Advances in Small Animal Care 1 (2020) 35–47
ADVANCES IN SMALL ANIMAL CARE

Whole-Body Computed Tomography Imaging in Cancer Staging

Francesco Collivignarelli, DVM, Francesca Del Signore, DVM, Francesco Simeoni, DVM*, Roberto Tamburro, DVM, PhD, Ilaria Falerno, DVM, Massimo Vignoli, DVM, PhD, Dipl. ECVDI
Faculty of Veterinary Medicine, University of Teramo, SP 18, Teramo 64100, Italy

KEYWORDS
• Computed tomography • Whole body • Cancer • Staging • Dog • Cat

KEY POINTS
- Whole-body computed tomography (WBCT) is a diagnostic tool that rapidly provides detailed information of the body.
- This technique is applied in veterinary medicine to fully characterize lesions in dogs and cats with polytrauma.
- In oncology, WBCT is of paramount importance to assess for the presence of metastasis, in particular in pulmonary and muscular locations.
- WBCT is recommended for the staging of oncology patients, especially for primary tumors characterized by high metastatic rate.

INTRODUCTION

Whole-body computed tomography (WBCT) is an imaging examination that provides a detailed view of the entire body and, for that reason, it is mainly applied to assess trauma or oncologic conditions in human and veterinary medicine. Particularly in human medicine, mortality and disability-adjusted life-years attributable to blunt multiple traumas have increased in the past decades, increasing the need for prompt diagnosis and management in industrialized countries [1]. WBCT is particularly useful for patients with polytrauma because it allows quick and early diagnosis of injury and improves survival rates [2–5]. However, WBCT diagnosis as standard of care is still under debate, because of the risk of developing cancer after long-term radiation exposure, expense, and limited access to unstable patients [6–10]. Recent studies have shown that radiation reduction with low-dose protocols does not lead to underestimating lesions in traumatized patients [11–15].

At present, WBCT is considered a useful tool in veterinary medicine to assess traumatic injuries in small animal patients. This technique provides the prompt detection of pneumothorax, and pleural and peritoneal fluid, thus permitting a complete evaluation of trauma-based injuries.

Alongside the use of WBCT for assessment of trauma, this technique is useful in oncology, in particular if applied to cancer staging.

Accurate and detailed tumor staging is essential in cancer management, to provide optimal therapeutic options and a more accurate prognosis in both human and veterinary medicine. The development of advanced diagnostic tools capable of scanning the whole body, such as WBCT, has proved to be an important tool to diagnose, stage, and manage malignancies [16]. In veterinary medicine, 3-view thoracic radiography and abdominal ultrasonography are conventionally performed to detect pulmonary and visceral metastasis [17–19], but, with the improvement of more advanced

*Corresponding author, *E-mail address:* fsimeoni@unite.it

https://doi.org/10.1016/j.yasa.2020.07.004

tools, such as WBCT, a thorough staging of patients with cancer can now be performed to obtain more detailed information to characterize neoplastic conditions.

With computed tomography (CT) scanners, images are acquired in slices, and the superimposition of structures is eliminated [20]. Although CT has decreased spatial resolution compared with radiographs, the reduced anatomic superimposition and superior contrast resolution result in CT being more sensitive to detect lesions throughout the body [20,21]. To perform an optimal WBCT examination, slice thickness should be between 1.25 and 2.5 mm depending on the patient's size. Thin-slice imaging is more challenging on older scanners, because the heat load on the x-ray tube can slow the scanning time. Newer-generation CT scanners, particularly multislice helical scanners, have largely overcome this limitation by allowing faster examination for larger areas, also reducing slice thickness. This aspect deserves particular consideration, because it affects both image noise and partial volume averaging artifacts.

Partial volume averaging can result in indistinct margins, false attenuation measurements, and the appearance of pseudolesions. Thin-slice images have increased noise, which can be offset by increasing the milliampere setting. This increase improves image quality but also increases the radiation dose to the patient. The scan field of view (SFOV) is the area from which the image can be reconstructed. Because the reconstruction matrix size is constant, keeping the SFOV sized to the anatomy to be imaged improves spatial resolution. Multiplanar reformatting (MPR) or three-dimensional reformatting of images can provide more complete assessment [20].

Dogs and cats are usually under general anesthesia during the WBCT examination. With the increasing availability of faster multislice scanners, more CT examinations are being performed with sedation alone.

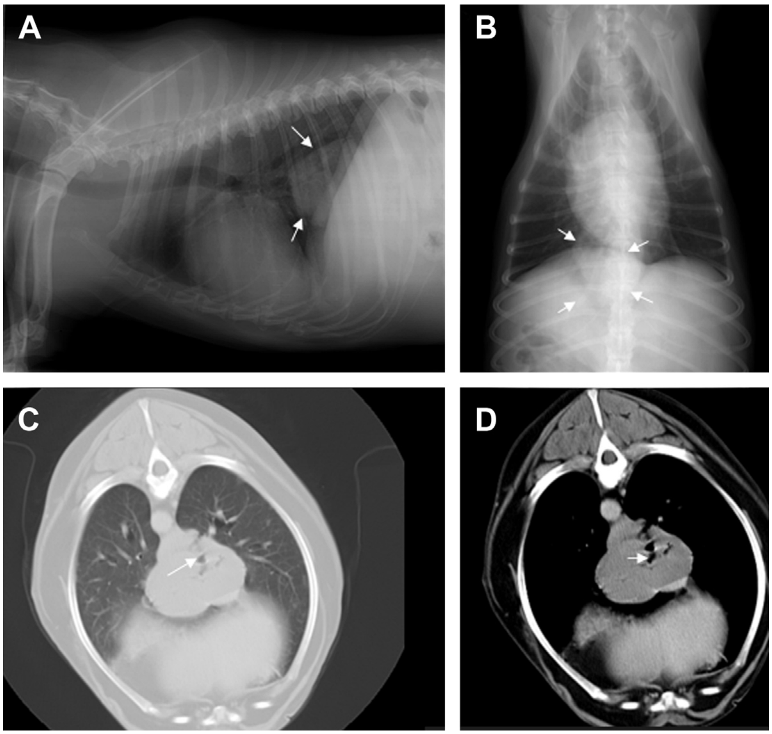

FIG. 1 (**A, B**) Thoracic radiographs of a 9-year-old spayed female mixed-breed dog. A soft tissue opaque mass is visible in the area of the caudal mediastinum along midline (*arrows*). Masses in this location can be difficult to localize in the lung or the mediastinum. (**C, D**) Transverse CT images of the same dog, in respective lung and postcontrast soft tissue windows, detail algorithm, showed internal air bronchograms (*arrows*), indicating the mass is pulmonary in origin and located in the accessory lung lobe (**C, D**). This mass was subsequently diagnosed as a carcinoma.

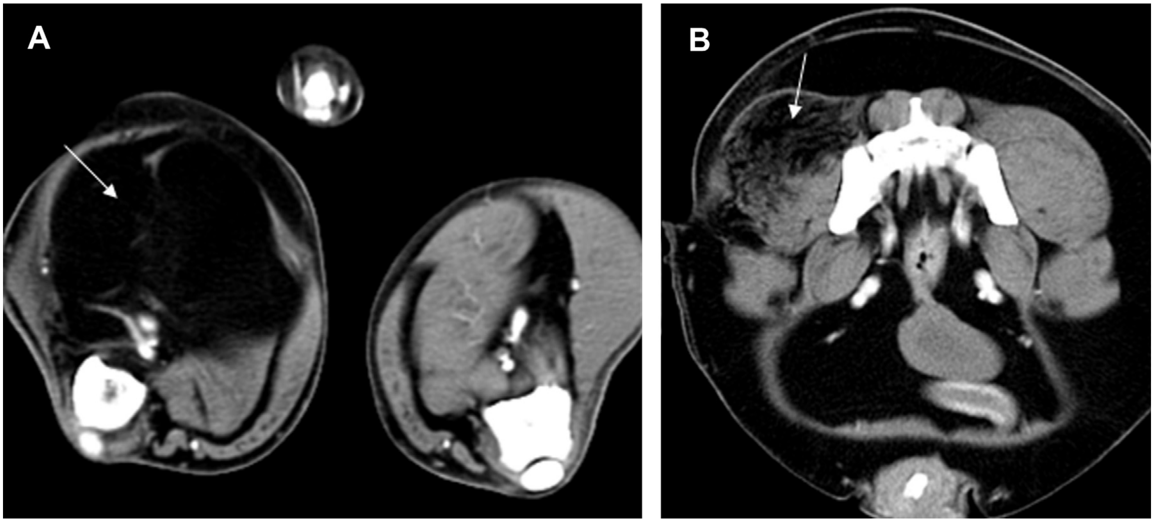

FIG. 2 Transverse CT images of the pelvic limbs postcontrast soft tissue window and algorithm. (**A**) Fat tissue attenuation mass is present in the caudal aspect of the right pelvic limb (*arrow*). Normal musculature in the left limb. (**B**) Scanning more cranially, fat tissue infiltrating the gluteal muscles is visible (*arrow*). Final diagnosis was an infiltrative lipoma.

However, it is the authors' opinion that this tool can be useful in emergency cases rather than in oncology.

WBCT imaging is discussed here, with a specific focus on the application of WBCT in small animal oncology. The current literature is discussed, this technique is described, and conditions are highlighted for which WBCT improves diagnosis and staging of neoplastic disorders in companion animals.

WHOLE-BODY COMPUTED TOMOGRAPHY TECHNIQUE

- After the patient has been anesthetized, placement in sternal recumbency is preferred, possibly with the aid of special foam cradles for optimal placement. To avoid imaging respiratory motion artifacts, patients may be manually hyperventilated just before slice acquisition to optimize lung visualization by

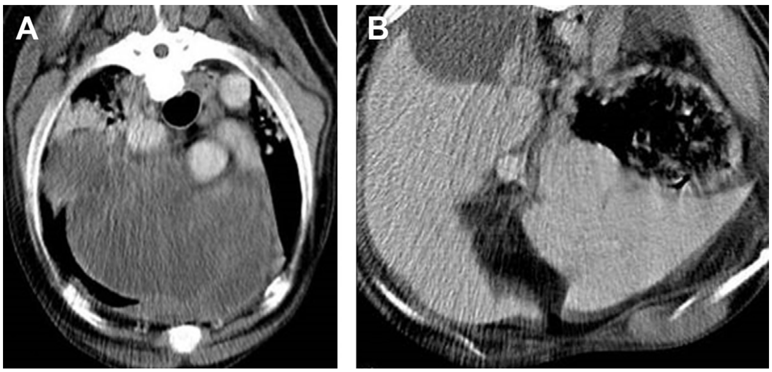

FIG. 3 An 8-year-old male Labrador retriever who underwent a CT scan for a mediastinal mass. Transverse CT image postcontrast with soft tissue window and algorithm (**A**) shows a large mediastinal soft tissue attenuation mass, with secondary dorsal displacement of the trachea, esophagus, vessels, and partial lung collapse. More caudally there was a second, smaller mass in the ventral left thoracic wall, involving a rib (**B**). The mediastinal mass was diagnosed as a thymoma, whereas the thoracic wall mass was a mastocytoma.

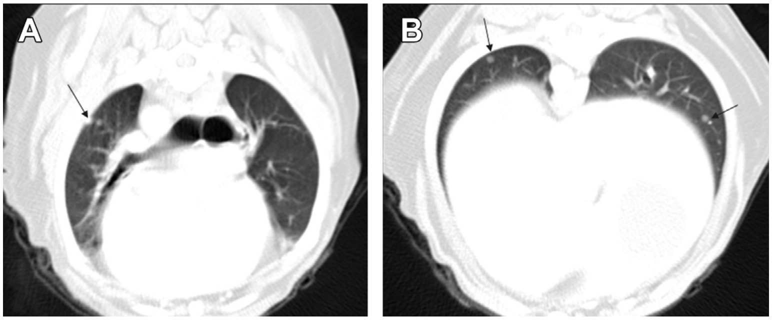

FIG. 4 A 12-year-old male Pomeranian dog underwent WBCT after a pancreatic mass was diagnosed via ultrasonography. Transverse CT images of the caudal thorax with lung window and medium algorithm highlighted several subpleural (***A***) and intraparenchymal (***B***) millimetric lung nodules (*arrows*).

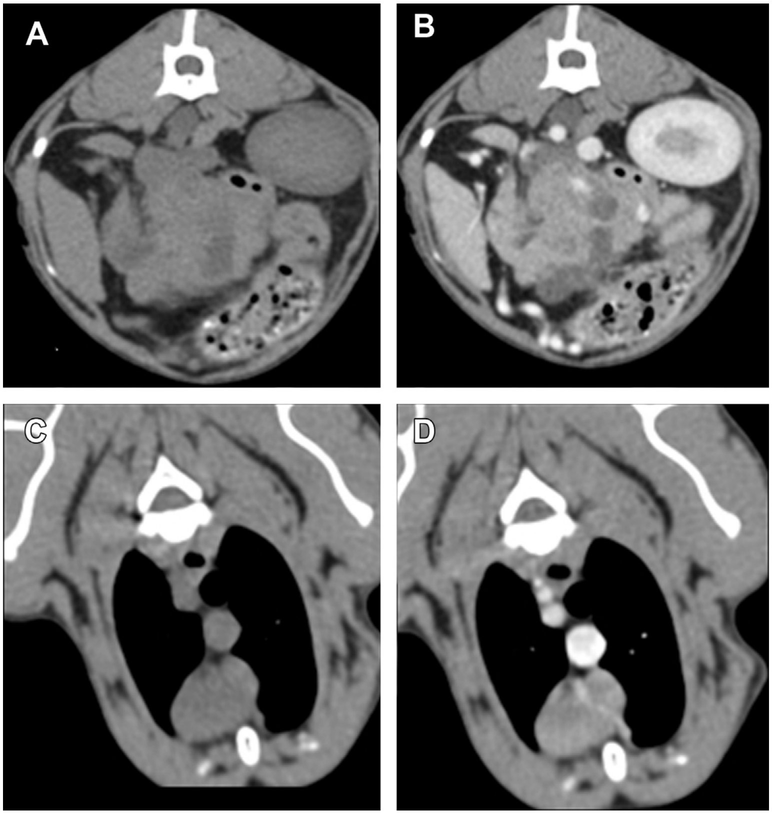

FIG. 5 A 12-year-old male castrated domestic shorthair cat with a pancreatic mass, cytologically diagnosed as pancreatic carcinoma. Transverse precontrast and postcontrast CT images with soft tissue window and algorithm reveal the pancreatic multicystic and heterogeneously contrast-enhancing mass (**A, B**), and sternal lymphadenomegaly. An enlarged heterogeneously contrast-enhancing sternal lymph node is present (**C, D**), cytologically confirmed as metastatic after ultrasonography-guided aspiration.

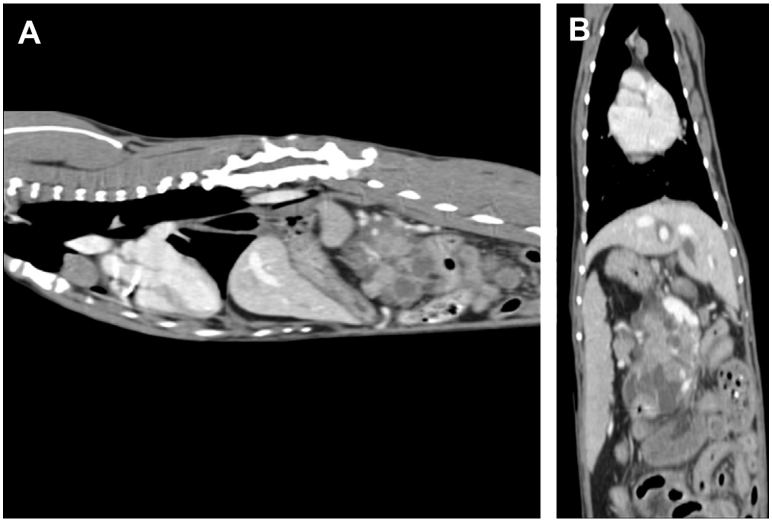

FIG. 6 Same cat as in Fig. 5. The postcontrast MPR images in sagittal (**A**) and dorsal (**B**) planes show the pancreatic mass and a sternal enlarged lymph node.

reducing any areas of atelectasis caused by anesthesia [21].

- Routinely, precontrast and postcontrast medium images are acquired. Nonionic water-soluble iodinated positive contrast medium administered at a dose of 2 mL/kg (600 mg of iodine per kilogram), injected into a peripheral vein, is routinely used to assess contrast enhancement of tissues.
- Contrast administration is crucial in WBCT for oncological staging to assess tumor vascularity, perfusion, and invasion into adjacent tissues. It is possible to perform a specific vascular assessment of arterial and early and delayed venous phase in masses and organs through triple-phase CT angiography (CTA): a single bolus injection facilitates imaging during the phase of preferential arterial enhancement (ie,

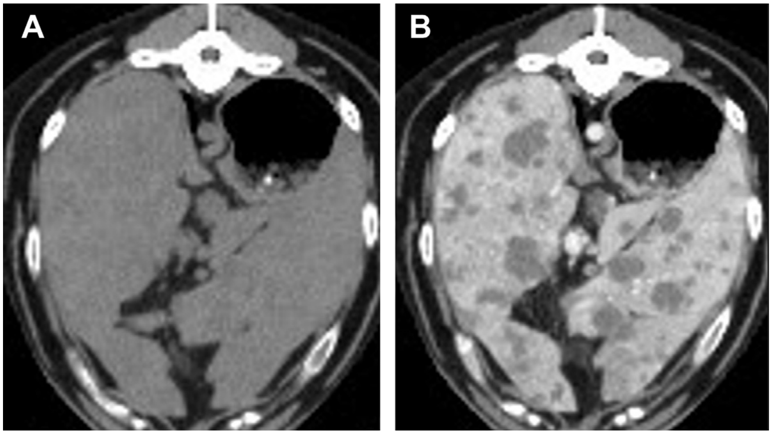

FIG. 7 A 6-year-old spayed female Czechoslovakian wolf with liver metastases from splenic hemangiosarcoma. Transverse CT images at the level of the liver precontrast and postcontrast with soft tissue window and algorithm. (**A**) Precontrast study showed mild heterogeneous liver parenchyma. (**B**) Postcontrast study highlighted multiple hypoattenuating nodules not previously visible.

the arterial phase), followed by the portal venous phase and delayed phase [22].

- Triple-phase CTA can improve the detection of small tumors, such as insulinoma and cardiac masses, and may help differentiate between benign and malignant lesions [23,24]. MPR can be helpful to better define lesions and may assist in predicting the malignancy of hepatic and splenic masses [24,25]. CT-guided biopsy is useful for the sampling of intracavitary lesions or pulmonary nodules, which are not readily identified or accessible with ultrasonography.

WHOLE-BODY COMPUTED TOMOGRAPHY ONCOLOGIC STAGING

- WBCT is an efficient and thorough imaging modality for the evaluation of multiple organs and structures. In oncology, WBCT is of paramount importance to assess (1) the correct localization of the tumor (Fig. 1), (2) its extension with or noninvolvement of the surrounding tissues/organs (Fig. 2), (3) concomitant diseases (Fig. 3), (4) metastatic lesions, and (5) follow-up after treatment. Specific structures evaluated on WBCT are discussed in more detail later.

THORAX EVALUATION

- CT imaging provides superior sensitivity in the identification of primary lung, mediastinal, heart base, and pleural tumors, and in assessment of pulmonary metastasis [26–30]. Because lesion identification with CT depends on the difference in Hounsfield units between lesions and their surroundings, with this technique it is possible to detect metastases as small as 1 mm in diameter (Fig. 4).
- CT allows detection of more lesions compared with conventional radiographs, so this technique is more sensitive in detecting pulmonary nodules [31].

LYMPH NODE EVALUATION

- Another important assessment is the cancer staging of lymph nodes for the evaluation of metastasis [32]. A study described lymph node findings using WBCT in cancer staging and found that lymphadenomegaly was commonly detected, thus alerting the clinicians to potential tumor spread [16].
- Enlarged lymph nodes may appear as oval to round soft tissue structures of homogeneous or heterogeneous attenuation and contrast enhancement. The pattern of tumor spread to regional or distant lymph nodes depends on the tumor type.
- Tracheobronchial lymph node enlargement is considered a prognostic factor for dogs with a primary lung tumor, thus making this information of paramount importance for clinicians to stage and formulate treatment planning [27].
- Sternal lymph node chain evaluation is important in cancer staging, because these nodes may drain either the thorax or cranial abdomen, including mammary tissue and dermal structures [16]. In particular, in human medicine, sternal and parasternal lymph nodes are staged in breast carcinoma, and, if enlarged, they represent metastasis to the internal mammary lymphatic chain, thus conferring poor prognosis for survival [33] Thorough evaluation of these nodes is of paramount importance with CT examinations [34] (Figs. 5 and 6).
- A recent retrospective study reported the usefulness of WBCT in the staging of gastric tumors in dogs [35,36]. The morphologic and contrast uptake parameters of primary gastric neoplasia and regional or peripheral lymph node involvement using dual-phase contrast WBCT in 16 dogs were evaluated. The dogs included were affected by adenocarcinoma, lymphoma, inflammatory polyps, and leiomyomas. Lymphadenopathy was regional in dogs affected by gastric adenocarcinoma, widespread in lymphomas, and not detected in leiomyomas. Also, lymph nodes measurements were reported to be larger in dogs with lymphomas than in dogs with adenocarcinomas [35].
- Definitive diagnosis of lymph node disorders is routinely performed with cytologic or histopathologic samples [32,37], but lymphatic draining patterns of certain type of tumors (eg, oral malignant melanoma or mast cell tumor) can diverge from the expected regional lymph node [38–40].
- In human medicine, the technique of sentinel lymph node mapping has been proved to be useful in cancer staging, considering the sentinel lymph node as the one receiving direct drainage from the tumor site [41,42]; in veterinary medicine, this technique is presently being investigated, with encouraging results and more detailed knowledge about the exact tumor lymphatic drainage [43,44].

LIVER EVALUATION

- Liver evaluation is crucial, not only for primary malignancies but also for potential metastatic spread from other primary tumors (Fig. 7). CT evaluation of the canine liver in both primary and metastatic hepatic neoplasm is reported in several studies describing the CT characteristics of liver masses [22,45,46]. Triple-phase CTA technique was used to evaluate the arterial, venous, and delayed phases to assess tumor type [22,45].

- Studies have compared hepatocellular carcinomas and nodular hyperplasia enhancement patterns and found that carcinomas had heterogeneous, marginal, or central arterial contrast enhancement and hypoattenuation in the later phases, whereas nodular hyperplasia had a diffuse enhancement pattern in the arterial phase and was isoattenuating in the delayed phase.
- Liver metastatic lesions were reported to be hypoattenuating in both arterial and delayed phases [22].

SPLEEN EVALUATION

- Another finding that can be detected with WBCT is splenomegaly, possibly caused by neoplasia, such as hemangiosarcoma, lymphoma, and mast cell tumor [16,47]. Standard precontrast and postcontrast CT findings are less specific in solid splenic masses, such as hematoma, nodular hyperplasia, hemangiosarcoma, and undifferentiated sarcoma in dogs.
- Three-phase CTA of splenic masses found nodular hyperplasia to have homogeneous normal enhancement pattern in all phases; hemangiosarcoma was characterized by 2 contrast enhancement patterns (a heterogeneous remarkable enhancement pattern in the arterial and portal venous phases and a homogeneous poor enhancement pattern in all phases) and, in addition, a heterogeneous normal enhancement pattern was detected

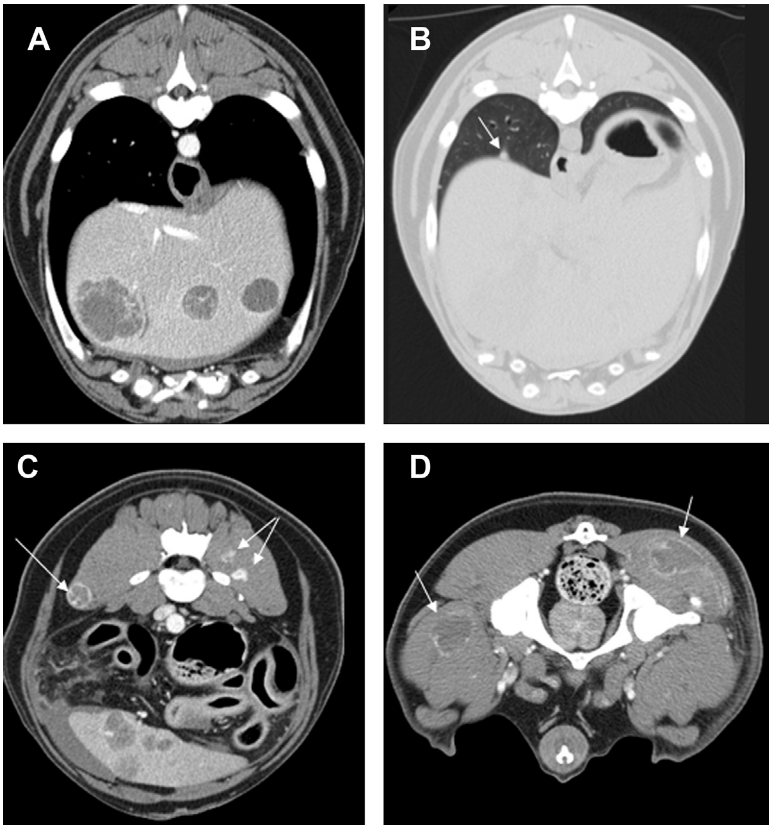

FIG. 8 A 7-year-old male boxer with a ruptured splenic hemangiosarcoma. Transverse CT images in multiple areas of the body. (**A**) Three hypoattenuating lesions are visible in the liver in the postcontrast study with soft tissue window and algorithm. (**B**) Lung window shows a small pulmonary nodule visible in the right caudal lung lobe (*arrow*). (**C, D**) several ring-enhancing (*arrows*) muscular nodules are visible in the epaxial, gluteal, and pelvic limb muscles. In (**C**), splenic nodules and free abdominal fluid are present.

in cases of hematoma and undifferentiated sarcoma [25] (Fig. 8D).

- When CT is used to stage multicentric lymphoma in dogs, in particular, the spleen and liver may appear normal or, when present, abnormalities are not pathognomonic for lymphoma. Fine-needle aspiration of the spleen and liver is recommended when using CT to stage dogs with multicentric lymphoma [48].
- Anesthetic drugs, in particular propofol, can also cause splenomegaly [49]. It has been suggested to minimize splenomegaly by using protocols that avoid drugs that could cause such effects and to combine spleen fine-needle aspiration or biopsy when the use of propofol cannot be avoided and splenomegaly is observed with CT scans [16].

