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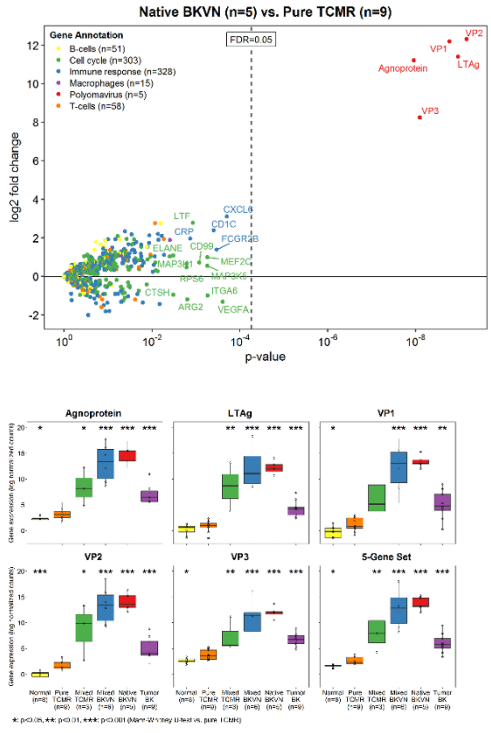
1674 Molecular Diagnosis of Polyomavirus Nephropathy Versus T-Cell Mediated Rejection in FFPE Tissue

Benjamin Adam[1], *Siegfried Wagner*[2], *Verena Broecker*[3], *Vivette D'Agati*[4], *Drachenberg Cinthia*[5], *Alton B Farris*[6], *Laurette Geldenhuys*[7], *Alex Magil*[8], *Volker Nickeleit*[9], *Parmjeet Randhawa*[10], *Michael Mengel*[11]. [1]University of Alberta, Edmonton, AB, [2]University of Alberta, [3]Sahlgrenska University Hospital, Gothenburg, Vöstra Götaland, [4]Tenafly, NJ, [5]University of Maryland, [6]Emory University, Atlanta, GA, [7]Dalhousie University, [8]St. Paul's Hospital, Vancouver, BC, [9]Univ. of North Carolina, Chapel Hill, NC, [10]University of Pittsburgh, Pittsburgh, PA, [11]Univ. of Alberta, Edmonton, AB

Background: Improved immunosuppression protocols have reduced the incidence of T-cell mediated rejection (TCMR) but still carry a significant risk of BK polyomavirus nephropathy (BKVN). Despite requiring opposite treatments, BKVN and TCMR often have overlapping clinical and histological presentations. Molecular testing may allow for more precise diagnosis and risk stratification.

Design: NanoString® was used to measure the expression of 800 genes in 40 formalin-fixed paraffin-embedded human samples. The genes included the 770-gene nCounter® PanCancer Immune Profiling Panel, 25 additional literature-based TCMR-related genes, and 5 polyomavirus (PV) genes (Agnoprotein, LTAg, VP1, VP2, VP3). The samples included native kidney BKVN (n=5), pure TCMR (n=9), SV40 immunohistochemistry-positive carcinoma (tumor BK, n=9), and normal implant kidney biopsies (n=8). Using six additional allograft nephrectomies with evidence of both BKVN and TCMR, regions showing histologic features of only BKVN (mixed BKVN, n=6) and only TCMR (mixed TCMR, n=3) were isolated with laser capture microdissection. Differential gene expression and diagnostic performance were assessed. Analysis was performed using nSolver and R.

Results: All five PV genes demonstrated statistically significantly increased expression (FDR<0.05) in native BKVN versus pure TMCR, but no human genes were differentially expressed (Figure 1). PV gene expression was also significantly higher (versus pure TCMR) in tumor BK (p<0.006), mixed BKVN (p<0.001), and mixed TCMR (p<0.036, except VP1) (Figure 2). Receiver operating characteristic curve analysis revealed excellent discrimination between BK-positive (including mixed TCMR) and BK-negative cases: LTAg, AUC=1.000; VP3, AUC=0.995; Agnoprotein, AUC=0.992; VP2, AUC=0.987; VP1, AUC=0.959. As a 5-gene set, the PV genes demonstrated near-perfect diagnostic performance (AUC=0.992) with improved sensitivity (0.957) over histology (0.870).



Conclusions: These data suggest that PV gene expression is more sensitive than histology and can more precisely discriminate BKVN and TCMR. However, at the molecular level, no significant difference in human immune response was identified. An independent cohort of BKVN patients treated with a standardized clinical protocol and showing either (a) BKVN resolution (n=15), (b) BKVN persistence (n=15), or (c) de novo rejection (n=15) is currently being assessed to validate these findings and assess the potential utility of gene expression testing for risk stratification purposes.

1675 Renal Manifestations in Neurofibromatosis

Osamah AL Badri, Lynn Cornell, Kriselle Maris Lao, Jorge Torres-Mora, Mariam Priya Alexander. Mayo Clinic, Rochester, MN

Background: Neurofibromatosis (NF) types 1 and 2 are diseases with peripheral nerve sheath tumors. The renal manifestations in NF have only been sparsely described in the literature. We present the largest series of renal pathology in patients with NF.

Design: We searched our renal biopsy and autopsy databases for patients with NF. Light microscopy slides were reviewed, and IF and EM reports or images were reviewed. Demographic data with clinical information and the causes of death were recorded. Immunoperoxidase staining was performed for S100 and alpha-smooth muscle actin (aSMA) to evaluate vascular lesions..

Results: We identified 17 cases of NF and kidney specimens from January 1996 to June 2017, including 9 autopsy cases and 8 kidney biopsies. Among autopsy cases, 7 had NF-1 and 2 had NF-2. The mean decedent age was 52 years (range 33-68). The mean serum creatinine at 3 weeks prior to death was 1.9 mg/dL (range 0.7-2.8); 4/9 (44%) autopsy patients had renal insufficiency. The mean patient age at renal biopsy was 54 years (range 21-76). The mean creatinine at time of biopsy was 3.1 mg/dL (range 2-5.1). The type of NF was not available for biopsy cases. The primary indication for renal biopsy was renal insufficiency in 6; 5 patients had proteinuria and 3 had hematuria. Histologically, subendothelial eccentric pericytic like nodular proliferation (SEPNP) in focal arteries was seen in 89% of autopsies, including both NF-2 cases. The subendothelial proliferative cells showed a smooth muscle phenotype (Focal immune-reactive to aSMA, while no reactivity to S100), as observed on all autopsy cases. SEPNP was seen in 2/8 (25%) renal biopsies. Renal biopsies showed a variety of other findings, including glomerulonephritis in 75%: IgA nephropathy (2), membranous nephropathy (2), MPGN (1) and focal necrotizing crescentic C3 glomerulonephritis (1). None of the autopsy or biopsy cases showed sclerosing peritubular nodules or schwannomas.

Conclusions: Patients with NF show a variety of renal diseases on biopsy that occur in the general population. In addition, we describe a distinct vascular lesion, the SEPNP, that can occur in NF-1 and NF-2. Recognition of this pattern can alert the pathologist to a diagnosis of NF.

1676 High Risk Variants of APOL-1 Are Associated with Parietal Epithelial Cell Activation in Arterionephrosclerosis

Jorge R Almeida[1], *Justin C Hsueh*[2], *Huma Fatima*[3], *Haichun Yang*[4], *Agnes Fogo*[5]. [1]Universidade Federal Fluminense, Capes, Brazil, [2]Vanderbilt University, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Vanderbilt University, Nashville, TN, [5]Vanderbilt University Medical Ctr, Nashville, TN

Background: Arterionephrosclerosis shows more solidified glomerulosclerosis in African American (AA) than Caucasian patients. APOL1 risk variants are commonly present in AA, and have been linked to podocyte injury. Activated parietal epithelial cells (PECs) express CD44, and may migrate to glomeruli in response to podocyte injury and contribute to matrix accumulation. We studied the correlation of APOL-1 variants and PEC activation in arterionephrosclerosis.

Design: We identified 652 renal biopsies diagnosed as arterionephrosclerosis without other lesions from 1988 to 2014. DNA from paraffin block tissue was genotyped for APOL1 risk alleles in all AA (n=189) and a subset of Caucasian patients (n=117). Clinical parameters at time of biopsy were obtained. Histologic scores, including extent and type of glomerulosclerosis, interstitial fibrosis, and vascular sclerosis were analyzed. PEC activation was assessed by CD44 immunostaining.

Results: No Caucasian patients had APOL1 risk variants. Compared to AA with 0 risk allele (n=60, AA-0), Caucasians had higher blood pressure, but similar creatinine clearance (Ccr), proteinuria and overall injury severity. 59 AA patients had 1 risk allele (AA-1) and 70 had 2 risk alleles (AA-2 high risk). Compared to AA with low risk variants

(AA-0+AA-1), AA with high risk variants were younger, had more proteinuria, more solidified and disappearing glomerulosclerosis, and interstitial fibrosis, although they had similar Ccr. CD44 positivity along Bowman's capsule did not differ. In contrast, more CD44+ cells were observed in glomerular tufts in the high risk group (3.60±0.62 $X10^4/\mu m^2$) than in low risk group (2.32±0.24 $X10^4/\mu m^2$).

Conclusions: Our data suggest that PEC activation with migration to the glomerular tuft is increased in patients with two APOL-1 risk allele variants. Such activated parietal epithelial cells could potentially contribute to renal injury, including increased solidified and disappearing glomerulosclerosis, in the subgroup of AA patients with arterionephrosclerosis and two APOL-1 risk allele variants.

1677 Glomerular Capillary Thrombi in Post Perfusion Biopsy of Transplanted Kidney: Are They Clinically Significant?

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Background: Post-perfusion donor kidney biopsies are often performed during renal transplantation. Glomerular capillary thrombi (GCT) can be seen in these biopsies. Many aspects of GCT remain poorly understood, including pathogenesis, morphologic spectrum, clinical significance, optimal management and impact on graft outcome. This study aimed to address these questions.

Design: All post-perfusion renal biopsies of transplanted kidneys over a 6-year period (2010-2016) were reviewed to identify those with GCT. These biopsies were reviewed with immunostains for CD61 (platelet marker), and PAX8 & RCC (proximal tubular cells markers) and electron microscopy (EM). Follow-up renal biopsies were also reviewed. The biopsy findings were correlated with clinical and laboratory findings of the donors around the transplantation period. They were also correlated with clinical course of the recipients and the outcome of their transplants.

Results: Out of a total of 812 post-perfusion biopsies, 44(5.4%) biopsies from 44 donors showed GCT. In each of these biopsies, only a few glomeruli were affected and only a rare glomerular capillary showed thrombus. The thrombi were composed predominantly of platelets with a minor contribution of fibrin as shown by CD61 immunostain and EM. Donor information included: mean age 41 years (range 14-72); 24 males, 17 females; 15 live, 29 deceased. The causes of death in deceased donors included stroke, motor vehicle accident, head trauma, anoxia, blunt injury and CNS tumor. The cold ischemic time ranged from 41 minutes to 35 hours. Graft preparation and preservation were similar for the deceased and living donors. Delayed graft function was noted in 12 recipients (10 deceased, 2 live donors). Among the 30 follow up biopsies (6-511 days post-transplant) in 21 patients, none showed any residual GCT. At a mean follow up of 49 weeks (range 22 - 62), 40 grafts functioned and 4 were lost. Six recipients were deceased, with graft lost in 4 of them.

Conclusions: GCT are often seen in post-perfusion renal transplant biopsies. They are composed predominantly of platelets and noted in both deceased and living donors. Although head trauma is a significant pathogenic factor, other causes remain unknown. The thrombi resolve quickly and are not seen in any follow-up biopsies. They are not associated with worse graft outcome and should not by themselves be a reason for rejection of the donor kidneys.

1678 Nephrosclerosis is Frequently Identified in Young Patients With Renal Cell Carcinoma.

Tiffany N Caza[1], *Ivy John*[2], *Gennady Bratslavsky*[3], *Stephen Blakely*[3]. [1]SUNY Upstate Medical University, Clay, New York, [2]University of Pittsburgh Medical Center, Pittsburgh, PA, [3]SUNY Upstate Medical University

Background: The purpose of this study was to determine the relative and absolute prevalence of nephrosclerosis in young patients with renal cell carcinoma (RCC) in comparison to age-matched controls.

Design: Fifty-nine patients up to 50 years of age who underwent nephrectomy for RCC, 11 patients who underwent trauma nephrectomy, and 43 kidney sections from autopsy cases from decedents under 50 years of age were examined retrospectively. In the autopsy group, to limit autolytic artifacts, only cases autopsied within 48 h from time of death were evaluated. Clinical data were extracted from the electronic medical record. Non-neoplastic renal parenchyma was evaluated for the presence of nephrosclerosis, defined as two of the following three features: arteriosclerosis or arteriolosclerosis, glomerulosclerosis, and interstitial fibrosis. To avoid local ischemic changes/compression artifact by the tumor, parenchyma furthest from the tumors was analyzed. We compared the prevalence of nephrosclerosis in the groups using a two-tailed Fisher's exact test; means and standard deviations for patient characteristics were compared using unpaired student's t-tests.

Results: There was a significant increase in arteriolosclerosis, atherosclerosis, and glomerulosclerosis in nephrectomies with renal cell carcinomas compared to trauma nephrectomies (arteriolosclerosis 5.0-fold increase p=0.001, atherosclerosis 6.3-fold increase p = 0.003, glomerulosclerosis 5.0-fold increase p=0.008) and to autopsy kidney sections (arteriolosclerosis 2.8-fold increase p=0.00002, atherosclerosis 2.5-fold increase p = 0.0004, glomerulosclerosis 3.0-fold increase p=0.00004). The amount of interstitial fibrosis was not significantly affected. Overall, significant nephrosclerosis was present in 70.1% of RCC patients, 36.4% of trauma nephrectomy, and 53.5% of autopsy control specimens (p=0.001 RCC vs. autopsy, p=0.009 autopsy vs. trauma). In the small subset of RCC patients without any risk factors such as HTN, DM or cigarette smoking, 9 of 12 (75%) exhibited nephrosclerosis.

Conclusions: Nephrosclerosis in non-neoplastic renal parenchyma is more common in RCC patients than in age-matched controls. These histopathologic changes could contribute to the rate of post-operative renal insufficiency after partial nephrectomy for RCC. The presence of nephrosclerosis, in young patients in particular, offers support for a nephron sparing approach in those individuals who will predictably, undergo further age-related decline in renal function.

1679 Rapid Formalin-Fixation of Donor Kidney Biopsies Shows Superior Interobserver Reproducibility Compared to Frozen Section

Jie Chen, Satoru Kudose, Marianna Ruzinova, Horacio Miguel Maluf, Joseph Gaut. Washington University, Saint Louis, MO

Background: Pathologic evaluation of donor kidneys is a key parameter used to determine whether or not an organ is acceptable for transplantation. A recent study by a Banff working group showed fair interobserver reproducibility for routinely used histologic parameters using frozen kidney biopsies. Rapid formalin-fixation and paraffin-embedding of needle core biopsies has been proposed as a potentially superior alternative to frozen section. In this study, we compared the interobserver reproducibility for key histologic parameters using frozen wedge and rapid formalin-fixed needle core donor kidney biopsies.

Design: Twenty consecutive frozen wedge biopsies and twenty consecutive rapid formalin-fixed core biopsies were evaluated using digital pathology by two experienced general surgical pathologists, one renal pathologist, and one trainee. The following 9 parameters were scored: number of glomeruli, number of globally sclerotic glomeruli, glomerular thrombi, focal segmental glomerulosclerosis, nodular glomerulosclerosis, interstitial fibrosis, acute tubular injury, arterial intimal fibrosis, and arteriolar hyalinosis. The intraclass correlations (ICCs) were compared between these two methods. Correlation is interpreted as excellent (>0.75), good (0.5 – 0.75), fair (0.25 – 0.5), and poor (<0.25).

