INTRODUCTION
Diagnostic imaging often plays an essential role in the work-up and management of cases and while radiography and ultrasonography will remain mainstays in veterinary medicine due to availability, cost and ease of use, advanced diagnostic imaging has and will continue to become more utilized in veterinary medicine due to its increased diagnostic capability and increasing availability. This lecture will describe some of the increasingly common uses of advanced diagnostic imaging in small animals, focusing on CT, MRI and contrast-enhanced ultrasound, with a brief introduction of each imaging modality followed by a case-based discussion of their utility in a variety of disease conditions. A brief description of newer, innovative techniques in advanced diagnostic imaging will also be presented.

COMPUTED TOMOGRAPHY (CT)
CT is well known for its excellent nasal, bone, and lung imaging capabilities as well in imaging soft tissue structures in the head/neck, thorax and abdomen/pelvis. Due to its tomographic (cross-sectional) acquisition, superimposition of structures (as is a problem with radiography) or lack of visibility of tissues deep to gas or bone (as is a problem with ultrasonography) is not an issue. Speed is another benefit of CT, as the fast image acquisition is useful in minimizing anesthesia time or in quickly imaging patients under light sedation (note: most of our CT studies are done under general anesthesia, as this allows for best control of respiratory motion and negates any patient movement which therefore improves image quality).

One of the areas in which we are utilizing CT more often is in patients with chylothorax. Thoracic CT with pre and post intravenous contrast is useful in assessing for any mass lesions that may be the underlying cause for chylous effusion, and has increased sensitivity/specificity compared to thoracic radiographs in this regard. In addition to this, we are now commonly performing CT lymphangiography, via injection of contrast into a lymph node, usually the popliteal lymph node. Since there is a large amount of variability in thoracic duct anatomy in dogs and cats, this technique allows for assessment of an individual patient’s thoracic duct morphology (e.g. location and number of ducts) which is useful in surgical planning. To perform this technique, we use ultrasound to visualize the lymph node and then guide the injection of iodinated contrast (same as used for IV contrast) directly into the node. Immediately after the injection (and often several times after this), CT images of the abdomen and thorax are acquired and we can then visualize the cisterna chylii and thoracic duct(s). We are hoping that by utilizing this technique, we will have increased success at the surgical treatment of this disease.

CT is being utilized more often in cases with vascular anomalies, such as vascular ring anomalies, to better understand the vascular anatomy in a patient prior to surgery. This involves
performing CT angiography, which requires use of a power injector to ensure that the contrast medium is injected quickly (which is needed for a good contrast enhancement of vessels, especially arteries), and the use of timing techniques (e.g. we often use something called a timing bolus, which helps us precisely plan when the contrast medium arrives in the vessel of interest). With these studies, we may find additional vascular anomalies, i.e. those concurrent with persistent right aortic arch (PRAA), or vascular anomalies other than PRAA, such as double aortic arch.

We also use CT angiography for cases with suspected pulmonary thromboembolism (PTE). Classically, there will be hypoattenuating filling defects in the pulmonary arteries, which should otherwise be strongly enhancing during the arterial phase. Unfortunately, CT angiography for the diagnosis of PTE is not 100% sensitive, as PTEs in the small peripheral arteries can be missed with this method. In those cases, however, we may still suspect PTE based on finding abnormal lung infiltrates, with the classic appearance being a wedge-shaped region of consolidation in the periphery of the lung.

CT angiography has many other uses, including: assessment for vascular invasion in patients with various tumors, e.g., adrenal, cranial mediastinal, or thyroid tumors; assessment of lesion vascularity for diagnostic purposes, e.g., pancreatic angiography for insulinoma; assessment of lesion vascularity for therapeutic purposes, e.g., planning embolization of unresectable liver masses or arteriovenous malformations; or, better evaluating vascular anatomy in patients with intrahepatic portosystemic shunts (to plan for interventional radiologic treatment) or assisting in extrahepatic portosystemic shunt detection (in cases where ultrasound is equivocal). For example, in a dog with suspected insulinoma, abdominal ultrasound may or may not be able to locate a nodule/mass in the pancreas, especially in large breed dogs with intestinal gas; or a nodule(s) is found on ultrasound, but it cannot be distinguished from a benign lesion such as nodular hyperplasia. Additionally, nodal or liver metastases can also be difficult to detect or confirm on ultrasound. Neuroendocrine tumor types, such as insulinoma, usually demonstrate intense arterial enhancement differing from the normal pancreatic parenchyma, which makes CT angiography a better diagnostic test than ultrasound, with the added benefit of better assessment of the regional lymph nodes and liver for metastatic disease.

