INTRODUCTION
Diagnostic imaging plays an essential role in the diagnosis and staging of cancer in small animal patients. Radiography and/or ultrasonography are the first line diagnostic imaging tests, but diagnosis and staging can be greatly improved with advanced imaging. This lecture will discuss the utility of advanced imaging techniques, including computed tomography, magnetic resonance imaging, contrast-enhanced ultrasound and positron emission tomography, with a brief introduction of each modality followed by a case-based discussion.

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).

CT with intravenous contrast (pre- and post-contrast images acquired) is frequently used at our hospital in patients with suspect nasal tumors to define lesion location and extent, including any potential paranasal bone or cribriform plate involvement, and for the assessment of regional lymph nodes. The information gained with CT guides rhinoscopic biopsies and allows for radiation treatment planning.

Pre- and post-contrast thoracic CT is commonly performed in patients with lung tumors seen on thoracic radiographs, as it allows for better lesion definition and location and is better at assessment for metastatic disease in the lungs, lymph nodes or pleural space (carcinomatosis). The smallest lung nodule detectable on radiographs has been reported at 3mm, although 5-10mm is a more typical size at which nodules are detected; on CT, lung nodules as small as 1mm are easily detectable. More precise location of a lung mass and assessment of regional lymph nodes also aids in surgical planning (e.g. thoracoscopy vs. thoracotomy, lymph node biopsy). Mediastinal masses are another common reason for thoracic CT, as better lesion definition and extent (e.g. looking for involvement of regional vasculature) is possible. Ultrasound may be unable to detect cranial vena cava invasion with tumors such as chemodectoma or thymoma, whereas contrast-enhanced CT can detect such vascular invasion, which obviously affects possible treatment options in those patients.

Abdominal CT pre- and post-contrast is often performed in patients with a mass identified on abdominal ultrasound (e.g., liver mass, adrenal mass, mass of unknown origin), as better lesion
definition, location and extension is appreciable on CT (particularly in large breed dogs that are more difficult to image with ultrasound). For example, CT is useful in dogs with retroperitoneal masses of indeterminate origin, as it can determine mass origin (adrenal vs. kidney vs. retroperitoneal tissue), look for any vascular invasion, and can help distinguish mass from hematoma (e.g. retroperitoneal hemangiosarcoma or adrenal mass with mass-like hematomas from spontaneous rupture). Another good use for abdominal CT includes cases with large liver masses, in which assessment of other liver lobes and hepatic lymph nodes may be difficult on an abdominal ultrasound exam due to mass effect and intestinal contents. Masses in the pelvic canal (e.g. mass associated with colon/rectum, genitourinary tract or soft tissues) may be partly visible on ultrasound if the masses extend into the caudal abdomen, but CT is often needed to assess lesion origin.

CT angiography is also commonly performed in our hospital for assessment of vascular invasion (e.g., adrenal, cranial mediastinal, or thyroid masses) or for assessment of lesion vascularity for diagnostic (e.g., pancreatic angiography for insulinomas) or therapeutic purposes (e.g., guiding interventional procedures as with embolization of a liver mass). For example, in a dog with suspect 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 of these cases. Neuroendocrine tumor types, such as pancreatic insulinoma, usually demonstrate intense arterial enhancement differing from the normal pancreatic parenchyma,\(^3\) which makes CT angiography a better alternative for diagnosis than ultrasound, with the added benefit of better assessment of the regional lymph nodes and liver for metastatic disease.

Finally, pre- and post-contrast CT can be used for assessing soft tissue masses, such as soft tissue sarcomas, with better lesion delineation than radiographs or ultrasound. MRI is better than CT for soft tissue lesions, although CT with contrast is often still excellent for mass assessment and its relationship to regional tissues, with the added benefit of much faster acquisition time. Another type of soft tissue imaging we commonly perform involves head/neck masses. A palpable neck mass could be of thyroid or lymph node origin and while ultrasound is often our first line imaging technique to assess such a mass, CT will give a better assessment of the mass and regional tissues. For example, ultrasound can demonstrate that a palpable cervical mass is an enlarged medial retropharyngeal lymph node and ultrasound-guided aspirate of this node could show metastatic carcinoma from an unknown primary neoplasm. Head/neck CT can then be used to identify the primary neoplasm, such as a tonsillar carcinoma.

**MAGNETIC RESONANCE IMAGING (MRI)**

MRI in small animals is best known for neuroimaging (brain, spine) but also excels in imaging soft tissue masses such as brachial plexus or other peripheral nerve tumors, soft tissue sarcomas (e.g. fibrosarcoma), abdominal/pelvic masses and some thoracic masses. As with CT, MRI has a huge advantage over radiography and ultrasound in terms of best defining lesion location and extent and in assessment for regional metastases (e.g. lymph nodes). MRI studies typically have a much longer acquisition time than CT, so at our institution, we tend to perform CT more often than MRI when imaging cancer patients (exception is neuroimaging). Additionally, MRI is often
more expensive than CT although currently at our hospital, the price difference is relatively small.

MRI can often better delineate tumor margins compared to CT, because of its excellent soft tissue contrast. While CT is known to excel at bone imaging, MRI is also excellent for bone imaging, including detection of osseous invasion by soft tissue tumors or in the assessment of primary bone tumors (e.g. osteosarcoma). MRI has proven better in tumor margin delineation compared to radiographs in primary bone tumors, which would be important if limb-sparing surgery was being considered. MRI will also show full tumor extension better than a modality such as ultrasound. For example, retrobulbar masses can be imaged with ultrasound, but areas of potential tumor extension (e.g. brain) can be missed due to the inability to image through the calvarium. Another example is using MRI for nasal tumors, which as with CT, is far superior to radiography. Note that MRI would be better than CT at detecting very subtle tumor invasion through the cribriform plate into the brain (would show meningeal enhancement along the olfactory lobes, which could be missed with CT), although CT would demonstrate lysis of the cribriform plate better than MRI (so modalities are relatively comparable in imaging nasal tumors).

Similar to CT, abdominal/pelvic MRI can be performed in patients with abdominal masses in which better lesion definition, location and extent is possible as compared to ultrasound. MRI can also be more specific for organ lesions (e.g. liver, spleen nodules) seen in such a patient. For example, in a patient undergoing MRI for a retroperitoneal mass that is suspected to be hemangiosarcoma, spleen nodules may be detected. The intensity of the spleen nodules on different sequences can be useful in distinguishing benign vs malignant lesions, i.e., benign nodules are usually hypointense on T2-weighted and T1-weighted images with contrast enhancement less than normal spleen, whereas malignant nodules are usually hyperintense on T2W and hypointense on T1W images and have increased contrast enhancement compared to normal spleen.

The usual gadolinium-based contrast agent utilized at our hospital is Magnevist® but we will occasionally use an agent called Multihance® which is taken up by hepatocytes and excreted in the bile and can therefore be used for more specific imaging of the liver. Nodules in the liver that are suspect for metastatic disease (i.e., hyperintense on T2W, hypointense on T1W with increased contrast enhancement) will be hypointense on a delayed “hepatobiliary phase” (performed ~20 minutes post contrast injection), which supports malignancy. Benign nodules will behave similar to normal liver parenchyma on these delayed scans (i.e., should be isointense) as the hepatobiliary tree 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 series.

MRI can be used for imaging the thorax, although at our institution, we mostly perform CTs for this purpose (e.g. lung, mediastinal, pleural and thoracic wall masses). The primary reason is that MRI is more sensitive to motion (although there is special equipment/software to deal with motion issues) and the lungs have low proton density along with increased artifacts from air-tissue interfaces (so overall anatomic detail is less than with CT). However, this does not mean
that MRI cannot be used for patients with various types of intra-thoracic masses and may be more commonly performed at some institutions. For example, lung masses and nodules can be imaged with MRI since the normal hypointense lung parenchyma allows for good contrast of pulmonary lesions. MRI has also been used for imaging cardiac tumors (with proper equipment in dealing with cardiac motion, e.g. ECG-gating).  

**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. Unfortunately, in terms of refining the diagnosis for the bleeding splenic mass, 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-reptured 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 reportedly are hyperenhanced 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 not replaced our more routine practice of CT for these types of tumors. For example, pancreatic insulinomas can be difficult to detect on standard abdominal ultrasound, especially in large dogs due to factors such as lesion depth and intestinal contents (which then means that CEUS cannot be used), whereas these factors do not hinder diagnosis in CT angiography.

**POSITRON EMISSION TOMOGRAPHY (PET)**
PET is a form of nuclear medicine imaging commonly used in human oncology, as it is very sensitive in identifying tumors and possible 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 a small amount of literature describing normal and abnormal findings on PET scans. 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 veterinary hospital currently, but we do have access to a PET scanner at the adjacent human hospital so are hoping to utilize this modality in some of our cancer patients.

References: