

# Assessment of the Efficacy and Potential Complications of Transjugular Liver Biopsy in Canine Cadavers

A.S. Levien, C. Weisse, T.A. Donovan, and A.C. Berent

**Background:** Transjugular liver biopsy (TJLB) is used in humans at risk of bleeding. There are no reports of its use in veterinary medicine.

**Objective:** To assess the efficacy and potential complications of TJLB in canine cadavers, and compare with samples obtained via needle liver biopsy (NLB) and surgical liver biopsy (SLB).

**Animals:** Twenty-five medium and large breed canine cadavers.

**Methods:** Prospective study. TJLBs were procured through the right jugular vein. After biopsy, intravenous contrast and gross inspection were used to assess the biopsy site. Minor and major complications were recorded. NLBs and SLBs were then obtained. Histopathology was performed, and TJLB and NLB were compared for number of complete portal tracts (CPTs), length, and fragmentation. Pathologic process and autolysis were assessed in all samples.

**Results:** All TJLBs yielded liver tissue. The proportion of minor complications was 12/25 (48%), and major complications 16/25 (64%); 13/16 (81%) of the major complications were liver capsule perforation. In 21/25 (84%), the histopathology in the SLB was reflected in the TJLBs. For cases with minimal autolysis, median number of CPTs in TJLBs was 7.5, compared with 4 in NLBs ( $P = .018$ ). Median length of TJLB specimen was 28 mm compared to 22 mm in NLBs ( $P = .007$ ). Fragmentation rate was median of 1.25 for TJLB compared to 1.50 in NLBs ( $P = .11$ ).

**Conclusions and Clinical Importance:** TJLB is technically feasible and achieves comparable results to NLB and SLB. The number of complications, in particular liver capsule perforation, was greater than expected. Further studies are indicated before clinical use is recommended.

**Key words:** Dog; Hepatic; Histopathology; Minimally invasive.

Liver biopsy is considered the gold standard for the diagnosis and management of liver disease.<sup>1</sup> In veterinary medicine, options for the procurement of liver tissue include fine needle aspiration, exploratory celiotomy, percutaneous needle liver biopsy (NLB; blind or imaging guided), and laparoscopic liver biopsy.

Both NLB and transjugular liver biopsy (TJLB) are commonly utilized minimally invasive techniques for liver biopsy in human medicine, particularly in coagulopathic patients with diffuse liver disease. Advancement in interventional radiologic skills, as well as improvements in equipment, has resulted in TJLB yielding comparable samples to NLB.<sup>2</sup> The main indications for TJLB include humans with moderate-to-severe ascites, small hard cirrhotic livers, morbid obesity, severe coagulopathies (prolonged prothrombin time, partial thromboplastin times, international normalized ratio (INR)  $\geq 1.5$ –2, thrombocytopenia:  $<60 \times 10^3/\mu\text{L}$ ), and medical conditions such as hemophilia.<sup>3–5</sup>

The theoretical benefit of TJLB is reduced risk of hemorrhage because a biopsy specimen is acquired through the hepatic vein, and thus any bleeding from

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## Abbreviations:

CPT	complete portal tract
CT-A	computed tomography angiogram
CVC	caudal vena cava
INR	international normalized ratio
NLB	needle liver biopsy
PPT	partial portal tract
SLB	surgical liver biopsy
TIPS	transjugular intrahepatic portosystemic shunting
TJLB	transjugular liver biopsy
TPT	total portal tract

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the puncture site remains in the systemic venous system, thereby avoiding intraperitoneal blood loss through liver capsule penetration that occurs with other techniques.<sup>4,6,7</sup> Patient discomfort might also be reduced after the procedure because the diaphragm is not irritated by intraperitoneal blood and the technique is minimally invasive.<sup>6</sup> In addition, other procedures can be performed concurrently via the transjugular approach including measurement of hepatic venous wedge pressure, placement of sampling catheters, and in humans, the transjugular intrahepatic portosystemic shunting procedure, which is a technique used to treat portal hypertension.<sup>8</sup>

To assess the quality of TJLB samples, physicians have assessed factors including length, width, fragmentation rate, and number of complete portal tracts (CPTs) and compared these with the traditional percutaneous NLB.<sup>1,9</sup> The number of CPTs is considered to be the best method of assessing the adequacy of a liver biopsy.<sup>1,10</sup> In humans, samples  $\geq 15$  mm length that contain at least 6 CPTs are sufficient for diagnosis of

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diffuse or chronic liver disease, whereas specimens 20 mm length and 11 CPTs are optimal for staging and grading chronic viral hepatitis.<sup>1,2,10</sup> Guidelines for optimal length of specimen and number of hepatic portal tracts in dogs have not been established.

