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Whole Body Computed Tomography for Tumor Staging in Dogs: Review of 16 Cases

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Abstract

Precise tumor staging encompassing the patient's entire body is essential in cancer management. While more advanced imaging modalities for tumor staging are available, in veterinary medicine, three-view thoracic radiography and abdominal ultrasonography are conventionally performed to screen for pulmonary and abdominal metastases. The objective of this retrospective study was to describe the use of whole-body computed tomography as an alternative in detecting lesions likely to be associated with primary or metastatic neoplasia in dogs. Sixteen dogs that underwent whole-body computed tomography were identified. Fifteen dogs had a histopathologic diagnosis of cancer. One dog had a cytologic diagnosis of thyroid carcinoma. The most common tumor types in this population included mast cell tumors [4; hind limbs (2), sternum (1), prepuce (1)], oral malignant melanomas (2), and spindle cell sarcomas [2; flank (1), cecum (1)]. The most commonly detected thoracic computed tomographic lesions were positional atelectasis (68.8%) and pulmonary nodules (12.5%). The most commonly detected abdominal computed tomographic lesions were splenomegaly (43.8%) and lymphadenomegaly (18.8%). The most commonly detected extra-thoracic/extra-abdominal computed tomographic lesions were cervical and retropharyngeal lymphadenomegaly (31.3%) and thyroid tumors (18.8%). No complications associated with anesthesia or contrast agents given during the procedure were observed and all dogs recovered uneventfully. Median scan time was 37.5 minutes. This study demonstrates that whole-body computed tomography is a safe and time-efficient imaging modality that is effective in identifying a range of pathologic changes important to tumor staging. Further prospective studies are needed to correlate the sensitivity and specificity of whole-body computed tomography with those of a combination of three-view thoracic radiography and abdominal ultrasonography.

Keywords: Computed tomography; Malignancy; Metastasis; Neoplasia; Tumor staging

Abbreviations: WBCT: Whole-Body Computed Tomography; CT: Computed Tomography.

Introduction

Accurate clinical staging is essential to pre-treatment evaluation of cancer patients to determine optimal therapeutic options and accurate prognosis. Therefore, precise tumor staging encompassing the entire body is critical to cancer management. Thirty to 40 years ago, the introduction of instruments capable of Whole-Body Computed Tomography (WBCT) scanning heralded the use of this technology for the detection of intra-abdominal and intra-thoracic disease in human patients [1]. Since then, numerous reports in medical journals emphasize the value of WBCT in the diagnosis, staging, and management of malignancies [2]. While more advanced imaging modalities for tumor staging are available in veterinary medicine, three-view thoracic radiography and abdominal ultrasonography are still conventionally performed to detect pulmonary and visceral metastases, respectively [3-6].

This report details our cumulative clinical experience with the use of WBCT in detecting and defining either primary or metastatic cancer in veterinary patients. The case material was drawn from patients with documented neoplasia, and it was not our intention to statistically compare the efficacy of WBCT versus other diagnostic modalities. Rather, our goal was to assess the feasibility of using WBCT in a clinical setting to demonstrate the range of lesions which can be visualized by WBCT and to underscore the potential diagnostic benefits that WBCT may yield.

Materials and Methods

Medical records of dogs that underwent WBCT at VCA All Care Animal Referral Center (VCA-ACARC) between January 2010 and December 2012 were reviewed. Dogs with confirmed histological or cytological diagnosis for malignancy were included. Clinical information obtained included signalment, laboratory findings, results of histologic or cytologic examination, WBCT scan findings, results of pertinent ancillary diagnostics (thoracic radiography, abdominal ultrasonography) and patient clinical outcome.