Results: For 5 of 9 parameters, rapid formalin-fixed core biopsies showed significantly improved ICCs compared with frozen wedge biopsies: arteriolar hyalinosis (0.734 vs 0.100), arterial intimal fibrosis (0.401 vs 0.217), glomerular thrombi (0.383 vs no thrombi detected), nodular glomerulosclerosis (0.213 vs 0.009), and focal segmental glomerulosclerosis (0.204 vs 0.078). Assessment of the number of glomeruli (0.958 vs 0.848) and number of globally sclerotic glomeruli (0.785 vs 0.840) showed similar ICCs. Identification of acute tubular injury (0.002 vs 0.014) was poor regardless of the technique used. The only parameter that showed marginally improved ICC using the frozen wedge technique was interstitial fibrosis (0.237 vs 0.370).

Conclusions: For 7 of 9 parameters, ICCs were better or comparable in rapid formalin fixation core biopsies than in frozen wedge biopsies. Our results indicate that interpretation of rapid formalin fixed core kidney biopsies using digital pathology has superior reproducibility between pathologists compared to frozen wedge biopsies, especially for the glomerular and vascular parameters.

1680 Study on Tubular Injury in Light Chain-Associated Acute Tubulointerstitial Nephritis

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Background: Monoclonal light chain-associated acute tubulointerstitial nephritis (LC-ATIN) is a variant of light chain proximal tubulopathy (LCPT). Recognition of the presence of proximal tubular injury is important for an accurate diagnosis of this entity. In this study, renal biopsies with LC-ATIN were investigated with immunohistochemical staining for tubular injury markers including KIM-1, p53, bcl-2 and Ki-67.

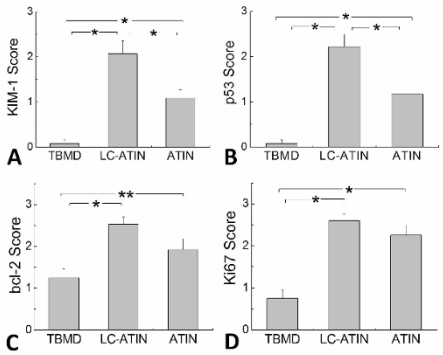
Design: Fifteen renal cases from patients with LC-ATIN were studied. Twelve cases with thin basement membrane disease (TBMD) served as negative controls and twelve cases with acute tubulointerstitial nephritis (ATIN), not monoclonal LC-associated, served as positive controls. Cases were stained immunohistochemistically for: KIM-1, p53, bcl-2 and Ki-67. The findings were scored: markedly increased (3, >10 cells/HPF), increased (2, 5-10 cells/HPF), rare (1, <5 cells/HPF) and negative (0, no staining). Specimens with markedly increased (3+) and increased (2+) staining in tubular cells were judged as positive, while cases with rare (1+) and negative (0) staining were considered negative. Fisher exact test and one-way ANOVA in conjunction with Tukey's post hoc test were used to test for statistical significance.

Results: As summarized in table 1, the IHC staining of KIM-1 was positive in 12 of 15 (80%) LC-ATIN cases, 3 of 12 (25%) ATIN cases, and 0 of 12 (0%) TBMD cases. P53 stain was similar to KIM-1, positive in 10/15 (67%) LC-ATIN cases and 3/12 (25%) ATIN cases, and negative in all TBMD (0/12) cases. Ki-67 was positive in 14 of 15 (93%) LC-ATIN cases, 10 of 12 (83%) ATIN cases, and 1 of 12 (8%) TBMD cases. With bcl-2, 14/15 LC-ATIN (93%) cases and 8/12 (67%) ATIN cases were positive, while 9/12 TBMD cases were negative. 10 of 15 (67%) LC-ATIN cases and 3 of 12 (25%) ATIN cases were positive for all of the four markers, whereas only 3 of 12 TBMD cases were positive for one or two of these markers. The average score of the four markers in three groups is shown in figure 1. LC-ATIN and ATIN cases showed significantly increased staining of KIM-1, Ki-67, p53 and bcl-2 when compared to TBMD cases. LC-ATIN also had a higher KIM-1 and p53 score than ATIN.

Table 2. Renal biopsies with positive IHC staining (staining score ≥ 2+).

Groups	KIM-1 + (%)	p53 + (%)	Bcl-2 + (%)	Ki-67 + (%)	Quadruple + (%)
LC-ATIN (n=15)	12 (80%)*	10 (67%)*	14 (93%)	14 (93%)	10 (67%)*
ATIN (n=12)	3 (25%)	3 (25%)	8 (67%)	10 (83%)	3 (25%)
TBMD (n=12)	0 (0%)	0 (0%)	3 (25%)	1 (8%)	0 (0%)

* Significantly higher than ATIN group (p<0.05)



Conclusions: This study demonstrates that proximal tubular injury in LC-ATIN is more severe and extensive than in ATIN, suggesting that both accumulation of light chains in tubular lysosomes and interstitial inflammation may be involved in the tubular injury formation in LC-ATIN.

1681 Acute Tubular Injury (ATI) Secondary to Thrombotic Microangiopathy Can be Morphologically Different from Primary ATI Due to Ischemia

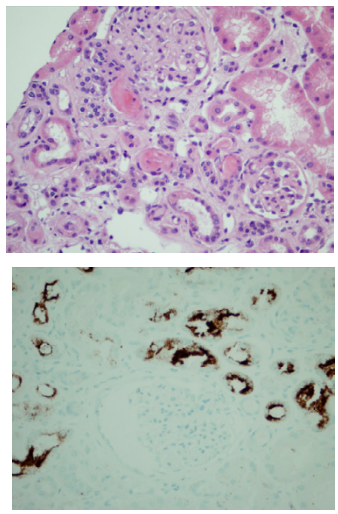
Craig Cousineau[1], *Ping Zhang*[2], *Hassan Kanaan*[3], *Wei Li*[3]. [1]Royal Oak, MI, [2]William Beaumont Hospital, Birmingham, MI, [3]Beaumont Health

Background: ATI can occur in all three segments of proximal tubules (PT); S1 occurs mainly in convoluted PT, S2 mainly in medullary rays, and S3 at cortico-medullary junctions. In-vivo experimental investigations and our human biopsy studies all demonstrate that S2 and S3, likely due to their low oxygen supplies, are more vulnerable to ischemic injury compared to the S1 segment of PT. The goal of this study was to investigate whether ATI secondary to thrombotic microangiopathy (TMA) was morphologically different from ATI due to ischemic/toxic injury (primary ATI, so called acute tubular necrosis [ATN]).

Design: Seventeen (17) TMA cases with dominant glomerular involvement and 18 primary ATN cases were stained for a specific injury marker of PT, kidney injury molecule-1 (monoclonal anti-KIM-1 antibody AKG7), whereas some were also stained for the injury markers CD133 and CD68 by immunohistochemical method. The expression of both KIM-1 and CD133 in S1 vs S2/S3 (S3 was often absent in core biopsies) were recorded as either: 0 (no staining), +/- (focal weak staining), 1+ (entire luminal weak staining), 2+ (entire luminal moderate staining), or 3+ (entire luminal strong staining). Cytoplasmic granular staining of CD68 was also graded from 0 to 3+. Twelve (12) cases without kidney injury were also stained with all three markers as negative controls.

Results: Negative controls without kidney injury (n=12) all stained negative for the three markers. In 17 TMA cases, 15 of 17 cases (88%) show higher or similar S1 staining for the injury markers when compared to S2/S3 segments of PT. By contrast, only 8 out of 8 primary ATN cases (44%) revealed higher or similar S1 staining for the injury markers when compared to S2/S3 segments, whereas the remaining 56% of cases with primary ATN demonstrated dominant injury staining in S2/S3 segments of PT

	S1 >/= S2/3	S1
TMA cases (n=17)	15 (88%)	2 (12%)
ATN cases (n=18)	8 (44%)	10 (56%)



Conclusions: Our data indicate that TMA often results in ATI, which mainly affected the S1 segment of PT around the thrombotic glomeruli, as well as some of the S2 segment, a feature which helps us support a diagnosis of TMA when no definite thrombi are present. Primary ATN, often due to overall renal ischemia, can affect all segments from S1 to S2/S3, with more injury seen in the S2/S3 segments, which are supplied by low oxygen blood and thus more vulnerable to further ischemic insults.

1682 Novel Genes Related to Human Diabetic Nephropathy

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Background: The pathophysiology of diabetic nephropathy (DN) is not well understood. By using RNAseq technology, we discovered that 288 genes exhibited significantly altered expression levels in experimental DN (db/db/eNOS$^{-/-}$) vs. control mice (db/eNOS$^{-/-}$). We assessed whether a subset of these genes were also altered in human DN, and possibly involved with mechanisms of injury in DN.

Design: We selected 29 from 288 genes, which have homologs in humans, have not been researched in depth, and are plausibly relevant to DN pathophysiology. RNA was extracted from 24 human DN biopsies and 24 normal nephrectomy cases. Gene expression levels of the selected genes were measured using Nanostring Technologies. Renal function and morphologic score were assessed.

Results: Of the 29 genes analyzed, 17 genes showed significantly altered expression ($p<0.05$) in DN samples when compared to control. 13 of these genes showed similar change as in our murine model. Among these 13 genes, 4 correlated with increased serum creatinine (sCr, R^2=0.23~0.36), 8 correlated with increased glomerulosclerosis (R^2=0.22~0.51), 7 correlated with interstitial fibrosis (R^2=0.19~0.28), and 8 correlated with glomerular hyalinosis (R^2=0.23~0.41). 4 genes, including adhesion molecule, pantothenate kinase, and antiplasmin, correlated with both increased sCr and worse morphologic injury.

Conclusions: The results of this study affirm the usefulness of the mouse model for selecting novel candidate genes that plausibly could be involved in human DN. Further study is required to determine whether the proteins encoded by these genes exhibit a similar change in expression levels, and are causal in injury, or represent epiphenomena.

1683 CD34-CD45 Stain Increases Reproducibility of ptc Score in Renal Allograft Biopsies

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Background: Microvascular inflammation (MVI) is the most prominent histologic lesion in antibody mediated rejection (AMR) and is defined by leukocyte margination in glomerular (g) and peritubular capillaries (ptc). The gold standard stain for evaluation of MVI is periodic acid Schiff (PAS), as defined by Banff international working group for classification of renal allograft pathology. Nevertheless, recognition and scoring of these lesions can be difficult and several studies have shown poor interobserver reproducibility.

Design: We developed a dual immunohistochemical stain (anti-CD34 and anti-CD45 for endothelium and leukocytes, respectively) as an ancillary stain to improve assessment of semiquantitivative Banff scores (Figure 1). A set of renal allograft biopsies obtained from 2004 to 2016 were independently reviewed by three renal pathologists to assess the reproducibility of Banff ptc scores with conventional stains (PAS and/or H&E, 68 cases) and CD34-CD45 IHC stain (63 cases). Reproducibility of histologic score was assessed with kappa test.

Results: The kappa-values for the grading of Banff ptc and for the evaluation of peritubular capillaritis extent (focal vs diffuse) with conventional stains were fair (0.28 to 0.30) and fair-to-moderate (0.38 to 0.42) respectively. The use of IHC CD34-CD45 stain slightly increased the kappa-values of both evaluations, with fair-to-moderate reproducibility for Banff ptc (0.36 to 0.48) and moderate-to-good reproducibility for ptc extent (0.49 to 0.67). (Table 1)

	Conventional Stains	CD34-CD45 IHC
ptc score (0,1,2,3)	K = 0.28-0.30	K = 0.36-0.48
ptc extent (focal **vs** diffuse)	K = 0.38-0.42	K= 0.49-0.67

Table 1. Use of CD34-CD45 stain increases reproducibility of ptc score and evaluation of extent of peritubular capillaritis.

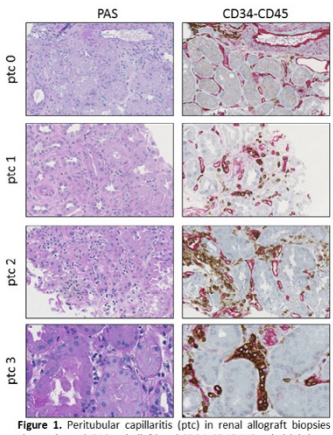

Figure 1. Peritubular capillaritis (ptc) in renal allograft biopsies shown through PAS stain (left) and CD34-CD45 IHC stain (right)

Conclusions: When used to evaluate standard Banff lesions, CD34-CD45 stain increased interobserver reproducibility of ptc score intensity (ptc0, 1, 2 and 3) and extent (focal vs. diffuse ptc).

1684 Second Harmonic Generation as a Novel Non-Destructive Technique for Evaluation of Interstitial Fibrosis in Renal Allograft Biopsies.

Marco Delsante[1], *Suman Ranjit*[2], *Alexander Dvornikov*[2], *Serena Bagnasco*[3], *Enrico Gratton*[2], *Moshe Levi*[4], *Avi Rosenberg*[5]. [1]Johns Hopkins Hospital, Baltimore, MD, [2]University of California, Irvine, [3]Johns Hopkins University, Baltimore, MD, [4]Georgetown University, Washington, DC, [5]Johns Hopkins University School of Medicine, Baltimore, MD

Background: Interstitial fibrosis (ci) and tubular atrophy (ct) are central features of chronic allograft nephropathy and show strong correlation with decline of renal function and risk of allograft failure. Thus, consistent evaluation of ci and ct in renal allograft biopsy is cardinal and is one of the main drivers for immunosuppression tailoring. Currently, ci and ct semi-quantitative scores are based on conventional histologic stains for fibrotic tissue. Second harmonic generation (SHG) and fluorescence imaging have been used to measure fibrosis in tissues, including kidney (Strupler M et al, J Biomed Opt 2008; Ranjit S at al, Kidney Int 2016). Fibrillar collagens have a non-centrosymmetric structure and thus can give rise to SHG. The second harmonic can be detected and the signal intensity will depend on the amount of collagen in the tissue.

Design: 13 renal allograft biopsies were imaged using SHG to assess the presence of collagen (Figure 1). SHG signal was expressed as the ratio of positive pixels from SHG signal and total number of pixels per tissue section. The results were correlated with conventional ci scores and with clinical outcomes.

Results: SHG signal shows fair correlation with Banff ci scores (Figure 2A). When used to predict transplant outcome, a mean SHG density below 0.45 was correlated with better allograft survival (Figure 2B).

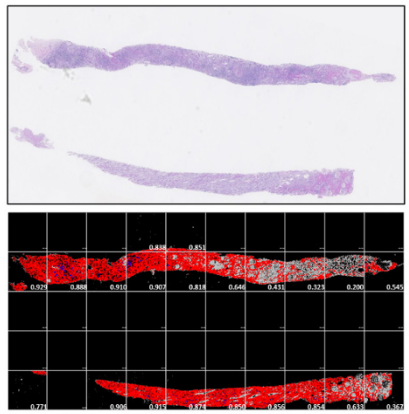

Figure 1. Renal allograft biopsy. Top image shows an H&E stained allograft biopsy with severe interstitial fibrosis (ci3); the same sample showed high mean SHG density (0.719, bottom figure).

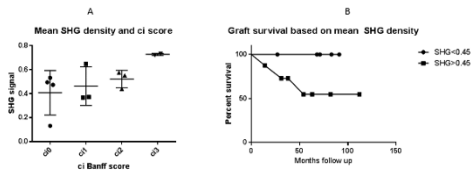

Figure 2. Mean SHG density shows fair correlation with Banff ci classes (A). With a threshold of 0.45, mean SHG density predicts long term graft survival (B).

Conclusions: SHG signal can be used to quantitatively estimate the degree of fibrosis in renal allograft biopsies and the quantitative value shows correlation with clinical outcome. More studies are needed to confirm clinical correlations, feasibility and reproducibility of this novel non-destructive approach for unbiased assessment of interstitial fibrosis and allograft integrity.

1685 Staining Characteristics of PLA2r and IgG Subclasses in Different Membranous Nephropathy

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Background: Membranous nephropathy (MN) can be secondary to a systemic condition (2MN) or "idiopathic" (iMN). Phospholipase A2 receptor (PLA2r) is the most common target antigen in iMN, and IgG4 frequently is the dominant IgG subclass that binds to it. Staining for PLA2r and IgG subclasses has been routine practice for last few years. Here we review the sensitivity and specificity of these stains.

Design: Renal biopsies with MN pattern of injury over last 4 years are studied using light microscopy, electron microscopy (EM), and immunofluorescence microscopy (IF) with antibodies specific for IgA, IgM, IgG, κ, λ, C3, C1q, PLA2r, and IgG subclasses1-4. IF intensity is graded into 6 classes: negative, trace, 1+ - 4+. Biopsies are classified into four EM stages by the criteria of Ehrenreich and Churg. Causes of MN and their chronological expression can be elusive, so 2MN in this study is defined morphologically by the presence of subendothelial and/or mesangial and/or tubular basement membrane deposits on EM and IF.

Results: 235 cases are included in the study, of which 94 (40%) are classified as 2MN and 141 (60%) are iMN. 43 of 94 2MN cases have clinical history of well-accepted MN causes including 20 lupus, 9 malignancy, 4 GVHD, 3 IgG4 disease, 3 HCV, 2 syphilis, 1 Lyme disease, and 1 HIV. 8 of 141 morphologic iMN cases are associated with well-accepted MN causes including 2 GVHD, 1 Lyme disease, 1 HIV, 1 HCV, 1 syphilis, 1 CLL, and 1 renal tumor.

PLA2R positivity: Of the 141 iMN cases, 110 (78%) are PLA2R positive. Of the 94 2MN cases, 32 (34%) are PLA2R positive. There is an increasing trend of PLA2R positivity as iMN progressing to higher stages (figure 1).

Intensity of IgG subclasses: IgG4 most frequently dominates in PLA2r-positive iMN cases, followed by IgG1 especially in early stages (figure 2). 57% stage I and 88% stage III & higher cases show IgG4 dominance. 36% stage I biopsiesbut not stage III & higher cases show IgG1 only dominance (table 1). Of 31 PLA2r-negative iMN cases, 11 show dominance of IgG1, 10 IgG1 & IgG4, and 10 IgG4. Of 31 PLA2r-positive 2MN case, 8 show IgG1 dominance, 3 IgG1 & IgG4, and 18 IgG4. Of 62 PLA2r-negative 2MN cases, only 5 (8%) are IgG4 dominant, and up to 30 cases show either dominance of all classes or IgG3 and/or IgG2.

Table 1. Dominance of IgG1 and IgG4 in MN cases.

Cases		IgG1 dominant	IgG1 and IgG4 co-dominant	IgG4 dominant	other
PLA2r-positive iMN (111)					
	Stage I	5	1	8 (57%)	0
	Stage I-II	0	3	8 (73%)	0
	Stage II	5	15	31 (60%)	0
	Stage III & up	0	3	30 (88%)	1
PLA2r-negative iMN (31)		11	10	10 (32%)	0
PLA2r-positive 2MN (31)		8	3	18 (58%)	3
PLA2r-negative 2MN (62)		21	6	5 (8%)	30

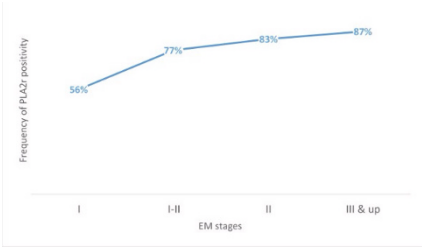

Figure 1. Frequency of PLA2R positivity in iMN cases at different EM stages.

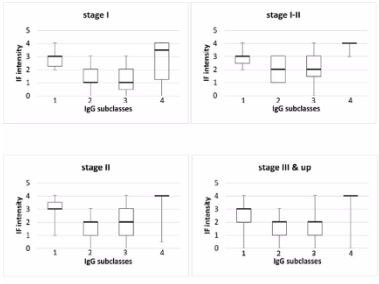

Figure 2. Box and whisker plots showing distribution of IgG subclasses in PLA2r-positive iMN cases.

Conclusions: Advanced cases of MN are more likely to be PLA2r-positive. However, we have not observed reactivity switch on second biopsies. The IgG subclass distribution patterns in PLA2r-negative 2MN cases are markedly different from other MN cases.

1686 C3 Glomerulopathy in Children: A Clinicopathological Study

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Background: C3 glomerulopathy is defined by dominant glomerular deposition of C3 with minimal or no immunoglobulin. Two subtypes, dense deposit disease (DDD) and C3 glomerulonephritis (C3GN), are recognized based upon electron microscopy features. The pathogenesis involves dysregulation of the alternative complement pathway. We sought to determine the prevalence of C3 glomerulopathy among patients biopsied at a pediatric hospital and correlate the subtypes with clinical characteristics, results of complement studies and renal outcomes in children.

Design: All patients with native kidney biopsies fulfilling diagnostic criteria for C3 glomerulopathy were identified from the case files of a single pediatric hospital from April 2007 to February 2017. The clinical history was reviewed and pertinent information including age, gender, indication for biopsy, complement studies, and renal outcome were collected for each patient.

Results: Out of 589 total native kidney biopsies, 9 patients were identified including 4 with DDD, 4 with C3GN, and 1 indeterminate resulting in a prevalence of 1.5%. Mean age at diagnosis was 11 years (range: 8-16), and the majority were females (55%). All patients presented with hematuria and proteinuria. At onset, the mean serum creatinine was 0.7 (range: 0.3-1.7). C3 was decreased in all cases except 1 with DDD. In patients with DDD, C3 nephritic factor was positive in 2/3 patients tested; C4 nephritic factor was positive in 0/3; factor H autoantibodies were positive in 1/3; C5b-9 was abnormal in 1/2; and C3d was high in 1/2. In patients with C3GN, C3 nephritic factor was positive in 1/2 patients tested; C4 nephritic factor was positive in 2/2; factor H autoantibodies were negative in 2/2; C5b-9 was abnormal and C3d was elevated in 2/2. Genetic screening was performed in 4 patients, but no causative variants were found. Six cases were treated with steroids, 5 of which also received immunosuppressants. The mean follow-up was 33 months (range: 2-120). Three patients showed progressive renal dysfunction, including 2 patients with DDD, 1 of which required a kidney transplant.

Conclusions: DDD and C3GN in children have many overlapping complement abnormalities. Our study found positive C4 nephritic factor in C3GN patients only which underscores the complexity of the autoantibody milieu in C3 glomerulopathy. Patients with DDD had worse renal outcome with 2 having progressive renal dysfunction, 1 of which required a renal transplant.

1687 Banff Renal Allograft v2 Arteritis: Heterogeneous Clinicopathologic Entity Confirmable by Morphometry Representing Acute Cellular Rejection, Type IIB or not IIB?

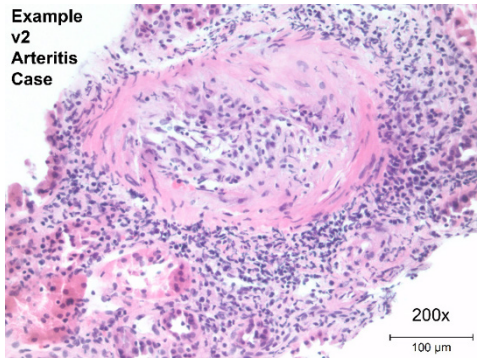
Alton B Farris, Carla L Ellis, Harold Sullivan, Robert A Bray, Howard Gebel, Thomas E Rogers, Payaswini Vasanth. Emory University, Atlanta, GA

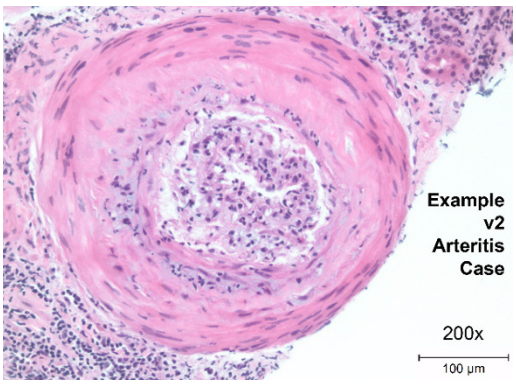
Background: Type IIB acute cellular rejection (ACR) in renal allografts is diagnosed based on the presence of arteritis at the Banff v2 level (≥25% of arterial lumen lost in ≥1 arterial cross section). The aim of this study was to assess clinicopathologic features of v2 arteritis & the utility of morphometric techniques in the assessment of these cases.

Design: Renal biopsies with v2 arteritis were retrieved during the era of current immunosuppression (2012-2016) & human leukocyte antigen (HLA) DSA testing & were confirmed with ImageJ morphometry; & clinicopathologic features were assessed, including single antigen bead donor specific antibody (DSA) assays.

Results: In the study period, v2 arteritis was present in 40 of 2,436 allograft kidney biopsies (1.6% of allograft biopsies), occurring at a mean of 503±115 (± standard error [SE]) days after transplant & peaking with a median creatinine of 3.8±0.74 mg/dL (±SE) during rejection compared to a median prerejection baseline = 1.47±0.49 mg/dL (±SE). Treatment prevented graft failure in 75%; the remainder returned to dialysis. Dialysis return only occurred in 3/26 (12%) belatacept patients vs. 7/14 (50%) non-belatacept patients (p=0.007). HLA DSAs, present in 30% of patients, included: class II(n=4 patients), class I(n=2), & class I+II(n=6). DSAs were only present in 19% of belatacept vs. 50% of nonbelatacept patients (p = 0.04). Other Banff criteria included mean±SE=t2.6±0.1,i2.6±0.1,g1.0±0.2,ptc0.9±0.2,ci0.8±0.1,ct0.8±0.1,cg0.1±0.1, & immunohistochemistry C4d0.5±0.2 [C4d0(negative)(n=29), C4d1(n=5), C4d2(n=2), & C4d3(n=4)]. Concurrent "borderline changes" "suspicious" for ACR were present in 97.5% of patients, & concurrent type IA or IB ACR was present in 85%. By morphometry, 41.6-99.5% of the arterial luminal area was lost due to arteritis (mean=77.7±2.9 [±SE]), confirming the original diagnoses made visually. Arteritis was superimposed upon neointima formation/intimal fibrosis in 58% of patients (cv0=17

patients,cv1=3,cv2=7, & cv3=13); & in patients where cv≥1, morphometry revealed 14.2-99.7% narrowing (mean=31.1±5.0 [±SE]).





Conclusions: Type IIB ACR, confirmed here by morphometry, constitutes an aggressive form of rejection with creatinine elevation, was commonly associated with tubulointerstitial cellular rejection ± antibody-mediated rejection, & had characteristics influenced by immunosuppression; however, there was heterogeneity in the clinicopathologic presentation, prompting the question whether all cases should be IIB or not IIB.

1688 Transplant Glomerulopathy in the Contemporary Immunosuppression Era: Clues to a Diverse Pathogenesis, Including Etiologies Other Than Donor Specific Antibody

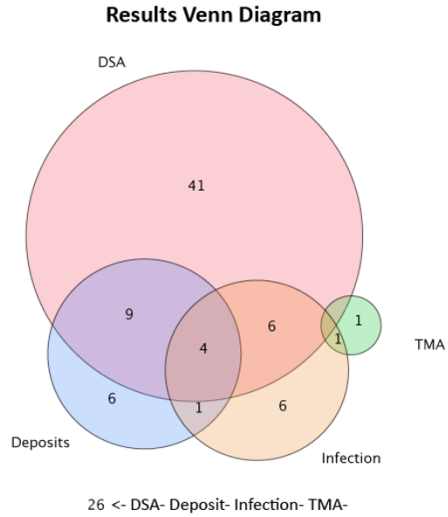
Alton B Farris, Carla L Ellis, Harold Sullivan, Robert A Bray, Howard Gebel, Thomas E Rogers, Payaswini Vasanth. Emory University, Atlanta, GA

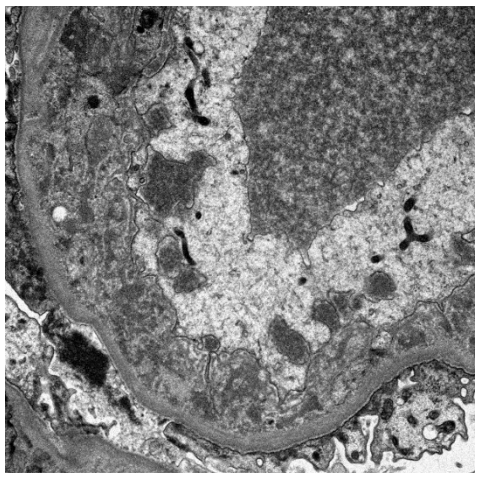
Background: Transplant glomerulopathy (TG) consists of glomerular basement membrane duplication/lamination & is typically associated with chronic, active antibody-mediated rejection (AMR); thrombotic microangiopathy (TMA); membranoproliferative-type glomerulopathies due to infections; autoimmune disease; complement defects; & occasional cases of cell-mediated rejection. The proportion that each etiology contributes to TG varies according to the population. Our aim was to determine the etiology of TG in our population in the era of our current immunosuppression regimen & single antigen bead donor specific antibody (DSA) assays.

Design: Renal biopsies with TG (Banff cg score ≥1) were retrieved during the era of current immunosuppression (2012-2016) to determine the incidence of TG; & to assess well-developed TG, cg≥2 were studied in more detail through examination of clinicopathologic features.

Results: In the study period, 265 of 2,436 allograft kidney biopsies (11% of allograft biopsies) were cg≥1. Focusing on cases cg≥2 (n=101), 45 were cg=2; & 56 were cg=3. Other Banff criteria included mean±standard error = t0.9±0.1,v0.3±0.1,i1.0±0.1,g1.6±0.1,ptc1.1±0.1,-ci2.1±0.1,ct2.0±0.1,mm1.8±0.1,cv1.4±0.1 & immunohistochemistry C4d1.2±0.1 [C4d0(negative)(n=40), C4d1(n=26), C4d2(n=14), & C4d3(n=21)]. At least borderline acute cellular rejection (ACR) changes were seen concurrently in 66 (65%), on a prior biopsy in 55 (54%), & either previously or concurrently in 73 (72%). DSAs were present in 60 (59%) & in only 1/10 belatacept patients vs. 59/91 nonbelatacept patients, a statistically significant difference (p=0.0008). Prior infections included BK virus, cytomegalovirus, Epstein-Barr virus, & hepatitis C virus; some patients had >1 infection. Considering the status of DSA, glomerular deposits, prior infections, & TMA, there were 10 patterns that could be seen, including a mixture of AMR (42 C4d+, 18 C4d-), immune complex glomerulonephritis (GN), possible infection-related factors, & TMA (Table).