An advantage of TJLB is that the biopsy instrument may be passed (deployed for biopsy) multiple times without theoretically increasing the risk of complications.<sup>10</sup> Although 3 passes of the TJLB device has been demonstrated to be sufficient, 4 passes per patient has been found to be superior in obtaining a longer sample with more CPTs without an increase in complication rate.<sup>1,10</sup> This is different from NLB, where in humans, only 1 or 2 passes (biopsies) per patient is recommended, as any increase in biopsy number is associated with increased risk of hemorrhage.<sup>11–13</sup> The World Small Animal Veterinary Association Liver Standardization Group recommends 2 to 3 well-taken NLB samples as adequate for histopathology in dogs.<sup>14</sup>

Transjugular liver biopsy was first described experimentally in dogs in 1964 utilizing a coil spring derived from a spout cleaner.<sup>15</sup> Significant improvements have led to the commercial availability of adult (9 French) and pediatric (7 French) transjugular access sets and associated biopsy instruments for humans. Children as small as 8 kg and as young as 11 months have undergone TJLB with few complications reported.<sup>5,7</sup> Although TJLB is utilized in human medicine, TJLB has not been investigated in veterinary medicine. Therefore, the aims of this study were to assess the efficacy and potential complications of TJLB in canine cadavers, and to compare the samples obtained with other options including NLB and SLB. It was hypothesized that TJLB would yield comparable samples to NLB and SLB without complications.

## Materials and Methods

Canine cadavers greater than 15 kg were recruited. The dogs were euthanized at the Animal Medical Center (AMC) for reasons unrelated to this study. Consent for cadaver use was obtained from owners, and the study was approved by the Institutional Animal Care and Use Committee. Patient age, breed, sex, weight, and reason for euthanasia were recorded. Cadavers were stored at 0°C (32°F) for up to 48 hours before the procedure. All biopsies were performed once the bodies had been allowed to adjust to room temperature. Before undertaking the study, the AMC computerized digital imaging database was reviewed for computed tomography angiograms (CT-A) of the abdomen from medium- and large-breed dogs. The CT-As were analyzed to determine whether there was sufficient liver parenchyma (>20 mm, which is the size of the throw of the biopsy needle) to enable safe intrahepatic biopsy from the hepatic veins. From these measurements, sufficient liver was observed, justifying progression with the study. However, the authors suspected that the left lateral lobe would be the safest to biopsy as this is the largest liver lobe in the dog and is not adjacent to the gall bladder.

## Equipment

Equipment (Fig 1) included donated unused transjugular access and biopsy sets with 7 French introducers and 18-gauge

(G) biopsy needles.<sup>a,b</sup> Both systems used a spring loaded sheathed cutting needle (“Tru-cut” style). Either the Cook or Dextera system was used based on availability of the device. The device used in each case was recorded. To perform NLB, a single-action 18-G biopsy needle was utilized.<sup>c</sup> Fluoroscopy was performed using a commercially available portable C-arm unit.<sup>d</sup> Because of limitations in equipment, undamaged TJLB and NLB biopsy devices were reused as appropriate.

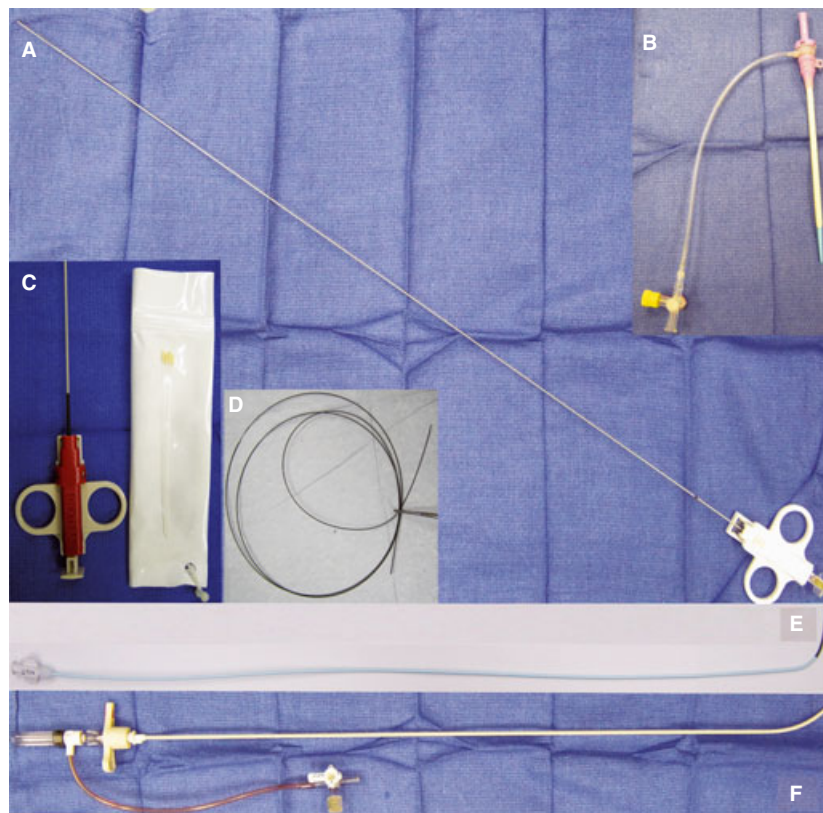
## Technique

The cadavers were positioned in dorsal recumbency with the C-arm positioned in a ventro-dorsal (VD) viewing position (Fig 2). Appropriate VD alignment was checked fluoroscopically and adjusted as required. To maintain position, the fore limbs and hind limbs were abducted out of the field and taped to the table. The head was extended and rotated slightly to the left, such that the right jugular vein was centered toward the midline. The ventral cervical region and abdomen were clipped. The procedures were performed by a single operator (A.S.L.) with minimal prior interventional radiology training to better reflect anticipated efficacy and potential complications if more routinely implemented.

A jugular cut-down was performed to the right jugular vein. The vein was cannulated using a modified Seldinger technique (single puncture) and a 9Fr vascular access sheath was placed. Under fluoroscopic guidance, a straight or angled hydrophilic 0.035 inch guidewire and 5Fr multipurpose angled (MPA) catheter<sup>a</sup> were manipulated through the right atrium and caudal vena cava (CVC) into the desired hepatic vein. In the first 8 cases, the left hepatic vein was selected, as the authors hypothesized that this would be most suited for biopsy. When it was apparent that complications occurred on the left side, the right and caudate hepatic veins of the liver were selected. In a number of cases, gas distension of the gastrointestinal tract caused shifting of the liver in which case the most easily accessed hepatic vein was selected.

Angiograms with digital subtraction were performed as needed to facilitate catheter placement.<sup>c</sup> Once the desired position was achieved, the hydrophilic guidewire was exchanged for a 150–180 cm 0.035 inch Amplatz extra or super stiff guidewire. The MPA catheter was removed and the transjugular introducer sheath/stiffening cannula with a dilator within was advanced over the guidewire and positioned within the hepatic vein. The dilator was then removed followed by the guidewire. The directional arrow on the introducer was used to point in the direction of the greatest hepatic bulk and away from the gall bladder. Gentle forward pressure was applied with the introducer. The biopsy needle was then loaded and advanced into the access set until the appropriate position was achieved, and then deployed. Four specimens were retrieved as per recommendations in humans.<sup>10</sup> To minimize fragmentation of the biopsy samples, tissue removal swabs<sup>a</sup> were used to place the samples in a cassette and then 10% formaldehyde solution. After each biopsy, contrast mixed with Diff-Quik solution III<sup>f</sup> was injected to assess for liver capsule perforation. This was done using digital subtraction. After a contrast study, water was injected through the introducer to dilute contrast remaining in the vessels. Through a midline celiotomy, which was performed after the first biopsy, the location of the TJLB needle was palpated and the respective liver lobe identified and recorded. Also, the liver was repeatedly examined after each biopsy to verify the presence/absence of capsule perforation.

After each TJLB, complications were logged. Complications were classified as minor and major. Minor complications were those which would likely not have affected patient outcome, whereas major complications were those which could have potentially led to patient morbidity or mortality.



**Fig 1.** Transjugular liver biopsy equipment: (A) Transjugular biopsy needle, (B) 9 French vascular access sheath, (C) Close-up of transjugular biopsy needle and tissue removal swabs, (D) 0.035 inch 150 cm hydrophilic guidewire, (E) 5 French multipurpose angled catheter, (F) 7 French introducer with protective sheath.

Directly following the TJLB, NLB was performed. This was done by advancing the biopsy needle directly into the liver with the abdomen open. The reason for performing the procedure with the abdomen open was to mimic the accuracy achievable by a board-certified radiologist who would normally perform this procedure. Two samples were taken as a balance between the recommendations in veterinary and human medicine, which suggest from 1 to 3 biopsies.<sup>11,12,14,16–18</sup> Finally, an SLB no smaller than 1 cm<sup>3</sup> was taken from a representative section of the liver.<sup>14</sup> If any pathology was noted grossly, the biopsy was taken from this region to mimic surgical accuracy and therefore not to miss any pathology.