All the patients had CT scans of the thorax and abdomen; additional body parts were scanned at the attending clinician's discretion. The CT images were acquired using a HiSpeed NX/I dual-slice unit (General Electric, United States). With this unit, lung scans can be performed in a single breath hold. Multi-phase studies of abdominal organs such as the liver and pancreas also benefit from its increased speed. All scans were performed within one month of confirmed cancer diagnosis. All dogs were scanned while under general anesthesia, having been induced with propofol, and maintained on isoflurane and 100% oxygen. Dogs were positioned in sternal recumbency and head first within the CT gantry. The CT protocol consisted of a whole body scan, from the nose to the ischii. In general, 3-5 mm thick slices were obtained in transverse plane with the majority of the thoracic scans having 3 mm slices and abdominal scans 5 mm slices. Prior to thoracic CT acquisition, the dogs were hyperventilated with 4-5 breaths followed

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by breath holding at 20 cm H_2O for the length of the thoracic scan. No additional manipulation was performed for the abdominal CT scan or to scan any other additional body part. Thirteen of the 16 cases had pre- and post-contrast CT scans carried out after intravenous administration of iodine-containing contrast material (Isovue*, Bracco Imaging, Italy).

All CT studies were evaluated by a single board-certified radiologist who was blind to the clinical diagnosis and from the original imaging reports at the time of retrospective analysis. The radiologist reviewed the location, size, margins, internal architecture, and density of lesions detected. Sternal lymph node height was measured when sternal lymphadenomegaly was observed.

Results

Signalment

Medical records of 31 dogs that underwent WBCT during the study period were reviewed and 16 cases met the criteria for inclusion in the study. For dogs included in the study, median age at time of CT scans was 9.5 years (range, 5-14 years). There were eight castrated males, two sexually intact males, and six spayed females. Three were mixed-breed dogs, and 13 were purebred, representing 11 breeds. The most common purebred breeds were Labrador Retrievers (2) and American pit bull terriers (2). One dog represented each of the following breeds: boxer, dachshund, golden retriever, Great Dane, Rottweiler, Shar-Pei, Siberian husky, standard poodle, and toy poodle.

Laboratory findings

Eleven of the 16 hemograms available had complete blood counts with no abnormalities. The remaining five had mild changes: lymphocytosis (1), lymphopenia (1), non-regenerative anemia (1), regenerative anemia (1), and thrombocytosis (1). Seven dogs out of 16 had normal serum chemistry panels. The most common serum chemistry abnormality was elevated liver enzyme activity in seven of the remaining nine dogs. Additional chemistry abnormalities in these nine dogs included: hyperamylasemia (2), hypercholesterolemia (2), hypocalcemia (2), hypercalcemia (1), hypoalbuminemia (1), and hypoglobulinemia (1). Urinalyses available in nine of the 16 dogs were acellular and sediment-free. Five out of nine dogs had isosthenuria and three dogs had proteinuria. Thyroid function was normal for nine of 11 dogs and the two other dogs that were tested had a low free T4.

Results of tumor types evaluated

One out of the 16 dogs had a cytological diagnosis of thyroid carcinoma. Histopathological diagnosis of neoplasia was confirmed in 15 out of the 16 dogs (Table 1). The neoplasias included: four mast cell tumors [hindlimb area (2), sternal area (1) and left peripreputial

