A New Resource for Integrated Anatomy Teaching: The Cadaver's Kidney PG (Pathology Guide)

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Abstract
The purpose of this study was to create a guide to assist students in evaluating an embalmed cadaveric kidney for pathologic lesions and to assess the guide as an effective teaching tool. Seventy-six kidneys were screened grossly and histologically for pathology. The most common pathologic incidences discovered during the screening were: neoplasms, nephrosclerosis, chronic pyelonephritis, cysts and acute kidney injury. Based on the anatomic screening, an educational resource was created and validated for content. Then, an educational intervention was performed with nursing and medical students using the guide. In both student populations, the student group that used the guide significantly outperformed the control group in evaluating organs for pathology ($p < 0.01$). These results suggest that the pathology resource can be an effective way to teach students to identify pathologic lesions in an embalmed cadaveric kidney. doi: 10.21692/haps.2017.051

Key words: kidney pathology, cadaver, gross anatomy, pathology, anatomy education

Introduction
Gross anatomy courses in health professional schools commonly involve cadaveric dissection. During these dissection activities, students often discover pathologic lesions and artifacts that are caused by the embalming process. Currently, educational resources that teach the identification of pathologic lesions are constructed from photographs of fresh (unembalmed) tissue at time of autopsy (Cooke and Stewart 2004, Riede and Werner 2004). Also, the gross characteristics that are described in pathology atlases refer to fresh tissue only, which casts doubt as to whether these resources are accurate when describing pathologic lesions in embalmed cadavers.

Although pathology is not usually taught in gross anatomy courses, the cadaver is becoming a source for integrative learning opportunities based on the pathologic lesions that are found during dissection (Chun *et al*. 2007, Alyafi *et a*l. 2012, Zhang and Fenderson 2014, Eisenstein *et al*. 2015, Wood *et al*. 2015, Geldenhuys *et al*. 2016, Rae *et al*. 2016). To complete these types of educational integration activities however, it takes a multi-disciplinary knowledge base from the standpoint of the faculty members. Faculty members who teach anatomy at health-related professional schools in the United States commonly hold a PhD or an MD degree (McCuskey *et al*. 2005). If a faculty member has a MD, they have completed training in pathology. However, training in pathology is not usually included in doctoral level training programs for anatomists (Lawrence *et al*. 2008, Brokaw and O'Loughlin 2015). Therefore, if pathology discovered in the gross anatomy laboratory is to be used for integrative learning opportunities, there may be a gap between what an anatomist knows and the resources that are available to identify and discuss pathologic lesions in an embalmed cadaver. The purpose of this study was to identify the pathologic lesions that are present in an embalmed cadaveric kidney and create an effective educational guide to assist users in identifying pathologic lesions.

Methods
The Institutional Review Board (IRB) of Louisiana State University Health Sciences Center deemed the protocol exempt from IRB oversight (IRB# 8406).
Seventy-six cadaveric kidneys were obtained from the gross anatomy laboratory after completion of the dissection process.

Collection of Data for the Construction of the Pathology Guide
Gross evaluation of the organs
A scale was used to measure the weight of each kidney in grams. The cortical surface of the organ was examined for lesions. Any discolorations, cysts, hard or soft regions were

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photographed and recorded. Any granularity or scarring of the cortical surface was noted. The renal arteries were sliced every 0.5 cm to check for the presence of eccentric or concentric stenosis. Using a cell-path knife, the kidney was cut in a frontal plane to allow for inspection of the parenchyma. If lesions were palpable but not visibly seen in the section, additional slices were cut to examine the parenchyma. One tissue sample was taken from kidney, extending from the cortical surface to the minor calyx. Additional tissue samples of lesion areas were also taken during the inspection process.

Histologic examination of organs
The tissue cassettes, disposable plastic containers used to hold and identify tissue samples, were processed and the tissues were embedded with paraffin wax using a standard overnight protocol using an Excelsior ES tissue processor. After placing the tissue in paraffin blocks using a Shandon Histocentre 3, the tissue was sectioned at five micrometers using a Leica RM 2135 microtome and manually stained with Hematoxylin and Eosin. A board certified pathologist examined the slides for histopathology (two pathologists with 10+ years experience and a senior resident). The clinicians were blinded as to the gross observations that were described with each case.