TG Findings (Also see diagram)	#	Probable Etiology
DSA+Deposit-Infection-TMA-	41	AMR
DSA-Deposit-Infection-TMA-	26	Idiopathic
DSA+Deposit+Infection-TMA-	9	AMR+GN
DSA-Deposit-Infection+TMA-	6	Infection
DSA-Deposit+Infection-TMA-	6	GN
DSA+Deposit-Infection+TMA-	6	AMR+Infection
DSA+Deposit+Infection+TMA-	4	AMR+GN+Infection
DSA-Deposit-Infection-TMA+	1	TMA
DSA-Deposit-Infection+TMA+	1	Infection+TMA
DSA-Deposit+Infection+TMA-	1	GN+Infection
Total	101	




DSA+Deposit+Infection+TMA- Case

Conclusions: TG occurred with a diverse set of findings in our cohort. As in prior studies, AMR was the largest contributor; however, there was a proportion without AMR. Possible contributors to the TG cohort without identifiable AMR include immune complex GN, infections, TMA, AMR due to an unidentified non-human leukocyte antigen (HLA) antibody, & a result of past/ongoing ACR. Future non-HLA antibody assays as well as molecular profiling may help in clarifying the heterogeneous etiologic spectrum in TG.

1689 Kidney Biopsy Adequacy, a Metric-based Study

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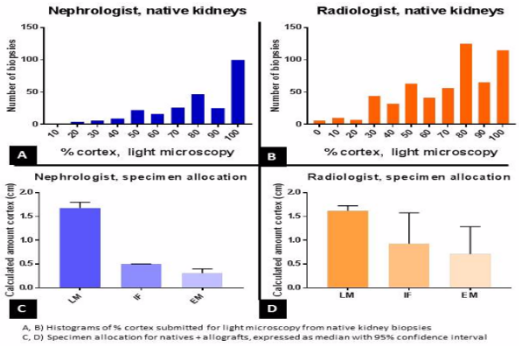
Background: Empiric observations and recent published data suggest a difference in renal biopsy yield related to method of obtainment and operator, among other factors. We sought to characterize and understand these differences in a metric-based study.

Design: We collated adequacy-associated data from consecutive native and allograft kidney biopsies over a 22 month period. Data included operator, biopsy length, % cortex, # of glomeruli, and whether the sample was considered adequate, each for light (LM), immunofluorescence (IF) and electron microscopy (EM). Statistics were performed using non-paramentric analyses in GraphPad Prism 7; results are provided in medians.

Results: Data from 1332 biopsies (native: 873, allograft: 459) were available, 617 of which were obtained by nephrologists, 663 by radiologists. With natives and allografts combined, biopsies from nephrologists had a greater percentage of cortex for LM (90% vs 75%, p<0.0001), IF (100% vs. 75%, p<0.0001) and EM (100% vs 90%, p=0.0009) than those from radiologists. Conversely, radiologists sampled more tissue for each study (LM: 2.3 vs 2.0 cm, p<0.0001; IF: 1.3 vs 0.6 cm, p<0.0001; EM: 0.85 vs 0.4 cm, p<0.0001), in more core segments for LM (3 vs 2 cores, p<0.0001). These differences remained statistically significant when examining only native or only allograft renal biopsies. Radiologists and nephrologists submitted similar calculated amount of cortex for LM (1.62 vs 1.68 cm, respectively), but differed significantly in the distribution of cortical tissue, with radiologists allocating more for both IF (0.8 vs 0.5 cm, p<0.0001) and EM (0.6 vs 0.3 cm, p<0.0001). Radiologists were significantly more likely to submit samples considered inadequate or limited for LM (18.25% vs 12.69%, p=0.006), and IF (13.19% vs 5.0%, p<0.0001). The number of total glomeruli did not linearly correlate with percentage of cortex obtained.



A, B) Histograms of % cortex submitted for light microscopy from native kidney biopsies
C, D) Specimen allocation for natives + allografts, expressed as median with 95% confidence interval

Conclusions: Although renal biopsies obtained by nephrologists contain less tissue than those by radiologists, they yield greater percent cortex for each sample (LM, IF, and EM) in fewer core segments, and are more likely to be considered adequate biopsies. In order to improve yield, radiologists' biopsies may also benefit from better specimen triaging. These qualitative and quantitative differences may have an impact on the rendition of pathologic diagnoses.

1690 Utility of GLUT1 Immunohistochemistry in Kidney Biopsy Interpretation

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Background: Glucose transporter 1 (GLUT1) is an integral membrane protein that facilitates transport of glucose across the membrane of mammalian cells. In adults, GLUT1 is highly expressed on erythrocytes. We sought to determine the utility of GLUT1 immunohistochemistry (IHC) in localizing red blood cells (RBCs) and RBC fragments in certain glomerular and vascular diseases of the kidney. We also hypothesized that GLUT1 expression may be altered in diseases with erythrocyte abnormalities.

Design: IHC for GLUT1 was performed on formalin-fixed, paraffin-embedded tissue samples from kidney biopsies with the following diagnoses: normal (3), thrombotic microangiopathy (TMA, 4), pauci-immune glomerulonephritis (2), sickle cell nephropathy (2), and diabetic nephropathy (3). Immunostains were compared to the H&E, PAS, and Jones methenamine silver stains.

Results: In the normal kidneys, GLUT1 IHC demonstrated moderate, diffuse membranous staining of RBCs in the glomerular and peritubular capillaries, arterioles, and arteries. There was also cytoplasmic expression of GLUT1 in the proximal (weak) and distal (moderate) convoluted tubules. There was no staining of the glomerular capillary tufts, interstitium, or blood vessel walls. In cases of TMA, GLUT1 IHC demonstrated granular staining of the glomerular capillary walls, mesangial areas, and larger blood vessel walls, correlating with fragmented RBCs. In cases of pauci-immune glomerulonephritis, GLUT1 IHC was notable for demonstrating intratubular RBCs and RBC casts. The RBCs in sickle cell nephropathy showed very intense membranous GLUT1 expression (strong). The staining pattern in diabetic nephropathy was similar to normal kidney.

Conclusions: GLUT1 expression is altered in several medical renal diseases, and may contribute to kidney biopsy interpretation. GLUT1 IHC may have diagnostic utility in cases of TMA, especially when the relevant findings are subtle or focal. Specifically, GLUT1 IHC highlights fragmented RBCs in the glomeruli and blood vessel walls in TMA. Additionally, GLUT1 staining highlights intratubular RBCs and RBC casts, which suggests a glomerular source of hematuria in the absence of diagnostic lesions. Larger studies are needed to further determine how expression of GLUT-1 may be altered in various erythrocyte and kidney diseases.

1691 Cardiomyopathy and IgA Nephropathy: Coincidence or a Potential Clue to Concomitant Thrombotic Microangiopathy?

Alexander Gallan, *Kammi Henriksen*, *Anthony Chang*. University of Chicago, Chicago, IL

Background: While IgA nephropathy (IgAN) is the most common glomerulonephritis in the world, thrombotic microangiopathy (TMA) has been observed in the setting of IgAN and in some cases may represent the main cause of glomerular and tubulointerstitial scarring. Yet, the second diagnosis of TMA may be subtle, focal, or simply not recognized. Atypical hemolytic uremic syndrome (HUS) may manifest with systemic findings such as cardiomyopathy. We conducted this study to determine if the presence of cardiomyopathy was associated with concurrent TMA in the setting of IgAN.

Design: We identified 5 kidney biopsies with IgAN and a documented history of cardiomyopathy in the Department of Pathology archives (2000-2017). Slides were reviewed with particular attention to the presence or absence of TMA.

Results: Clinicopathologic features of the five identified cases are listed in Table 1. None of the patients had known thrombotic thrombocytopenic purpura, classical HUS, or antiphospholipid antibody syndrome. Four (80%) of the five cases had TMA and the additional component of TMA in two (40%) of these was only diagnosed upon review. These patients had few or no crescents, minimal or no endocapillary hypercellularity (ECH), and only mild to moderate mesangial hypercellularity (MH) compared to more active lesions in the one IgAN patient without TMA.

Patient	Age	History	Revised Dx	IgAN Features
1	29	Hematuria, proteinuria, Cr=7 mg/dL, cardiomyopathy	IgAN, TMA	6% crescents, no ECH, moderate MH, 4+ IgA IF
2	28	Proteinuria, no hematuria, cardiomyopathy	IgAN, TMA	No crescents or ECH, mild MH, 2+ IgA IF
3	67	Hematuria, Cr=5 mg/dL, cardiomyopathy	IgAN, TMA	No crescents, mild ECH, moderate MH, 3+ IgA IF
4	28	Hematuria, proteinuria, colitis, cardiomyopathy	IgAN, TMA	No crescents, ECH, or MH, 2+ IgA IF
5	46	Proteinuria, pulmonary edema, cardiomyopathy	IgAN only	17% crescents, moderate ECH and MH, 2+ IgA IF

Conclusions: IgAN is commonly diagnosed in kidney biopsies, but may not be the primary driver of renal dysfunction in a subset of patients. In our cohort, cardiomyopathy in the setting of IgAN was frequently associated with a concomitant TMA. Therefore, a history of cardiomyopathy, particularly in younger patients, should prompt the pathologist to assess for the presence of a concurrent TMA. Further studies are needed to determine the pathophysiologic link between these disorders, and if the TMA in these patients is caused by atypical HUS.

1692 Donor Characteristic, Recipient Outcomes, and Histologic Findings of Kidney Allografts with Diffuse Donor-Derived Glomerular Fibrin Thrombi

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Background: Given the shortage of kidneys available for transplantation, major efforts are being made to lower discard rates of deceased donor kidneys. Limited data is available regarding whether

it is safe to use donor kidneys with diffuse glomerular fibrin thrombi (GFT). In this study, the clincopathologic characteristics of allografts with diffuse donor-derived GFT were examined.

Design: All time zero kidney transplant biopsies between January 2011 to July 2017 with diffuse (>50%) glomerular involvement by fibrin thrombi were included. For each patient, all subsequent kidney biopsies were reviewed to assess histologic changes. Associated clinical data were extracted from electronic medical records, including donor information.

Results: Eighteen recipients received donor kidneys with diffuse GFT from 11 deceased donors. Average donor age, body mass index, kidney donor profile index, and cold ischemia time were 30 years, 26.7 kg/m^2, 38%, and 35 hours, respectively. All donor kidneys were preserved with hypothermic machine perfusion. All donors died from severe head trauma; six due to motor vehicle accident, three due to gunshot wound, one due to physical altercation, and one from falling down a flight of stairs. On time zero (reperfusion) biopsy, average percentage of glomeruli involved with fibrin thrombi was 82% (range 52-100%). All cases showed moderate to severe acute tubular injury and no significant interstitial fibrosis or tubular atrophy. 15 cases had subsequent biopsy within the first 6-months following transplant, all of which revealed resolution of GFT. Mean clinical follow up time was 18 months (range 5-73 months). Delayed graft function was experienced in 63% of cases. Only one graft failed within the first year while all others showed good graft function. Notably, the failed graft had the shortest cold ischemia time (10 hours) and it's sister donor kidney experienced no complications.

FOR TABLE DATA, SEE PAGE 621, FIG. 1692

KDPI, kidney donor profile index; GS, glomerulosclerosis; ATI, acute tubular injury; CTI, cold ischemia time; DGF, delayed graft function; Cr, creatinine; F/U, follow up.

Conclusions: Deceased donor kidneys with diffuse GFT appear to be safe to use given that nearly 95% of recipients in this cohort who received such allografts experienced good clinical outcomes even in the setting of relatively long cold ischemia times. Histologically, GFT demonstrated rapid resolution following transplantation. Interestingly, severe head trauma seems to be a predisposing factor for diffuse GFT development in the donor.

1693 Tubulointerstitial Macrophages in IgA Nephropathy Assessed by Digital Image Analysis

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Background: Tubular atrophy/interstitial fibrosis (TA/IF) assessed according to the Oxford classification (T score) is highly reproducible and a strong predictor of renal survival. Tubulointerstitial inflammatory infiltrate, consisting in large parts of macrophages, is more difficult to evaluate by light microscopy and its prognostic significance remains unclear. Digital image analysis could potentially clarify the relevance of tubulointerstitial macrophages in IgA Nephropathy.

Design: CD68-positive cells were quantified in glomeruli and the tubulointerstitiumby digital image analysis in 97 renal biopsies from a previously reported IgA Nephropathy cohort, which was used to study the prognostic value of the Oxford Classification. Macrophage numbers were correlated with criteria of the Oxford classification (MESTC) and clinical parameters as well as manual counts of glomerular macrophages.

Results: A strong correlation between the number of glomerular macrophages assessed by image analysis and manual counting was demonstrated (r=0.80, r^2=0.64, p=<0.0001). The number of tubulointerstitial macrophages correlated moderately with the % TA/IF (r=0.59, r^2=0.35, p=<0.001) and GFR at the time of biopsy (r=0.54, r^2=0.29, p=<0.0001). There was weak correlation with % segmental sclerosis (r=0.31, r^2=0.10, p=0.0017) and crescents (r=0.22, r^2=0.05, p=0.0334), and no significant correlation with mesangial and endocapillary hypercellularity. The number of tubulointerstitial macrophages did not correlate with rate of loss of renal function and was not an independent predictor of renal survival.

Conclusions: Digital image analysis is a reliable method to assess macrophages in IgA Nephropathy, demonstrated by the good correlation between digital and manual macrophage count in glomeruli. Considering its relationship to the T score and clinical parameters of renal function, the number of tubulointerstitial macrophages is a marker for chronic kidney damage but not disease activity.

1694 Relationship of Bartonella to Renal Disease

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Background: *Bartonella* spp. are a common cause of culture negative endocarditis (CNE). Although glomerulonephritis is a known complication of endocarditis, there is a growing appreciation for *Bartonella* spp. CNE associated with ANCA positive pauci-immune glomerulonephritis that distinguishes it from glomerulonephritis usually seen with endocarditis. This association is poorly understood and a limited number of cases have been reported, although cases published to date have been associated with serologies positive for c-ANCA. Interestingly, the relationship of pauci-immune glomerulonephritis and *Bartonella* has not been described with p-ANCA positive serology or in patients without endocarditis.

Design: In our department's surgical pathology database, we searched the past 30 years for cases of *Bartonella* exposure or infection and identified 19 specimens. Among these cases we stratified according to ANCA serology and organ type, including medical renal biopsy specimens.

Results: We found 19 surgical pathology specimens from patients with serologic evidence of *Bartonella* spp. exposure. Three *Bartonella*-positive cases were native kidney biopsy specimens of which two patients had ANCA-positive pauci-immune glomerulonephritis and endocarditis (one MPO+/56 year-old male and one PR3+/52 year-old male). The third patient was ANCA-negative (7 year-old male), had acute tubular necrosis without glomerulonephritis or vasculitis on renal biopsy, but had encephalitis attributed to *Bartonella*. A 4th *Bartonella*-positive patient with lymphadenopathy and no known ANCA testing (8 year-old female) had two biopsy specimens from her renal allograft, of which the second specimen showed a membranoproliferative pattern with full-house immune complex deposits by immunofluorescence.

Conclusions: *Bartonella* is an important pathogen that may trigger renal disease, including ANCA positive crescentic glomerulonephritis. We identified two adult patients with ANCA positive serology (one p-ANCA, one c-ANCA), renal biopsy-proven crescentic glomerulonephritis, and *Bartonella* infection. Recognition of this association is critical for diagnosis and treatment. To our knowledge this is one of the largest case series reported for patients with *Bartonella* infection and associated renal biopsy-proven kidney disease.

1695 Perfusion of Monoclonal Light Chains (Lcs) Associated With Proximal Tubulopathies without Crystals: A Morphologic and Pathogenetic Study

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Background: LC-associated tubulointerstitial manifestations include cast nephropathy (CN) and proximal tubulopathies (PT). PTs have been divided into 4 different variants: one associated with crystal formation and 3 additional categories without crystals including acute tubular necrosis (ATN), acute tubulointerstitial nephritis (ATIN) and lysosomal indigestion-constipation (LIC). The present study was conducted to better understand non-crystalline PTs.

Design: LCs *10 μg/ml* purified from the urine of patients with biopsy proven non-crystalline PTs n=18, CN n=2 and minimal change disease (MCD, control), n=2 were perfused into rat proximal tubules, and n=12 through the renal artery into isolated rat kidneys using an ex-vivo platform n=6. Sections from the kidneys were processed for light (LM), immunofluorescence (IF), electron microscopy (EM) and ultrastructural gold immunolabeling (UIL).

Results: The perfused LCs resulted in identical renal pathology as observed in the corresponding renal biopsies. In three PT variants, there was proximal tubular damage identifiable by LM and clearly demonstrable by EM with proximal tubular cells showing vacuolization apical blebbing, desquamation, and an abundance of lysosomes, some enlarged and atypical in shape. By UIL LCs were present in lysosomes and intracytoplasmic vacuoles. In the ATIN variant similar evidence of tubular damage was noted, along with inflammation, tubulitis and deposition of LCs in lysosomes and along tubular basement membranes (transcytosis). In the LIC variant the proximal tubular cells were filled with enlarged, sometimes atypical lysosomes containing monoclonal LCs. There were distal tubular casts in those cases perfused with LCs from patients with CN. Patients with MCD revealed LCs endocytosed into proximal tubules and catabolized by endosomes.

Conclusions: The features of the various PTs were reproduced in the ex-vivo system validating the fact that different LCs produce distinct morphological lesions in the proximal tubules. This study also clarifies pathogenesis in these different PTs, emphasizing the various pathologic mechanisms involved in each of the variants including lysosomal bursting in the ATNPT, transcytosis in the ATIN type and inability to digest LCs in the indigestion/constipation variant. These LCPT variants can be explained on the basis of different physicochemical characteristics of the tubulopathic LCs involved resulting in lysosomal inability to properly catabolize them and subsequent pathological alterations.

1696 Receptor on Mesangial Cells For Glomerulopathic Light Chains: The Search Continues

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Background: It has been proven that glomerulopathic (G), but not tubulopathic (T) light chains (LCs) interact with mesangial cells (MCs) using a not yet characterized receptor. Both light chain deposition disease (LCDD) and amyloid- producing (Am) LCs use the same receptor. Tubulopathic LCs do not interact with MCs.

Design: Two Am, one LCDD and one tubulopathic-LCs were crossed linked with MCs using DSTTP as the cross linker. LCs at 10 ug/ml were incubated with G and TLCs and a SPS-PAGE gel was run to identify bands. Bands above 70kD were cut and analyzed using mass spectroscopy (MS). Proteins obtained from various LCs cross linked to MCs were compared to identify receptors shared by the GLCs. TLC was used as a control.

Results: Several mesangial cell receptors were shared by the 3 GLCs including: G-protein coupled, ligand-gated ion channel, extracellular matrix linker protein receptor, and cell adhesion-molecule extracellular matrix glycoprotein receptors.

Conclusions: MCs display a particular receptor complex that interacts with GLCs which is the same for both Am and LCDD-LCs. This receptor complex only becomes available when GLCs are interacting with MCs and not when TLCs are incubated with MCs. This receptor is a unique receptor with characteristics that are not present in other described MC receptors when compared with data base of existing MC receptors.

1697 The Focal Adhesion Protein hic-5 Maintains Basal Autophagy in Podocytes and Protects from Genotoxic Injury

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Background: Podocytes are an integral part of the glomerular filtration barrier. Podocyte loss is a marker of progression in many glomerular diseases. As suggested by other groups, basal autophagy protects against podocyte injury and death. We demonstrated previously that hic-5, a focal adhesion scaffolding protein, is upregulated in glomeruli in a subset of podocytopathies, and that the presence of hic-5 in podocytes promotes a pro-survival phenotype after genotoxic injury *in vitro* and ameliorates nephron loss and FSGS in mice.

Design: We created hic-5-deficient (hic-5 KD) podocytes and scr control cells using a lentiviral-based shRNA approach. Cells were exposed to 0.5 µg/ml adriamycin (ADR) to induce genotoxic injury for 0, 2, 12 and 20 hrs. We performed quantitative discovery proteomics using mass spectrometry at 0 and 12 hrs, and immunocytochemistry (ICC) and Western blot analysis of all timepoints. Results were further verified by IHC *in vivo* in *hic-5*$^{-/-}$ mice and their WT littermates after a single injection of 11ug/g BW ADR.

Results: Consistent with previous reports, scr control podocytes showed significant basal autophagy, as indicated by LC3I+II expression and presence of LC3-positive autophagosomes, as well as expression of beclin-1 and p62. In hic-5 KD cells, LC3B abundance by WB/ICC and beclin-1 were markedly reduced while p62 was increased both at baseline and immediately following genotoxic injury, demonstrating a profound impairment of autophagy. Proteomic analysis confirmed an exceptionally strong effect on several autophagy pathways after hic-5 KD. Furthermore, hic-5 KD cells showed sustained JNK activation after ADR exposure past 12h and activation of caspase 3 prior to cell death, which were absent in scr control cells. In ADR-treated, highly proteinuric hic-5$^{-/-}$ mice, but not WT littermates with 3-fold lower proteinuria, caspase 3-positive podocytes could be readily observed as early as 1 wk after exposure in the absence of ultrastructural and immunohistochemical **features of autophagy.**

Conclusions: Our results are in support of the crucial role of autophagy in podocyte protection, and further demonstrate that the focal adhesion protein hic-5 plays an important role in maintaining this system, implicating hic-5 as a direct link between the focal adhesion hub and autophagy regulation. In conclusion, we provide additional evidence that autophagy deficiency represents an important contributing factor to podocyte loss which may lend itself well to therapeutic intervention.

1698 Diabetic Nephropathy in Kidney Donor with Diabetic Mellitus, Implication of Renal Biopsy Findings at Time of Transplantation

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Background: Deceased diabetic donor kidneys are increasingly utilized. Whether there is diabetic nephropathy (DN) in these kidneys is unknown. The post-transplant evolution of DN and its impact on graft survival are poorly understood.

Design: Postperfusion biopsies of 26 deceased diabetic donor kidneys were studied. DN was classified in to four classes (0 = no DN, I = no DN by LM, but DN by EM; IIa = mild mesangial expansion; IIb = marked mesangial expansion; III = nodular sclerosis; IV = advanced glomerulosclerosis). The findings were compared with follow-up biopsies and correlated with clinical findings at the time of transplantation and at follow-up.

Results: Among these 26 biopsies, no DN (Class 0) was seen in 20, Class I in 2, and Class IIa in 4. No correlation was found between the DN class and duration of diabetes in the donors. At follow-up (36-136 months), 4 recipients died with functional grafts and others were alive with functional grafts. Follow-up biopsies (5-342 weeks post-transplant) were performed in 17 recipients, in whom the post reperfusion biopsies showed no DN in 12 and DN in 5. For the 12 recipients in whom the post reperfusion biopsies showed no DN (Class 0), the follow-up biopsies showed no DN (Class 0) in 9 biopsies and DN in 3 (two Class I and one Class IIa). For the 5 recipients in whom post reperfusion biopsies showed DN, the follow-up biopsies showed no changes in 1(Class IIa/Class IIa); mild progression in 3(Class IIa/ Class IIb), and regression in 1(Class IIa/ Class I). DM was noted in 11 recipients before transplantation. After transplantation, DM regressed in 2 recipients, but developed de novo in 10 recipients. No correlation was noted between the evolution of DN and the course of DM.

Conclusions: DN is noted in a small percentage of diabetic donor kidneys. It is often mild and in early stages. After transplantation, DN may stabilize, regress or progress with mild increase in severity and at a slow pace. In cases where DN is not present in the diabetic donor kidneys, DN often does not develop post-transplant, even in diabetic recipients. DN in diabetic donor kidney or in post transplant period may not by itself impart significant adverse effect on graft survival.

1699 The Oxford Classification System and Crescents in Pediatric Henoch–Schönlein Purpura

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Background: The Oxford classification system of IgA nephropathy stratifies patient risk for progression based on pathologic lesions. Though histopathologic findings of Henoch–Schönlein purpura (HSP) and IgA nephropathy have common characteristics, cases of HSP were excluded from the original study cohort. Thus, this study serves to assess the revised Oxford Classification system (ROCS) with the addition of crescent scores in the pathologic classification of pediatric HSP.

Design: 41 renal biopsies from 40 patients with HSP from our academic center (April 1998-November 2016) were evaluated by the ROCS. Estimated GFR (eGFR) and urine protein/creatinine (Upc) at the time of biopsy, one year post-biopsy and at last follow-up were used to evaluate the prognostic value of the ROCS. Treatment was also included in this retrospective analysis.

Results: There was a median of 18 glomeruli per biopsy (range, 3-56). 33 patients (80.5%) had mesangial proliferation (M1), 28 (68.3%) had endocapillary proliferation (E1), 27 (65.9%) had segmental sclerosis/ adhesion (S1), and only 1 (2.4%) had significant tubulointerstitial fibrosis (T1). Crescents were present in 27 patients (65.9%); 19 had crescents in <25% of glomeruli (C1; 70.4% of patients with crescents) and 8 had crescents in ≥ 25% of glomeruli (C2; 29.6% of patients with crescents). Glomerular necrosis was present in 20 (48.8%), and global

glomerulosclerosis (range 2.9-13.3% of glomeruli involved) was present in 5 (12.2%) cases. Treatment included ACEi/ARBs, steroids, and immunosuppressants ([IS], azathioprine, cyclophosphamide, or MMF). After a median follow-up of 27.4 months, 20/40 patients showed normal Upc and all patients had normal eGFR. Mesangial hypercellularity (p=0.01) and glomerular necrosis (p=0.04) demonstrated significant association with proteinuria at biopsy, while no lesions showed significant relationship with eGFR at biopsy, one-year follow up, or last visit. However, children with cellular crescents and glomerular necrosis tended to have lower eGFR at time of biopsy. Patients exhibiting endocapillary proliferation and crescents were more likely to be treated with IS in addition to steroids (E0C0 50%; E1C0 80%; E1C1 88%; E1C2 100% treated with IS).

Conclusions: Mesangial hypercellularity and glomerular necrosis were associated with greater proteinuria at time of biopsy. Additionally, those children with crescents were more likely to have low eGFR at the time of biopsy and to receive IS therapy.

1700 Computerized Image Recognition of Glomeruli in Donor Kidney Frozen Sections

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Background: Computerized image recognition has the potential to transform the practice of pathology by improving efficiency and interobserver reproducibility. Recent studies have shown high rates of interobserver variability amongst pathologists examining donor kidney frozen sections, compromising the assessment of organ quality prior to transplantation. Evaluation of these tissues typically include laborious and time-consuming enumeration of globally sclerotic and non-sclerotic glomeruli. We sought to train a convolution neural network (CNN) to detect and enumerate sclerotic and non-sclerotic glomeruli in frozen wedge donor kidney biopsies to improve pathologist efficiency and reproducibility.

Design: Whole-slide images (WSIs), scanned at 20x with an Aperio Scanscope CS scanner, were acquired from frozen wedge donor kidney biopsies between 4/2015 and 7/2017. Pathologist annotations were created by manually outlining and labeling non-sclerotic and globally sclerotic glomeruli in each of 49 WSIs, using in-house software to generate pixel-wise label masks. The CNN was tasked with assigning labels to individual pixels in the original WSI to match the provided annotations. Starting with the pre-trained VGG16 CNN, we replaced the final fully connected layers with 4 convolutional layers. This CNN was trained against 1024x1024-pixel partially overlapping image patches (n~50,000) extracted from 39 WSIs for ~10 epochs. The network was evaluated on a holdout set of 10 WSIs.

Results: The network assigned labels to interstitial tissue, normal glomeruli, and sclerotic glomeruli with AUROC scores of 95%, 97%, and 97%, respectively. Sensitivity for each label was 98%, 75% and 67%, respectively. Linear regressions of the predicted percentage of sclerosed glomeruli (measured by total glomerular area and probability) against target values of percentage sclerosed area and number are shown in the table below for the holdout set of 10 WSIs. The trained model applied to an example validation image is shown in the figure below, illustrating the correspondence between glomeruli (blue=normal, red=sclerosed) in the mask and predictions.

	Predicted area vs Target area	Predicted probability vs Target area	Predicted area vs Target number	Predicted probability vs Target number
Slope	1.031	0.873	0.524	0.442
Intercept	1.869	3.545	1.075	2.903
p-value	0.0002	0.001	0.001	0.004
r^2 value	0.833	0.758	0.741	0.670

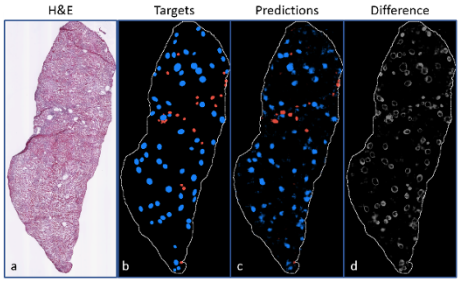

Figure 1: a) H&E micrograph of frozen kidney biopsy sample; b) manually created annotations for normal (blue) and globally sclerosed (red) glomeruli; c) CNN prediction probabilities mapped to red and blue, for sclerosed and normal glomeruli, respectively; d) absolute difference of panels b) and c).

Conclusions: Computerized image recognition is a viable tool to assist pathologists in recognition of glomeruli in frozen section evaluation of donor kidney biopsies. Further studies are required to evaluate the impact of this technology on the efficiency and reproducibility of donor kidney evaluation.

1701 Collapsing FSGS in Older Adults

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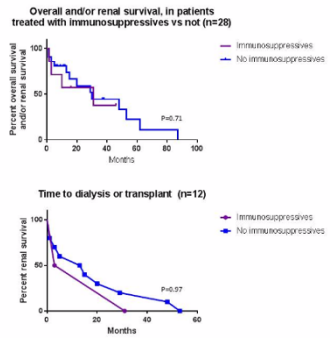
Background: Collapsing focal and segmental glomerulosclerosis (FSGS) has been described in settings of viral infections, certain drugs, genetic, ischemic, and idiopathic conditions. It has a worse prognosis than other morphologic variants of FSGS, and may be treated with aggressive immunosuppression. In this study, we sought to characterize the clinical and morphologic findings in older adults with collapsing FSGS.

Design: Renal biopsies and associated clinical data from patients aged 65 or older with a diagnosis of collapsing FSGS or FSGS with collapsing features from 2000 thru 2016 were retrospectively reviewed at 3 academic institutions. Cases with advanced diabetic or other significant nephropathies were excluded. Statistics were performed using GraphPad Prism 7.

Results: Renal biopsies from 42 patients (25 men, 17 women) were identified. The median age was 71.5 years, and of those with available information, 88% had a history of hypertension and 91% had nephrotic range proteinuria; median serum creatinine was 2.5 (range 1-5.9 mg/dL). Renal biopsies revealed a median of 40% globally and 16% segmentally sclerotic glomeruli, moderate tubular atrophy and interstitial fibrosis, moderate arteriosclerosis, and mild-to-moderate arteriolar hyalinosis; 7% had evidence of atheroembolic disease. 63% of cases had segmental podocyte foot process effacement by electron microscopy. Follow up information was available in 28 (67%) of patients. Eight (19%) were treated with immunosuppressives, including steroids (8), cyclosporine (2), and rituximab (1), which were not tolerated by 3 patients. In one patient, pamidronate was discontinued. Primary outcome was overall or renal survival. At a median time to follow up or primary outcome of 14 (range 1 – 87) months, 5 (17%) patients had died, 12 (41%) had ESRD on dialysis or had received a transplant, and 12 were alive with renal insufficiency and proteinuria. There was no significant difference in overall or renal survival between patients who were treated with immunosuppressives vs. those who were not (Fig). One patient died 6 weeks after biopsy as a result of high dose steroids, with invasive rhinoorbital Rhizopus infection. Other patients died of multifactorial or unknown causes.