Case	Diagnosis	Thoracic CT findings	Abdominal CT findings	Additional CT findings	Additional imaging diagnostics	Sternal LN height (mm)
1	Right thoracic wall spindle cell sarcoma	NSF[a]	NSF	n/a[b]	n/a	7L[c], 10R[d]
2	Lingual malignant melanoma	Atelectasis	-Left adrenomegaly -Prostatomegaly	Bilateral retropharyngeal lymph node enlargement	AUS[e] – prostatomegaly	n/a
3	Left metatarsal Mast cell tumor	Contrast enhancing sternal soft tissue subcutaneous nodule	NSF	n/a	n/a	4L, 5R
4	Thyroid carcinoma	Atelectasis	Caudate liver nodules	Left thyroid mass	n/a	10L, 9R
5	Left stifle Mast cell tumor	Atelectasis	Splenomegaly	n/a	n/a	4L, 6R
6	Left radial osteosarcoma	Atelectasis	Splenomegaly	-Aggressive bony lesion distal aspect left radius - Left superficial cervical lymph node enlargement	CXR[f] – unremarkable	n/a, 5R
7	Sternal Mast cell tumor	NSF	Splenomegaly	n/a	n/a	n/a, 3R
8	Right anal sac adenocarcinoma	NSF	-Right anal sac inflammation -Splenomegaly	n/a	CXR – unremarkable	n/a, 2R
9	Salivary gland malignant mixed tumor	-Atelectasis	Splenomegaly	-Left ventral cervical mass -Left retropharyngeal lymph node enlargement	n/a	n/a
10	Mediastinal lymphoma	-Large soft tissue mediastinal mass -Atelectasis	-Splenomegaly -Hepatic lymph node enlargement	n/a	CXR – unremarkable	n/a
11	Pulmonary adenocarcinoma	-right and left caudal lung lobe nodules -Atelectasis	-Splenomegaly	n/a	n/a	3L, 4R
12	Hepatocellular carcinoma	NSF	-Multiple liver lobe masses -Hepatic lymph node enlargement	n/a	-CXR – unremarkable -AUS – liver lobe masses	8L, 6R
13	Right ear ceruminous adenocarcinoma	Atelectasis	NSF	-Right ear mass -Right retropharyngeal lymph node enlargement -Left thyroid nodule	n/a	2L, 6R
14	-Left nasal bridge soft tissue sarcoma -Left peripreputial mast cell tumor	-left cranial lung lobe nodule -Atelectasis	NSF	Soft tissue swelling left nose	n/a	7L, 4R
15	Maxillary malignant melanoma	Atelectasis	NSF	-left maxillary mass with bone lysis -Cervical lymph node enlargement -Right thyroid nodule	n/a	5L, 5R
16	Cecal spindle cell tumor with omental metastasis	Atelectasis	-Multiple abdominal lymph node enlargement -Right adrenal mass invading caudal vena cava	n/a	-CXR – unremarkable -AXR[g] – cranial abdominal mass effect	6L, n/a

[a]NSF: No Significant Findings; [b]n/a: Not Applicable; [c]L: Left; [d]R: Right; [e]AUS: Abdominal Ultrasonography; [f]CXR: Thoracic Radiography; [g]AXR: Abdominal Radiography

Table 1: Summary of description of imaging findings for 16 dogs with confirmed diagnosis of neoplasia.

area (1)], two oral malignant melanomas, two spindle cell sarcomas [cecum (1) and flank area (1)], and one each of apocrine gland anal sac adenocarcinoma, ceruminous adenocarcinoma, hepatocellular carcinoma, malignant mixed tumor of the salivary gland, mediastinal lymphoma, osteosarcoma, pulmonary adenocarcinoma, and left nasal bridge soft tissue sarcoma. One out of the 15 dogs (case 14) was evaluated for two concurrent neoplasias (left peripreputial mast cell tumor and left nasal bridge soft tissue sarcoma).

Radiographic and/or abdominal ultrasonographic findings

Five of the 16 dogs (cases 6, 8, 10, 12, and 16) had three-view thoracic radiographs available at the time of the CT scan; no radiographic abnormalities were detected. Only one dog (case 16) had abdominal radiographs available, which showed evidence of abdominal masses. Two dogs (cases 2 and 12) had abdominal ultrasonography performed, which showed prostatomegaly and liver lobar masses, respectively.