The TJLBs, NLBs, and SLB were fixed in formalin for a minimum of 24 hours. The TJLBs and NLBs were then measured for total length (adding up the fragment lengths using a ruler), and the number of tissue fragments was counted.<sup>1,9,10</sup> The biopsy was then embedded in a paraffin block, and serial sections 5 µm thick were cut and stained with hematoxylin and eosin (H&E). All biopsies were read by a single pathologist (T.A.D.) who was not blinded to the origin of the biopsies.

Portal tracts in each of the TJLB and NLB were counted as described in other studies.<sup>1,10,19</sup> Briefly, portal tracts were considered complete portal tracts (CPT) when at least 3 quarters of the circumference and 3 luminal structures (portal vein, hepatic artery and bile duct) were visible.<sup>1,10</sup> A partial portal tract (PPT) was defined as incomplete when its circumference was incomplete and contained any 2 luminal structures.<sup>1,10</sup> The total number of portal tracts (TPT) was the summation of complete and partial portal tracts. Histopathology of each liver biopsy was interpreted, and then the pathologist subjectively assessed (1) whether

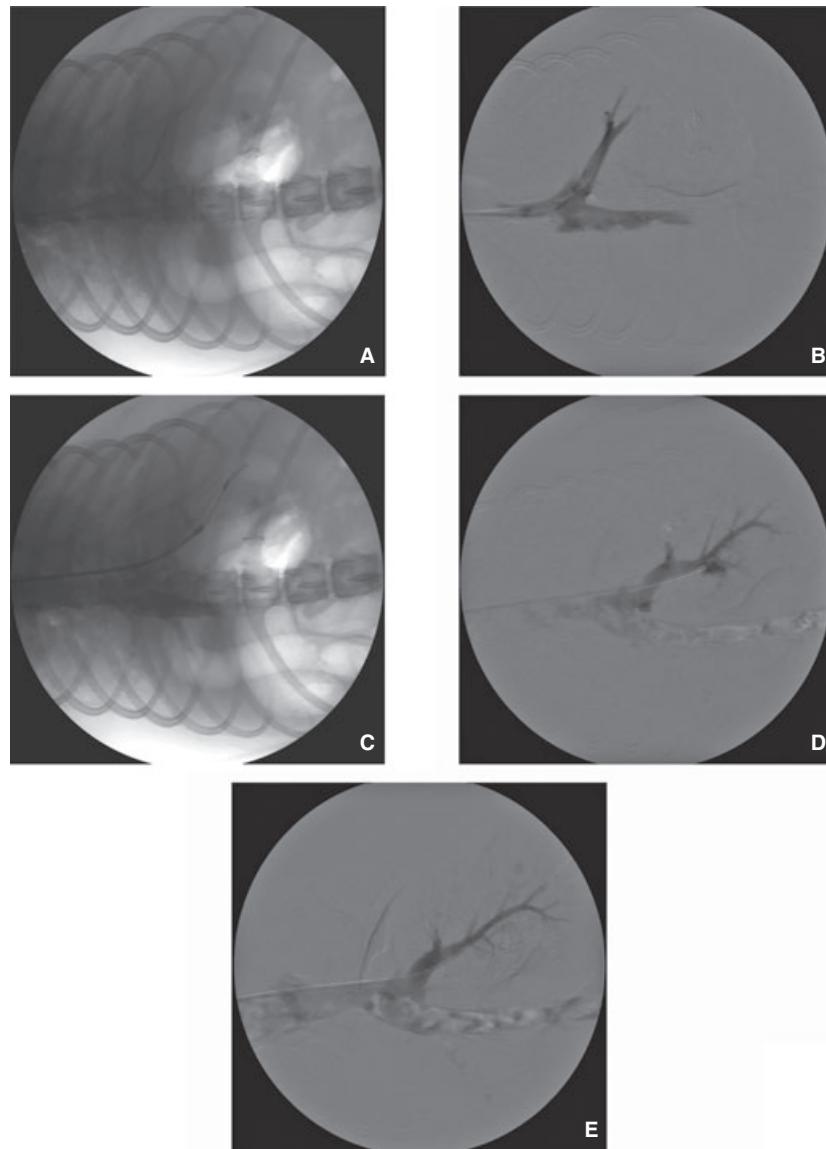
pathology seen in the SLB was reflected in the TJLB, (2) whether the TJLB was inferior, superior, or equivalent to the NLB, and (3) the degree of autolysis observed, which was graded 1 (mild autolysis) to 3 (severe autolysis).