Conclusions: Collapsing FSGS in older patients is accompanied by significant chronic injury in glomeruli, vasculature, and tubulointerstitium. Aggressive immunosuppression contributed to one death, and did not yield an overall or renal survival advantage in this cohort.

1702 Spectrum of PLA2R Staining Pattern in a Large Cohort of Immune Complex Glomerulonephritis: Pitfalls and Challenges

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Background: Immunohistochemistry (IHC) stain for M2-type Phospholipase A2 receptor (PLA2R) is employed to diagnose primary membranous glomerulonephritis (MGN). However, the current literature on PLA2R emphasizes the result of positive staining without adequately addressing the spectrum of staining patterns that results in interpretational challenges. This study examines PLA2R expression in largest to date cohort including entire spectrum of immune complex-mediated glomerulonephritides (GN) and addresses the pitfalls and challenges.

Design: 260 renal biopsy cases with diagnosis of immune-mediated GN and minimal change disease were collected from our database from 2010 to present. IHC was performed on formalin-fixed paraffin tissue sections using PLA2R monoclonal antibody (CL0474, 1:1500 dilution) and IgG4 monoclonal antibody (HP6025, 1:500). PLA2R and IgG4 results were blindly scored as described below in table 1.

Results: The spectrum of cases with PLA2R and IgG4 results is outlined in table 1, including scoring criteria of PLA2R stain. 18/21 (86%) primary MGN showed either a 2 or 3+ PLA2R expression compared to 15/196 (8%) of all other immune complex GN ($p<0.0001$). 7/84 (8%) of all lupus nephritis showed 2 or 3+ PLA2R expression as it did in 5/23 (22%) of nonlupus MGN due to other medical conditions such as autoimmune conditions. We recommend a low-magnification approach to initially assess the global pattern of peripheral accentuation, followed by a higher manigification for evaluation of a diffuse pattern of capillary stain. The stain pattern should take precedence over the stain intensity, so that intermediary to weak stain may be interepreted as poitive **if criteria** of capillary stain with decreased podocyte pattern are fulfilled. IgG4 by IHC was positive in only 6/261 (2%) cases with 4 of them representing primary MGN (67%).

Table 1: Categorization of variable PLA2R staining patterns: negative is when there is no stain or shows a blush, 1+ is when a stain shows exclusive peripheral pattern (negative result), 2+ is when the stain shows capillary loop pattern with staining of visceral epithelium (borderline positive) and 3+ is when the stain shows capillary loop pattern with decreased visceral epithelial staining (positive). IgG4 stain was scored as either negative (no stain) or positive (capillary loop staining).

Diagnosis	cases	PLA2R				IgG4
		Negative	1	2	3	
Minimal Change	44	41	3	0	0	0
IgA/HSP	52	41	11	0	0	0
PIGN	11	10	1	0	0	0
MPGN	13	11	2	0	0	0
Crescentic GN	6	6	0	0	0	0
Lupus proliferative nephritis	42	28	12	2	0	1
Lupus MGN	42	20	17	1	4	1
Primary MGN	21	0	3	8	10	4
Non lupus MGN	23	18	0	0	5	0
Miscellaneous	7	2	2	2	1	0
Total	261	177	51	13	20	6

Conclusions: The presence of characteristic granular capillary basement membrane staining with a decreased visceral epithelial expression of PLA2R is extremely specific for the diagnosis of primary membranous glomerulonephritis. However, a careful assessment of staining pattern regardless of intensity is necessary to accurately interpret PLA2R result, which should also be correlated with morphologic, immunofluorescence and electron microscopic findings to accurately distinguish primary from secondary MGN. The consideration that immunofluorescence may be a better modality compared to IHC in the assessment of IgG4 expression should be further investigated.

1703 Temporal Histopathology of INF2-Associated Steroid Resistant Nephrotic Syndrome

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Background: Next-generation sequencing is increasingly used to identify genetic etiologies in patients with steroid resistant nephrotic syndrome. The Inverted Formin 2 gene (*INF2*) encodes a cytoskeleton subfamily actin-regulating protein for which mutations are associated with autosomal dominant focal segmental glomerulosclerosis (FSGS). Despite this association, examination of the temporal changes to pathology of patients with *INF2* variants has received little attention. This study examines the biopsy findings over time in two patients with *INF2* variants.

Design: Here we describe two unrelated females who presented with proteinuria at ages 26 (patient 1) and 6 (patient 2) years. Next-generation sequencing with targeted bioinformatic analysis was performed for *ACTN4, APOL1, CD2AP, INF2, LAMB2, MYH9, NPHS1, NPHS2, PLCE1, TRPC6,* and *WT1* using DNA collected from peripheral blood. Renal biopsies performed approximately 6 years apart were examined for each patient.

Results: Non-synonymous variants in *INF2* were identified in both patients. Patient 1 had a heterozygous p.R177C mutation, classified as likely pathogenic by the American College of Medical Genetics and Genomics guidelines and has previously been reported. No other significant variants were identified. The initial kidney biopsy showed FSGS, 22% global glomerulosclerosis, 10% interstitial fibrosis, and diffuse podocyte foot process effacement. The follow up biopsy showed no FSGS, 21% global glomerulosclerosis, no interstitial fibrosis and 40% foot process effacement. A heterozygous p.K1240T *INF2* mutation was identified in patient 2, classified as a variant of uncertain significance. No other significant variants were identified. Patient 2's initial biopsy showed minimal change disease with no interstitial fibrosis or global glomerulosclerosis. The follow up biopsy showed minimal change disease, acute interstitial nephritis, 6% global glomerulosclerosis, and no interstitial fibrosis.

Conclusions: These results demonstrate variability in clinical and pathologic presentation for patients with *INF2*-related nephrotic syndrome, illustrating the variable expressivity of *INF2* variants. Patients may show relatively slow pathologic evidence of disease progression and may present with minimal change disease on biopsy. Genetic testing for such patients may assist with management by guiding therapy and identification of appropriate living-related organ donors.

1704 HIV and the Kidney; Clinicopathological Analysis of Biopsy-Proven Renal Disease in Johannesburg

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Background: Human immunodeficiency virus (HIV) is associated with a wide spectrum of pathological manifestations of kidney disease and is an important cause of renal failure. The HIV prevalence in South Africa is 18,9% with a prevalence of HIV-Chronic Kidney Disease of 6%. This study explores differences in biopsy-proven renal disease by HIV status.

Design: A retrospective review of 190 consecutive renal biopsy reports from the National Health Laboratory Service (NHLS) Charlotte Maxeke Hospital in Johannesburg from January to June 2013 was undertaken. The renal biopsies were studied by light, immunofluorescence and electron microscopy. The data was collected and stratified according to age, gender, clinical presentation, HIV status and histological diagnosis.

Results: Of the 190 biopsy reports reviewed, 114 native renal biopsies met the inclusion criteria, 59 males and 55 females (103 blacks and 11 whites). Thirty patients (24.6%) were HIV positive, of whom 12 were on HAART therapy. The CD4 count ranged from 98-672 cells/mm^3. The mean age at biopsy was 27.6 years (range 3 months to 77 years).

The most common clinical indication for biopsy in both HIV positive and HIV negative patients was nephrotic syndrome (16/30 and 56/84) followed by nephritic syndrome (14/30 and 28/84) and systemic lupus erythematosus (3/30 and 19/84) respectively.

HIV Positive: FSGS was the most common diagnosis 9/30 (29.9%) followed by HIV immune complex kidney disease (HIVICK) 5/30 (16.6%), Minimal Change 4/30 (13.9%), Human immunodeficiency virus associated nephropathy (HIVAN) 3/30 (9.9%) and a single case of IgA Nephropathy was recorded in a Caucasian male.

HIV Negative: Lupus nephritis was the most common diagnosis 25/84 (29.8%) followed by FSGS 24/84 (28.6%), Minimal Change 18/84 (21.4%), and Membranous Glomerulonephritis 10/84 (11.9%).

Conclusions: HIV positive patients were less likely to be diagnosed with lupus nephritis - odds ratio 0.14 (95% CI 0.03-0.66). Other than HIVAN and HIVICK, which exclusively occured in HIV positive patients, there were no other significant associations in histological diagnoses by HIV status. The prevalence of HIVAN was much lower than previously documented in earlier studies. This may indicate a

possible decline in HIV-related renal disease consequent to HAART therapy which is now widely available.

1705 Comparison Between Pretransplant Frozen Section and Multifocal Zero Hour Kidney Allograft Biopsies: Associations With Clinical Outcomes

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Background: The gap between patients waitlisted for kidney transplants and available organs is enormous, leading to longer wait times for suitable organs and increasing waitlist mortality. One key strategy to address this crisis is to reduce the rate of discarded organs. Studies have demonstrated that the primary driver for discard is histology from frozen section wedge biopsy (FWB), despite its known limitations. We evaluated the performance of FWB, by comparing them to multifocal, zero hour needle core biopsies (ZHB) and classic outcome predictors, nadir serum creatinine (Cr) and Kidney Donor Profile Index (KDPI).

Design: FWB were reviewed, and matched back table, fixed and embedded ZHB were examined for all transplants performed from 2/2017-9/2017 with available material (n=42). These results were evaluated in the context of graft KDPI score and correlated with initial graft function using nadir Cr. Delayed graft function (DGF) was defined as dialysis within a week post-transplant.

Results: 8 patients received living and 34 deceased donor kidneys. Median KDPI was 60%, and mean KDPI was 49.2% (range 4-99%; n=32). Mean % globally sclerotic glomeruli was 2.2% on FWB (range 0-16%, n=25), 7.2% on upper pole ZHB (range 0-66%, n=41), and 5.0% on lower pole ZHB (range 0-30%, n=33). Clinically significant diagnoses were seen on 7 ZHB, but not on paired FWB. 12 cases (38%) demonstrated DGF (n=32). KDPI averaged 68% for those with DGF and 43.8% with immediate function (IF) (n=12 for both). Cr at 1-2 mo. was 1.84 and 1.24 for DGF and IF respectively. 3 of the DGF and 1 of the IF cases had >20% obsolescent glomeruli on ZHB, but not on FWB (n=17).

Conclusions: ZHB provide a more accurate representation of graft quality and are a better predictor of DGF than FWB. FWB misses clinically significant histologic findings. KDPI appears to predict IF more accurately than either type of biopsy. We confirm that ZHB are superior to FWB; conventionally processed biopsies may add to available data and could lead to a lower discard rate for usable organs.

1706 Pathologic Features of Mesoamerican Nephropathy in Honduras

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Background: Mesoamerican Nephropathy (MeN) is recently described after the observation that chronic kidney disease (CKD) in Central America has a higher prevalence and a distinct epidemiological and clinical pattern. MeN is endemic chronic kidney disease of unknown cause (CKDu) affecting rural inhabitants of Central America. It affects young and otherwise healthy men working in physically demanding agricultural work in a hot climate. Significant association has been found with hypertension (HTN), NSAID use, pesticide exposure and family history of CKD. Patients are thus exposed to nontraditional (occupational and toxic factors) as well as traditional risk factors (DM, HTN, obesity, dyslipidemia). The pathologic features described include: extensive glomerulosclerosis (29%-78%), chronic glomerular ischemia, tubular atrophy, interstitial fibrosis, mild vascular lesions and podocytic injury by EM.

Design: Patients were recruited after obtaining informed consent to participate in the study at the Hospital Escuela Universitario in Honduras. Inclusion criteria were: Age 18 to 69 years, CKDu, history of physically demanding agricultural work and eGFR of 30-60 ml/min/1.73m^2. Patients with DM or HTN were excluded. Data was collected between January and November 2016.

Results: Fourteen patients were enrolled. The most common histopathological findings in the glomeruli included: global sclerosis, obsolescence, glomerulomegaly, tuft retraction, periglomerular fibrosis and podocyte hypertrophy. Interstitial findings included fibrosis and interstitial nephritis. The tubular changes were hypertrophy, dilation, thyroidization and accumulation of Tamm-Horsfall protein. Arteriolopathy was found in 100% of cases.

The vascular features are presented in Table 1

Patient	Arteriolopathy	Arteriolar Hyalinosis
1	1+	1
2	3+	0
3	3+	0
4	2+	0
5	1+	1
6	2+	0
7	2+	0
8	2+	0
10	3+	0
11	3+	0
12	3+	0
13	2+	0
14	2+	0
%	100%	15%

Conclusions: The pathologic features of MeN are described. Compared with a previous study, our biopsies showed marked arteriolopathy in the absence of hypertension. The nature of this entity is still in need to be unravelled in order to implement preventive measures. MeN is an emerging health problem and measures are control it such as avoiding excessive exposure to heat during hard, physical work drinking adequate fluids, avoidance of fructose containing drinks and NSAIDs need to be investigated and implemented .

1707 Peritubular Capillary Injury in Diabetic Nephropathy

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Background: Patients with diabetic nephropathy (DN) typically present with gradual progression of proteinuria. Heavy proteinuria with or without features of nephrotic syndrome in diabetic patients may be associated with superimposed primary glomerular and systemic diseases. However, in many patients with DN and nephrotic range proteinuria (DN-N), neither superimposed glomerular nor tubulointerstitial diseases are identified. Peritubular capillary (PTC) injury is characterized by peritubular capillary basement membrane multilayering (PTCM). We hypothesized that degree of PTC injury as measured by the number of layers in the basement membrane may be associated with degree of DN and proteinuria.

Design: We selected a subset of native kidney biopsies from diabetic patients with proteinuria at VUMC (2009-2014) and divided them into groups based on the degree of proteinuria and histologic findings of DN. These groups included DN-N, DN with non-nephrotic range proteinuria (DN-P), and diabetic patients with proteinuria without DN (NonDN). LM and EM morphologic evaluation was performed.

Results: 23 diabetic patient biopsies were selected, 12 women and 11 men, age 23-77 yrs, (mean 52 yrs). 10 DN-N patients , 6 DN-P and 7 Non-DN patients. All patients had proteinuria with mean 9.0, 0.5, and 5.2 g/d in DN-N, DN-P, and NonDN, respectively. Glomerular mesangial matrix (G) score was 2.3 (scale 0-3) in DN-N and 1.5 in DN-P ($p < 0.05$). Ultrastructural evaluation showed PTCM with mean 3.7 layers in DN-N, 2.7 in DN-P, and 1.3 layers in NonDN ($p < 0.001$, Kruskal-Wallis ANOVA test).

Conclusions: The number of layers in the PTC basement membrane increased as expected from NonDN to DN-N. PTC injury is limited in NonDN patients. We speculated that pathogenic mechanisms of PTCM are complex and may involve megalin-mediated endocytic handling of glomerular filtered advanced glycation end products and albumin causing autolysomal dysfunction via autophagy impairment leading to hypertrophic senescent changes of tubular epithelial cells. In addition, these processes may be associated with the increase production of profibrotic mediators, which activate interstitial fibroblasts and PTC pericytes to induce interstitial fibrosis. PTC basement membranes would thereby become damaged and multilayering by these complex mechanisms. We speculated that increase in PTC resistance can induce retrograde pressure loading to glomeruli, and thus promotes more glomerular hypertrophy and mesangial expansion.

