Perfusion- and diffusion-weighted magnetic resonance imaging of the liver of healthy dogs

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OBJECTIVE
To describe the perfusion and diffusion characteristics of the liver in healthy dogs as determined by morphological, perfusion-weighted, and diffusion-weighted MRI.

ANIMALS
11 healthy adult Beagles.

PROCEDURES
Each dog was anesthetized and underwent morphological, perfusion-weighted, and diffusion-weighted MRI of the cranial aspect of the abdomen. On the MRI images, a region of interest (ROI) was established for each of 6 structures (aorta, caudal vena cava, portal vein, hepatic parenchyma, splenic parenchyma, and skeletal [epaxial] muscle). The signal intensity was determined, and a time-intensity curve was generated for each ROI. The apparent diffusion coefficient (ADC) was calculated for the hepatic and splenic parenchyma in diffusion-weighted MRI images, and the normalized ADC for the liver was calculated as the ratio of the ADC for the hepatic parenchyma to the ADC for the splenic parenchyma. Dogs also underwent abdominal ultrasonography, and ultrasound-guided fine-needle aspirate samples and biopsy specimens were obtained from the liver for cytologic and histologic examination.

RESULTS
Cytologic and histologic results suggested that the liver was clinically normal in all dogs. Perfusion-weighted MRI parameters varied among the 6 ROIs. The mean ± SD ADC of the hepatic parenchyma was 0.84 X 10−3 mm²/s ± 0.17 X 10−3 mm²/s, and the mean normalized ADC for the liver was 1.8 ± 0.4.

CONCLUSIONS AND CLINICAL RELEVANCE
Results provided preliminary baseline information about the diffusion and perfusion characteristics of the liver in healthy dogs. Additional studies on dogs of various breeds with and without hepatopathies are necessary to validate and refine these findings. (Am J Vet Res 2016;77:463–470)

Magnetic resonance imaging of the liver is an important tool for the detection and characterization of focal hepatic lesions and evaluation of diffuse liver disease. Diffuse infiltrative liver disease is a common problem in dogs and cats. In veterinary medicine, ultrasonographic examination is an integral part of the assessment for liver disease; however, because many parenchymal changes have a similar ultrasonographic appearance, its ability to discriminate among the various categories of diffuse liver diseases is not clinically acceptable. Additionally, factors such as the patient’s body weight and ultrasonographer’s skill can affect ultrasonographic examination and interpretation. Quantitative determination of hepatic echogenicity is possible with histogram analysis and may be useful for evaluation of diffuse hepatic parenchymal disease, but it is not routinely used in clinical practice.

In veterinary medicine, the availability of cross-sectional imaging modalities is increasing, and the use of such modalities to assess the liver is garnering interest. Assessment of the liver by MRI relies largely on visual assessment of unenhanced T1-weighted, T2-weighted, and contrast-enhanced images. Those conventional imaging sequences are frequently used for detection and characterization of liver diseases. Structural alterations to the liver often develop late in the disease process, and the ability to identify pathological changes associated with the earlier stages of liver disease on conventional MRI images is limited. Thus, the use of functional imaging techniques such as PW-MRI and DW-MRI to provide additional information is gaining popularity.

Diffusion is the thermally induced motion of water molecules in biological tissues and is also called Brownian motion. The movement of water within bio-

ABBREVIATIONS
ADC Apparent diffusion coefficient
DW-MRI Diffusion-weighted magnetic resonance imaging
PW-MRI Perfusion-weighted magnetic resonance imaging
ROI Region of interest
SI Signal intensity
logical tissues is not completely free. Instead, it is influenced by interaction among tissue compartments and is categorized as intravascular, intracellular, or extracellular. Tumors, cytotoxic edema, abscesses, and fibrosis impede diffusion. Tissues with low cellularity or that consist of cells with disrupted membranes permit unimpeded movement of water molecules.9

Although a description about the generation of DW-MRI images is beyond the scope of the study reported here, the contrast of DW-MRI images is derived on the basis of differences in the mobility of protons between tissues.10 The ADC measures the amount of signal loss between images obtained with different b values and represents the magnitude of water molecule diffusion within the tissues. Diffusion-weighted MRI has been used primarily to image the brain for evaluation of acute ischemic stroke, intracranial tumors, and demyelinating disease.11 The objective of the study reported here was to describe the PW-MRI and DW-MRI characteristics of the liver in healthy dogs. That information could be used as preliminary baseline information against which changes in the livers of dogs with focal and diffuse hepatopathies can be compared.