MUSCULAR AND CARDIAC EVALUATION

- WBCT is also useful in cancer staging to detect muscular and cardiac metastasis, especially in primary tumors characterized by a high metastatic rate. Skeletal and cardiac musculature has been described in the literature as a rare metastatic target and this metastasis behavior is not completely understood. Inhibition of tumor cell proliferation by lactic acid, proteinase, and low pH in muscles are considered to be the most plausible reasons [50–53].
- In human medicine, cancers characterized by muscle metastasis are typically breast cancer, gastrointestinal adenocarcinoma, pulmonary adenocarcinoma, squamous cell carcinoma, and renal carcinoma [50,54–59]. In veterinary medicine, previous reports described muscle metastasis in pulmonary, mammary, and prostatic carcinoma, lymphoma, and

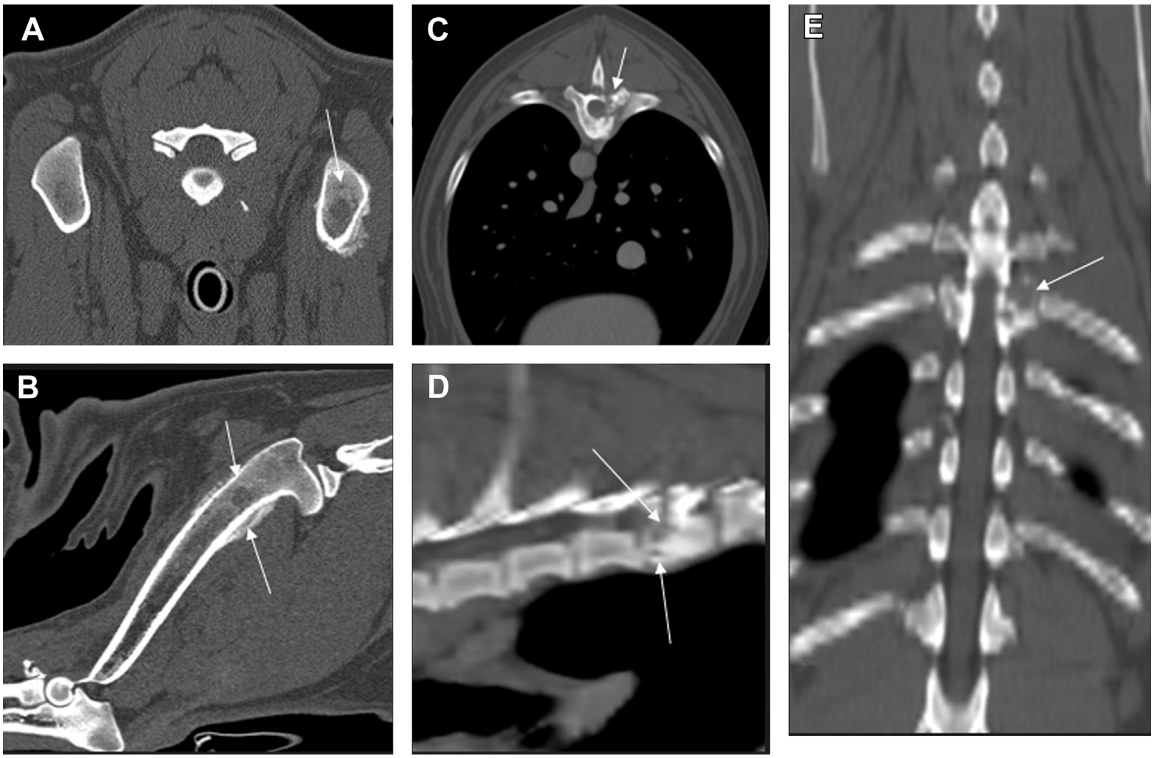

FIG. 9 A 4-year-old female Bernese mountain dog with osteosarcoma of the left proximal humerus. Bone window (**A–E**), bone algorithm (**A, B**), and soft tissue algorithm (**C–E**). (**A, B**) The transverse and sagittal MPR images, respectively, of the humeral lesion, with a mixed pattern of moth-eaten bone lysis and adjacent periosteal reaction (*arrows*). (**C**) Transverse view at the level of the eighth thoracic vertebra, where a lytic lesion of the left pedicle and lamina, and mixed bone lysis and sclerosis in the body, are visible (*arrow*). The vertebral lesion in sagittal (**D**) and dorsal (**E**) MPR reconstructions (*arrows*).

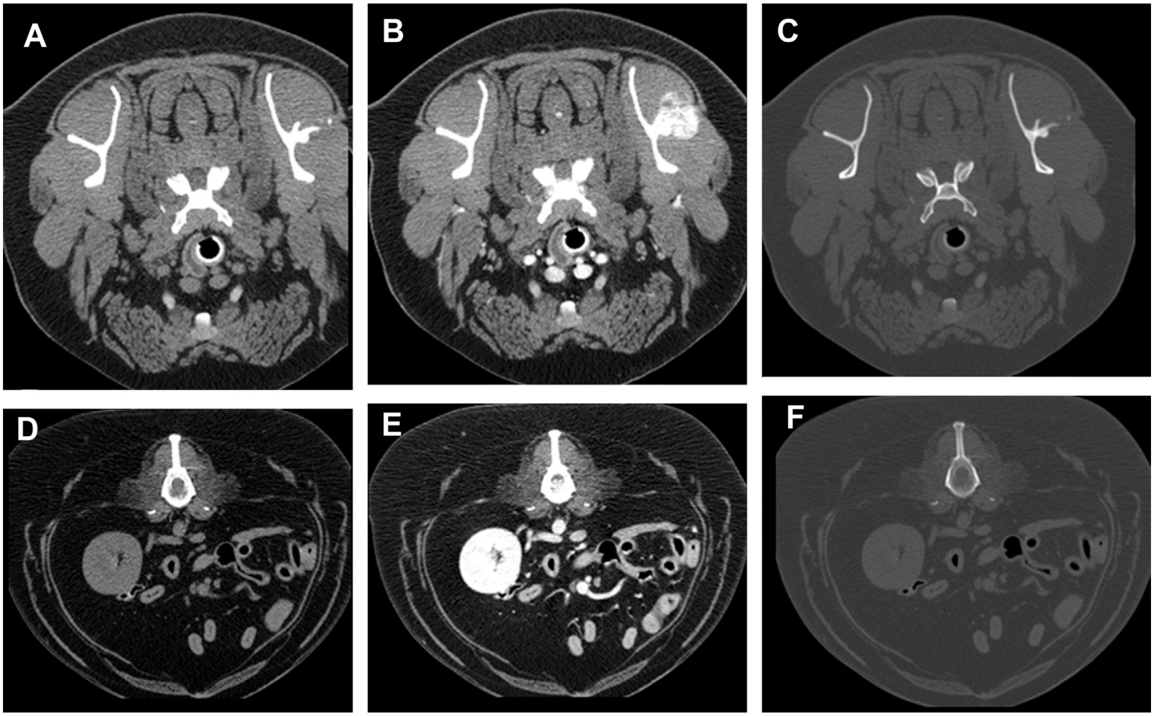

FIG. 10 An 8-year-old female spayed Rottweiler, 6 months after splenectomy for hemangiosarcoma. Transverse CT images, soft tissue algorithm, with precontrast (**A, D**) and postcontrast (**B, E**) soft tissue window. (**C, F**) Bone windows. The WBCT study showed multiple bone lysis, especially in the left scapula, with marked surrounding soft tissue enhancement (**A–C**), and lysis in several lumbar vertebrae, with vertebral canal invasion visible as contrast-enhanced tissue (**D–F**).