1708 Monoclonal Immunoglobulin-Associated C3G (Mlg-C3G): A Distinct Subtype

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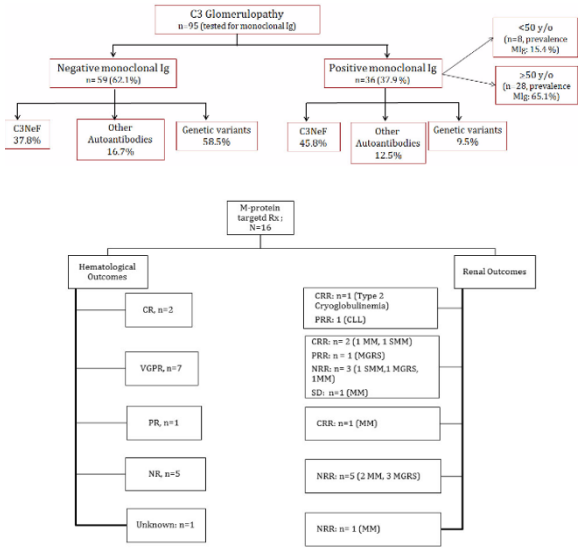
Background: Monoclonal immunoglobulins (Mlg) play a causal

role in C3 glomerulopathy (C3G) by impairing regulation of the alternative pathway of complement. We provide a detailed evaluation of clinicopathological features, complement abnormalities, treatment and outcomes of MIg-C3G.

Design: Ninety-five C3G patients evaluated for a MIg were included. Renal outcomes were classified into: i) Complete (CRR) with ≤ 0.5 g/24 hours proteinuria and ≤10% decrease in eGFR, ii) partial (PRR) with ≥ 50% reduction proteinuria post-treatment from baseline, iii) stable (SD) with eGFR within 10% baseline and stable proteinuria, and iv) no response (NRR). Hematological response was assessed according to IMWG criteria for myeloma and International Society of Amyloidosis criteria for MGUS/MGRS patients and were classified as complete (CR), very good partial response (VGPR), partial response (PR) and no response (NR).

Results: 36 (37.9%) patients were positive for MIg (32 C3GN, 4 DDD). The median age at diagnosis was 60 years (range: 20-85). Twenty-six were classified as MGUS/MGRS, 5 as multiple myeloma, 2 smoldering multiple myeloma, 1 CLL, and 2 were positive for cryoglobulins. Among patients ≥50 years, prevalence of MIg was 65.1%. Complement evaluation (figure 1) revealed C3Nef in 45.8% and genetic variants in only 9.5%. Kidney biopsies showed MPGN in 23 patients, mesangial proliferative GN in 10, crescentic GN in 2, diffuse proliferative GN in 1. IF was positive for bright staining for C3 (2-3+) in all cases. Fifteen (41.7%) biopsies had pronase IF studies performed on paraffin embedded material to rule out masked Ig deposits. Only 1 (6.7%) case showed masked Ig deposits. Treatment and outcomes were- 3 received conservative therapy (2 NRR, 1 unknown), 17 received non-targeted therapy (all had MGUS/MGRS of which 5 achieved CRR, 2 PRR, 7 NRR, 3 unknown). 16 patients received targeted MIg therapy: 10 patients achieved complete/very good/partial hematologic response, of these 7 (70%) also achieved CRR/PRR/SD (figure 2). 1 patient was lost to follow-up. Importantly, 5 (31.3%) patients receiving targeted treatment did not achieve hematologic response; none of these had a renal response.



Conclusions: Our study shows MIg-C3G is a distinct subtype of C3G that is seen in mostly older patients, is associated with autoantibodies to complement proteins, and targeted treatment of MIg results in remission and stabilization of kidney function in a subset of these patients.

1709 The Effect of Time and Media in Renal Biopsy Specimens

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Background: Evaluation of medical renal biopsies is increasingly being performed at referral institutions. The University of Iowa Diagnostic Laboratories (UIDL) interprets approximately 1000 medical renal biopsies per year, some of which travel internationally via postal services prior to processing for electron microscopy (EM) or direct immunofluorescence (IF). Travel delays, accidents and misuse of transport media have led to questions of interpretation validity. This study is designed to explore the accuracy of EM and IF findings across various time intervals and tissue preservation conditions.

Design: This prospective study utilized kidney tissue from 5 medical autopsy cases performed at the University of Iowa Hospitals and Clinics from May 2016 to August 2017. Post-mortem interval was limited to less than 24 hours. Renal tissue was obtained and divided into various collection media and conditions: (1) formalin, (2) Michel's solution (MS), (3) glutaraldehyde (GLUT), (4) moist in saline gauze, and (5) saturated in saline. Samples were then processed at a specified set of time intervals for EM and IF. Samples evaluated by EM were submitted in GLUT at 24 hours, 1 week, and 2 weeks, moist in saline at 1 and 2 weeks, and saturated in saline at 1 and 2 weeks. Samples evaluated by IF were submitted in MS at 24 hours, 1 week, and 2 weeks, moist in saline at 1 and 2 weeks, and saturated in saline at 1 and 2 weeks. Samples collected in formalin were processed for light microscopy for reference.

Results: The diagnoses were: Case 1: IgA nephropathy (IGAN), Case 2: Chronic advanced diabetic nephropathy (DN), Cases 3 and 4: Foot process effacement of uncertain significance, Case 5: Chronic vascular hypertensive disease. IGAN and DN could be reproduced with certainty in specimens in media up to 2 weeks and up to 1 week if kept moist. Podocyte injury (cases 3, 4 and 5) were reliably reproducible in specimens kept for up to 1 week in transport media.

Conclusions: Biopsy interpretation of immune complex glomerulonephritis and chronic diabetic nephropathy were reproducible if specimen was kept in transport media (GLUT for EM and MS for IF) for up to 2 weeks. Specimens kept moist were interpretable for up to 1 week. EM interpretation of podocyte injury was reproducible only in specimens kept in GLUT for up to 1 week.

1710 The Pathology and Clinical Characteristics of Proliferative Glomerulonephritis with Monoclonal IgG Deposits in the Renal Allograft

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Background: Recent case reports have documented recurrence of proliferative glomerulonephritis with monoclonal IgG deposits (PGNMID) in the transplant (Tx). Here, we report the first clinicopathologic series of PGNMID in Tx.

Design: We retrospectively reviewed our pathology archives from 1/1996-9/2017 and identified 23 patients (pts) with PGNMID diagnosed by renal transplant biopsy (TxBx), including 17 who were followed at our Tx center where protocol biopsies are performed 3-4 months (mo), 1, and 5 years.

Results: PGNMID in Tx was classified as recurrent in 16 (native biopsy proven), probably recurrent in 4, and undetermined in 3. Mean age at Tx was 53 years (26-76). Median time from Tx to the first diagnostic TxBx was 5 mo (1-116); PGNMID was detected in 11 of 13 (85%) pts who had TxBx **at 3-4** mo postTx. The first diagnostic TxBx was done for increased creatinine and/or proteinuria in 70% and was protocol in 30%; median proteinuria was 0.5 g/day (>1 g/day in 36%), 61% had increased creatinine from baseline, 61% hematuria, and 9% nephrotic syndrome. Serum immunofixation was positive in 4 (17%, IgGκ in 2 a**nd** IgGλ in 2). 9% had hematologic malignancy (1 MM and 1 CLL), 40% had hypocomplementemia, and none had hepatitis or cryoglobulinemia. The first diagnostic TxBx showed mesangial proliferative (MesGN)(43%), endocapillary proliferative (EPGN)(22%), MPGN(17%), membranous GN (MGN)(9%) or normal glomeruli (9%). MesGN or normal patterns were seen mostly within 4 mo postTx (75%) and were associated with proteinuria in only 33%, whereas the other patterns were seen mostly >6 mo postTx (73%) and all had proteinuria. On immunofluorescence, all cases showed monoclonal IgG deposits (IgGκ in 16 and IgGλ in 7) with IgG subclass restriction (IgG3 in 82% of cases). Electron microscopy showed granular mesangial (100%), subendothelial (52%), and subepithelial (33%) deposits.

On follow up in 22 pts (mean 89 mo, 12-252), 21 pts eventually developed proteinuria (median peak 2.5 g/day), 8 (36%) lost their Tx within a mean of 75 mo (21-132) mostly due to PGNMID and 2 died. 21 (91%) pts had repeat TxBxs (total =62) which showed persistent PGNMID. The last TxBx showed MesGN (43%), MPGN (43%), EPGN (5%), MGN (1%), and normal glomeruli (5%).

Conclusions: PGNMID recurs early in the allograft and detection is enhanced by protocol biopsies. Most cases are IgG3-driven and hematologic malignancy is rare. Proteinuria and activity of GN are milder than native kidney PGNMID. About 1/3 of pts lose their graft within 6 years.

1711 Clinical Characteristics of De Novo Collapsing Focal Segmental Glomerulosclerosis (cFSGS) in Kidney Allografts

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Background: In the native kidney, cFSGS is characterized by heavy proteinuria and rapid progression to end stage renal disease. A few small studies have shown that post-kidney transplant (post-KTx) cFSGS is associated with variable proteinuria and poor allograft survival. We describe our experience of the natural history, presenting features, and prognosis of de novo post-KTx cFSGS.

Design: All cases of de novo post-KTx cFSGS in adult patients (≥ 18 years old) treated at our institute between 1/2005 and 1/2017 were identified retrospectively (n=39). Selected clinicopathologic characteristics were compared to all patients transplanted at our institute between 2005 and 2009 or total allograft biopsies assessed at our institute between 2005 and 2017.

Results: The patients were 61±12 year-old and included 14 (36%) women, 12 (31%) African American (AA), and 24 (62%) had received an allograft from a deceased donor. Notably, 18 (46%) of donors were AA [compared to 146/975 (15%) of all donors, P<0.001]. The biopsies were obtained 813 ±1304 days post-transplantation with a serum creatinine of 5.2 ±2.6 mg/dl, urine protein/creatinine of 4.6 ±4.1 g/g (range 0.3-16.5), and full nephrotic sundrome in only 7 (18%) patients. Possible causes of cFSGS included viral infections [6 (15%); CMV (3), HIV (1), Parvovirus (1), EBV (1)] and acute vaso-occlusive disease [11 (28%); cortical necrosis (6), thrombotic microangiopathy (2), athero-embolization (2), renal vein thrombosis (1)]. Concurrent acute rejection, including "borderline changes", was present in 23 (59%) cases [compared to 3327/9978 (33%) of all biopsies; P=0.001)].

Twenty-three (59%) patients developed allograft failure at 540 ±686 days post-biopsy. By univariable Cox regression, acute vaso-occlusion was associated with superior graft survival while post-transplant interval to biopsy, % global glomerulosclerosis, and Banff histologic scores of interstitial fibrosis, arteriosclerosis, and arteriolar hyalinosis were each associated with poor graft survival. On multivariable analysis, only interstitial fibrosis predicted allograft failure (HR: 2.6, P=0.03).

Conclusions: We confirmed that de novo post-KTx cFSGS is associated with variable proteinuria and poor prognosis. We showed that interstitial fibrosis is the best predictor of long-term outcome. In addition to viral infection and acute vaso-occlusion, acute rejection and AA donor race may be contributing factors, possibly reflecting elevated interferon production and nephropathic APOL1 variants.

1712 Integrated Regulatory Genomic Analysis Reveals an Unexpected Role for SOX17 in Primary Human Podocytes

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Background: The glomerular podocyte is an important cell type with limited proliferative/regenerative potential that is the target of many proteinuric kidney diseases. Despite extensive cell biological characterization, very few studies have focused on an integrated characterization of the podocyte-specific epigenetic architecture and transcriptome. In particular, global chromatin accessibility profiling (DNase-seq) holds the potential to identify novel genome regulatory mechanisms that are uniquely specific to the podocyte and that are upstream of and control gene expression programs. Such studies have not been previously performed on primary podocytes due to technical challenges.

Design: Using optimized techniques, we generated high resolution chromatin accessibility (DNase-seq) and gene expression (RNA-seq) data for primary cultures of human podocytes (n=4), and compared them to similar datasets generated from primary cultures of human kidney proximal tubule cells (n=3). We utilized state-of-the-art genomic analysis tools to analyze transcriptomic and chromatin accessibility datasets in an integrated fashion.

Results: 1807 genes and several thousand DNase-hypersensitive sites (DHSs) showed differential regulation between the primary human podocytes and proximal tubule cells. Analysis of DHSs revealed enrichment of the SOX sequence-specific transcription factor binding motif within DHSs with increased accessibility in podocytes. Of the SOX family of transcription factors, only SOX17 shows a podocyte-specific expression pattern, which has not been previously described. DHSs containing SOX17 motifs are located in proximity to genes associated with negative regulation of the canonical Wnt signaling pathway, activation of which is associated with podocyte injury and dysfunction.

Conclusions: Our first-of-kind integrated epigenomic analyses reveal an unexpected role for SOX17 in primary human podocytes. SOX17 has been mostly studied in early embryonic development, but patients with SOX17 mutations have urogenital developmental abnormalities. We show that SOX17 expression in podocytes exerts a genome-wide influence which may suppress canonical Wnt signaling to preserve normal podocyte function. Our results shed light on the mechanisms of genome regulation in this important cell type and could calibrate and improve commonly used and emerging (e.g. iPSC-derived) podocyte cell culture systems.

1713 Thrombotic Microangiopathy with Intraglomerular Monoclonal IgM Pseudothrombi

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Background: Renal disease in the setting of Waldenstrom macroglobulinemia or monoclonal IgM most commonly includes amyloidosis, monoclonal IgM deposition disease, light chain deposition disease, cast nephropathy, and lymphoplasmacytic lymphoma infiltration. Here we report an unusual constellation of thrombotic microangiopathy (TMA) with intraglomerular monoclonal immune globulin pseudothrombi.

Design: A single institution's pathology database was retrospectively searched for kidney biopsies with a combination of findings of TMA with monoclonal immune globulin deposition. All biopsy samples were processed for light microscopy (LM), immunofluorescence (IF) and electron microscopy (EM).

Results: Five cases from 4 patients were retrieved. All patients had a known monoclonal gammopathy, with 3 having or suspected to have Waldenstroms macroglobulinemia (WM). Three presented with worsening renal function, 3 with proteinuria, and none had systemic TMA. All 4 patients had intraglomerular monotypic IgM deposits by IF, found in capillary lumina, capillary walls, and in the mesangium. Interestingly, 2 patients also had deposits in arteriolar lumina and/or walls by light or IF. All showed TMA changes including mesangiolysis and basement membrane duplication, red blood cell fragments in 2, and artery/arteriolar involvement in 1. Mesangial and/or endocapillary proliferation was seen in 3 patients. Intracellular crystalline structures in intraglomerular macrophages were seen on EM in two cases with significant kappa-monotypic deposition, appearing needle-like in one and rhomboid in another. An atypical lymphoid infiltrate was seen in 2 of 5 cases. All showed at least focal acute tubular injury.

Conclusions: TMA has rarely been reported in the setting of MGUS or Waldenstrom, but not with associated monotypic pseudothrombi. Here we report the co-existence of IgM pseudothrombi and TMA in glomeruli in the setting of monoclongal gammopathy; this is an intriguing association in need of further characterization.. We speculate on the following possibilities: 1) mechanical injury of the endothelium by paraprotein or crystalline deposit; 2) paraprotein auto-antibody activity against the endothelium; 3) paraprotein auto-antibody activity against an alternate complement pathway analogous to that seen in C3 glomerulopathy.