Materials and Methods

Animals

All study procedures were reviewed and approved by the Cantonal Veterinary Office of Zurich. Eleven adult Beagles that were specifically bred for experimental studies were enrolled in the study. The study population consisted of 5 sexually intact females and 6 sexually intact males with a mean age of 49 months (range, 3 to 6 years) and mean weight of 14.8 kg (range, 10 to 15 kg). All dogs were considered healthy and assigned an American Society of Anesthesiologists grade of 1 on the basis of results of a physical examination.

Study design

Each dog was anesthetized and underwent MRI, followed by abdominal ultrasonography and ultrasound-guided fine-needle aspiration and biopsy of the liver. The fine-needle aspirate samples and biopsy specimens were submitted for cytologic and histologic analysis to rule out liver disease.

Anesthesia and instrumentation of dogs

Each dog was premedicated with methadone (0.2 mg/kg, IM), and a catheter was aseptically placed in a cephalic vein. Oxygen was administered via a facemask for 30 minutes prior to anesthesia induction. Anesthesia was induced with midazolam (0.1 mg/kg, IV) and propofol (2.2 to 3.3 mg/kg, IV to effect). Each dog was intubated with a cuffed endotracheal tube, which was connected to a rebreathing system. Anesthesia was maintained with sevoflurane administered to effect in an oxygen-air gas flow rate of 50 mL/kg/min, with an inspired fraction of oxygen of 0.5%.

Each dog was mechanically ventilated with a volume-cycled ventilator set to maintain an end-tidal Pco2 of 35 mm Hg. Infusion of lactated Ringer solution (5 mL/kg/h, IV) was initiated. Cardiovascular and respiratory variables were measured continuously and recorded by a multiparameter monitor that included an MRI-compatible wireless respiratory sensor, vectorcardiography, and pulse oximeter (the probe was placed on the dog’s tongue). Mean arterial blood pressure was monitored by noninvasive methods and maintained between 70 and 85 mm Hg by adjustment of the inspired fraction of sevoflurane as necessary. For dogs that became hypotensive (mean arterial blood pressure, < 60 mm Hg), the inspired fraction of sevoflurane was decreased by 0.5%. If hypotension persisted, a fluid bolus (2 mL/kg, IV) was administered. Dogs that remained hypotensive following the fluid bolus were administered a constant rate infusion of dobutamine (5 µg/kg/h, IV).

MRI

Each dog was positioned in dorsal recumbency and scanned with a 3-T MRI system with a phased-array anterior coil.12 Morphological imaging included a transverse scan of the cranial portion of the abdomen on T2-weighted (turbo spin echo; repetition time, 1,250 milliseconds; echo time, 80 milliseconds; flip angle, 90°; field of view, 220 mm; voxel size, 0.60 X 0.73 X 3.00 mm; slice thickness, 3 mm; slice gap, 0.3 mm) and T1-weighted (T1 turbo field echo; repetition time, 10 milliseconds; echo time, 3.5 milliseconds; flip angle, 15°; field of view, 250 mm; voxel size, 1.31 X 1.21 X 3.00 mm; slice thickness, 3 mm; slice gap, 0.5 mm) images. Functional sequences performed included DW-MRI (3b imaging performance sensitivity encoding; repetition time, 1,301.5 milliseconds; echo time, 125 milliseconds; flip angle, 90°; field of view, 250 mm; voxel size, 2.98 X 3.13 X 3.00 mm; slice thickness, 3 mm; slice gap, 0.5 mm; number of directions, 4; number of b values, 3 [0, 500, and 1,000]) obtained on the transverse plane. Then, contrast medium (2 mL/s, IV) was administered with an MRI-compatible pump injector followed by IV injection of 10 mL of saline (0.9% NaCl) solution. A bolus-tracked T1 PW-MRI sequence with a breath-hold technique was performed over the cranial abdomen (multitransmit-enhanced high-resolution isotropic volume examination, dynamic parallel imaging performance sensitivity encoding, T1 turbo field echo; repetition time, 3.1 milliseconds; echo time, 1.5 milliseconds; flip angle, 10°; field of view, 280 mm; voxel size, 1.49 X 1.51 X 3.00 mm; slice thickness, 3 mm; slice gap, 1.5 mm; number of dynamics, 6). The scan was started when contrast medium was visible in the descending aorta in the premonitoring window and was repeated 6 times consecutively on a transverse plane. A breath-hold technique was used for MRI sequences that required the dog to hold its breath (maximum scan duration, 42 seconds). Briefly, controlled mechanical ventilation was intermittently discontinued to allow expiratory apnea to develop. Immediate-
ly after 1 sequence was obtained, controlled mechanical ventilation was resumed until an end-tidal $P_{CO_2}$ of 35 mm Hg was achieved. This stabilization period minimized the likelihood of spontaneous breathing induced by expiratory apnea during the subsequent breath-hold sequence. The duration of the stabilization period varied between sequences and among dogs.

**Abdominal ultrasonography and liver biopsy**

After all MRI sequences were obtained, 1 investigator (FDC) performed abdominal ultrasonography on each dog while it was still anesthetized. With ultrasound guidance, 2 fine-needle (22 gauge, 0.7 × 30 mm) aspirate samples and 2 biopsy (automatic gun with a 16-gauge needle) specimens were obtained from the liver of each dog. Following the biopsy procedure, each dog received methadone (0.2 mg/kg, IV) and was allowed to recover from anesthesia.

Dogs were maintained in an intensive care unit for 4 hours following discontinuation of anesthesia to monitor them for potential complications associated with the biopsy procedure. For each dog, an ultrasonographic examination of the liver and cranial aspect of the abdomen was performed between 110 minutes and 4 hours after the biopsy procedure. If no complications were identified, the dog was discharged from the intensive care unit and returned to the research colony.

**Cytologic and histologic evaluation**

All fine-needle aspirate samples were submitted for cytologic examination. Biopsy specimens for 7 of the 11 dogs were submitted for histologic examination; the biopsy specimens for the remaining 4 dogs were submitted for biochemical analysis in a concurrent study.

All cytologic and histologic examinations were performed by 1 board-certified veterinary clinical pathologist (PG) who was unaware of (ie, blinded to) the study protocol. Fine-needle aspirate samples were stained with a modified Wright stain. Biopsy specimens were fixed in 4% neutral-buffered formaldehyde solution, embedded in paraffin wax, processed in accordance with standard laboratory procedures, and stained with H&E stain and Sudan stain to identify lipid.

**Processing of MRI data**

All processing of MRI data was conducted on a dedicated extended workstation. Quantitative ADC maps were derived from the DW-MRI scans. Four ROIs (right and left cranial aspects, central aspect, and right caudal aspect) were manually drawn on the hepatic parenchyma in areas with homogenous SI. Care was taken to ensure that large blood vessels and the gallbladder were not included in those ROIs. Two ROIs were also drawn in the splenic parenchyma, with care taken to avoid large blood vessels and the organ boundary. The ADCs were calculated for both the hepatic and splenic parenchyma. For each dog, the ADC for the liver was normalized by dividing the ADC for the hepatic parenchyma by the ADC for the splenic parenchyma.

For each dog, 1 PW-MRI image in which both hepatic and splenic parenchyma were present was selected for analysis. Six ROIs (aorta, caudal vena cava, portal vein, hepatic parenchyma, splenic parenchyma, and skeletal muscle [typically the epaxial muscle in the left lumbar region]) were manually drawn and propagated through all the scans. When drawing the ROIs for the hepatic and splenic parenchyma, care was taken to avoid large blood vessels, the gallbladder, and organ boundaries.