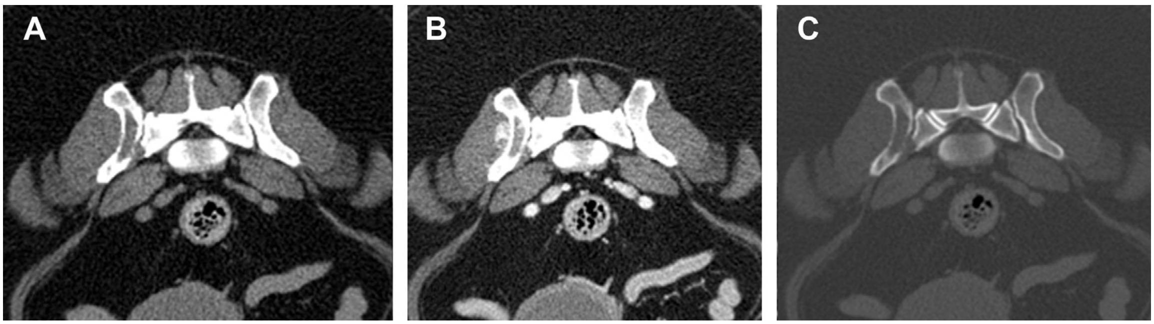

FIG. 11 Same dog as in Fig. 10. Transverse CT images, soft tissue algorithm, precontrast (**A**) and postcontrast (**B**) soft tissue window and bone window (**C**) of the pelvis. The lysis of the right ileum and sacrum is visible as well as the surrounding soft tissue contrast enhancement.

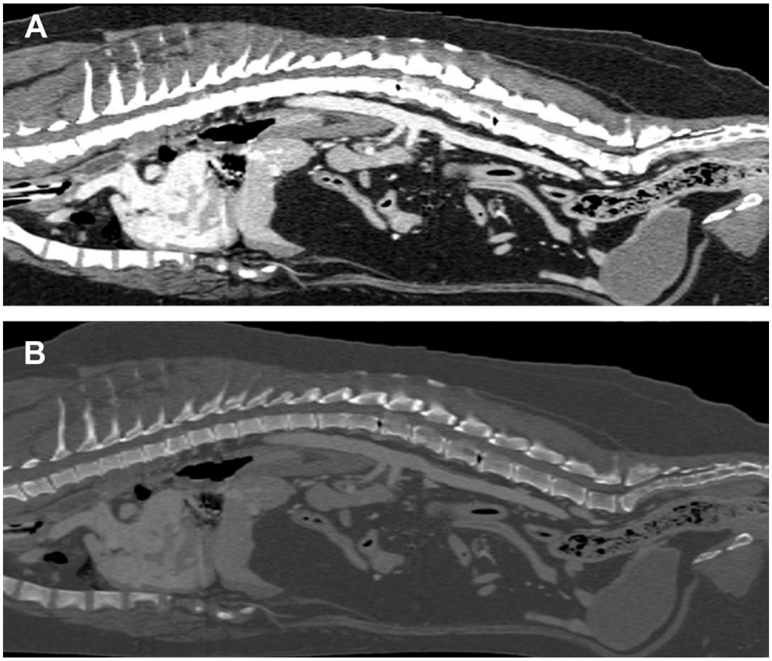

FIG. 12 Same dog as in Figs. 10 and 11. Soft tissue algorithm, sagittal MPR of the postcontrast soft tissue window (**A**), and bone window (**B**). The vertebral bodies L1 to L3 appear to be lytic, and contrast tissue enhancement is present in the vertebral canal. At the level of the intervertebral discs T13 to L1 and L3 to L4, gas is visible, representing a vacuum phenomenon secondary to disc degeneration.

mast cell tumors, with cardiac muscle metastasis described as originating from carcinoma, lymphoma, and hemangiosarcoma [60–63].

- Until CT was used to detect muscle metastasis, these metastases were detected either with necropsy or with biopsy [60–62] Studies have highlighted the importance of WBCT to visualize muscle metastasis in different kinds of neoplasia (mainly hemangiosarcoma and adenocarcinoma in dogs and adenocarcinoma in cats) to guide biopsy or cytology sample collection.
- CT patterns of the metastasis were also described, with the most frequent pattern being ring enhancement with hypoattenuating centers (Fig. 8), histologically characterized as necrotic areas [64]. Interestingly, most of the patients did not show clinical signs specifically attributable to their metastatic disease, underscoring the importance of WBCT to fully characterize and stage tumors with high metastatic rate [64].
- A recent study investigated the use of WBCT to detect muscle metastasis in canine hemangiosarcoma, with the prevalence of this kind of lesion higher compared with previous studies in both human and veterinary oncology. The investigators recommended WBCT as a routine staging procedure in canine hemangiosarcoma to detect lesions missed by clinical examination and traditional diagnostic imaging modalities [65].

SKELETAL EVALUATION

- With WBCT, bone metastasis (Figs. 9–12) can be properly assessed. A recent report described the role of WBCT in detecting urinary transitional cell carcinoma (TCC) metastasis and evaluated survival rate of the patients as well. The investigators observed that urethral TCC had higher metastasis rates and shorter survival time than dogs with urinary TCC [66].
- Sternal lymphadenomegaly and bone metastasis were identified as significant findings associated with WBCT screening at diagnosis because bone metastasis has been observed to be a poor predictor [67]. Furthermore, with WBCT it is possible to detect concurrent malignancies in patients, thus having more complete diagnosis by detecting lesions otherwise missed [19,68].

PRESENT RELEVANCE AND FUTURE CONSIDERATIONS

- WBCT in cancer staging of small animals is an extremely useful technique able to detect various sites for metastasis and further characterize the primary tumor.
- Further studies are needed to investigate the role of WBCT in feline oncology.
- In human medicine, careful attention is paid to the radiation dose per patient [12,69]. Similar studies may be useful in veterinary medicine.
- In addition, along with more advanced imaging such as PET/CT in oncology, the role of total-body MRI in cancer staging is now under investigation. The most recent reports described this technique as effective in detecting metastases, with reduced time, costs, and increased safety because of the lack of ionizing radiation [70–72].

SUMMARY

WBCT is considered useful in cases of malignant neoplasia characterized by a high metastatic rate, to thoroughly detect metastases affecting common and atypical tissues throughout the body. A complete and thorough characterization of the tumor is of paramount importance to properly manage the patient and plan effective treatment, and WBCT is an effective tool to be applied in routine oncologic practice.