1714 Incidental Identification of Non-Neoplastic Renal Diseases in Renal Mass Biopsies

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Background: The concern for tumor seeding has historically limited the utility of the renal mass biopsy, but no such reports have occurred in the modern era since the application of coaxial sheath biopsy techniques. Given that renal function preservation is of high priority in the management of small renal masses and up to 25% of renal neoplasms may be benign, the renal mass biopsy is an increasingly viable option. We and others have demonstrated the common occurrence of non-neoplastic renal diseases in kidney cancer patients in nephrectomy specimens, but this has not been studied in the setting of renal mass biopsy to our knowledge. Therefore, we conducted this study to determine the feasibility of evaluating the non-neoplastic renal parenchyma in such a limited tissue sample

Design: We identified 117 needle biopsies for renal lesions in adults from the Department of Pathology archives (2007-2017). Additional stains for PAS or Jones methenamine silver were obtained as needed. The pathologic findings were correlated with the clinical data.

Results: Of the 117 cases, non-neoplastic renal parenchyma was absent in 91 cases (78%), and present in 26 cases (22%). After review of the H&E slides, 6 cases (5.1%) had significant diffuse and/or nodular mesangial sclerosis. Additional review of the PAS and Jones stains demonstrated that 2 cases (1.7% of total cases, 7.7% of cases with non-neoplastic renal parenchyma) showed diffuse and focally nodular mesangial sclerosis that was consistent with diabetic nephropathy as both patients had an established clinical diagnosis of diabetes. Table 1 summarizes the findings of this study.

Diagnosis	No. cases (%)	No. cases with non-neoplastic renal parenchyma
Papillary urothelial carcinoma	45 (38%)	1
Renal cell carcinoma, clear cell	19 (16%)	6
Renal cell carcinoma, papillary	10 (12%)	3
Renal cell carcinoma, poorly differentiated	5 (4%)	4
Renal medullary carcinoma	1 (0.8%)	0
Metastasis	4 (3.4%)	2
Oncocytoma	3 (2.6%)	1
Amyloidoma	1 (0.8%)	0
Other disease processes*	29 (25%)	9

Table 1. Summary of diagnoses, number of cases, and number of cases with non-neoplastic renal parenchyma. Other disease processes includes benign urothelial mucosa, benign renal parenchyma, xanthogranulomatous pyelonephritis, non-diagnostic specimens.

Conclusions: The needle biopsy is increasing useful in guiding the management of patients with small renal masses. Although less than 25% of renal mass biopsies had sufficient incidental non-neoplastic renal parenchyma for pathologic evaluation, medical renal diseases, such as diabetic nephropathy, could be diagnosed. On the other hand, the biopsy specimen for urothelial lesions rarely yields sufficient adjacent non-neoplastic renal parenchyma for pathologic evaluation.

1715 High Susceptibility of Histoplasmosis in Renal Allografts Compared with Non-Renal Allografts

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Background: Histoplasmosis is an opportunistic fungal infection caused by *Histoplasma capsulatum*. The overall incidence is estimated 3.4 cases per 100,000 in adults aged 65 and older with a higher incidence of 6.1 per 100,000 in Midwest. Manifestations of this infection range from self-limited infection to disseminated systemic disease with a particularly adverse impact on immunocompromised patients. In transplant patients, this infection can cause graft failure and potential fatality. However, there is scarce data on this infection in renal allografts in US endemic regions. This study is aimed to understand the susceptibility of renal allografts to *Histoplasma* infection by analyzing pathology data.

Design: Medical records were retrieved and retrospectively reviewed from all renal and non-renal (including liver, heart and pancreas) transplant patients for biopsy-proven *Histoplasma* infection in any organs between 1/2015 to 8/2017 in our institution. Renal transplant patients with only re-perfusion or inadequate biopsies were excluded from this study. The pathology data on *Histoplasma* infection in all patients with records available in our PowerPath database were also gathered for review in the same period of time.

Results: Histoplasmosis was identified in 64/63,560 (0.1%) patients with or without transplants, of which, 5 (8%) patients had renal transplants, including 3 with renal biopsies (results below) and 2 with no records in our pathology database. The rest 59 of 64 patients had no history of any transplants. Renal transplantation was identified in a total of 258 patients with 532 renal biopsies. Among these 258 patients, 3 (1.2%) patients had *Histoplasma* infection, including 2 with organisms in renal allografts and 1 with organisms in Bronchoalveolar lavage only. As a comparison, a total of 155 non-renal transplant patients were identified in the same period of time, with 232 biopsies available for review. No Histoplasmosis was diagnosed in any organs of these 155 patients.

Conclusions: Histoplasmosis occurred in 1.2% renal transplant patients overall and 67% in kidney allografts if Histoplasmosis was identified in any other organs. No *Histoplasma* infection was diagnosed in liver, heart and pancreas transplant patients in our institution. Taken together, renal transplant patients are at a higher risk of histoplasmosis than non-renal transplant patients. Thus, high suspicion of Histoplasmosis in renal allografts is warranted if *Histoplasma* infection is present in any other organs.

1716 Renal Biopsy Characteristics in HIV-Negative to HIV-Positive Kidney Transplants - an Institutional Experience

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Background: Renal transplantation in HIV-positive patients is known to be associated with a higher rate of acute rejection. HIV-positive to HIV-positive transplantations are also being performed, thus increasing the availability of transplantable kidneys. The role of performing protocol biopsies in this setting is understudied. In this context, our study aims to examine renal biopsy characteristics of HIV-positive renal transplant recipients in our institution.

Design: All HIV-positive kidney transplant biopsies obtained from 1/1/2000 to 1/30/2017 were included. Rates of rejection, other diagnoses, clinical characteristics and patient demographics were collected. Older cases were re-classified based on current Banff criteria.

Results: A total of 141 biopsies from 81 patients were identified. All cases were HIV-negative donor to HIV-positive recipient transplantations. Acute rejection was seen in 40 of 141 biopsies (28.4%). Chronic active rejection with or without transplant glomerulopathy and/or transplant arteriopathy was seen in 14 of 141 biopsies (9.9%). Focal segmental glomerulosclerosis, not otherwise specified type (FSGS, NOS) was seen in 4 of 141 (2.4%) biopsies, with no cases showing collapsing morphology. One patient showed HIV-associated "lupus-like" immune complex mediated glomerulonephritis on two consecutive biopsies. 18 of 35 (51.4%) protocol biopsies had significant findings including 12 diagnoses of borderline change, 2 diagnoses of acute T-cell mediated rejection and 4 diagnoses of polyomavirus nephropathy. Detailed results are summarized in Table 1.

Patient demographics (n=81)		
	Male Female	61 (75.3%) 20 (24.7%)
	Age (range)	31-73 years
	Deceased donor Living unrelated donor Living related donor	73 (90.1%) 5 (6.2%) 3 (3.7%)
Biopsy/clinical characteristics (n=141)		
	Time after transplant (range)	2 days to 132 months
	Protocol biopsies	35 (24.8%)
	Cause biopsies	106 (75.2%)
	Proteinuria	23 (16.3%); 6 nephrotic range
Banff diagnoses (n=141)		
	Non-diagnostic	1 (0.7%)
	Negative for rejection	55 (39%)
	Borderline change	48 (34%)
	Acute T-cell mediated rejection	26 (18.4%): Type 1: 13; Type 2: 12; Type 3: 1
	Acute antibody mediated rejection	10 (7.1%); C4d positive: 7; C4d negative: 3
	C4d staining without histologic rejection	1 (0.71%)
	Chronic active antibody mediated rejection	4 (2.8%)
	Transplant glomerulopathy	8 (5.7%)
	Transplant arteriopathy	2 (1.4%)
Other diagnoses (n=141)		
	Acute tubular necrosis	25 (17.7%)
	Polyomavirus nephropathy	9 (6.4%)
	Acute/chronic tubulointerstitial nephritis	4 (2.8%)
	FSGS, NOS type	4 (2.8%), no collapsing type
	Diffuse nephrocalcinosis	4 (2.8%)
	HIV-associated lupus-like glomerulonephritis	2 (1.4%), same patient
	IgA nephropathy	2 (1.4%)
	Thrombotic microangiopathy	1 (0.7%)
	Acute pyelonephritis	1 (0.7%)

Conclusions: In our institution, rates of acute rejection in HIV-positive recipients are higher than historical rates of rejection seen in HIV-negative recipients. Recurrent or de-novo HIV-associated glomerular disease was infrequent. Protocol biopsies were helpful

in this clinical setting to identify subclinical allograft injury. Further studies involving long term follow-up, morphologic characteristics via digitized slides, and tissue based studies are underway for this cohort.

1717 Molecular Risk Prediction in Crescentic Glomerulonephritis

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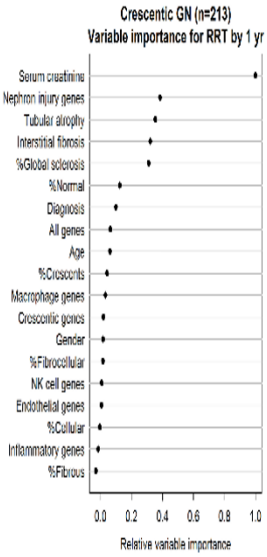
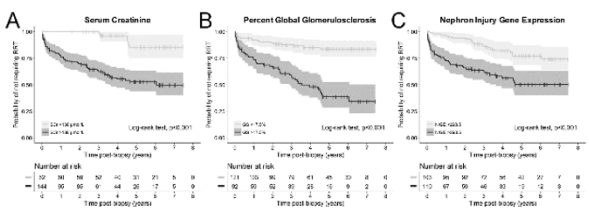
Background: Molecular diagnostics have the potential to improve the classification, activity staging, and risk stratification of native kidney diseases. We aimed to employ the NanoString® nCounter® platform to assess the utility of gene expression quantification in formalin-fixed paraffin-embedded (FFPE) native kidney biopsies with crescentic glomerulonephritis (GN) for predicting patient outcomes.

Design: The expression of a 54-gene set for inflammation, and glomerular and nephron injury genes was quantified using NanoString® on mRNA isolated from 213 native kidney biopsies with crescentic GN of varying etiologies. Gene set expression was correlated with biopsy histology, clinical parameters, and outcome.

Results: Random forest multivariate regression demonstrated the variable most strongly associated with the need for permanent renal replacement therapy (RRT) by 1 year post-biopsy to be serum creatinine at the time of biopsy (Figure 1). This was followed by nephron injury gene expression, tubular atrophy, interstitial fibrosis and percent global glomerulosclerosis (relative variable importance = 39%, 35%, 32%, and 31%, respectively). Three variables were associated with increased risk of permanent RRT: serum creatinine at time of biopsy (HR=3.75, p=0.013), percent global glomerulosclerosis (HR=3.07, p=0.003), and nephron injury gene expression (HR=2.82, p=0.002). Corresponding univariate Kaplan-Meier curves for these variables are demonstrated in Figure 2. Biopsies with high nephron injury gene expression included a significantly greater proportion of ANCA-associated GN (40% vs. 21%, p=0.037) and smaller proportion of IgA nephropathy (25% vs. 46%, p=0.020).





Conclusions: Our results demonstrate the potential for long-term molecular prognostication from routine FFPE native kidney biopsies. Quantification of nephron injury gene expression using the NanoString® platform provides additional information that may allow for more precise risk stratification of patients with crescentic glomerulonephritis.

1718 PLA2R in Non-lupus Patients with Membranous Nephropathy and Crescents

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Background: Anti-phospholipase A2 receptor (PLA2R) antibodies are positive in about 70% of primary membranous nephropathy (MN). Crescents in MN are unusual, except in lupus nephritis, and suggest additional injury, such as ANCA or anti-GBM associated glomerulonephritis. The coexistence of MN with crescents has been postulated to reflect injury by one of these mechanisms that may unmask cryptic epitopes and lead to the second auto-antibody. Thus, we hypothesized that if crescentic injury was the initial insult, the ensuing MN would likely be PLA2R negative, and conversely if MN were the first injury, it more commonly would be PLA2R positive. We studied PLA2R staining in non-lupus patients with MN and crescents.

Design: 14 non-lupus patients with 17 native renal biopsies (2008-2017) with MN and crescents were assessed for PLA2R staining.

Results: The patients included 5 women and 9 men, age 22-81 yrs, (mean 58 yrs) at time of biopsy. All had proteinuria (mean 4.97 g/d; range 0.31-8.40 g/d) and elevated serum creatinine (mean 4.53 mg/dl; range 1.84-20.00 mg/dl); all except one had hematuria. Two patients had positive anti-GBM antibody. 7/9 patients tested for ANCA were positive, with p-ANCA (n=3), c-ANCA (n=2), or both (n=1), with one not specified. On average, 28% of glomeruli (range 5%-89%) had crescents, mostly cellular (51%, range 0%-100%); 13% of glomeruli (range 0%-56%) had fibrinoid necrosis. One patient had MN, and 4 years later had MN with crescents. One patient had ANCA-associated vasculitis, and 5 years later had MN and crescents. The remaining 12 patients had concurrent diagnoses of MN and crescents. PLA2R was positive in 4 cases, 2 with ANCA positivity, 2 with unknown ANCA status, and none with anti-GBM disease. Importantly, the patient with initial MN was PLA2R positive; and the patient with initial ANCA-associated vasculitis was PLA2R negative.

Conclusions: Patients with concomitant MN and crescents mostly had ANCA-associated disease, with only 17% with co-existing anti-GBM disease. PLA2R was positive in only 29% of patients, suggesting most cases are likely secondary MN. The rare occurrence of initial MN, PLA2R positive, followed by crescents, suggests the possibility of unmasking of cryptic epitopes in primary MN. Conversely, initial ANCA positivity may result in a secondary, PLA2R negative MN. Further study will be necessary to determine the epitopes involved.

FIG. 1692

Donor			Recipient									
Case	Cause of Death	KDPI (%)	Case	GFT	GS	ATI	CIT (hr)	DGF	Failed	Cr (3 mo)	Latest Cr	F/U Time (mo)
D1	head trauma, blunt inj, accident (non-MVA)	-	R1	81%	5%	++	23.8	Yes	No	0.98	1.27	73
			R2	78%	1%	++	34.9	Yes	No	1.04	1.26	25
D2	head trauma, blunt inj, MVA	17%	R3	52%	0%	++	49.7	Yes	No	1.5	1.14	36
D3	head trauma, gunshot wound, suicide	39%	R4	97%	0%	++	36.1	No	No	1.37	1.17	30
			R5	75%	0%	++	30.1	No	No	0.71	0.57	24
D4	head trauma, blunt inj, MVA	33%	R6	85%	0%	++	32.8	No	No	0.82	0.68	29
			R7	85%	0%	+++	27.5	No	No	1.69	1.46	10
D5	head trauma, blunt inj, MVA	63%	R8	55%	0%	++	34.1	Yes	No	1.51	1.29	16
D6	head trauma, blunt inj, homicide	52%	R9	100%	0%	+++	35.2	Yes	No	1.08	1.05	6
D7	head trauma, gunshot wound, homicide	36%	R10	76%	3%	++	37.6	Yes	No	1.19	1.03	6
			R11	70%	0%	++	42.4	No	No	1.39	1.31	13
D8	head trauma, blunt inj, MVA	20%	R12	85%	0%	+++	46.4	Yes	No	1.58	1.32	6
			R13	83%	0%	+++	35.6	Yes	No	1.32	1.24	6
D9	head trauma, blunt inj, MVA	41%	R14	94%	10%	+++	16.2	Yes	No	1.48	1.43	11
			R15	89%	7%	+++	10.0	Yes	Yes	4.07	6.71	11
D10	head trauma, blunt inj, MVA	46%	R16	98%	2%	+++	41.8	Yes	No	1.19	1.23	5
			R17	82%	0%	+++	46.4	Yes	No	1.32	1.37	5
D11	head trauma, gunshot wound, suicide	29%	R18	87%	0%	+++	41.1	No	No	1.48	1.42	12