Computed tomography scan findings

The scan time for all dogs ranged from 12-90 minutes; the median scan time was 37.5 minutes for dogs undergoing WBCT. Twelve of 16 dogs had lesions detected on thoracic CT scans. The most common CT abnormality was positional atelectasis, which was detected in 10 of 12 dogs. Two of 12 dogs had lung nodules detected on thoracic CT scans, and three dogs had additional single lesions: large mediastinal mass (1), right lateral thoracic wall subcutaneous nodule (1), and a contrast-enhancing soft tissue sternal subcutaneous nodule (1). Sternal lymph nodes were visible in 13 dogs and were measured accordingly (Table 1). The median left sternal lymph node height was 6.6 mm in 10 dogs and right sternal lymph node height was 5.3 mm in 12 dogs.

Abdominal lesions were detected in 11 of 16 dogs, with splenomegaly being the most common finding (7), followed by abdominal lymphadenomegaly (3), liver nodules (2), left adrenomegaly (1), right adrenal mass invading the caudal vena cava (1), prostatomegaly (1), and right anal sac inflammation (1).

Additional body parts evaluated by CT scan included the head, neck, and extremities; these scans were performed on seven of the 16 dogs. All seven dogs had detectable extra-thoracic/extra-abdominal CT lesions which included retropharyngeal lymphadenomegaly in three dogs (cases 2, 9, and 13), thyroid mass or nodule in three dogs (cases 4, 13, and 15), cervical lymphadenomegaly in two dogs (cases 6 and 15). One dog each was observed to have each of the following lesions: ventral cervical mass, left nasal soft tissue swelling, left maxillary mass with bone lysis, right ear canal mass, and an aggressive lesion located at the distal aspect of the left radius.

Discussion

The results of our current study show that WBCT can play a primary or complementary role in staging canine patients with known or suspected malignancy via lesion localization. Since CT allows visualization of normal anatomic structures as well as pathologic processes, this imaging modality provides information regarding the texture and internal architecture of lesions under investigation. In the assessment of the primary tumor, CT is particularly helpful for identifying tumor spread into adjacent tissues. In this study, we assessed primary tumors of the skull and oral cavity, thorax (primary lung tumors, mediastinal tumors), abdomen, and of the integument and extremities. CT imaging can readily define the presence of compression and/or invasion of surrounding structures, as was seen in case 16 (Figure 1). Whole body CT identified this right adrenal mass invasion of the caudal vena cava. Although histopathology was not performed to confirm malignancy, this invasion may be correlated with extension of malignancy, which in turn could impact treatment approach and prognosis for the patient [7-9].

Contrast agents are applied in CT protocols to aid differentiation of anatomic structures, improve lesion localization, and support lesion characterization. With the aid of injected contrast, solid lesions can be further categorized into hypovascular or hypervascular masses [10]. An example is demonstrated in case 4 (Figure 2). Studies of human patients comparing contrast-enhanced with non-enhanced CT protocols in the experimental setting, as well as in standard radiology practice, demonstrate a substantial benefit of the contrast-enhanced approach [9,11]. Violante and Dean show an increase in accuracy for detection of liver lesions, from 63% to 90%, when applying intravenous contrast agents [11]. Schultz et al. reports the sensitivity and specificity of contrast-enhanced CT for vascular invasion, compared with observation at surgery or necropsy, to be 92% and 100%, respectively [9].

Lymphadenomegaly was a lesion most commonly detected on CT in our patients. This finding may alert the clinician to potential tumor

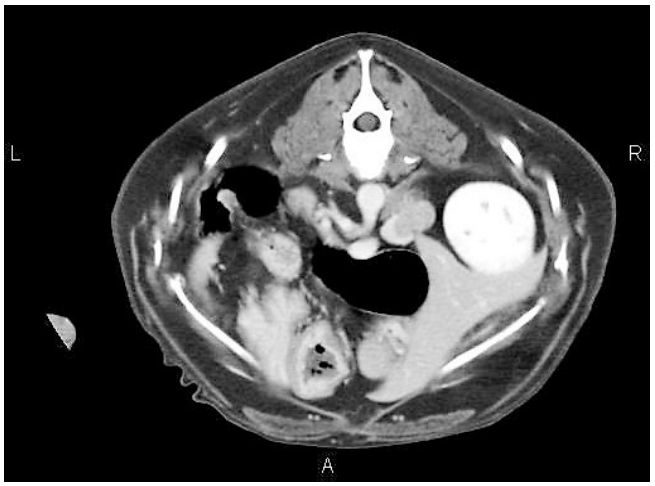

Figure 1: Case 16 - right adrenal tumor with caudal vena cava invasion; contrast-enhancement.