Methods of qualitative analyses
All of the gross observations were placed in categories using a qualitative content analysis approach that included both an open coding process followed by a selective coding process (see below). Content analysis is a method of qualitative research where words are coded, grouped and recoded to identify themes that exist within documents. For this process, an anatomist (PhD trained) with experience in qualitative research methodology read the written notes that were compiled after the gross and histologic evaluations. The documents were then coded in a two-phase process as described below.

Open coding process
Each individual raw observation was taken from the notes made at the time of gross examination of the kidney. The observations were listed in their original language. Then, they were grouped together based on common themes and attributes. For example, individual categories such as "brown discoloration" and "black discoloration" were grouped together into one category, "brown or black discoloration". There were three rounds of grouping until the categories could not be condensed without losing their individuality. For example, "fine granular surface" and "pitted surface" would not be grouped together because this would not allow an analysis between a granular or pitted cortical surface**.**

Selective coding process
After the grouping of observations, the list of categories was considered to be the proposed selective code. Then, using the selective coding system, the notes of the gross observations for each organ were re-read and the observations were placed in one of the categories from the selective code system. Saturation was achieved when all observations fit into a category and no additional categories were needed for completion of the analysis. The same coding process was used for the microscopic observations made by the pathologist. The most common selective codes for the gross and microscopic evaluations are presented in Tables 1 and 2.

Table 1. Most prevalent kidney gross observations

Observation	Prevalence
Reddish isolated spots/area	56.10%
Granular surface	53.70%
Outer cysts	41.50%
Lobular in shape	39%
Spider-like arteries	36.60%
Red discoloration of cortex	36.60%
Congested parenchyma	31.70%
Red spots in cortex	26.80%
Thin cortex	26.80%
Brown black discoloration / spots	19.50%

Table 2. Most prevalent kidney microscopic observations

Observation	Prevalence
Glomerulosclerosis	29.30%
Arteriolosclerosis	24.40%
Autolysis	19.50%
Acute tubular necrosis	14.60%
Chronic interstitial nephritis	14.60%
Tubulointerstitial chronic nephritis	12.20%
Coarse calcifications	9.76%
Interstitial fibrosis	4.88%
Metastatic carcinoma	4.88%
Nodular glomerulosclerosis	4.88%
Thyroidization of tubules	4.88%

Statistical analysis
A Phi correlation (φ) analysis was conducted among all categories in the selective coding systems (gross and histologic) to determine statistical significance of correlations between the categories. This statistical analysis was conducted using the Graphpad Prism 6 software program. All correlations with a p value less than 0.05 were considered significant.

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Development of the cadaver pathology guide for the kidney

After statistically analyzing all of the correlations between the gross and microscopic observations, a list of significant correlations was generated. The list was then analyzed based on basic pathologic principles to determine whether any of the correlations were indirect, or artificially created by the categorization process; those items were removed from the results. The remaining correlations were considered of importance for creating the pathology guide (Table 3).

Table 3. Significant correlations between gross and histologic observations

Primary Kidney Correlations		
Gross observation	Histologic observation	phi coefficient
Bright red inner (soft)	Acute tubular necrosis	rφ = .358)
Dilated pelvis	Chronic pyelonephritis	rφ = .696)
Fine granularity of surface	Arteriolosclerosis	rφ = .437)
-	Glomerulosclerosis	rφ = .437)
Hard lesions	Metastatic carcinoma	rφ = .696)
Pale surface	Metastatic carcinoma	rφ = .697)
Pitted surface	Metastatic carcinoma	rφ = .537)
	Nodular glomerulosclerosis	rφ = .325)
Red splotches inner and outer	Arteriolosclerosis	rφ = .367)
Red splotches on surface	Acute tubular necrosis (AKI)	rφ = .375)

Table 3: This table lists the significant correlations between the gross and histologic observations. The phi coefficient is used to detect an association between two variables. All of the significant correlations were positive, meaning that if one variable was present there was an association of another variable being present. Values represent a weak (0.3-0.5), moderate (0.5-0.7) and strong positive correlation (0.7-1.0).

Interpreting the results of the statistical analysis

The correlation between gross and microscopic observations suggested that those two observations occurred together but did not necessarily suggest any causative relationship between them. The clinically or diagnostically important correlations can do two things: assist an examiner in identifying likely microscopic observations that would be present if the gross characteristic is observed and support the current theories in the field of pathology that those gross and microscopic findings are related to each other. The correlations that were determined as having diagnostic or clinical importance are seen in Table 3. The justification for their inclusion into the pathology guide is discussed below.

There was a positive correlation between red splotches on the surface of the kidney and acute tubular necrosis (Figure 1). Acute tubular necrosis, which is one of the main factors present in acute kidney injury, is a condition that commonly results from either severe hypo-perfusion of the kidneys or exposure of the tubules to toxic elements (Kumar *et al*. 2014). The tubular epithelium of the kidney is particularly sensitive to ischemia and toxins, and the acute damage that ensues as a result of this exposure causes severe renal dysfunction. Clinically, the dysfunction can progress to acute kidney injury that may be fatal if not treated aggressively (Bellomo *et al*. 2012).

Red splotches on the surface and inner parenchyma of the kidney were also correlated with another condition, arteriolosclerosis. Both acute tubular necrosis and arteriolosclerosis are conditions that probably involve a disruption in the normal renal blood flow. The impaired circulation of the kidney may inhibit the distribution of embalming fluid during the embalming process. The artifacts (red splotches) did not histologically resemble any pathology, although 60% of the kidneys that were poorly preserved had these red discolored regions. Therefore, the red discolorations probably are a sign that the kidney had impaired blood flow. The statistical correlation of the red discolorations with two diseases that involve impaired circulation as a mechanism of the disease development may nonspecifically highlight the kidney's circulatory dysfunction.

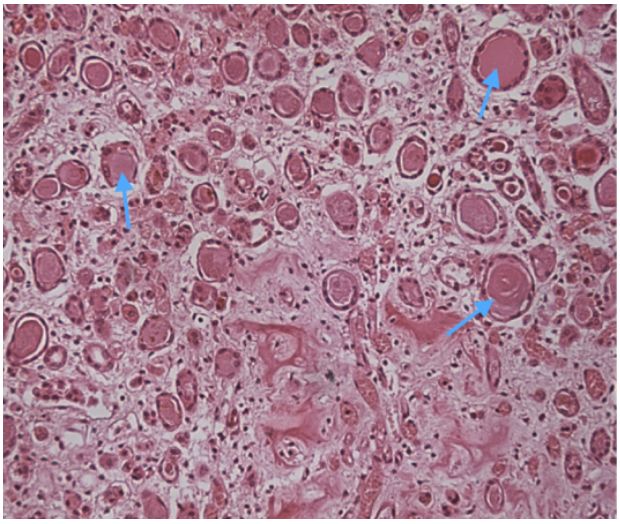

Figure 1. Acute Tubular Necrosis. The histologic presentation of acute tubular necrosis with desquamation of epithelial cells into the tubular lumen.

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The observation that the kidney surface was deeply pitted and distorted was positively correlated with both nodular glomerulosclerosis, and metastatic carcinoma. It is well documented that the surface of the kidney can be an indicator of renal disease (Kumar *et al*. 2014). In many diseases of the kidney, the normal smoothness of the cortical surface is replaced with scars that give the kidney an irregular contour. Nodular glomerulosclerosis, which is a specific sign of diabetic nephropathy, tumors and chronic pyelonephritis cause chronic injury to the kidney's architecture that can result in diffuse scarring. In addition, tumor growth is highly irregular and can cause distortion of the kidney's overall shape.

A pale surface was positively correlated with metastatic carcinoma (Figure 2). Due to the small sample size in our population, the only tumors that were present were metastatic carcinoma. Disruption of the normal renal blood flow as a result of the tumor most likely resulted in the pale-appearing cortical surface. This paleness is most likely non-specific to the fact that the tumors were metastatic, because a primary renal cell carcinoma would most likely also cause blood flow disruption.

