Canine Appendicular Osteosarcoma Pathology Quick Reference Guide (QRG)
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Authors: Donald Meuten*, Keren E. Dittmer*, Courtney R. Schott*, Laura Selmic
* *Denotes communication authors;* contact communication authors to suggest updates, provide edits and comments: Don Meuten (don_meuten@ncsu.edu)

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Introduction: QRGs for neoplasms are designed for diagnostic pathologists so they are aware of the gross or microscopic information needed by clinicians to assign prognoses and offer therapy options. **For canine osteosarcoma (OSA) the information needed from a pathologist is the diagnosis.** This QRG is to be used for canine appendicular OSA and is not intended for canine axial or extraskeletal OSA or feline OSA.

Appendicular OSA is the most common primary bone tumor of dogs and is one of the most aggressive tumors in animals. Most dogs with OSA live less than one year after the diagnosis; the timing of euthanasia influences outcome data. Pulmonary metastases will eventually occur in >85% of dogs, and <15% will have detectable metastases at presentation. Clinicians will create treatment recommendations and assign a prognosis based on all the data gathered for that patient. Clinical data that aid the pathologist include breed, age, location on the limb, and radiographs or the radiology report of the primary bone lesion and thorax.[1] Each of these may add to the certainty of the diagnosis. See the OSA Guideline which provides additional information on OSA in dogs and the importance of differentiating reactive bone from bone produced by neoplastic cells. A full Protocol for canine OSA is under development.

Diagnostic report: The only piece of data needed by a clinician from the pathologist to aid in assigning a prognosis and offer therapeutic options for canine appendicular OSA is the diagnosis. The presence of osteoid produced by neoplastic cells within a sarcoma located in the metaphyseal region of an appendicular bone is sufficient evidence for a microscopic diagnosis of OSA. The osteoid in OSA arises from neoplastic mesenchymal cells that have variable atypia and there is no orderly maturation of the osteoid. Reactive bone should have a rim of osteoblasts lining the osteoid with intertrabecular spaces containing fibrovascular stroma, and the maturation is orderly. The various histologic subtypes of OSA or the grading systems have not been proven to predict clinical outcomes. The oncologist will integrate the pathologist's diagnosis with all the data known for the dog.[1] Additional histologic or cytological assessments by the pathologist beyond the diagnosis are not needed for the clinician/oncologist to make recommendations to owners. However, it is recommended to also report the mitotic count (MC), presence of lymphovascular invasion (LVI), and lymph node (LN) status, if available. **Staging** is performed by clinicians.

Lymph Node status: Report findings on any LN submitted; if the specimen is a limb amputation, the pathologist should search for a LN and if found submit for histopathology; <5% of canine appendicular OSA metastasize to LN; Validation studies are needed to confirm whether OSA in a LN correlates with survival metrics.[2,3]

Histologic grading: Grading systems for canine appendicular OSA[4,5] could not be replicated by an independent group of pathologists; grading does not correlate with prognosis and does not predict appropriate treatment.[6,7]

Other histologic assessments: None of the following are known to be predictive of outcomes in canine OSA however, it is our philosophy that these three parameters (more info on https://vcgp.org/guidelines-and-protocols/) should be reported on all aggressive neoplasms:

[8]MC in 2.37 mm^2
[9]LVI – Soft and strict criteria; see VCGP LVI guideline
Surgical margins

Surgical margin evaluation:
For limb-sparing – minimum of 4 samples that include the soft tissues and the bone from each end of the bone should be evaluated.

Full limb amputation – histological assessment at the excision margin is not necessary if there is at least one joint present between the tumor and the excision (amputation) margin. For OSA located in proximal femur and proximal humerus, soft tissue margins should be assessed due to possible local infiltration; recommend at least 4 sites. It would be helpful if the surgeon indicated the closest margin they observed or any specific points along the excision margin they would like evaluated histologically.

***Core* vs *Noncore* information supplied by the pathologist to help clinicians assign prognosis:**

What is critical to be provided by the pathologist- Core	***What is not critical but highly recommended to be provided by the pathologist- Noncore***	***What is not needed to be provided by the pathologist- Noncore***
• Histopathologic interpretation/morphologic diagnosis (e.g. canine appendicular osteosarcoma) • Cytologic interpretation/ diagnosis	• Mitotic count (MC) • Presence of lymphovascular invasion (LVI) • Lymph node (LN) status • Surgical margin evaluation	• Histopathologic subtype* • Grading systems* • Description

** Independent studies could not replicate previous published results; Pathologist preference to write a description – descriptions are not needed for synoptic reports.*

Future investigations should evaluate a wide array of clinical, pathological, and molecular parameters correlated with accurate clinical outcome data to determine what, if any, further testing beyond a microscopic diagnosis will help predict outcome and or guide clinician options. If advances in clinical screening, imaging, liquid biopsy or other factors enable identification of OSA at an earlier stage than is currently possible, we may discover histological findings which correlate with specific outcomes. If such data emerges this Pathology QRG will be updated.

SELECTED REFERENCES:

1. Dittmer KE, Pemberton S. A holistic approach to bone tumors in dogs and cats: Radiographic and histologic correlation. *Vet Pathol* 2021; 58: 841–857.
2. Hillers KR, Dernell WS, Lafferty MH, et al. Incidence and prognostic importance of lymph node metastases in dogs with appendicular osteosarcoma: 228 cases (1986-2003). *J Am Vet Med Assoc* 2005; 226: 1364–1367.
3. Marconato L, Buracco P, Polton GA, et al. Timing of adjuvant chemotherapy after limb amputation and effect on outcome in dogs with appendicular osteosarcoma without distant metastases. *J Am Vet Med Assoc* 2021; 259: 749–756.
4. Kirpensteijn J, Kik M, Rutteman GR, et al. Prognostic significance of a new histologic grading system for canine osteosarcoma. *Vet Pathol* 2002; 39: 240–246.
5. Loukopoulos P, Robinson WF. Clinicopathological relevance of tumour grading in canine osteosarcoma. *J Comp Pathol* 2007; 136: 65–73.
6. Schott CR, Tatiersky LJ, Foster RA, et al. Histologic grade does not predict outcome in dogs with appendicular osteosarcoma receiving the standard of care. *Vet Pathol* 2018; 55: 202–211.
7. Meuten D, Munday JS, Hauck M. Time to standardize? Time to validate? *Vet Pathol* 2018; 55: 195–199.
8. Meuten DJ, Bertram CA, Moore FM, et al. Mitotic Count Guideline, version 1.0. *Veterinary Cancer Guidelines and Protocols*, http://vetcancerprotocols.org (accessed 31 August 2024).
9. Moore FM, Craig L, Donovan TA, et al. Lymphovascular Invasion Guideline, version 1.0. *Veterinary Cancer Guidelines and Protocols*, http://vetcancerprotocols.org (accessed 31 August 2024).