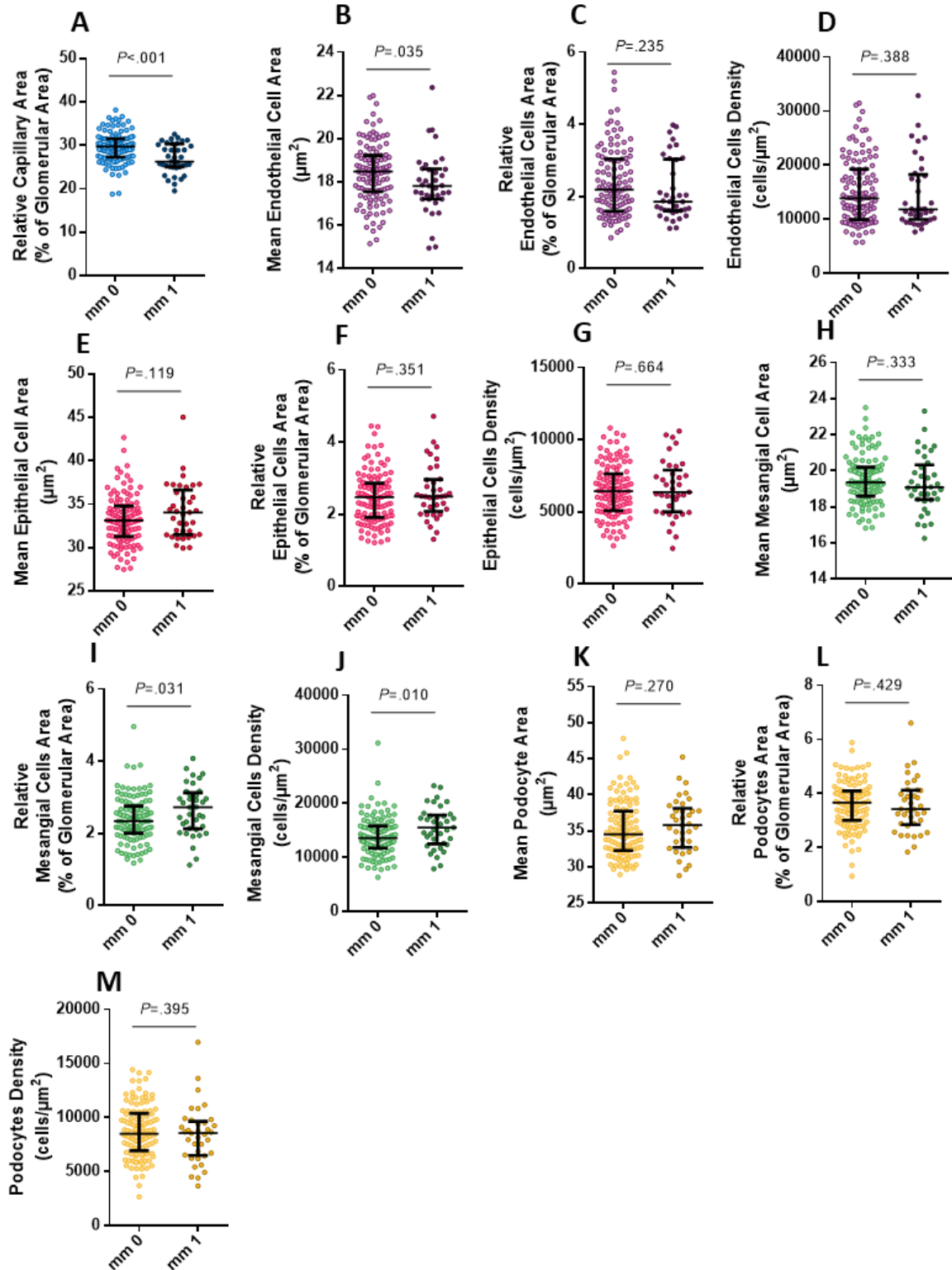
CI: Confidence Interval, BMI: Body Mass Index, IF/TA : interstitial fibrosis/ tubular atrophy
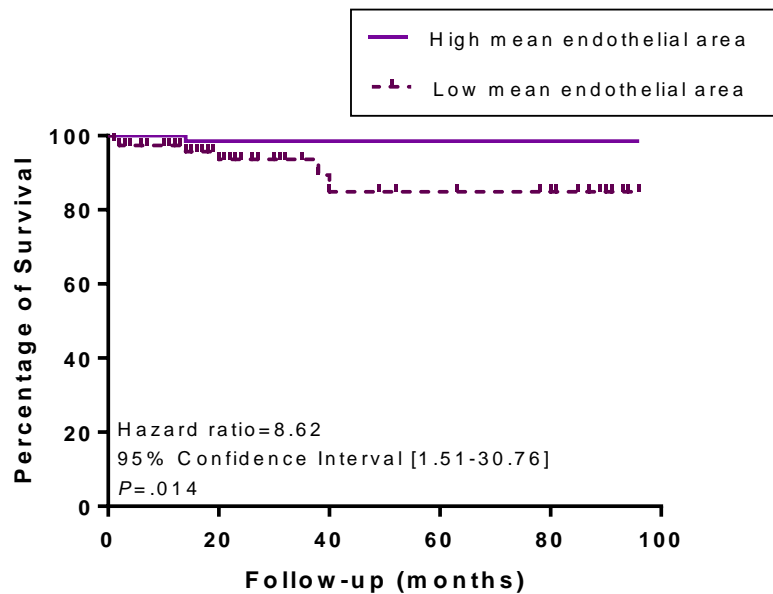
Supplemental Figure 1: Example of glomerular inclusion from a transplant biopsy in the training cohort. Biopsy stained with Masson's trichrome. A. Rectangles of 3840x2176 pixels are centered on cortical areas containing glomeruli. The borders of the rectangles do not pass through the glomeruli. B. The randomly chosen rectangle contains 2 glomeruli (*, #). One of the glomeruli (#) cannot be included as some parietal epithelial cells are not observable outside the biopsy border. C. Image at 40x zoom of the included glomerulus. During preprocessing for training, software will automatically center its analysis on a 1024x1024 pixel square (dotted square).

Supplemental Figure 2: Association between proteinuria and mean podocyte area for Minimal Change Diseases (MCD) and protocol transplant biopsies. Patients with MCD were from the Test cohort, and transplant biopsies were from the Application cohort. A. Comparison of mean podocyte area between MCD and Transplants. Mann-Whitney test. B. Correlation curve between proteinuria and mean podocyte area for Transplant and MCD patients analyzed together. Spearman's test.

Supplemental Figure 3: Comparison of histological data predicted by the neural network based on mesangial thickness score (mm score) in the Application cohort. mm 0: mm score = 0, mm 1: mm score ≥1. The bars depict medians and interquartile ranges. Mann-Whitney test.

Supplemental Figure 4: Kaplan-Meier curves for survival analysis of rejection occurrence based on whether relative endothelial areas were above or below the medians. Included acute, chronic, antibody-mediated, and T-cell-mediated rejections.

Supplemental References

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