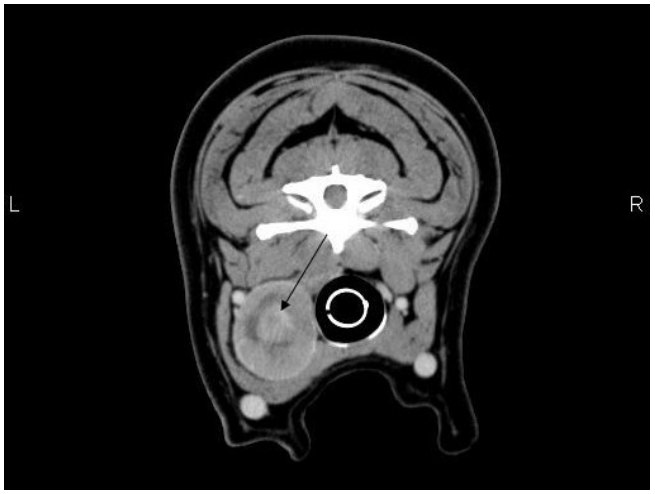

Figure 2: Case 4 - left thyroid carcinoma; contrast enhancement.

spread. The pattern of tumor spread to regional and distant lymph nodes depends on the tumor type and the use of CT examination must be tailored to include the appropriate areas. Enlarged lymph nodes often appear as soft tissue masses of homogenous density. A recent study evaluated CT characteristics of canine tracheobronchial lymph node metastasis for thoracic neoplasia and identified that lymph node enlargement, as well as contrast enhancement, was associated with metastatic disease [12]. Moreover, tracheobronchial lymph node enlargement is a prognostic factor for dogs with primary lung tumors [13]. In our study, the one dog with pulmonary adenocarcinoma (case 11) did not have associated lymph node enlargement, and this information was helpful in staging and formulating treatment planning.

The sternal lymph node chain may drain either the thorax or cranial abdomen. These lymph nodes are located in the intercostal spaces and may drain organs from the liver, to the diaphragm, to the thoracic wall, including mammary tissue. These lymph nodes may also drain dermal structures in this region. In human medicine, (para)sternal lymph nodes are staged in women with breast carcinoma, and when enlarged, are found to represent metastasis to the internal mammary lymphatic chain, which confers a poor prognosis for survival [14]. A recent veterinary study described radiographic findings of sternal lymphadenomegaly in cats and dogs. Neoplastic disease is the most prevalent condition associated with sternal lymphadenomegaly [15]. In that study, the median height of the left and right sternal lymph nodes in dogs with neoplastic, inflammatory, and hematologic diseases was 18 mm and 20 mm, respectively.

We measured sternal lymph nodes to assess for potential metastatic disease. To the authors' knowledge, there are no studies that measure sternal lymph nodes via CT in veterinary cancer patients. In our study, sternal lymph nodes were visible in 13 dogs; the median left sternal lymph node height was 6.6 mm in 10 dogs, and right sternal lymph node height was 5.3 mm in 12 dogs. Although the imaging modalities are different, one can conclude that sternal lymph nodes in our dogs were not enlarged compared to those observed in the dogs in the Smith and O'Brien study [15]. The results of our study appear to describe normal sternal lymph node size in dogs by CT scan, and thus could serve as a potential reference; however, cytological or histopathological confirmation is needed. Prospective studies are needed to further investigate this finding.