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

[1] Haagsma JA, Graetz N, Bolliger I, et al. The global burden of injury: incidence, mortality, disability-adjusted life years and time trends from the Global Burden of Disease study 2013. Inj Prev 2016;22(1):3–18.
[2] Ahmadinia K, Smucker JB, Nash CL, et al. Radiation exposure has increased in trauma patients over time. J Trauma Acute Care Surg 2012;72(2):410–5.
[3] Huber-Wagner S, Mand C, Ruchholtz S, et al. Effect of the localisation of the CT scanner during trauma resuscitation on survival – a retrospective, multicentre study. Injury 2014;45(Suppl 3):S76–82.
[4] Çorbacıoğlu ŞK, Aksel G. Whole body computed tomography in multi trauma patients: Review of the current literature. Turk J Emerg Med 2018;18(4):142–7.
[5] Huber-Wagner S, Biberthaler P, Häberle S, et al. Whole-Body CT in Haemodynamically Unstable Severely Injured Patients – A Retrospective, Multicentre Study. PLoS One 2013;8(7). https://doi.org/10.1371/journal.pone.0068880.
[6] Mathews JD, Forsythe AV, Brady Z, et al. Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. BMJ 2013;346:f2360.
[7] Miglioretti DL, Johnson E, Williams A, et al. The Use of Computed Tomography in Pediatrics and the Associated Radiation Exposure and Estimated Cancer Risk. JAMA Pediatr 2013;167(8):700–7.
[8] Berrington de Gonzalez A, Salotti JA, McHugh K, et al. Relationship between paediatric CT scans and subsequent risk of leukaemia and brain tumours: assessment of the impact of underlying conditions. Br J Cancer 2016;114(4):388–94.
[9] Sierink JC, Saltzherr TP, Beenen LF, et al. A multicenter, randomized controlled trial of immediate total-body CT scanning in trauma patients (REACT-2). BMC Emerg Med 2012;12:4.
[10] Yeguiayan J-M, Yap A, Freysz M, et al. Impact of whole-body computed tomography on mortality and surgical management of severe blunt trauma. Crit Care 2012;16(3):R101.
[11] Elmokadem AH, Ibrahim EA, Gouda WA, et al. Whole-Body Computed Tomography Using Low-Dose Biphasic Injection Protocol With Adaptive Statistical Iterative Reconstruction V: Assessment of Dose Reduction and Image Quality in Trauma Patients. J Comput Assist Tomogr 2019;43(6):870–6.
[12] Stengel D, Mutze S, Güthoff C, et al. Association of Low-Dose Whole-Body Computed Tomography With Missed Injury Diagnoses and Radiation Exposure in Patients With Blunt Multiple Trauma. JAMA Surg 2020. https://doi.org/10.1001/jamasurg.2019.5468.
[13] Oliveira CR, Mitchell MA, O'Brien RT. Thoracic computed tomography in feline patients without use of chemical restraint. Vet Radiol Ultrasound 2011;52(4):368–76.
[14] Shanaman MM, Schwarz T, Gal A, et al. Comparison between survey radiography, B-mode ultrasonography, contrast-enhanced ultrasonography and contrast-enhanced multi-detector computed tomography findings in dogs with acute abdominal signs. Vet Radiol Ultrasound 2013;54(6):591–604.
[15] Dozeman ET, Prittie JE, Fischetti AJ. Utilization of whole body computed tomography in polytrauma patients. J Vet Emerg Crit Care 2020;30(1):28–33.
[16] Bonaparte A, Dhaliwal RS, Murtaugh RJ. Whole Body Computed Tomography for Tumor Staging in Dogs: Review of 16 Cases. J Vet Sci Technol 2016;7(4). https://doi.org/10.4172/2157-7579.1000344.
[17] Armbrust LJ, Biller DS, Hoskinson JJ. Case examples demonstrating the clinical utility of obtaining both right and left lateral abdominal radiographs in small animals. J Am Anim Hosp Assoc 2000;36(6):531–6.

[18] Mattoon JS, Bryan JN. The future of imaging in veterinary oncology: learning from human medicine. Vet J 2013; 197(3):541–52.

[19] Oblak ML, Boston SE, Woods JP, et al. Comparison of concurrent imaging modalities for staging of dogs with appendicular primary bone tumours. Vet Comp Oncol 2015;13(1):28–39.

20 Randall EK. PET-Computed Tomography in Veterinary Medicine. Vet Clin North Am Small Anim Pract 2016; 46(3):515–33, vi.

[21] Forrest LJ. Computed Tomography Imaging in Oncology. Vet Clin North Am Small Anim Pract 2016;46(3): 499–513, vi.

[22] Kutara K, Seki M, Ishikawa C, et al. Triple-phase helical computed tomography in dogs with hepatic masses. Vet Radiol Ultrasound 2014;55(1):7–15.

[23] Buishand FO, Vilaplana Grosso FR, Kirpensteijn J, et al. Utility of contrast-enhanced computed tomography in the evaluation of canine insulinoma location. Vet Q 2018;38(1):53–62.

[24] Leela-Arporn R, Ohta H, Shimbo G, et al. Computed tomographic features for differentiating benign from malignant liver lesions in dogs. J Vet Med Sci 2019;81(12): 1697–704.

[25] Kutara K, Seki M, Ishigaki K, et al. Triple-phase helical computed tomography in dogs with solid splenic masses. J Vet Med Sci 2017;79(11):1870–7.

[26] Prather AB, Berry CR, Thrall DE. Use of radiography in combination with computed tomography for the assessment of noncardiac thoracic disease in the dog and cat. Vet Radiol Ultrasound 2005;46(2):114–21.

[27] Paoloni MC, Adams WM, Dubielzig RR, et al. Comparison of results of computed tomography and radiography with histopathologic findings in tracheobronchial lymph nodes in dogs with primary lung tumors: 14 cases (1999-2002). J Am Vet Med Assoc 2006;228(11):1718–22.

[28] Ballegeer EA, Adams WM, Dubielzig RR, et al. Computed tomography characteristics of canine tracheobronchial lymph node metastasis. Vet Radiol Ultrasound 2010; 51(4):397–403.

[29] Marolf AJ, Gibbons DS, Podell BK, et al. Computed tomographic appearance of primary lung tumors in dogs. Vet Radiol Ultrasound 2011;52(2):168–72.

[30] Reetz JA, Buza EL, Krick EL. CT features of pleural masses and nodules. Vet Radiol Ultrasound 2012;53(2):121–7.

[31] Nemanic S, London CA, Wisner ER. Comparison of thoracic radiographs and single breath-hold helical CT for detection of pulmonary nodules in dogs with metastatic neoplasia. J Vet Intern Med 2006;20(3):508–15.

[32] Erhart EJ, Kamstock DA. The Pathology of Neoplasia. In: Withrow V, editor. Withrow and MacEwen's small animal clinical oncology. St. Louis (MO): Elsevier Saunders; 2013. p. 51–67.

[33] Maalej M, Hentati D, Afrit M, et al. Sternal or parasternal involvement from breast cancer: a misleading clinical sign. Tunis Med 2013;91(1):54–8.

[34] Smith K, O'Brien R. Radiographic characterization of enlarged sternal lymph nodes in 71 dogs and 13 cats. J Am Anim Hosp Assoc 2012;48(3):176–81.

[35] Tanaka T, Akiyoshi H, Mie K, et al. Contrast-enhanced computed tomography may be helpful for characterizing and staging canine gastric tumors. Vet Radiol Ultrasound 2019;60(1):7–18.

[36] Terragni R, Vignoli M, Rossi F, et al. Stomach wall evaluation using helical hydro-computed tomography. Vet Radiol Ultrasound 2012;53(4):402–5.

[37] Langenbach A, McManus PM, Hendrick MJ, et al. Sensitivity and specificity of methods of assessing the regional lymph nodes for evidence of metastasis in dogs and cats with solid tumors. J Am Vet Med Assoc 2001;218(9): 1424–8.

[38] Worley DR. Incorporation of sentinel lymph node mapping in dogs with mast cell tumours: 20 consecutive procedures. Vet Comp Oncol 2014;12(3):215–26.

[39] Skinner OT, Boston SE, Souza CHM. Patterns of lymph node metastasis identified following bilateral mandibular and medial retropharyngeal lymphadenectomy in 31 dogs with malignancies of the head. Vet Comp Oncol 2017;15(3):881–9.