Finally, CT is being utilized more often in complex orthopedic cases (e.g. angular limb deformities) prior to surgery, to assist with surgical planning. CT images can also be used for 3D printing, which creates a 3D model of the particular area of interest (e.g. skull, long bone) and assists in surgical planning, including practicing a complex surgical procedure prior to the actual surgery. For a great example of how 3D printing was paramount in treating a clinical case, see [http://www.vet.upenn.edu/about/press-room/publications/penn-vet-extra/penn-vet-extra-march-2016/3d-printing-key-to-success](http://www.vet.upenn.edu/about/press-room/publications/penn-vet-extra/penn-vet-extra-march-2016/3d-printing-key-to-success).

MAGNETIC RESONANCE IMAGING (MRI)

MRI in small animals is best known for neuroimaging (brain, spine) but also excels in imaging musculoskeletal structures and soft tissue structures in the head/neck, abdomen/pelvis and to some extent, the thorax. As with CT, MRI has a huge advantage over radiography and
ultrasonography given its cross-sectional nature, but it is also advantageous due to its increased sensitivity for even subtle soft tissue or bone lesions.

Musculoskeletal MRI is very useful in imaging dogs with lameness, such as that due to supraspinatus tendinopathy or bicipital tenosynovitis. Currently, imaging the shoulder is the most commonly performed musculoskeletal MRI at our institution, although other conditions are being imaged with increasing frequency. We often use intravenous contrast in these cases to look for evidence of more acute tendinopathy (contrast enhancement) and to distinguish it from more chronic or fibrotic tendinopathy (lesser to no contrast enhancement). It has been demonstrated that intra-articular contrast allows for better visualization of regional soft tissue structures, e.g. joint capsule and ligaments of the shoulder, compared to standard sequences alone, so for example, we sometimes perform arthography for shoulder MRI after the acquisition of standard sequences. This involves temporarily removing the patient from the MRI scanner, clipping and aseptically preparing the area and then having one of our surgeons perform an intra-articular injection of dilute gadolinium (same contrast as used IV, but it is diluted 1:100 with sterile saline). Other musculoskeletal abnormalities, such as iliopsoas muscle strain/tear or fibrosis3,4 or fibrotic gracilis myopathy,5 can also be visualized on MRI examination in both acute and chronic (fibrotic) stages. These conditions are usually seen in mature, active/athletic dogs and fibrotic gracilis myopathy in particular has a predilection for German Shepherd dogs. Iliopsoas muscle strain is more commonly associated with trauma and dogs present with pain on hyperextension of the hips, which can be confused with hip dysplasia.3 Fibrotic gracilis myopathy is of unknown etiology, although many dogs with this condition are working dogs (e.g. dogs that might perform sprinting or jumping exercises).5 This condition creates a classically abnormal gait, with a shortened stride, internal rotation of the foot, external rotation of the hock and internal rotation of the stifle during the mid to late swing phase of the stride.5 Numerous other muscles can be affected by strain or fibrosis/contracture and MRI would also be useful for diagnosis.

MRI is also very useful in bone imaging, which at our institution is usually utilized in oncology cases. It is excellent at the detection of osseous invasion by soft tissue tumors, in the assessment of primary bone tumors (e.g. osteosarcoma) and their intramedullary margins6 and in the assessment of metastatic or multicentric neoplasia (e.g. metastatic osteosarcoma, lymphoma).7 Neoplastic bone lesions of any kind are typically hyperintense on routine T2W sequences, however, fatty infiltration of bone marrow, as is typical in older patients, is also hyperintense and could be confused with neoplasia. We therefore often use additional sequences with either fat nullification (e.g. STIR [Short Tau Inversion Recovery]) or fat suppression (e.g. TW1 post contrast with fat suppression) to delineate normal fatty marrow change from neoplastic infiltration of the bone.

A final increasingly common use for MRI that will be discussed is imaging the liver with a liver-specific contrast agent. The usual gadolinium-based contrast agent utilized at our hospital is Magnevist® but if we want to image the liver more specifically, we will use an agent called Multihance® which is taken up by hepatocytes and excreted in the bile and allows for determination of benign vs. malignant liver lesions. For example, nodules in the liver that are suspect for metastatic disease on routine sequences (i.e., hyperintense on T2W, hypointense on T1W, with contrast enhancement) will be hypointense on a delayed “hepatobiliary phase” (performed ~20 minutes post contrast injection), which supports malignancy.8 Benign nodules
will behave similar to normal liver parenchyma on these delayed scans (i.e., should be isointense to the rest of the liver) as the normal hepatic vasculature should be intact in benign lesions (with the exception of cysts, which do not have normal parenchyma within them). Sensitivity for nodule detection is also better in the delayed phase, often showing more lesions than seen on the routine T2W and T1W post-contrast series. If MRI of the entire abdomen is to be performed in addition to the liver specific scan, this contrast agent can also be utilized for routine T1W post contrast scans of the rest of the abdomen.