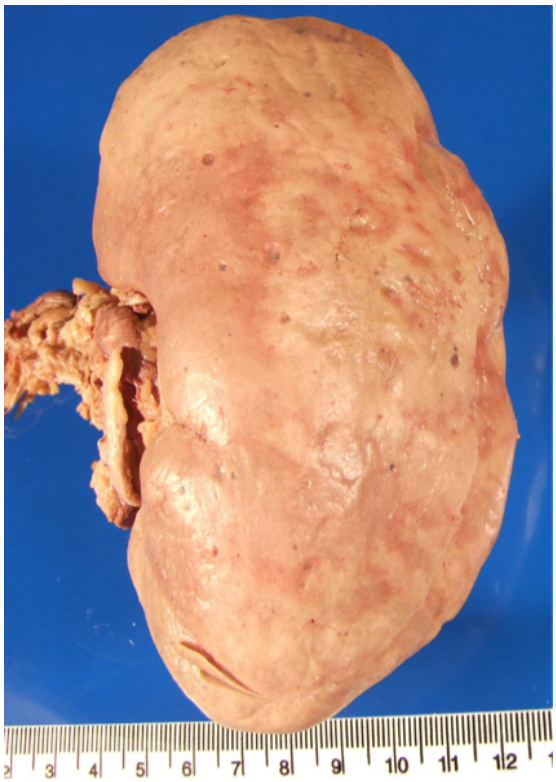

Figure 2. Pale cortical surface of the kidney. The pale cortical discoloration of a kidney with metastatic cancerous lesions.

In addition to the pale surface, the presence of the renal tumor was also positively correlated with hard lesions in the parenchyma. As in other organs, neoplasms of the kidney are usually hard lesions due to the density of the tissue. This characteristic was present in both of the kidneys where tumors were present, but was not observed in any other kidney. Therefore, hard lesions are most likely a dependable marker for the presence of tumor.

A dilated renal pelvis was positively correlated with the presence of chronic pyelonephritis (Figure 3). Chronic pyelonephritis is a disease of the renal interstitium that involves chronic inflammation and fibrosis (Kumar *et al*. 2014). Of the renal interstitial diseases, chronic pyelonephritis is the only one that involves damage to the calyces. Overall, urinary obstruction is the most frequent cause of this condition resulting in permanent dilation of the renal pelvis.

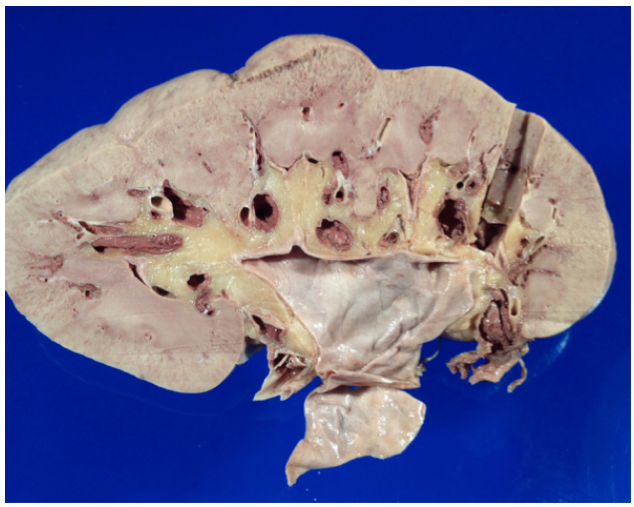

Figure 3. Dilated Pelvis. The gross presentation of a kidney with a dilated pelvis due to chronic pyelonephritis**.**

There was a positive correlation between a bright red inner surface of the kidney and acute tubular necrosis. Acute tubular necrosis was previously defined (see first primary correlation for the kidney). The bright red inner areas were most likely areas of necrosis that received insufficient amounts of the embalming fluid and, subsequently, experienced autolysis. Acute tubular necrosis is a common contributing factor in the renal failure patient, and this relationship between the gross and histologic observation is most likely non-specific to severe renal injury.

Fine granularity of the cortical surface was positively correlated with both arteriolosclerosis and glomerulosclerosis. This condition is called nephrosclerosis (Kumar *et al*. 2104) (Figure 4). Arteriolosclerosis involves the proliferation of the endothelial cells of small arteries and arterioles in the kidney or the deposition of hyaline deep to the endothelial layer in the same vessels (Figure 5). Hypertension is a common cause of arteriolosclerosis, inducing arterial remodeling and the deposition of extracellular proteins such as hyaline. In early phases, arteriolosclerosis does not impair blood flow within the affected vessels. However, as the disease progresses, the blood vessel's ability to remodel is reduced and the lumen may become obstructed. The obstruction results in decreased blood flow to the glomerulus, renal tubules, or both depending on the location and severity of obstruction. The destruction of the small blood vessels in the cortex causes

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atrophy and fibrosis of the cortex that causes changes in the cortical surface of the organ seen as a fine granularity. The subsequent damage that results from arteriolosclerosis is varied, although glomerulosclerosis is a common disease that accompanies arteriolosclerosis. This is probably why glomerulosclerosis was also positively correlated with the appearance of a granular cortical surface. Glomerulosclerosis is a term that means sclerosis, or scarring, of the glomerulus. Infection, which causes glomerulonephritis, is a common cause of glomerulosclerosis, as is diabetes, reflux nephropathy, and drug toxicity (Kumar *et al*. 2014).

Glomerulosclerosis can be focal, which means that it only affects some of the glomeruli, or global which means that it affects the glomeruli more diffusely. The end effect of glomerulosclerosis regardless of its cause is decreased functioning renal tissue, induces changes within the kidney's normal architecture. Compensatory mechanisms involve enlargement of the still functioning glomeruli and short-term increases in the glomerular filtration rate. Although glomerulosclerosis often accompanies arteriolosclerosis, because it can be a result of disease progression, the granularity of the surface is most likely a result of fibrotic scarring of the cortex due to small vessel damage than it is a result of damage to the glomeruli.

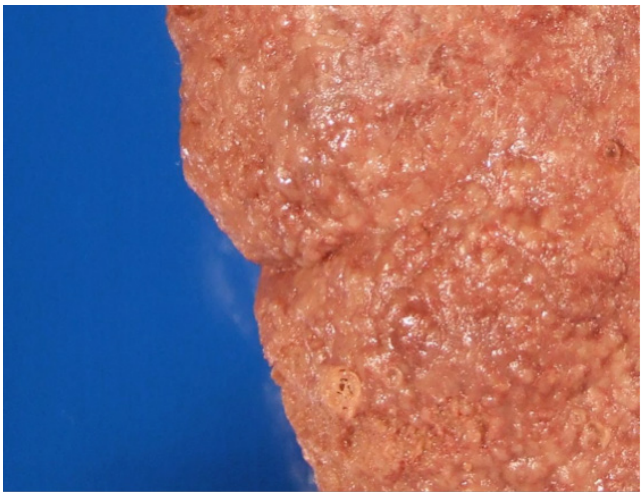

Figure 4. Nephrosclerosis. The cortical surface of the kidney has a fine granularity in nephrosclerosis.

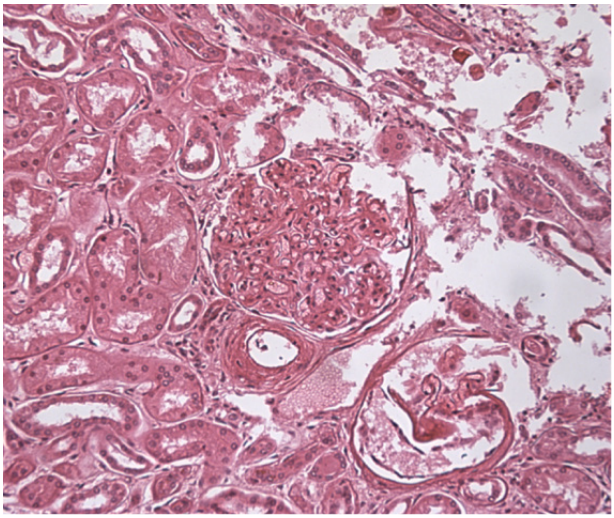

Figure 5. Arteriolosclerosis. In the center of the photomicrograph, there is a glomerulus with a sclerotic arteriole.