[40] Williams LE, Packer RA. Association between lymph node size and metastasis in dogs with oral malignant melanoma: 100 cases (1987-2001). J Am Vet Med Assoc 2003;222(9):1234–6.

[41] Uren RF, Howman-Giles R, Chung D, et al. Imaging sentinel lymph nodes. Cancer J 2015;21(1):25–32.

[42] Nakagawa M, Morimoto M, Takechi H, et al. Preoperative diagnosis of sentinel lymph node (SLN) metastasis using 3D CT lymphography (CTLG). Breast Cancer 2016;23(3):519–24.

[43] Soultani C, Patsikas MN, Karayannopoulou M, et al. Assessment of sentinel lymph node metastasis in canine mammary gland tumors using computed tomographic indirect lymphography. Vet Radiol Ultrasound 2017; 58(2):186–96.

[44] Suga K, Ogasawara N, Yuan Y, et al. Visualization of breast lymphatic pathways with an indirect computed tomography lymphography using a nonionic monometric contrast medium iopamidol: preliminary results. Invest Radiol 2003;38(2):73–84.

[45] Fukushima K, Kanemoto H, Ohno K, et al. CT characteristics of primary hepatic mass lesions in dogs. Vet Radiol Ultrasound 2012;53(3):252–7.

[46] Taniura T, Marukawa K, Yamada K, et al. Differential diagnosis of hepatic tumor-like lesions in dog by using dynamic CT scanning. Hiroshima J Med Sci 2009; 58(1):17–24.

[47] Johnson KA, Powers BE, Withrow SJ, et al. Splenomegaly in dogs. Predictors of neoplasia and survival after splenectomy. J Vet Intern Med 1989;3(3):160–6.

[48] Jones ID, Daniels AD, Lara-Garcia A, et al. Computed tomographic findings in 12 cases of canine multicentric lymphoma with splenic and hepatic involvement. J Small Anim Pract 2017;58(11):622–8.

[49] Baldo CF, Garcia-Pereira FL, Nelson NC, et al. Effects of anesthetic drugs on canine splenic volume determined via computed tomography. Am J Vet Res 2012;73(11): 1715–9.
[50] LaBan MM, Nagarajan R, Riutta JC. Paucity of muscle metastasis in otherwise widely disseminated cancer: a conundrum. Am J Phys Med Rehabil 2010;89(11): 931–5.
[51] Al-Alao BS, Westrup J, Shuhaibar MN. Non-small-cell lung cancer: unusual presentation in the gluteal muscle. Gen Thorac Cardiovasc Surg 2011;59(5):382–4.
[52] Paget S. The distribution of secondary growths in cancer of the breast. 1889. Cancer Metastasis Rev 1989;8(2): 98–101.
[53] Seely S. Possible reasons for the high resistance of muscle to cancer. Med Hypotheses 1980;6(2):133–7.
[54] Pop D, Nadeemy AS, Venissac N, et al. Skeletal muscle metastasis from non-small cell lung cancer. J Thorac Oncol 2009;4(10):1236–41.
[55] Tuoheti Y, Okada K, Osanai T, et al. Skeletal muscle metastases of carcinoma: a clinicopathological study of 12 cases. Jpn J Clin Oncol 2004;34(4):210–4.
[56] Muzamil J, Bashir S, Guru FR, et al. Squamous Cell Carcinoma Lung with Skeletal Muscle Involvement: A 8-year Study of a Tertiary Care Hospital in Kashmir. Indian J Med Paediatr Oncol 2017;38(4):456–60.
[57] Ong N, George M, Dutta R, et al. CT imaging features of skeletal muscle metastasis. Clin Radiol 2019;74(5): 374–7.
[58] Marioni G, Blandamura S, Calgaro N, et al. Distant muscular (gluteus maximus muscle) metastasis from laryngeal squamous cell carcinoma. Acta Otolaryngol (Stockh) 2005;125(6):678–82.
[59] Lennartz S, Große Hokamp N, Abdullayev N, et al. Diagnostic value of spectral reconstructions in detecting incidental skeletal muscle metastases in CT staging examinations. Cancer Imaging 2019;19. https://doi.org/10.1186/s40644-019-0235-3.
[60] Meyer A, Hauser B. Lung tumor with unusual metastasis in a cat–a case report. Schweiz Arch Tierheilkd 1995; 137(2):54–7 [in German].
[61] Krecic MR, Black SS. Epitheliotropic T-cell gastrointestinal tract lymphosarcoma with metastases to lung and skeletal muscle in a cat. J Am Vet Med Assoc 2000; 216(4):524–9, 517.
[62] Langlais LM, Gibson J, Taylor JA, et al. Pulmonary adenocarcinoma with metastasis to skeletal muscle in a cat. Can Vet J 2006;47(11):1122–3.
[63] Aupperle H, März I, Ellenberger C, et al. Primary and secondary heart tumours in dogs and cats. J Comp Pathol 2007;136(1):18–26.
[64] Vignoli M, Terragni R, Rossi F, et al. Whole body computed tomographic characteristics of skeletal and cardiac muscular metastatic neoplasia in dogs and cats. Vet Radiol Ultrasound 2013;54(3):223–30.
[65] Carloni A, Terragni R, Morselli-Labate AM, et al. Prevalence, distribution, and clinical characteristics of hemangiosarcoma-associated skeletal muscle metastases in 61 dogs: A whole body computed tomographic study. J Vet Intern Med 2019;33(2):812–9.
[66] Charney VA, Miller MA, Heng HG, et al. Skeletal Metastasis of Canine Urothelial Carcinoma: Pathologic and Computed Tomographic Features. Vet Pathol 2017; 54(3):380–6.
[67] Iwasaki R, Shimosato Y, Yoshikawa R, et al. Survival analysis in dogs with urinary transitional cell carcinoma that underwent whole-body computed tomography at diagnosis. Vet Comp Oncol 2019;17(3):385–93.
[68] Talbott JL, Boston SE, Milner RJ, et al. Retrospective Evaluation of Whole Body Computed Tomography for Tumor Staging in Dogs with Primary Appendicular Osteosarcoma. Vet Surg 2017;46(1):75–80.
[69] Karpitschka M, Augart D, Becker H-C, et al. Dose reduction in oncological staging multidetector CT: effect of iterative reconstruction. Br J Radiol 2013;86(1021): 20120224.
[70] Lee DH, Lee JM. Whole-body PET/MRI for colorectal cancer staging: Is it the way forward? J Magn Reson Imaging 2017;45(1):21–35.
[71] Machado Medeiros T, Altmayer S, Watte G, et al. 18F-FDG PET/CT and whole-body MRI diagnostic performance in M staging for non-small cell lung cancer: a systematic review and meta-analysis. Eur Radiol 2020. https://doi.org/10.1007/s00330-020-06703-1.
[72] Taylor SA, Mallett S, Miles A, et al. Whole-body MRI compared with standard pathways for staging metastatic disease in lung and colorectal cancer: the Streamline diagnostic accuracy studies. Health Technol Assess 2019;23(66):1–270.