Descriptive statistics were used to compare NLB and TJLB in terms of biopsy length, complete portal tract number, fragmentation rate, and pathologist assessment. Fragmentation rate was defined as the total number of biopsy cores (fragments) divided by number of samples. All statistical analysis was conducted by a commercially available statistical package<sup>g</sup> and a type 1 error probability of 0.05 was utilized as an indication of statistical significance. Normality was assessed using a frequency distribution histogram as well as skewness and kurtosis values. As data were not normally distributed, nonparametric tests were used. All categorical variables were analyzed by a chi-square test for independence, whereas continuous variables were assessed by the Mann-Whitney *U*-test or Kruskal-Wallis test as appropriate.

## Results

### Dogs

Twenty-five medium- and large-breed canine cadavers were recruited for the study. Age was median 12 years (range 1–19 years) and weight was median 27.2 kg (range 15–68 kg). Sex distribution included 3 male intact, 13 male neutered, 1 female intact, and 8 female neutered. The TJLB obtained liver tissue in 25/25 (100%) of cases. This included biopsies from left



**Fig 2.** (A) Catheterization of the left hepatic vein, (B) angiogram of the left hepatic vein, (C) introducer placed into hepatic vein over guidewire, (D) angiogram pre-TJLB, (E) angiogram post-TJLB demonstrating no contrast extravasation.

hepatic vein: 10 from the left lateral lobe, 5 from the papillary process (where the papillary process meets the left hepatic vein); right hepatic vein: 7 from the right lateral lobe and 2 from the right medial liver lobe; and caudate hepatic vein: 1 from the caudate process of caudate liver lobe. The Cook system was used in 5 cases and the Dexter system in 20 cases. Although not officially recorded, catheterization of the hepatic vein became faster during the study leading to a decrease in the procedure time. An estimate of TJLB procedure time was 20 minutes in the cadavers once experience was gained with the technique.

### Complications

**Major Complications.** Nine cases had no major complications (36%) and these included 4 biopsies from

the left hepatic vein and 5 biopsies from the right hepatic vein.

Sixteen cases had major complications (64%), which included perforation of the liver capsule in 13, perforation of the CVC in 1, perforation of the gall bladder in 1, and perforation of the left hepatic vein in 1. Of the 16 major complications, 10 were taken from the left hepatic vein, 5 from the right hepatic vein, and 1 from the caudate hepatic vein. There was no statistically significant association of a complication with which hepatic vein was selected ( $P = .95$ ).

**Minor Complications.** Twelve minor complications (48%) were recorded during the TJLB. These included 5 cases in which the azygos vein was catheterized when attempting to gain access to the CVC. There were 3 cases in which extreme difficulty was encountered gaining access to the CVC from the right atrium. In one of



the 3 dogs, this was caused by severe kinking of the CVC secondary to abdominal distension (which was caused by a severely distended urinary bladder). In 2 cases, severe gaseous distension of the stomach was noted causing compression of the CVC and hepatic veins complicating access. There was 1 case where the phrenic vein was inadvertently catheterized and another case where the TJLB system was not an optimal length for the size of the dog (68 kg Mastiff).

No significant difference in major or minor complication rate was observed between the first half of the procedures when compared with the second half ( $P = .10$ ).

### ***Autolysis Scores***

Median autolysis scores for TJLB and NLB were 2 (mean 1.96). TJLB specimens that were less autolysed (autolysis score 1) had significantly higher CPT counts compared with those that were more autolysed (autolysis score 3;  $P = .003$ ). Similarly for TJLB, PPT and TPT counts were significantly higher in samples less autolysed ( $P = .001$  and  $P < .001$ , respectively). For TJLBs with an autolysis score of 1, 6/8 (75%) had  $\geq 6$  CPTs, and 2/8 (25%) had  $\geq 11$  CPTs.

### ***Histopathology***

Review of the histopathology showed that in 21/25 (84%), the changes in the SLB were comparable to those observed in the TJLBs. Evaluating TJLB and NLB, the pathologist subjectively assessed that the TJLB was superior in 5 (20%), inferior in 5 (20%), and equivalent in 15 (60%). Considering samples only with an autolysis score of 1, the histopathology of 8/8 (100%) TJLBs contained similar histologic changes as compared to the SLB. Comparing TJLB with NLB with an autolysis score of 1, the TJLB was superior in 1 (13%), inferior in 0 (0%), and equivalent in 7 (88%).

Histopathology revealed nonspecific liver changes in all except for 3 cases. In these cases, neoplasia was detected on liver biopsy. For SLB, neoplasia was identified in each case, whereas for TJLB and NLB, neoplasia was detected in 2 of 3 cases each.

### ***TJLB versus NLB***

For TJLB with an autolysis score of 1, CPT counts were median 7.5 (range 3–13). For NLB with autolysis scores of 1, CPT count was median 4 (range 2–7). In relation to TPTs, for TJLB with autolysis scores of 1, there was a median of 18.5 (range 9–25) portal tracts, whereas for NLB, median TPT count was 6.5 (range 4–12). Comparing TJLB with NLB samples with autolysis scores of 1 revealed that TJLBs had significantly higher median CPT ( $P = .018$ ), PPT ( $P = .004$ ), and TPT ( $P = .002$ ) counts than NLB. Similarly, median length of the TJLB (28 mm; range 10–40 mm) was significantly longer than NLB (22 mm; range 7–33 mm;  $P = .007$ ). There was no significant difference in

median fragmentation rate between TJLB (1.25 fragments; range 0.75–2.50) and NLB (1.50 fragments; range 1.00–3.50,  $P = .11$ ).

### **Discussion**

The results of this study showed that transjugular liver biopsies were technically feasible, but associated with a high number of complications. In this study, the major complication rate was 64% and the minor complication rate 48%. This suggests that the procedure might be of considerable risk to the live animal. However, 81% of the major complications were liver capsule perforation, which always occurs during NLB and is most often subclinical in human TJLB.<sup>6</sup> In terms of quality of biopsy specimen, the TJLB was significantly longer, and had significantly more CPTs than the NLB. On histopathology, the TJLB correlated with the gold standard (SLB) in the majority (84%) of cases. Therefore, the results of the study suggest that although TJLB is efficacious, it does not appear to be without risk in dogs.

In an attempt to prevent complications, computed tomography angiograms (CT-A) in medium and large dogs were reviewed before the study. The goal was to determine whether there was enough liver tissue at the point where the left hepatic vein bifurcated, to enable a safe biopsy. Similar measurements were made from the right and central portions of the liver. The left lateral lobe of the liver was suspected to be best suited as this is the largest liver lobe in the dog and was not adjacent to the gall bladder. In the cases that were reviewed, sufficient liver tissue (>20 mm, which is the size of the biopsy needle throw) appeared to be present.

In choosing which portion of the liver to perform the TJLB, there are essentially only 3 choices, as there are only 3 hepatic veins large enough in dogs to be routinely accessed with the TJLB introducer. The largest hepatic vein is most cranial and on the left and drains the left lateral, left medial, quadrate lobes, and part of the right medial lobe and papillary process.<sup>21,22</sup> On the right, there are 2 major hepatic veins. The more cranial vein drains the right lateral liver lobe and part of the right medial liver lobe, and more caudally located is the hepatic vein from the caudate process of the caudate lobe.<sup>22</sup> In the majority of cases, it was relatively simple to guide the MPA catheter and guide-wire deep into the left lateral hepatic vein as planned. However, it was not possible to reliably position the introducer sheath in the corresponding position of the left lateral lobe. Instead, the introducer would often drop into the branch of the left hepatic vein draining the papillary process, which is a small liver lobe. The reason for this appears to relate to the relatively large curve present on the end of the TJLB introducer in comparison with the acute angle with which the left lateral hepatic vein meets the caudal vena cava. Similar problems have been noted in some human cases.<sup>8</sup> In contrast, the introducer sheath would smoothly and reliably gain access to the 2 hepatic veins draining the

right side of the liver. The problem on the right, however, was that the caudate process is relatively small and the right medial liver lobe is adjacent to the gall bladder.

The most frequently observed complication in this study was perforation of the liver capsule, which is also the most common complication reported in people.<sup>6</sup> In humans, this complication has been reported in up to 3.5% of TJLBs, whereas in this study, perforation occurred in 52% despite the technique being virtually identical.<sup>5</sup> A reason for the relatively higher complication rate encountered in this study compared with the human literature might be attributable to anatomic differences between human and canine liver.<sup>22,23</sup> The human liver is "brick-like," having only 4 lobes and lacking the deep fissures that characterize the canine liver. In contrast, the canine liver is divided into 4 lobes, 4 sublobes, as well as 2 processes by deeply running fissures, which is thought to be an adaptation to prevent injury.<sup>22,23</sup> In our experience, it is these deep fissures that make it difficult to obtain a similarly safe corridor for TJLB, resulting in the biopsy device being close to the liver capsular surface. Because of the deep fissuring of the canine liver, we suspect that the 20-mm throw of the biopsy needle might also be relatively oversized for the canine liver, particularly when the biopsy device is not pointed centrally in a liver lobe.