Generation of the guide

To assist individuals who are dissecting in the gross anatomy laboratory, it was pertinent to explain the common gross abnormal appearances of the kidney regardless of whether the abnormal appearances were due to pathology or artifact. The surface of the cortex can be considerably variable, and this variability can be used to estimate the general level of renal health. Although the estimation of renal health is nonspecific, the presence of smoothness can direct the observer to a conclusion that the kidney was not under chronic stress. The presence of fine granular imperfections may point the observer towards the conclusion that the kidney was under some sort of chronic vessel destruction, such as arteriolosclerosis. The presence of deeper surface distortions may indicate a larger chronic issue (chronic pyelonephritis, diabetic nephropathy) or the presence of tumors, all of which can be confirmed by other findings. If the observer does not have the ability to histopathologically confirm a diagnosis, then at least the general categorization of the surface features may give them more information toward the cadaver's overall renal health.

In addition to the cortical surface features, the presence of red discolorations, both bright red and the more subdued red splotches, can be an indication of acute kidney injury. Although the red discolorations are not histologically different from the normally pigmented cortex, grossly these areas are very noticeable. The gross observation may be an indication, according to the statistical support, that the kidney incurred a non-specific acute insult.

As in other organs, the presence of hard lesions is an indication of tumors, although the type of tumor will not be identifiable without histopathologic confirmation. Other characteristics that accompanied the tumors were an overall distortion of the kidney's surface and paleness of the cortical surface.

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These observations, although they are general, serve to assist the examiner to confirm the presence of tumor if access to histology is not possible.

There were also a large percentage of the kidneys that exhibited a pattern of coloration in the cortex that appeared "speckled". Histologically, there was no difference in these cases compared to other cases that lacked this discoloration. It is important to explain these abnormal characteristics as being artifact so that the observer does not confuse their presence with the presence of pathology.
Although cysts were common, they did not correlate with the presence of any renal pathology. Even so, their presence should be explained as being benign and non-specific in the guide to provide an explanation of their occurrence to the observer. Although there were no nephrolithiasis (kidney stones) in this study population, their presence should be explained in the guide to allow for identification in other populations when their presence is encountered.

Content validation of the guide

Content validation of the guide was performed by pathologists (n=3) and students (n=6; three second-semester nursing student and three second-year medical students). The guides were reviewed for the following categories: clarity in wording, relevance of items, use of standard English, absence of biased words or phrases, formatting of items, clarity of instructions (Fowler 2002). The content validation forms were qualitatively analyzed to identify themes in the reviewers' comments. The major suggestions were to add definitions to the beginning or end of the guide for selected terms and to add elaboration on the instructions.

Evaluation of the Effectiveness of the Pathology Guide

At Louisiana State University Health Sciences Center, both medical and nursing students take a gross anatomy laboratory that involves cadaver dissection. In addition, both student populations also take a course in pathology in their second year of study. After the students completed dissection during their gross anatomy course, but before they were enrolled in pathology, students were recruited to participate in a short educational intervention to measure the effectiveness of the pathology guides as a teaching resource.

Medical (n=87) and nursing (n=84) students were asked to use the guides or a definition sheet to identify pathology when examining cadaveric kidneys. Cadaveric specimens were arranged at seven stations around the laboratory. The students were assessed on their ability to correctly identify the following pathologic lesions: acute kidney injury (AKI), nephrosclerosis, neoplasms and chronic pyelonephritis. Half of the students used the provided pathology guide to assist them in their evaluation of the organ (experimental group) and half of the students had a laboratory guide that only included definitions of the pathologic terms (control group).

The control group scores were compared to the experimental group scores by performing a t-test using Graphpad Prism 6 software program. Effect size was estimated by calculating Cohen's d. The internal consistency of the assessment was determined by calculating KR-20.

Results

The group using the pathology guide, in both populations, had a higher average percentage of items correct than the control group ($p < .001$; medium effect size) (Figure 6). The internal consistency of the assessment was KR-20= 0.50, which is a good level for an instructor-made assessment. For the nursing population, the control group scored 36% correct for the control group and 51.30% correct for the experimental group. For the medical student population, the control group scored 45.7% correct for the control group and 64.7% correct for the experimental group. The results suggest that the pathology guide significantly improved student ability to accurately identify pathologic lesions in cadaveric kidneys, even after only 20 minutes of use. The students did not have any other direction or instruction in using the guide or evaluating the kidney besides the printed guide itself at the station.