Splenomegaly was the most commonly detected abdominal CT finding. One possible cause for splenomegaly in our dogs is neoplasia. The most common neoplastic diseases of the spleen include hemangiosarcoma, lymphoma, and mast cell tumors [16]. No dogs included in this study had diagnosed hemangiosarcoma, but one dog had mediastinal lymphoma (case 10), and four dogs had mast cell tumors (cases 3, 5, 7 and 14). Three of these five dogs had splenomegaly on CT scan. While biopsy of the spleen would have been optimal for staging purposes, two of the three dogs with splenomegaly (cases 5 and 7) had fine needle aspiration performed. Normal splenic cytology, as interpreted by a board-certified cytopathologist at a reference laboratory, make it less likely that splenomegaly was attributable to metastatic round cell tumor in those two dogs.

Another cause for splenomegaly is use of anesthetic drugs. The concern for the effect of drugs on spleen size has been recognized, and drug-induced (propofol) splenomegaly may be misdiagnosed as splenic disease, such as diffuse neoplastic infiltrates of the spleen [17]. In the present study, all dogs were anesthetized with propofol, and 11/16 dogs had splenomegaly. Despite this finding, one cannot exclude the possibility that splenomegaly detected on CT may be caused by neoplasia, which then warrants confirmatory needle aspiration or biopsy. Whenever possible, anesthetic protocols that minimize the potential for splenomegaly should be employed for WBCT procedures on patients being evaluated for metastatic neoplasia.

With WBCT, identification of a lesion depends on the difference in Hounsfield units between the lesion and its surroundings; therefore, smaller lesions can be detected by CT scans compared to conventional radiographic studies [18]. This is particularly important in the pulmonary parenchyma, where pulmonary metastases can be identified at sizes as small as one millimeter in diameter by CT scanning, compared to 7-9 mm by conventional radiography [19]. In recent veterinary studies that compared thoracic radiographs to CT scanning for detection of pulmonary nodules, CT was found to be more sensitive [5,19,20]. In our study, two cases (11 and 14) had evidence of pulmonary nodules on WBCT. Case 11 had two nodules: right caudal lung nodule (50 mm) and left caudal lung nodule (28 mm). Case 14 had one left cranial lung nodule (7 mm). These dogs did not have thoracic radiographs available for comparison, but one can infer that while the dog in case 11 had nodules that would be readily detectable on radiographs, the nodule in case 14, perhaps, would have been less obvious.

The same theory holds true for abdominal CT, in that abdominal CT may prove to be a better screening test for abdominal disease in veterinary patients when compared to abdominal radiographs and/or abdominal ultrasound findings [21]. Three of our dogs had abdominal ultrasonography (cases 2 and 12) or abdominal radiography performed (case 16). In case 2, abdominal CT and ultrasound detected prostatomegaly. The dog in case 12 had an abdominal ultrasound that detected liver masses, but CT was able to definitively identify the location and extent of the liver masses in the left and right medial liver lobe. Finally, case 16 had a cranial abdominal mass effect detected on abdominal radiographs, but CT was able to further characterize this mass effect as a right adrenal mass with multiple lymph node (mesenteric and medial iliac) rim enhancement lesions. A prospective study specifically comparing WBCT with thoracic radiography and abdominal radiography and/or abdominal ultrasound is warranted in the future.

Despite WBCT being an important, safe, and time-efficient diagnostic tool, there are some concerns associated with its use. Perhaps the most common concern for routine use of WBCT is the current necessity of employing general anesthesia in immune-compromised and often older cancer patients. Physiologic changes impede the body's ability to maintain homeostasis during times of physiological stress, with a subsequent decrease in physiological reserve. This can lead to physiological dysfunction, resulting in peri-anesthetic complications [22]. None of our patients had anesthetic complications; this was aided by a thorough pre-anesthetic patient evaluation to assess patient suitability for the procedure.

