Visualizing Variations of Renal Glomerulus Characteristics in Relation to Clinical Metadata

Amanda Alonzo, Saranjeet Singh Saluja, John Savage, Chunlin Yang

Indiana University Bloomington

Abstract

This is a review of data from the HuBMAP set of microscopic images of sections of donor kidneys [7]. The scope is limited to 20 images that have been annotated with glomerular and cortical borders in associated segmentation masks. These 20 images contained 6 pairs and 1 triplet of images from duplicate donors which combined leaves 12 distinct donor samples. The polygonal vertices of the glomerular and cortex annotations were processed to yield glomerular area (GA) and shape data (eccentricity, ECC) for the glomeruli and area data for the cortex. This data was processed to give our measures as statistical data regarding GA and ECC as well as glomerular area ratio (GAR) (total glomerular area/cortical area) and glomerular density (GD) (count of glomeruli/cortical area) for each donor. This data was compared across the 12 donors and their demographics (age, race, body mass index (BMI), body surface area (BSA), medical history) with visualizations. The comparison focused on parameters affecting renal function such as age, race, sex, and medical history. No measure of renal function such as glomerular filtration rate (GFR) or serum creatinine (SCreat) was in the dataset so a portion of the Modification of Diet in Renal Disease (MDRD) equation was used to estimate renal function independent of SCreat. The main findings were GA decreases with age, BMI and BSA did not correlate with any of the measures, trends relating race and sex were postulated but not significant, linear combinations of age power curve from GA, race, and sex simulated the MDRD equation with significance, and hypertension (HTN) likely reduces GAR. Thanks to our sponsor, Shriya Mandarapu, Indiana University, for her support and Jeff Spraggins, Vanderbilt University, who created the dataset. Links are provided for most visualizations. Key images are in a captioned sequential Tableau Story at **Glomerulus Metadata and Visualization Story | Tableau Public**. Scripts used for data transformation and datasets generation are included in supplementary datasets

Search terms: glomerulus, kidney imaging, Modification of Diet in Renal Disease (MDRD) equation, glomerular filtration rate (GFR), patient metadata, glomerular area, glomerular eccentricity

1. Introduction

Glomeruli are functional units of the kidney that filter blood and expel solutes in the urine. The kidney comprises the cortex which houses the glomeruli, and the medulla which houses tubules for concentrating urine. This project investigates how size, shape, and distribution of glomeruli vary in relation to clinical metadata, i.e., race, age, sex, BSA and BMI. The goal is to use clear visualizations to facilitate data exploration and effectively communicate any findings. Providing better understanding of the kidney at the cellular basis and correlations between glomerular properties and clinical metadata is the significance of this project.

Multiple related studies have been conducted previously. Michael Hughson et al [1] looked at the number of glomeruli in 37 Black and 19 White donors, examining factors that might impact the glomerular count and volume. Their findings showed factors like age, race, gender, and BSA did not have a significant result for the number or mean volume of glomeruli. But they found a negative correlation between the glomerular count and volume that was significant. Nyengaard, J.R. & Bendtsen [2], explored the Glomerular Number and Size in relation to age, kidney weight, and BSA in a normal man. They analyzed autopsy kidneys of 37 people of various age, sex, and BSA, to explore relationships of these factors with the number and volume of glomeruli. Unlike in the previous paper, there was no significant relationship between the number of glomeruli and the mean glomerular volume. However, a statistically significant result was obtained for BSA and age and the number of glomeruli. Hoy et. al [3], conducted a stereological study to identify and explore the relationship between the number and volume of glomeruli in different races. They observed that females had lower glomeruli numbers by 15% than males, but this relationship was not statistically significant. They also observed that the glomerular number in US whites was not significantly lower than in US Blacks.

2. Data Description

2.1 Data acquisition

The dataset is from the Kaggle competition with data on donors and their kidney images [4, 5]. The dataset contains 20 kidney images (15 training, 5 testing) and corresponding Anatomical Structure segmentation mask (JSON) and Glomeruli segmentation mask (JSON) that provide detailed polygonal coordinates to represent the cortical and glomerular boundaries which is the raw data for this project. These kidney tissue images are from 12 distinct donors. Six donors have two image files and one donor has three images. The datasets include the basic meta-data about the donors such as age, race, and gender. Fig. 1 summarizes the demographics of the 12 donors after combining images from duplicated donors. Table 1 shows basic donor demographics and data. Full demographics and data are available at Glomerulus Metadata and Visualization Donor Full Demographics | Tableau Public.

2..2. Data transformation

The Shoelace formula [8] used on the JSON files coordinates to calculate the polygon area giving the size of the

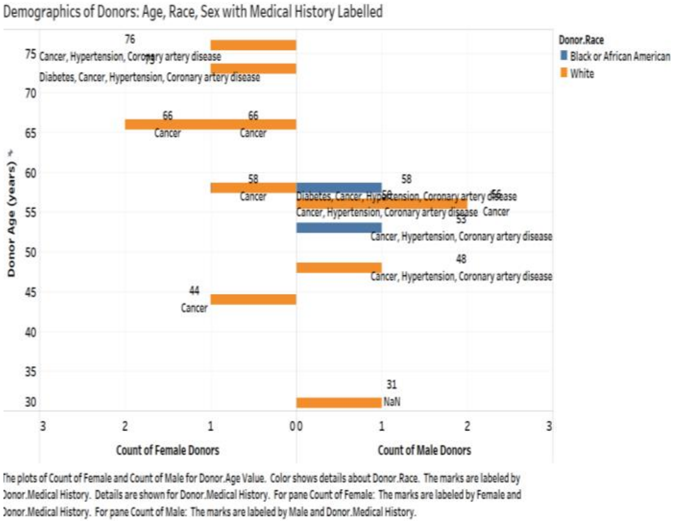


Figure 1. Demographics of donors. Shows demographics of donors: 6 female, 6 male, 10 white, 2 black, 6 with HTN. Glomerulus Metadata and Visualization Demographics | Tableau Public.