In humans, capsule perforation is considered a minor complication when subclinical but a major complication when clinically significant intraperitoneal hemorrhage occurs.<sup>2</sup> Most often, capsular perforations are subclinical.<sup>6</sup> In general, treatment is not required with clinically significant bleeding in 0.35% of TJLBs.<sup>5</sup> If treatment is considered necessary, it is recommended that tract embolization with coils or gelatin sponge<sup>h</sup> be performed to prevent bleeding.<sup>2,6,9</sup> In this study, capsule perforation was considered a major complication for 2 reasons. Firstly, significant intraperitoneal extravasation was grossly observed in cases of perforation. Secondly, capsular perforation defeats the purpose of the TJLB procedure, with coagulopathic animals potentially at most risk if capsular perforation occurred. The converse argument would suggest that given the limitations of a cadaver study, defibrinated blood unable to develop a clot, and equipment, the observed capsule perforation may not have been as clinically significant as we interpreted. It is also possible that in an attempt not to overlook leakage, contrast was injected at higher pressure than normal, exacerbating the hemoabdomen. In addition, while capsule perforation occurs with NLB, it likely does not always occur through a large hepatic vein as is the case with TJLB. Further studies are required to better understand the capsule perforation complication.

If capsule perforation would have been considered only a minor complication, the major complication rate would have fallen to 3/25 (12%). These 3 complications included gall bladder, hepatic vein, and CVC perforation, which were all likely related to operator inexperience. Perforation of the CVC has been

reported only once in the human literature and was a nonfatal complication. In that case, the pediatric patient was stabilized without surgical intervention.<sup>5</sup> In this study, perforation of the CVC occurred early in the series and was attributable to technical error associated with inexperience. With proper care, this situation should be very unlikely to reoccur. Subjectively, the technique became easier during the study and the procedure time decreased significantly, although was not officially recorded. There was, however, no difference in complication rate observed between the first half of the procedures when compared with the second half.

NLB is also not a benign procedure. Inherent to the technique of NLB is liver capsule perforation, which TJLB theoretically avoids. Accordingly, the most common complication of NLB is bleeding with an incidence in dogs and cats reported in 1 study of up to 22% (relative hematocrit decrease >10% with no required intervention) with 3.5% requiring blood products or resuscitative fluids following NLB.<sup>17,20,24</sup> Other complications reported in humans, dogs, and cats include perforation of the diaphragm, gall bladder, blood vessels, needle fracture/dislocation, seeding micro organisms or tumor cells, and vagal reactions (particularly in cats).<sup>11,13,17,18,20</sup>

The most common minor complications encountered were catheterization of the azygos vein and difficulty gaining access to the liver. Catheterization of the azygos vein was readily apparent on contrast angiography and occurred relatively frequently. This is likely because, anatomically, on a ventrodorsal fluoroscopic view, the azygos vein travels in a similar plane to the CVC. This could easily be remedied by positioning the c-arm in a transverse position across the dog during caudal vena cava access; however, the protocol was not changed during the study.

Aside from vascular and hepatic perforation, there are a variety of other TJLB complications reported in the human literature. These include abdominal pain, neck hematoma, transient Horner's syndrome, dysphonia, cardiac arrhythmias, pneumothorax, and formation of a fistula from the hepatic artery to portal vein or biliary tree.<sup>3,5,9</sup> The human complication rate ranges from 1.3 to 20.2%, with a recent literature review reporting an adult complication rate of 0.6% major and 6.6% minor.<sup>2,3</sup> A higher complication rate was noted in pediatrics, which is of interest, as they are more similar in size to canines. For pediatrics, the major complication rate was 1.9% and minor complication rate 20%, which is significantly lower than the complication rates seen in this study.<sup>2</sup>

The median number of CPTs found on TJLB (with autolysis scores of 1) in this study was 7.5 (3–13), which compares well with a median 6.5 (range 3.3–28) reported in a recent human literature review.<sup>2</sup> In 2 cases in this study, zero portal tracts were noted because the TJLB contained mostly neoplastic tissue. Incidentally, the 2 cases with neoplastic tissue were considered diagnostic; however, selective mass liver biopsy is not easily performed using the TJLB

technique. Median length of the sample was 28 mm (range 10–40), which compares favorably with that reported in similar human studies, median 23 mm (range 4–44).<sup>1</sup>