For each ROI, the workstation software generated an SI versus time curve (time-intensity curve). Other parameters generated for each ROI from the PW-MRI images included maximum enhancement, maximum relative enhancement, time to peak SI, wash-in rate, washout rate, brevity of enhancement, and area under the time-intensity curve. Maximum enhancement is the difference between initial intensity and peak intensity and is measured in arbitrary units. Relative enhancement is the measure of the signal enhancement of a pixel in the PW-MRI scan, compared with the signal enhancement for that pixel in an MRI scan obtained prior to administration of the contrast medium. Maximum relative enhancement is the maximum for all relative enhancements over all dynamics. Time to peak SI is the time from the start of the scan until maximum SI occurs. The wash-in rate is the maximum slope between the time of onset of contrast medium inflow and the time of peak intensity. The washout rate is the maximum slope between the time of peak intensity and time that the contrast medium is eliminated. The brevity of enhancement represents the time between the maximum wash-in rate and the maximum washout rate. The area under the time-intensity curve represents the sum of all intensities. For each dog, ratios were calculated in which each perfusion parameter for a given ROI was divided by the corresponding parameter for skeletal muscle.

**Statistical analysis**

Descriptive data were generated by the use of a commercially available software program. The distribution of data for each parameter was assessed for normality with the Shapiro-Wilk test. Results were reported as the mean ± SD for parameters that were normally distributed and as the median (range) for parameters that were not normally distributed.

**Results**

**Ultrasoundographic findings**

For all dogs, the liver and gallbladder were considered clinically normal on the basis of echogenicity and echoarchitecture. Cytologic evaluation of fine-needle aspirates obtained from the liver revealed no abnormalities for any of the dogs. Similarly, none of the
liver biopsy specimens had any remarkable histologic changes.

MRI findings

The mean ± SD duration of the PW-MRI scan was 3.5 ± 1.9 minutes. The structure and SI of the liver were considered clinically normal on all morphological images. On visual assessment of T2-weighted images, the SI of the liver was homogenously hyperintense, compared with that of the epaxial muscle, and hypointense, compared with that of the spleen. On visual assessment of the T1-weighted images, the SI of the liver was homogenously and mildly hyperintense, compared with that of the epaxial muscle.

For the DW-MRI images, the mean ± SD size of the ROI was 39.6 ± 11.8 mm² for the hepatic parenchyma and 38.7 ± 8.6 mm² for the splenic parenchyma. The mean ± SD ADC was 0.84 ± 10⁻³ mm²/s ± 0.17 ± 10⁻³ mm²/s for the hepatic parenchyma and 0.48 ± 10⁻³ mm²/s ± 0.1 ± 10⁻³ mm²/s for the splenic parenchyma (Figure 1). The mean ± SD normalized ADC for the liver (ie, ADC of the hepatic parenchyma/ADC of the splenic parenchyma) was 1.8 ± 0.4.