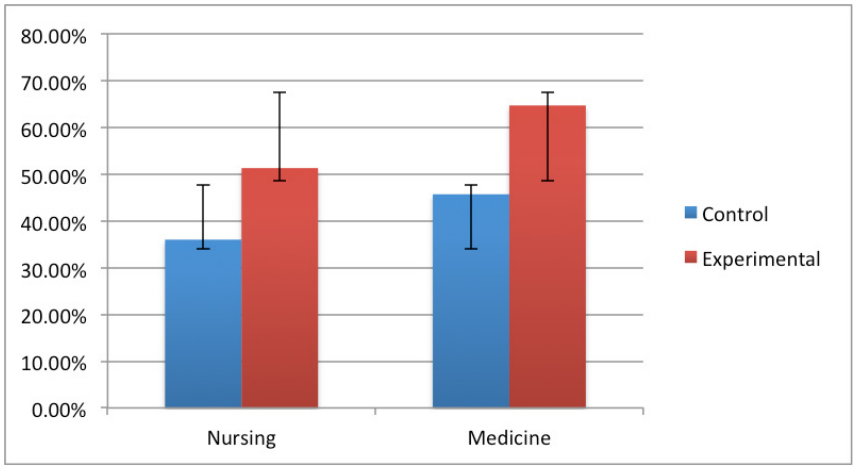

Figure 6. Assessment scores for nursing and medical student population.
In both populations, the experimental group was significantly higher than the control group, $p<0.01$. Values represent the percent of the total number of questions the student got correct.

Discussion

Results from this anatomic screening suggest that the most common pathologic lesions of the kidney that can be identified in embalmed cadavers are: renal neoplasms, nephrosclerosis, chronic pyelonephritis, cysts and acute kidney injury. Discoloration of the cortical surface and medullary regions were the most common observed artifacts from the embalming process. Previously, there have been small

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anatomic studies that describe renal pathology in embalmed cadavers. One gross survey of twelve cadavers found renal cysts and hydronephrosis (Wood *et al*. 2010) and another anatomic survey of seventeen cadavers reported renal cysts, renal stones, and a renal neoplasm (Wood *et al*. 2015). A larger anatomic survey of thirty-six embalmed cadavers reported the presence of renal cysts, renal cancer, and renal atrophy (Magrill *et al*. 2008). However, the most complete study (n=127) that involved histopathologic confirmation of many incidences of pathologic lesions suggests the prevalence of renal lesions to be: chronic pyelonephritis (18.9%), renal tuberculosis (10.2%), hypertensive nephrosclerosis (6.3%) acute pyelonephritis (2.4%) and malignant renal neoplasms (1.6%; Geldenhuys *et al.* 2016). The results in this current study are consistent with the previous findings of Geldenhuys *et al*., except that there were no observed cases of renal tuberculosis. This discrepancy may be regionally connected, because the previous study was conducted in South Africa that the current study was conducted in New Orleans, Louisiana.

After the guide was constructed, its effectiveness as a teaching resource was assessed. In a short twenty-minute session, students evaluated organs for the presence of renal pathologic lesions using either our guide or a definition sheet prepared from pathology resources. The results indicate that even after a short session and no further instruction, the guide was effective at statistically improving student assessment abilities. It is plausible that given more time and perhaps even supplemental instruction by a faculty member, that students could quickly learn how to detect renal pathologic lesions in the embalmed cadaver in which they are dissecting.

The ability to detect renal pathologic lesions can impact health professional education programs in several ways. The ability to take advantage of learning opportunities such as pathologic lesions, gives faculty the opportunity to practice integration between basic science disciplines such as anatomy, physiology, histology and genetics. Students can also get exposure to lab experiences that involve histology and pathology that is currently declining in medical education.

Virtual histology databases have decreased face-to-face lab time for both of these courses and availability for an autopsy experience has also declined, further limiting students exposure to pathologic organs. On an ethical level, the identification and teaching of pathologic lesions in the willed body donor during anatomic dissection serves to deepen the impact that the willed body donor has on the advancement science. In turn, this may come closer to the donors intended impact that he/she wanted their gift to have on the field.

The authors would like to acknowledge the individuals who donated their bodies for the advancement of science. Their contribution made the development of these resources possible.

The Cadaver Kidney PG guide is freely available for download on LSUHSC's website at: http://virtualhumanembryo.lsuhsc.edu/GIFT/PathGuides%20-%20Copy.html.

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