Demographics Data by Patient

Patient ..	Donor..	Donor..	Donor.Race	Donor..	Bsa M..	Donor..	Donor..	Donor.Medical ..	Cortex..	Area Me..	Ecc M..	Glom ..	Glom ..	
VAN0014	76	Female	White	37.5	2.02	93	157.4	Cancer, Hypert..	320.73	22596.26	0.49	0.021	0.94	Abc
VAN0010	56	Male	White	32.5	2.06	91.2	167.6	Cancer, Hypert..	581.99	24748.2	0.45	0.022	0.89	Abc
VAN0009	53	Male	Black or Africa..	26.5	1.83	73	166	Cancer, Hypert..	243.79	20576.62	0.46	0.027	1.30	Abc
VAN0005	58	Female	White	23	1.62	59	160	Cancer	744.32	26507.83	0.46	0.037	1.38	Abc
VAN0016	56	Male	White	27.7	2.15	91.4	181.6	Cancer	666.36	24214.58	0.43	0.037	1.54	Abc
VAN0006	58	Male	Black or Africa..	22	2.06	79.9	190.5	Diabetes, Canc..	360.43	30921.45	0.48	0.039	1.27	Abc
VAN0007	66	Female	White	32.2	1.90	81.5	158.8	Cancer	84.23	20966.01	0.45	0.044	2.08	Abc
VAN0011	31	Male	White	32.6	2.31	106.1	180.3	NaN	87.56	30979.79	0.47	0.046	1.48	Abc
VAN0003	73	Female	White	33.2	1.99	87.5	162.3	Diabetes, Canc..	37.00	18311.33	0.49	0.049	2.68	Abc
VAN0008	48	Male	White	35.3	2.66	131.5	193	Cancer, Hypert..	94.05	26214.24	0.45	0.050	1.89	Abc
VAN0013	66	Female	White	25.4	1.82	71.3	167.6	Cancer	225.81	24957.81	0.45	0.053	2.14	Abc
VAN0012	44	Female	White	28	1.79	71.7	160	Cancer	146.21	24854.92	0.47	0.059	2.39	Abc

The view is broken down by Patient Number, Donor.Age Value, Donor.Sex, Donor.Race, sum of Donor.Body Mass Index Value, Bsa M^2, sum of Donor.Weight Value, sum of Donor.Height Value, Donor.Medical History, Cortex Area, Area Mean, Ecc Mean, Glom Area Density and Glom Count Density Glom/Sq Mm

Table 1. Basic Donor Demographics. Glomerulus Metadata and Visualization Donor Brief Demographics | Tableau Public

glomeruli. The pixel coordinates as integers were converted to length by 0.5-micrometer or 0.65-micrometer coefficients based on the donor. Glomeruli are ellipsoid so eccentricity $\sqrt{1-\frac{b^2}{a^2}}$ (a is major axis length and b is minor axis length) was chosen for the measure of the shape. Zero indicates a perfect circle, and one a very elongated ellipse.

The cortex area was calculated for each donor based on the coordinates of the Anatomic Structure segmentation mask. Python and Pandas were used to manipulate the data frames for merging and sorting data and performing calculations such as glomerular density (number of glomeruli for a donor per total cortex area of the donor) and glomerular area ratio (ratio of total glomerular area for a donor per total cortex area for the donor).

3. Data Visualizations and Insights

3.1. Distribution of GA and ECC Among Donors

A preliminary examination of GS and ECC distributions of the glomeruli across the kidney samples of each donor is depicted in Figure 2. Distributions of GA and ECC from the 12 donors with combined samples are shown in Fig. 3.

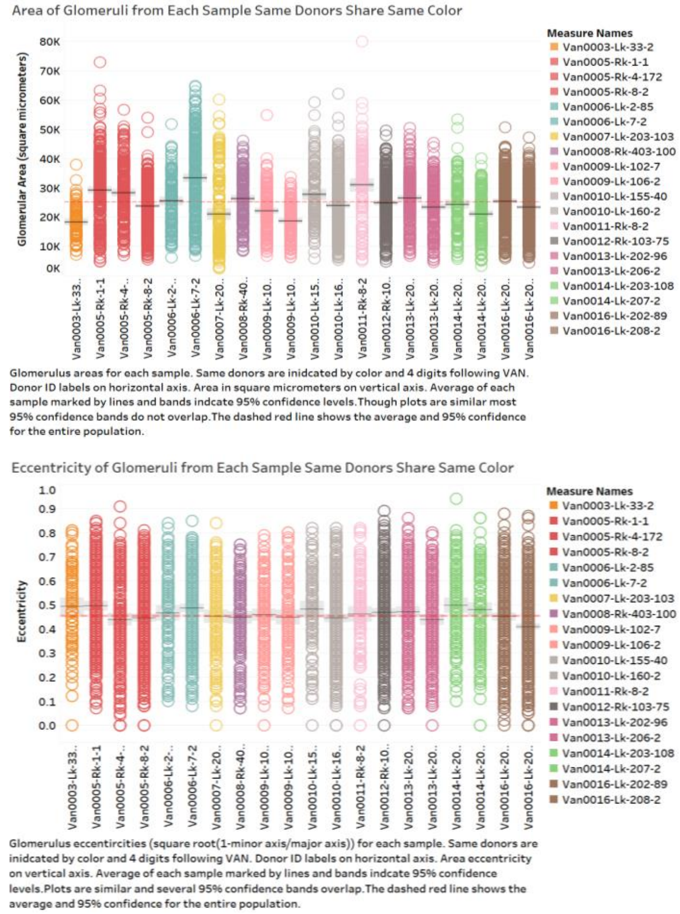


Figure 2. Area (up) and eccentricity (low) distributions of Glomeruli from each sample. Samples from the same donor share the same color. Tthe number indicates the donor, LK indicates left kidney and RK right kidney. Glomerulus Metadata and Visualization Raw Donor Data | Tableau Public

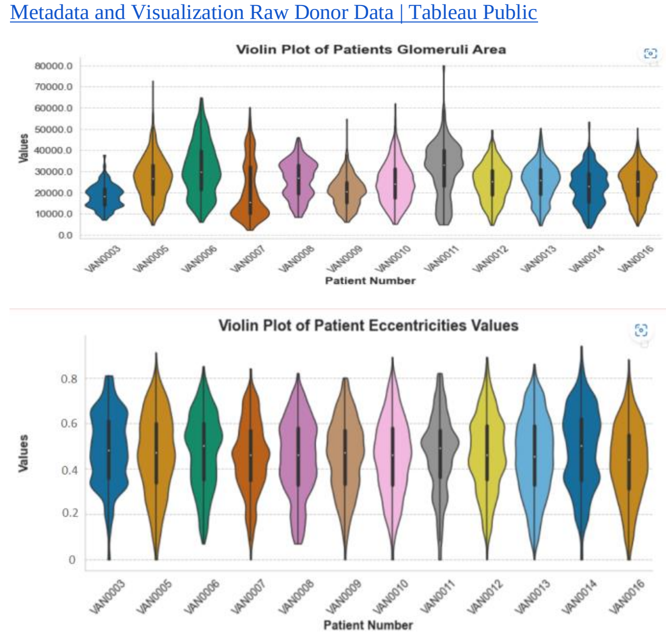
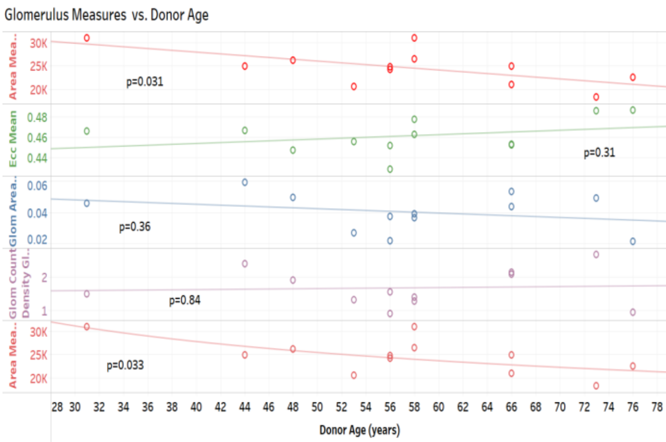


Figure 3. Violin charts show the distribution of the GA (upper) and ECC (lower) of the glomeruli of the 12 donors.

3.2. Glomeruli size decreases with age

The results of comparison of our measures against age is in Fig. 4, and shows a significant decrease in GA with increasing age. ECC tended to elongation with age but this was not significant. These findings imply that GA decreases with age and this may be due in part to loss of sphericity.

A slight decrease in GAR was observed with increasing age and GD is unchanged with age, but neither was significant. We fit the GA to a power curve to be discussed later($p = 0.033$).

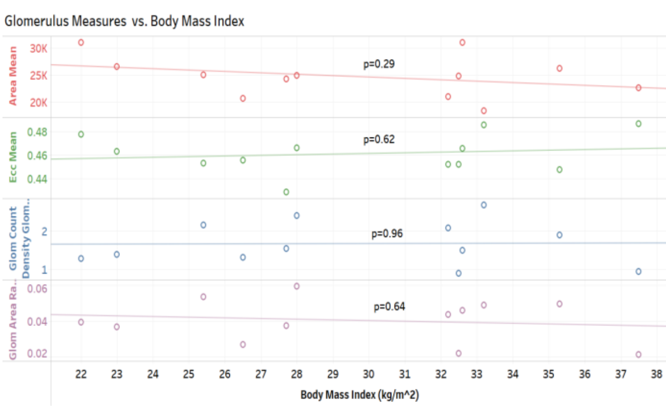


Donor.Age Value vs. Area Mean (square micrometers), Eccentricy Mean (square root(1-(minor axis/major axis)^2)), Glomerular Area Ratio (Total Glomerular Area/Cortex Area), Glomerular Count Density (Glom/square mm) and Area Mean plotted with power trend line. Correlation of age with mean glomerular area is signifciant at p<0.05. The power trend line is applied to modelling the MDRD age coefficient (area = 118187xage^-0.3927.in the bottom plot.

Figure 4. Glomerulus Measures vs. Donor Age. The charts, in descending order, depict linear correlations between donor age and GA, ECC, GAR, and GD. The final chart is a power curve fit for calculating MDRD Factor. Glomerulus Metadata and Visualization Measures vs Age | Tableau Public

3.3. Non-significant decrease in glomerular size with an increase in Body Mass Index (BMI)

The glomerular measures did not correlate with the BMI of the donors as presented in Fig. 5.