A critical component of the pre-anesthetic patient evaluation is laboratory analysis. There is no evidence to indicate the minimum time frame before anesthesia within which laboratory analysis should be performed. However, the timing should be reasonable to detect changes that impact anesthetic risk [23]. There was no clear association evident between the clinical pathological abnormalities in our patients and the results of their WBCT scans. Mildly elevated serum alkaline phosphatase activity was the most common serum chemistry abnormality in patients in our study. This elevation could represent a paraneoplastic elevation of serum alkaline phosphatase. Garzotto et al. describes the relationship between serum alkaline phosphatase and appendicular osteosarcoma and survival times [24]. The one dog in this

study with appendicular osteosarcoma (case 6) did not have elevated alkaline phosphatase activity, however. The relatively minor clinical pathological abnormalities noted in our patients did not complicate or contraindicate pursuing WBCT, and all similar patients should have pre-anesthetic testing in order to properly evaluate the patient's status and adjust anesthetic agents or protocols as needed. Fortunately, with the advance of CT scanning equipment, newer multi-slice models (16, 32, or 40-slice) will allow for shorter anesthesia time, and even allow some studies to be performed using sedation only. Faster scanning also helps to eliminate artifacts from patient motion such as breathing or peristalsis. The increased slice count is useful for cancer diagnosis because it offers better resolution, making it possible to diagnose and assess the extent of the disease. A higher-slice count CT should more accurately measure the margins of a mass and allow for a greater precision in surgery and radiation therapy.

Another concern for the routine use of WBCT in veterinary patients is adverse reactions to contrast media. There are reports of reactions to iodinated contrast media in the human and veterinary literature [25-27]. These reactions are reported to include allergic reactions, cardiovascular reactions, gastrointestinal disturbances, nephrotoxicity, shock, and even sudden death. No dogs in this study developed any adverse reactions. Furthermore, the adverse reactions in the two anesthetized dogs described in the case report by Pollard and Pascoe were secondary to an ionic iodinated contrast media, whereas the dogs in our study received nonionic iodinated contrast media. Minor acute reactions occur in only three percent of people given nonionic iodinated contrast media [26]. These results, combined with prior clinical experience, suggest that veterinary patients undergoing WBCT with nonionic contrast media are highly unlikely to develop an adverse reaction.

An additional concern to both the clinician and client related to CT evaluation is cost. At our facility, the average cost of WBCT is $800-$1,200, whereas the cost of thoracic radiographs and abdominal ultrasound together average a cost of $700-$900. The apparent utility of WBCT to detect and more completely evaluate primary or metastatic lesions, along with the relatively short time to perform the study, offer good clinical and financial value when compared to a combination of abdominal ultrasound and thoracic radiographs.

CT has been more readily available in the recent years to clinicians and clients. Results of a 1999 survey of the American College of Veterinary Radiology members on the availability of CT scanners reported that in-house CT scanners accounted for 56% of the CT scanning instruments available to veterinary radiologists; off-site transport to local imaging centers, 26%; and regularly scheduled mobile units on site, 5%. However, the availability of CT scanners is likely to be considerably greater at the time of this writing.

Conclusions

WBCT is safe and provides valuable information for clinical staging in cancer patients. In this study, we highlighted tissue findings that may not have been detected through more commonly used imaging modalities. We also described sternal lymph node size in a variety of veterinary cancer patients, which could provide an objective reference for future studies. The potential advantages of WBCT in comparison to radiography and ultrasonography for staging cancer patients will likely become more evident with the increased availability of more advanced equipment. Newer multi-slice CT scanning instruments will dramatically reduce scan times, further limiting anesthetic risk while simultaneously improving spatial resolution and facilitating multiplanar reconstruction. The results of our retrospective study support further work evaluating WBCT compared to radiographic and ultrasonographic evaluations for staging veterinary cancer patients.

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