The medians (ranges) for the PW-MRI parameters for the aorta, caudal vena cava, portal vein, hepatic parenchyma, splenic parenchyma, and epaxial muscle were summarized (Table 1), and the medians (ranges) for the ratios of each PW-MRI parameter for each structure (aorta, caudal vena cava, portal vein, hepatic parenchyma, splenic parenchyma, and epaxial muscle) for the dogs of Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aorta</th>
<th>Caudal vena cava</th>
<th>Portal vein</th>
<th>Hepatic parenchyma</th>
<th>Splenic parenchyma</th>
<th>Epaxial muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal enhancement</td>
<td>4,286.0 (2,053.1–5,582.5)</td>
<td>3,121.7 (2,262.6–6,747.2)</td>
<td>3,736.2 (2,665.6–6,409.1)</td>
<td>1,213.4 (879.3–3,055.5)</td>
<td>512.1 (344.4–563.9)</td>
<td>296.1 (127.7–430.5)</td>
</tr>
<tr>
<td>Maximal relative enhancement (%)</td>
<td>1,058.4 (673.8–1,584.5)</td>
<td>308.9 (187.6–504.7)</td>
<td>481.8 (298.4–716.0)</td>
<td>102.8 (64.8–209.4)</td>
<td>64.7 (30.5–70.5)</td>
<td>32.7 (11.6–39.8)</td>
</tr>
<tr>
<td>Time to peak SI (s)</td>
<td>24.1 (19.4–51.9)</td>
<td>49.4 (24.1–221.2)</td>
<td>63.6 (37.8–221.2)</td>
<td>73.7 (37.8–190.0)</td>
<td>142.7 (88.1–152.3)</td>
<td>116.2 (88.1–346.2)</td>
</tr>
<tr>
<td>Wash-in rate (s⁻¹)</td>
<td>177.9 (92.9–260.6)</td>
<td>122.3 (21.4–190.7)</td>
<td>91.0 (26.8–189.2)</td>
<td>30.7 (4.4–77.7)</td>
<td>8.3 (3.0–11.4)</td>
<td>5.2 (1.4–10.7)</td>
</tr>
<tr>
<td>Washout rate (s⁻¹)</td>
<td>20.5 (7.3–58.0)</td>
<td>10.9 (2.4–24.4)</td>
<td>7.3 (2.6–13.7)</td>
<td>2.1 (1.0–7.2)</td>
<td>0.6 (0.0–3.2)</td>
<td>0.6 (0.0–0.7)</td>
</tr>
<tr>
<td>Brevity</td>
<td>313.1 (194.6–63.5)</td>
<td>49.4 (18.8–221.2)</td>
<td>113.0 (26.3–232.5)</td>
<td>86.2 (27.2–190.0)</td>
<td>142.7 (88.1–152.3)</td>
<td>116.2 (66.7–346.2)</td>
</tr>
<tr>
<td>Area under the time-intensity curve (mm²)</td>
<td>7.3 X 10⁵</td>
<td>6.7 X 10⁵</td>
<td>6.6 X 10⁵</td>
<td>2.1 X 10⁵</td>
<td>7.9 X 10⁵</td>
<td>5.6 X 10⁵</td>
</tr>
<tr>
<td>Area (mm²)</td>
<td>285.9 (188–50.6)</td>
<td>42.6 (243–107.4)</td>
<td>32.3 (21.3–40.0)</td>
<td>61.8 (39.9–92.2)</td>
<td>30.1 (37.8–154)</td>
<td>38.8 (25.4–71.3)</td>
</tr>
</tbody>
</table>

Maximum enhancement is the difference between initial intensity and peak intensity and is measured in arbitrary units. Relative enhancement is the measure of the signal enhancement of a pixel in the PW-MRI scan, compared with the signal enhancement for that pixel in an MRI scan obtained prior to administration of the contrast medium. Maximum relative enhancement is the maximum for all relative enhancements over all dynamics. Time to peak intensity is the time from the start of the scan until maximum SI occurs. The wash-in rate is the maximum slope between the time of onset of contrast medium inflow and the time of peak intensity. The washout rate is the maximum slope between time of peak intensity and time that the contrast medium is eliminated. The brevity of enhancement represents the time between the maximum wash-in rate and the maximum washout rate. The area under the time-intensity curve represents the sum of all intensities.

### Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aorta</th>
<th>Caudal vena cava</th>
<th>Portal vein</th>
<th>Hepatic parenchyma</th>
<th>Splenic parenchyma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal enhancement</td>
<td>15.8 (10.6–43.7)</td>
<td>8.8 (83–33.5)</td>
<td>10.8 (10.6–36.0)</td>
<td>4.4 (3.0–11.4)</td>
<td>1.6 (1.1–4.4)</td>
</tr>
<tr>
<td>Maximal relative enhancement</td>
<td>35.3 (30.7–90.2)</td>
<td>9.4 (47–33.5)</td>
<td>12.4 (10.9–46.1)</td>
<td>3.8 (2.3–8.6)</td>
<td>2.0 (1.7–5.9)</td>
</tr>
<tr>
<td>Time to peak SI (s)</td>
<td>0.2 (0.0–0.2)</td>
<td>0.5 (0.0–0.6)</td>
<td>0.5 (0.0–0.6)</td>
<td>0.7 (0.5–0.7)</td>
<td>1.2 (1.0–1.6)</td>
</tr>
<tr>
<td>Wash-in rate (s⁻¹)</td>
<td>50.1 (19.5–106.7)</td>
<td>24.8 (15.0–55.3)</td>
<td>19.1 (11.7–23.6)</td>
<td>5.0 (3.1–7.2)</td>
<td>1.1 (0.8–2.2)</td>
</tr>
<tr>
<td>Washout rate (s⁻¹)</td>
<td>21.1 (20.1–257.3)</td>
<td>15.6 (42.2–218.1)</td>
<td>11.7 (4.6–12.5)</td>
<td>6.0 (1.5–3.6)</td>
<td>0.0 (0.0–29.0)</td>
</tr>
<tr>
<td>Brevity of enhancement</td>
<td>0.3 (0.1–0.4)</td>
<td>0.6 (0.4–0.6)</td>
<td>0.6 (0.2–1.0)</td>
<td>0.7 (0.5–1.0)</td>
<td>0.0 (0.0–1.3)</td>
</tr>
<tr>
<td>Area under the curve</td>
<td>12.2 (11.4–384.0)</td>
<td>11.1 (6.7–328.8)</td>
<td>11.8 (11.4–366.8)</td>
<td>4.5 (2.9–12.8)</td>
<td>1.8 (1.0–42.7)</td>
</tr>
<tr>
<td>Area (mm²)</td>
<td>0.8 (0.7–1.3)</td>
<td>0.8 (0.6–1.4)</td>
<td>0.8 (0.5–0.9)</td>
<td>1.6 (1.3–2.0)</td>
<td>1.3 (1.0–2.0)</td>
</tr>
</tbody>
</table>

For each dog, ratios were calculated by dividing each perfusion parameter for a given ROI by the corresponding parameter for the epaxial muscle. See Table 1 for remainder of the key.
ic parenchyma, and splenic parenchyma), compared with the corresponding PW-MRI parameter for the epaxial muscle, were likewise summarized (Table 2). A representative T1 PW-MRI image obtained in the transverse plane that shows each of the 6 ROIs evaluated (Figure 2) and the associated time-intensity curves for those ROIs (Figure 3) was provided for one of the study dogs. In the PW-MRI scans of all dogs, the hepatic parenchyma was enhanced sooner and had a higher peak SI, compared with the enhancement and peak SI of the splenic parenchyma and epaxial muscle. The median SI of the hepatic parenchyma was 4.4 times that for the epaxial muscle. For 9 of the 11 dogs, the peak SI of the hepatic parenchyma was greater than twice the peak SI of the splenic parenchyma, and the time-intensity curve for the enhancement of the splenic parenchyma was higher and grossly parallel to that for the epaxial muscle. For the remaining 2 dogs, the time-intensity curve for the enhancement of the epaxial muscle was slightly higher than but still parallel to that for the splenic parenchyma.

**Discussion**

The diagnosis of hepatic abnormalities such as fibrosis and inflammation by conventional MRI is difficult, and histologic evaluation of liver biopsy specimens is currently considered the gold standard for diagnosis of liver disease. Unfortunately, liver biopsy is frequently associated with complications such as hemorrhage, and obtaining a diagnostic biopsy specimen can be difficult owing to the heterogeneous distribution of most hepatopathies and is dependent on operator experience.

In human medicine, the ADC of cirrhotic hepatic tissue is lower than that of healthy hepatic tissue, and the ADC of hepatic tissue has been used to diagnose moderate and severe hepatic fibrosis. Threshold ADC values have been proposed for differentiation of benign from malignant hepatic lesions. Although the ADC varies among healthy humans, the results of multiple studies indicate a significant difference between the ADCs of clinically normal and diseased hepatic tissue. Thus, calculation of the ADC of hepatic tissue may represent an additional or ancillary method for diagnosis of liver disease.

In healthy humans, the ADC of hepatic tissue ranges from $0.69 \times 10^{-3}$ mm$^2$/s to $1.83 \times 10^{-3}$ mm$^2$/s as obtained with different numbers and $b$ values. The mean ± SD ADC of the hepatic parenchyma ($0.84 \times 10^{-3}$ mm$^2$/s ± $0.17 \times 10^{-3}$ mm$^2$/s) calculated for the healthy dogs of the present study was most similar to that reported in a study that involved human patients who were evaluated with $b$ values of 300 and 1,200 in a 1.5-T MRI system. The mean ADCs for the right ($0.85 \times 10^{-3}$ mm$^2$/s) and left ($0.89 \times 10^{-3}$ mm$^2$/s) brain parenchyma of healthy dogs in another study are similar to that for hepatic tissue of the healthy dogs of the present study. However, there is a fundamental difference between hepatic and brain parenchyma. Hepatic parenchyma has an isotropic structure, whereas the white matter of the brain has an anisotropic structure.

The $b$ values used in the present study were selected on the basis of published literature. The $b$ values used for DW-MRI typically do not exceed 1,000 s/mm$^2$, and $b$ values < 100 s/mm$^2$ and > 500 s/mm$^2$ are considered advantageous for hepatic imaging when the primary goal is to obtain accurate ADCs.

Because the ADC can vary among healthy individuals, investigators of another study proposed a method for normalizing the ADC for hepatic tissue in which the ADC of hepatic tissue is compared with the
ADC of splenic tissue. In human medicine, the spleen is considered a reliable internal standard and is often used as such when quantitative analysis is required. In the present study, the spleen was consistently present in the DW-MRI images of the liver and therefore could be used as an internal standard for each dog. Clinically normal splenic parenchyma has a high SI on images with high $b$ values because the hypervascularity of the spleen results in a restricted diffusion pattern and the lowest ADC of all visceral organs. The ADCs for splenic and hepatic parenchyma can vary substantially in patients with chronic viral hepatitis. Diffusion-weighted MRI images can be obtained over a fairly short scan time (1 to 5 minutes) without administration of an exogenous contrast medium. However, DW-MRI images of the liver frequently contain motion artifact caused by respiration. The development of stronger diffusion gradients, faster imaging sequences, and improvements in technology and MRI instrumentation than those currently available should partially overcome this challenge. Diffusion-weighted MRI images obtained by use of various techniques are used to minimize motion artifact, such as the multiple breath-hold, free-breathing, respiratory-triggered, and navigator-triggered techniques. The free-breathing technique has better reproducibility than other techniques. The acquisition of respiration-triggered sequences improves lesion detection and image quality but increases the scan time. We decided to use a breath-hold technique in the present study because it allowed the shortest sequence time ($\leq 42$ seconds) and minimized motion during single sequences.

Another important source of variation for the ADC is the location of the ROI within the hepatic parenchyma. Investigators of another study suggest that cardiac motion may cause signal loss during DW-MRI image acquisition, which can result in an artificially increased ADC for the parenchyma in the left cranial aspect of the liver, and intestinal peristalsis may affect the ADC for the parenchyma in the right inferior aspect of the liver. In the present study, the ADC was measured for 4 ROIs in the liver, each of which had homogenous parenchyma. Subjective visual examination could not detect a difference in SI between the right and left aspects of the liver or between the cranial and caudal aspects of the liver. To our knowledge, comparison of ADCs among different regions of the liver has not been performed.

Equipment differences can also contribute to difficulties in standardization of ADCs. Results of 1 study indicate that the ADCs of gray and white matter of the brain vary between 4% and 9% for images obtained with 1.5-T and 3.0-T MRI systems from the same vendor. Moreover, within the same system, simply changing the coil can alter the ADC by up to 8%. Diffusion-weighted MRI is also sensitive to chemical shift artifact. The DW-MRI sequences acquired in the present study used frequency-based fat suppression to minimize chemical shift artifact. However, chemical shift artifact was present in DW-MRI images obtained for all dogs and appeared as a hypointense halo around the gallbladder and major hepatic blood vessels. Care was taken to ensure that none of those areas were included in the ROIs.