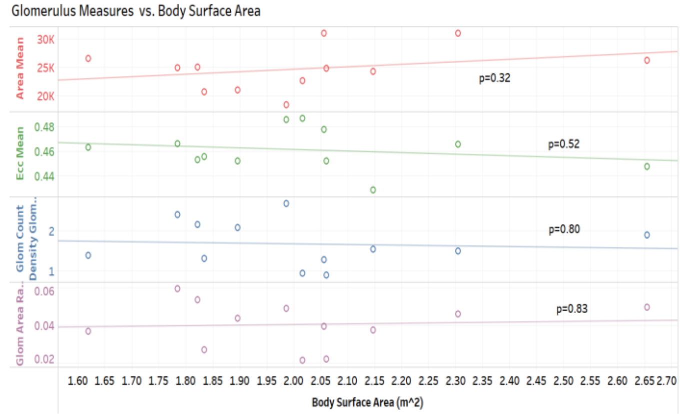


Donor.Body Mass Index vs. Area Mean (square micrometers), Eccentiricy Mean (square root(1-(minor axis/major axis)^2)), Glomerular Area Density (Total Glomerular Area/Cortex Area), and Glomerular Count Density (Glom/square mm). None of these correlations seem to be significant..

Figure 5. Glomerulus Measures vs. donor BMI. Linear correlations between BMI and GA, ECC, GAR, and GD. Glomerulus Metadata and Visualization Measures vs BMI | Tableau Public

3.4. Non-significant increase in glomerulus size with an increase in Body Surface Area (BSA)

Analysis of the correlation between the properties of glomeruli and BSA a non-significant increase in GA and a non-significant decrease in ECC with an increase in BSA (Fig. 6), different from Nyengaard, J.R. & Bendtsen [2].

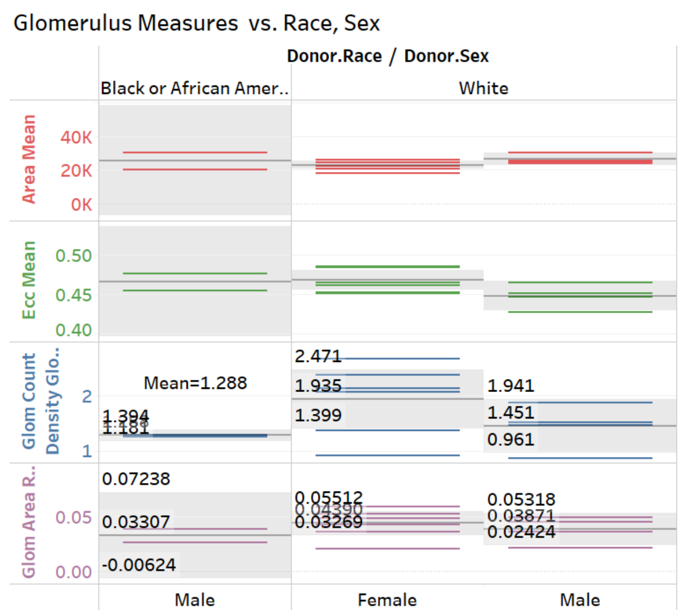


Donor.Body Surface Area vs. Area Mean (square micrometers), Eccentricy Mean (square root(1-(minor axis/major axis)^2)), Glomerular Area Density (Total Glomerular Area/Cortex Area), and Glomerular Count Density (Glom/square mm). None of these correlations seem to be significant..

Figure 6. Glomerulus Measures vs. Donor BSA. Linear correlations between donor BSA and their corresponding GA, ECC, GAR, and GD. Glomerulus Metadata and Visualization Measures vs BSA | Tableau Public

3.5. No significant relationship present between race and sex with glomerular properties

Our sample did not include Black females and only two Black males limiting our ability to draw conclusions about racial and gender disparities in glomerular properties. In Fig. 7, White females tend to have larger GA, smaller ECC, smaller GD, and smaller GAR compared with White males. These differences are not statistically significant.



Race and Sex vs. Area Mean (square micrometers), Eccentiricy Mean (square root(1-(minor axis/major axis)^2)), Glomerular Area Density (Total Glomerular Area/Cortex Area), and Glomerular Count Density (Glom/square mm). Means are shon with 90% confidence bands. The Count Density and Area Ratio trends correlate weil with the MDRD equation. Count Density ratios for sex and race based on means yield MDRD coefficients of: 0.750 and 1.127, whereas Area Ratio means yield MDRD coefficients of: 0.882 and 1.171

Figure 7 (previous column)**. Glomerular Measures vs. Race and Sex.** A visual representation of GA, ECC, GD, GAR across three donor groups: Black males, White males, and White females. Each line represents 1 donor. Gray lines are means and gray highlights are the 90% confidence bands. Glomerulus Metadata and Visualization Measures vs Race Sex | Tableau Public

3.6. Distribution of Glomerular Measures based on Age, BMI/BSA, Race, and Sex

Effect of BMI/BSA under race, and sex categorization was illustrated with the distribution of Glomerular Measures across these variables as shown in Fig. 8. We did not observe any significant trend based on the visualization.

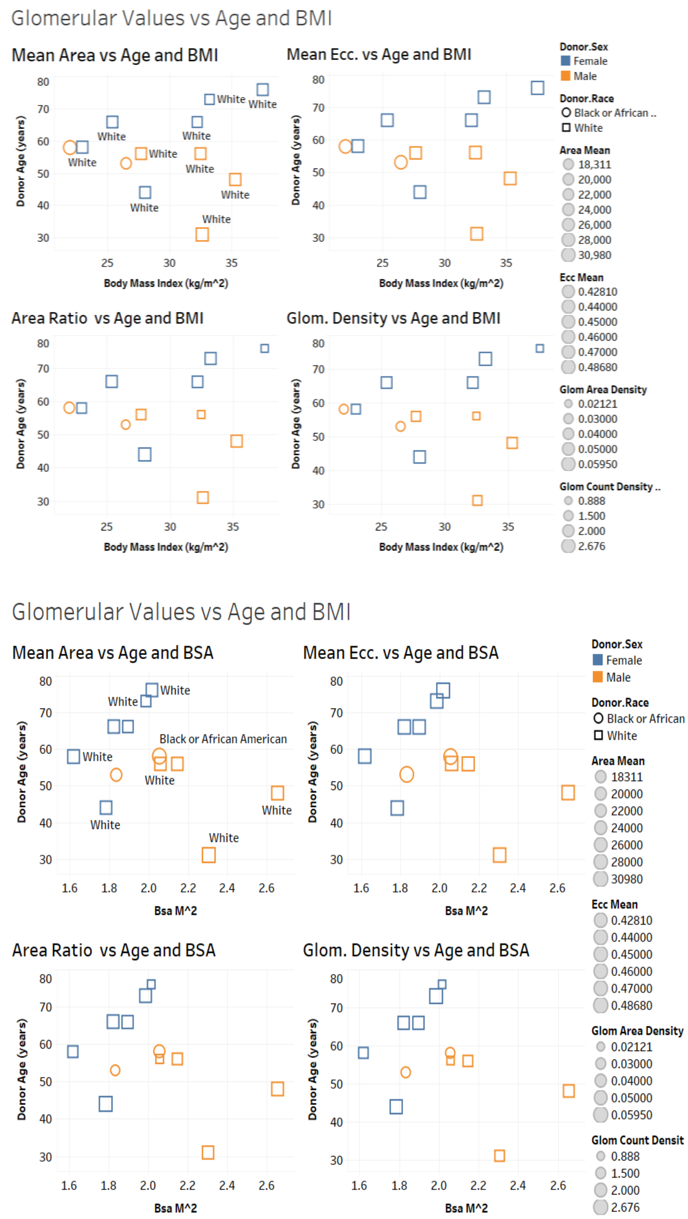


Figure 8. Distribution of Glomerular Measures based on Age, BMI/BSA, Race, and Sex. The charts depict the distribution of glomerular measures based on age, and BMI, under the categorization of race and sex. Glomerulus Metadata and Visualization Measures vs Age BMI dash | Tableau Public; Glomerulus Metadata and Visualization Measures vs Age BSA dash | Tableau Public

3.7. Glomerular measures vs MDRD Factor

Glomerular Filtration Rate (GFR) measures renal function. GFR is the amount of blood filtered through glomeruli per unit time and is the best indicator of renal function. MDRD is commonly used to estimate GFR based on serum creatinine levels, age, sex, and race [9] and is shown below.

GFR in mL/min per 1.73 m^2=175 x SerumCr$^{-1.154}$ x age$^{-0.203}$ x 1.212 (if black) x 0.742 (if female)

The data for the coefficients for female and black patients for the MDRD equation were compared to the measures in Fig. 6. The trend consistent with MDRD was only apparent for GD and GAR. The GD for sex and race categories was most consistent with MDRD. The coefficients were derived as ratios of male:female and white:black means of GD and GAR. The age term was derived from the power curve of GA to age as in Fig. 5.

Data includes no values for creatinine, so the last portion of the MDRD equation, MDRD factor, is compared to the derivation from the image data.

age$^{-0.203}$ x 1.212 (if black) x 0.742 (if female)

The analogous models for the MDRD Factor from the image-derived data are:

age$^{-0.3927}$x1.1264(if black)x0.8818(if female) - GAR
age$^{-0.3927}$ x1.127(if black)x0.7907 (if female) - GD

The coefficients derived from GD are closest to the MDRD as seen in Fig. 9. Fit of curves is significant (p<0.0001) and the maximum error after linear correction is less than 11% for any point.

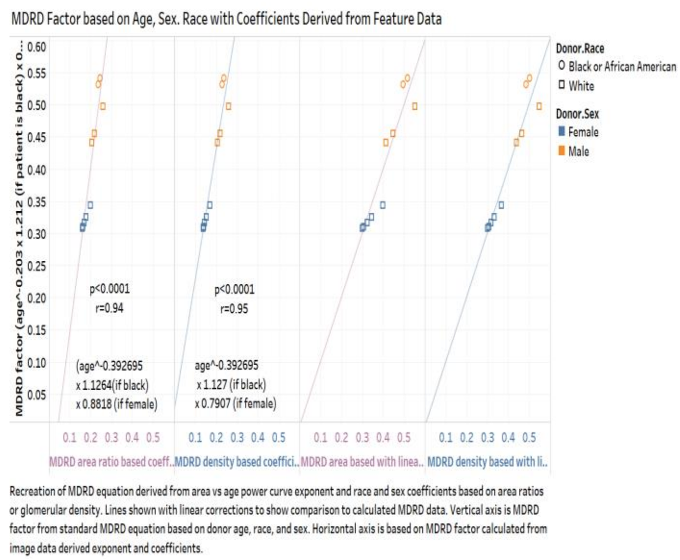


Figure 9. Linear models of the MDRD equation. Plots based on power curve of GA vs. age and coefficients from GAR (left) and GD (right) from race and sex data. Curves on right are linearly corrected to show accuracy of fit. Glomerulus Metadata and Visualization MDRD Models | Tableau Public

The MDRD Factor is used as a surrogate for GFR since GFR and SCreat are not in the data.. Comparing measures against the MDRD factor shows trends that the GA increases with MDRD Factor and GD decreases with MDRD Factor reeling to increased GFR, as in Fig, 10.

3.8. Change of Variance of GA, ECC with Age

There was no significant variation in the standard deviation of glomerular area or eccentricity with age as indicated by Fig. 11. There is no variation in the variance of ECC with age, and variance of GA with age is unlikely.

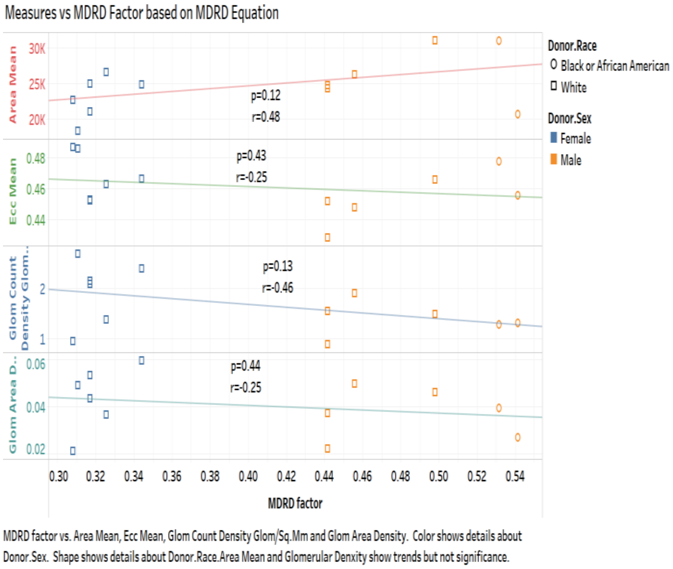


Figure 10. Glomerular measures vs MDRD Factor. No curves are significant but there are trends that GA increases with MDRD Factor (p=0.12) and GD decreases with MDRD Factor(p=0.13). GFR is proportional to MDRD Factor. [Glomerulus Metadata and Visualization Measures vs MDRD Factor | Tableau Public]

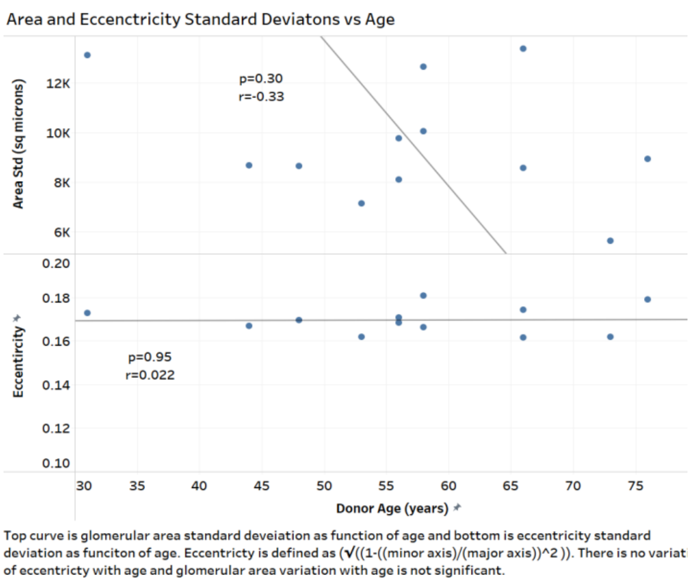


Figure 11. Variation of Standard Deviation of Glomerular Area and Eccentricity with Age. There is no significant change with age. [Glomerulus Metadata and Visualization Measure STD | Tableau Public]

3.9. Effect of HTN on Glomerular Measures

HTN is known to contribute to renal failure. Figure 12 shows that GA, GAR ratio, and GD decrease with HTN, and ECC increases with HTN.

The statistical significance tests conducted in this study used a significance level of 0.05. Most comparisons were not statistically significant because of the small sample size. The comparison of GD between patients with and without HTN showed a p-value of 0.0563, very close to the significance level. This suggests a potential trend. Further research with a larger sample size may establish a stronger link between HTN and GD.

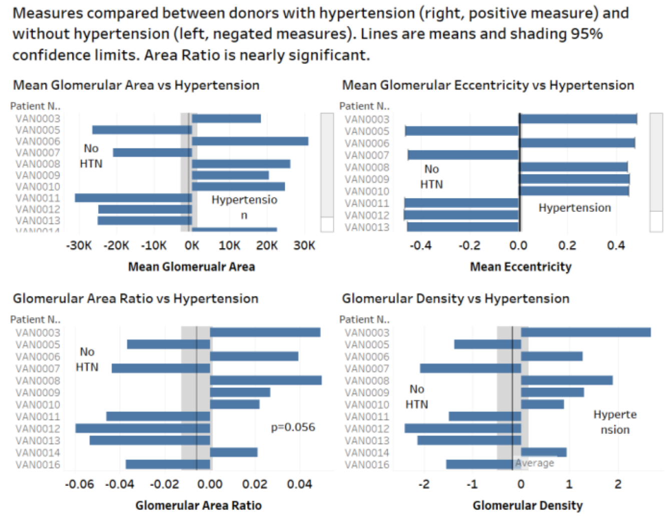


Figure 12. Glomerular measures vs Hypertension Status. No comparisons are statistically significant but there are trends as shown. Lines indicate means and shading indicates 95% confidence intervals. Glomerular area ratio is near significance. [Glomerulus Metadata and Visualization Measures vs HTN Dash | Tableau Public]

4. Conclusion

There is strong evidence that GA decreases with age (p=0.031). Some authors believe that the number of glomeruli decreases with age from nephrosclerosis with some compensation by hypertrophy of the remaining glomeruli. [10] This finding contradicts the compensatory hypertrophy theory unless there is an increase in atrophic glomerulus and glomerular hypertrophy in which case an increase in the variance of GA would be expected, but there was no significant change in the standard deviation of GA.

An equation analogous to a portion of the MDRD equation could be derived from values measured from the images using the power curve for glomerular size vs age and ratios of the glomerular density for sex and race. These derivations of the analogous MDRD equations were accurate despite the limited data (p<0.0001, rmse=6.8%). The MDRD is important because it gives us an indication of the trend of the GFR where we have no data for this important measure. The high level of significance and good accuracy is likely related to the significance of GA with respect to age and the linear combination of the coefficients for race and sex.

There are trends that GA is directly related to the MDRD factor (p=0.12) and GD is inversely related to the MDRD factor (p=0.13). The MDRD factor is presumed to correlate directly with GFR. The increase in GA with respect to MDRD Factor is supported intuitively as it would be expected that GFR would increase with GA. The inverse relationship between GD and MDRD Factor is contrary to the expectation that GFR would increase with an increase in the number of glomeruli, presumably directly related to the density of glomeruli. However, the MDRD equation clearly indicates that GFR increases with the black race and male sex. Our data shows a related trend to decreased glomerular density. There may be something physiologic causing this unexpected increase in GFR with decreased density such as a crowding phenomenon.

There are trends that GA, GAR (p=0.056), and GD decrease with hypertension and ECC increases with HTN.

These are all consistent with what might be expected with the loss of renal function over time related to HTN. The average age of the donors with HTN was 61. Declining GA, increased ECC (links to decreased area and perhaps altered glomerular function), decreased GAR and decreased GD in the cortex would all be expected to contribute to loss of renal function. References addressing these relationships were not found.

5. Resolving Problems during validation and solutions.

The images differed considerably. Combining samples from duplicate donors helped offset. There was a large variation in the number of glomeruli. The region of interest is the cortex which is the area of the kidney that contains the glomeruli. We mapped the location of glomeruli to the cortex boundaries to ensure the consistency of our analysis with the image data (see intermediate report). The glomeruli were consistently within the boundaries of the cortex; however, there were some areas of the cortex barren of the glomeruli. The variation in the number of glomeruli was consistent with the large variation of the cortex areas and concentration of glomeruli in those areas. We mitigated this variation by creating new measures, GD and GAR

There was very little correlation of p values of linear regressions of various relationships between the data. Significant findings were questionable because of the small number of samples and poor repeatability when looking at a different race or sex. However, when matching the data of GA to age, and GD to sex, and race, and applying this data to an analog of the MDRD equation to estimate GFR there were very low p-values when correlating with the MDRD equation.

There was a relatively small data set provided by the Kaggle competition, and we obtained more data directly from the HuBMAP site. The initial project description stated pixel size was 0.5 micrometers; however, the HubMAP metadata indicated there were two-pixel resolutions of 0.5 and 0.65 micrometers randomly distributed among the donors. This created errors and false conclusions initially and it added to the complexity of calculating measures.

6. Challenges and Opportunities

It is difficult to normalize this data to accurately compare one donor to the next as the data shows that data from the same donor is not repeatable and size and shape of the cortices vary considerably. Determining the best easy to normalize data is important.

There may be data variations with sectioning as relates to the relationship between glomerular and kidney geometries. The glomeruli do not appear to be closely packed based on the glomerular-to-cortex area ratio (typically <0.1). Therefore, images are dependent on the specific plane sectioned which would affect the apparent sizes (imagine cross-sections of spheres at different latitudes) and densities.

It would be beneficial to explore methods for normalizing imaging samples and data as a way of making accurate comparisons from one image to another given the limitations and variations in taking an arbitrary sample from one donor or lab to the next. For example, there is strict regulation and standardization in mammogram image samples. We applied normalization using the cortex area; however, the images of the cortex area may be lacking in precision when exploring the mappings. Given more time, it may be possible to modify the cortex mappings, perhaps even algorithmically using the glomerular dimensions.

There is the opportunity to process the raw TIFF image files with machine learning instead of relying solely on the JSON polygon coordinate data. This appears to be the purpose of the Kaggle competition from which our dataset was drawn. So, it may be possible to use the algorithm of the Kaggle competition winner to process more HubMAP images to create more data.

Any pre-processing of medical images for human consumption inherently loses information that can prove useful and can be detected in a machine learning algorithm. Given all the data contained within a single image, it is difficult or impossible for a human to digest but an algorithm can manage and infer insight to support the human process. Using other data available in the raw images may allow more learning opportunities.

From a wider research perspective, there is an opportunity to obtain, analyze and visualize longitudinal data meaning the same donor over time to see a baseline to measure the change in the glomeruli over time. However, these samples appear to be full sections from kidneys so each kidney was likely excised from cadavers precluding longitudinal studies unless similar data could be obtained from core biopsies which would be much smaller, but potentially repeatable.

Our desire would be to have clinical data such as glomerular filtration rate or creatinine and a thorough medical history. Correlating a larger dataset with clinical history would likely lead to more meaningful results that would help with predictive diagnoses and clinical decision support.

The process of imaging large kidney sections such as this and using image processing to identify glomerular boundaries and cortex boundaries lends itself to processing large numbers of samples with qualitative data which could translate to better understanding of the effects of aging and illness on renal physiology. Sample size in our references was typically less than 40. The Kaggle competition yielded algorithms that were 95% accurate.

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References

[1] Hughson, M., Farris, A.B., Douglas-Denton, R., Hoy, W.E., & Bertram, J.F. (2003). Glomerular number and size in autopsy kidneys: The relationship

to birth weight. Kidney International, 63, 2113-2122. Jackson, MS: University of Mississippi Medical Center; Clayton, Victoria, Australia: Department of Anatomy and Cell Biology, Monash University; Brisbane, Australia: Centre for Chronic Disease, University of Queensland.

[2] Nyengaard, J.R. & Bendtsen, T.F. (1992). Glomerular Number and Size in Relation to Age, Kidney Weight, and Body Surface in Normal Man. The Anatomical Record, 232, 194-201. Aarhus, Denmark: Stereological Research Laboratory, University Institute of Pathology and 2nd. University Clinic of Internal Medicine, Institute of Experimental Clinical Research, Aarhus University.

[3] Hoy, W.E., Douglas-Denton, R.N., Hughson, M.D., Cass, A., Johnson, K., & Bertram, J.F. (2003). A stereological study of glomerular number and volume: Preliminary findings in a multiracial study of kidneys at autopsy. Kidney International, 63(Suppl 83), S31-S37. Darwin, Northern Territory, Australia: Renal Unit, Menzies School of Health Research; Melbourne, Victoria, Australia: Department of Anatomy and Cell Biology, Monash University; Jackson, Mississippi, USA: Department of Pathology, University of Mississippi Medical Center.

[4] The HuBMAP Glomeruli FTU Segmentation Dataset:
https://www.kaggle.com/leahscherschel/dataset-details

[5] Glomeruli Detection Related Works:
https://www.kaggle.com/leahscherschel/glomeruli-detection-related-works

[6] Leah L. Godwin, Yingnan Ju, Naveksha Sood, Yashvardhan Jain, Ellen M. Quardokus, Andreas Bueckle, Teri Longacre, Aaron Horning, Yiing Lin, Edward D. Esplin, John W. Hickey, Michael P. Snyder, N. Heath Patterson, Jeffrey M. Spraggins, Katy Börner. 2021. "Robust and generalizable segmentation of human functional tissue units."bioRxiv 2021.11.09.467810; doi: 10.1101/2021.11.09.467810.

[7] HuBMAP datasets:

Datasets | HuBMAP (hubmapconsortium.org)

[8] Shoelace formula: https://en.wikipedia.org/wiki/Shoelace_formula

[9] Andrew S. Levey, MD, Josef Coresh, MD, PhD, MHS, Tom Greene, PhD, Lesley A. Stevens, MD, MS, Yaping (Lucy) Zhang, MS, Stephen Hendriksen, BA, John W. Kusek, PhD, & Frederick Van Lente, PhD (15 August 2006). Using Standardized Serum Creatinine Values in the Modification of Diet in Renal Disease Study Equation for Estimating Glomerular Filtration Rate, Annals of Internal Medicine, Volume 145, Issue 4, 247-254, https://doi.org/10.7326/0003-4819-145-4-200608150-00004.

[10] Denic A, Glassock RJ, Rule AD. Structural and Functional Changes With the Aging Kidney. Adv Chronic Kidney Dis. 2016 Jan;23(1):19-28. doi: 10.1053/j.ackd.2015.08.004. PMID: 26709059; PMCID: PMC4693148.

Appendix: Nephrology Terms

Glomerulus[a-1]: The functional unit of the kidney that filters the blood allowing the body to maintain homeostasis by ridding the body of toxins carried in the blood and maintaining the concentration of key electrolytes in the blood.

Glomerulus Anatomy[a-1]: The glomerulus contains capillaries within Bowman's capsule which empties into the proximal tubule. The glomerular capillaries are unique in that the blood flows in through afferent arterioles and out through efferent arterioles (higher pressure than venules which collect blood from capillaries in most organs). The capillaries are surrounded by a basement membrane and Bowman's capsule is lined by its own basement membrane.

Glomerulus Function[a-1]: The function of the glomerulus is to allow solutes to diffuse across the capillary walls and surrounding basement membrane while keeping cells such as red blood cells, white blood cells, and platelets within the capillaries along with key proteins such as albumin, enzymes, and antibodies. The selective retention of proteins occurs by limiting diffusion across the capillaries and basement membrane by keeping pore sizes small relative to proteins and maintaining a negative charge on the basement membrane that repels most proteins that tend to have a predominantly negative charge. The filtrate is collected within Bowman's capsule and then drains into the proximal tubule. The function of the total glomeruli is measured by the glomerular filtration rate.

Renal Cortex[a-2]: The outer area of the kidney and cortical columns extending toward the inner kidney between the medullary pyramids. The cortex is composed of glomeruli and renal tubules.

Renal Medulla[a-3]: This is pyramidal tissue extending from the cortex and between the cortical columns. The portion of the kidney contains various specialized blood vessels and the loops of Henley. This area of the kidney is important in reabsorbing water, electrolytes, and glucose from the filtrates collected in the glomerulus and thus is urine created as the remainder of the fluid within the distal tubules which empty into the collecting tubules. The concentrated filtrate drains into the collecting tubules and eventually into the renal pelvis and empties into the renal pelvis and the ureters to the bladder.

Glomerular Filtration Rate (GFR)[a-4]: This is the measure of how much fluid diffuses across the glomerular capillaries and is collected in the proximal tubules per unit time. This can be estimated by creatinine clearance.

Creatinine Clearance (CClr)[a-5]: This is an estimate of the Glomerular Filtration Rate because creatinine is released by muscle and protein metabolism at a constant rate based on muscle mass and enters urine as glomerular filtrate and proximal tubule secretions. The serum creatinine rises as GFR decreases and the urine creatinine decreases as the GFR decreases. Therefore, Creatinine Clearance is an estimate of GFR and CClr is estimated from the serum creatinine or the urine creatinine measured over unit time (typically 24 hours)

Modification of Diet in Renal Disease (MDRD) equation[a-4]: This is an equation used to estimate GFR based on serum creatinine, age, sex, and race based on empiric data from the Modification of Diet in Renal Disease study and is:

GFR in mL/min per 1.73 m^2 = 175 x $\text{SerumCr}^{-1.154}$ x $\text{age}^{-0.203}$ x 1.212 (if the patient is black) x 0.742 (if female)

Appendix References:

[a-1] Glomerulus (kidney) - Wikipedia

[a-2] Renal cortex - Wikipedia

[a-3] Renal medulla - Wikipedia

[a-4] Glomerular filtration rate - Wikipedia

[a-5] Assessment of kidney function - Wikipedia

Supplementary datasets

The supplementary datasets with this report include the scripts (two Jupyter notebooks) for data transformation and processing, the transformed and processed datasets. All other related materials are included in the Files on IU Canvas: https://iu.instructure.com/groups/888554/files.