For NLBs (with autolysis scores of 1), the median number of CPTs 4 (range 2–7) and length 22 mm (range 1–13) were less than the TJLBs and correlates with findings in human studies. Intuitively, TJLB should yield more CPTs than NLB if 4 versus 2 samples are taken, respectively. As we were comparing 2 different techniques, according to the recommendations of the human medical literature, this was the protocol we followed.<sup>10,11</sup> Given that CPTs are reported to be the best method for assessment of sample adequacy, it is apparent that the TJLB compares favorably to NLB, which concurs with data reported in the human literature.<sup>1</sup>

In humans, a minimum of 6 CPTs and length  $\geq 15$  mm is recommended for histologic diagnosis of diffuse liver disease, whereas  $\geq 11$  CPTs and  $\sim 20$  mm is recommended for staging and grading of chronic viral hepatitis.<sup>4</sup> In this study, for TJLBs with autolysis scores of 1, 75% of samples had  $\geq 6$  CPTs and 25%  $\geq 11$  CPTs. This compares favorably with human studies where it has been reported that 73% of samples had  $\geq 6$  CPTs and 26% had  $\geq 11$  CPTs.<sup>1</sup> Nevertheless, it is clear that there is a need for better samples to increase the number of CPTs to improve the quality of biopsy samples. In this study, it was apparent that lower numbers of portal tracts were highly correlated with a greater degree of autolysis. It is thus anticipated that live animals would yield higher numbers of portal tracts. Aside from using fresher specimens, another way to improve the number of CPTs is to obtain more samples. In humans, an advantage of TJLB is that multiple passes of biopsy device can safely be utilized to gather more samples.<sup>25</sup> This is unlike NLB, where more passes increases the risk of hemorrhage.<sup>1</sup>

In this study, we found that the 2 TJLB brands were effective, although the Dextera system appeared to have some small advantages including (1) the safety guide, which prevents overextrusion of the biopsy needle, (2) the Dextera system subjectively appeared to yield larger samples, and (3) included tissue removal swabs, which reduce fragmentation of the sample. Both systems are similar in price and available for between \$450 and \$500 per complete set. Although expensive, when considered in comparison with the costs of exploratory celiotomy or laparoscopy, the cost may be justifiable. Similarly, assuming that no complications occur, there is theoretically no need for blood products to reverse coagulopathies, which may add cost to the use of NLB.<sup>6</sup> Although reuse of the biopsy devices appears possible, further research is needed before this can be recommended.

There are a number of limitations of this study. Aside from limitations in equipment, the use of unpreserved cadavers, which had varying degrees of post-mortem autolysis, may have exacerbated complications, reduced

CPT counts, and obscured more subtle pathologic processes. In addition, it was not possible to blind the pathologist because of the processing protocol for the histopathology samples. Another limitation was that some of the pathology assessments were subjective. To overcome this limitation, objective assessments were made such as CPT counts, fragmentation, and length measurements. Lack of blood flow and the presence of blood clots increased the difficulty of passing the guide-wires and catheters, and in a number of animals, gaseous distension of gastrointestinal tract displaced the liver and CVC. Although TJLB is considered a relatively simple interventional procedure, a more experienced operator might have experienced fewer complications. Finally, there were limitations in the number of donated TJLB sets requiring that some devices be used more than once.

Future studies could repeat this procedure in research dogs to assess the safety and efficacy of the TJLB technique. Design modifications of the TJLB device could be considered including changing the diameter of the curve on the introducer (or manually shaping the device at the time of use), or creating a more flexible curved introducer to enable better access to the left hepatic vein. In designing this study, we also experimented with cup biopsy forceps deployed intravenously under fluoroscopic guidance as a means of procuring liver biopsies. Initial experience suggested that the forceps did not adequately grip and cut the vascular endothelium, although this technique could be further investigated.<sup>26</sup>

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## Footnotes

- <sup>a</sup> Dextera TLAB Patel Set, US Biopsy, Franklin, Indiana  
<sup>b</sup> Cook LABS-200 liver access and biopsy set, Cook Medical Inc, Bloomington, Indiana  
<sup>c</sup> E-Z Core, 18G biopsy needle, Products Group International Inc, Lyons, CO  
<sup>d</sup> BV Pulsera mobile C-arm, Philips, Andover, MA  
<sup>e</sup> Omnipaque, 240 mg of iohexol/mL, Amersham Health, Princeton, NJ  
<sup>f</sup> Dip-Quik solution III, Jorgensen Laboratories, Loveland, CO  
<sup>g</sup> SPSS Statistics V.17.0, Chicago, IL  
<sup>h</sup> Gelfoam, Upjohn Co, Kalamazoo, MI
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