Perfusion-weighted MRI refers to the imaging of tissue blood flow and microcirculation and tracks the passage of contrast medium through the blood vessels and parenchyma of solid organs such as the liver and spleen. Perfusion-weighted MRI is used to assess focal liver lesions and their vascular supply as well as diffuse liver diseases such as cirrhosis. Human patients with cirrhosis have alterations in hepatic arterial and portal blood flow, and PW-MRI has been used to grade disease severity in those patients. Perfusion-weighted MRI is also used to assess changes in hepatic perfusion in human patients with acute hepatitis and microscopic liver metastases. Various MRI methods have been used to assess hepatic perfusion in pigs, rabbits, and dogs. Hepatic perfusion has also been assessed with dynamic CT in healthy dogs and dogs with portal vascular anomalies before and after surgical correction of portosystemic shunts. Perfusion-weighted MRI may be an alternative to CT because it can be used to characterize hepatic blood flow and provides additional information about the hepatic parenchyma that is not provided by CT.

The present study used bolus-track technology, which means that the PW-MRI scan was initiated when the contrast medium became visible within the descending aorta in the premonitoring window. The use of that technology is likely the reason why peak enhancement of the aorta was missed in most of the dogs.

Compared with the values for the splenic parenchyma and epaxial muscle, the mean time to peak SI was shorter and the mean peak SI was higher for the hepatic parenchyma. This was expected because, unlike the spleen and skeletal muscle, the liver has a dual (portal and systemic) blood supply.

The duration of the MRI scans varied among dogs, likely because of the high variability in the area under the time-intensity curve, which was a function of the stabilization period between 2 sequences during implementation of the breath-hold technique. The stabilization period was dependent on the duration of expiratory apnea. The duration of apnea is positively correlated with blood carbon dioxide concentration. Therefore, as the duration of expiratory apnea increased, so did the blood carbon dioxide concentration and the longer it took to achieve the desired carbon dioxide concentration with controlled mechanical ventilation after apnea.

The anesthetic protocol used is critical for perfusion studies because several anesthetic drugs affect the cardiovascular system. In the present study, mean arterial blood pressure was maintained within a fairly narrow range (70 to 85 mm Hg) to keep hepatic blood flow stable. Anesthesia was induced with drugs that had no ef-
fects (midazolam) or only short-acting effects (propofol) on cardiovascular function. Anesthesia was maintained with sevoflurane, which preserves hepatic arterial blood flow. Sevoflurane also has a low blood-gas solubility coefficient and therefore is quickly eliminated from the body despite being partially metabolized by the liver.

Limitations of the present study included a small study population that was homogeneous in terms of breed and body weight and did not accurately represent the potential population of clinical patients with liver disease. Also, dogs were definitively determined to not have liver disease on the basis of histologic evaluation of 2 hepatic biopsy specimens, and focal hepatic changes might have remained undetected. However, that was considered unlikely given the homogenous appearance of the hepatic parenchyma on the MRI images and ultrasonographic examination.

To our knowledge, functional MRI imaging techniques have not been described or investigated for use in the diagnosis of hepatopathies in veterinary species. The present study provided a description of the use of PW-MRI and DW-MRI to evaluate the liver of healthy dogs. The MRI parameters calculated provided preliminary baseline information about the diffusion and perfusion characteristics of the liver in healthy dogs. Additional studies that involve dogs of various breeds with and without hepatopathies are necessary to validate and refine the findings of the present study and elucidate the potential clinical application and relevance of the use of PW-MRI and DW-MRI for assessment of the liver in dogs.

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Footnotes
a. Philips Ingenia scanner, Philips AG, Zurich, Switzerland.
b. Stream Torso, coil solution, 32 channels, Philips AG, Zurich, Switzerland.
c. Omniscan, 0.5 mmol/kg, GE Healthcare AG, 8152 Glattbrugg, Switzerland.
d. Philips iU22 ultrasound system, Philips Healthcare, Bothell, Wash.
e. MR WorkSpace, version 2.6.3.5, Philips Medical System, Best, The Netherlands.
f. SPSS Statistics, version 21.0.0.0, 64-bit edition, IBM Corp, Chicago, Ill.

References