CONTRAST-ENHANCED ULTRASOUND (CEUS)
CEUS is an ultrasonographic examination performed during and for several minutes after the intravenous injection of an ultrasound-specific contrast agent (we use one called Definity®), which requires special software on a high quality ultrasound machine. These ultrasound contrast agents are comprised of gas-filled microbubbles stabilized by an outer shell and are smaller than red blood cells, so travel freely through blood vessels including capillaries. Contrast agents give us information regarding tissue vascularity (imaging occurs during arterial, venous, and delayed parenchymal phases), which in some instances will allow for differentiation between benign vs. malignant lesions. Lesion perfusion characteristics can also potentially refine the differential diagnosis for some tumor types (e.g. pancreatic or adrenal tumors).

Currently, CEUS is primarily used in our hospital for imaging liver nodules, as 100% sensitivity and 94-100% specificity for distinguishing malignant from benign liver nodules has been reported. A common scenario with standard B-mode abdominal ultrasound is the finding of liver nodules in patients with hemoabdomen secondary to a bleeding splenic mass (primary differentials of hemangiosarcoma vs. hyperplasia/hematoma), where we usually cannot determine whether these nodules are metastatic lesions (e.g. metastatic hemangiosarcoma) or benign nodules (e.g. nodular hyperplasia). Malignant nodules have a different vascular supply compared with benign nodules (e.g. malignant lesions lack normal sinusoids), so these nodules will be seen as hypoechoic lesions (hypoperfused) within an otherwise diffusely enhanced liver parenchyma during CEUS. On the other hand, benign nodules have a relatively similar blood supply as the normal liver so will be isoechoic (i.e. not visible) to the rest of the liver during the parenchymal phase of enhancement. As for the assessment of bleeding splenic masses, it has been shown that CEUS is unable to distinguish between splenic hematoma and hemangiosarcoma, and therefore, we do not use CEUS to image a bleeding splenic mass prior to splenectomy. Although CEUS has shown some usefulness in imaging non-ruptured splenic lesions and can sometimes distinguish between benign and malignant nodules, the sensitivity/specificity is not high enough for routine incorporation into our practice.

Numerous other studies have looked at the utility of CEUS in imaging other cancers, such as pancreatic insulinoma (these tumors are hyperperfused during the arterial phase, which is similar to their behavior on CT angiography) or adrenal tumors (may be able to distinguish tumor type based on CEUS), but CEUS has generally not replaced our more routine practice of CT for these types of tumors. If a pancreatic nodule in a suspected insulinoma case is easily identified on routine abdominal ultrasound, then we may try CEUS to assess the nodule in lieu of CT angiography (e.g. if there are economic concerns, as CEUS is much cheaper than CT angiography). However, as previously discussed, pancreatic nodules can be difficult to detect on standard abdominal ultrasound in many cases, especially in large dogs due to factors such as
lesion depth and intestinal contents, and therefore, we often cannot use CEUS for diagnosis and would instead choose CT angiography.

OTHER ADVANCED IMAGING TECHNIQUES
Positron emission tomography (PET) is a form of nuclear medicine imaging commonly used in human oncology, as it is very sensitive in identifying neoplastic lesions including metastases. It is often used in concert with CT, with images being fused together after image acquisition, for the purpose of having the functional details (PET) overlying the anatomic details (CT). It is available at a few veterinary institutions and there is some literature describing normal and abnormal findings on PET scans.\textsuperscript{11,12} Expense and availability are the current primary reasons for PET not being used commonly in veterinary medicine. We do not have PET available at our institution currently; however, we could potentially have future access to a PET scanner at the adjacent human hospital.

Perfusion imaging utilizing CT or MRI has been briefly described in veterinary medicine.\textsuperscript{13,14} In humans, it is most commonly used in oncologic imaging or in imaging infarcts. In oncologic imaging, it can assist in the evaluation of treatment response and may better identify non-responders, which may in turn allow for more tailored therapies earlier in the course of treatment.\textsuperscript{15} There is some current work on perfusion imaging ongoing at our institution and others, such as examining whether CT perfusion imaging can help distinguish between adrenal tumor types. As for perfusion imaging using MRI, we are not currently performing this technique specifically; however, our standard brain MRI examination does include another special sequence called diffusion-weighted imaging (DWI). This sequence, along with a calculated apparent diffusion coefficient (ADC) map, allows for better evaluation of more acute brain infarcts, where movement of water molecules in cells is restricted due to cytotoxic edema.\textsuperscript{16}

MRI spectroscopy is a special technique utilized in conjunction with conventional MRI which gives biochemical information on metabolites within cells. This is most often used in human medicine for distinguishing neoplastic vs. non-neoplastic brain lesions. Two studies in veterinary medicine have shown that MRI spectroscopy was able to distinguish between intra-cranial neoplasia and inflammatory brain diseases in many cases.\textsuperscript{17,18} As more studies are performed, this may become a more popular technique for imaging the brain in small animals.

References: