Tumor Necrosis Quick Reference Guide

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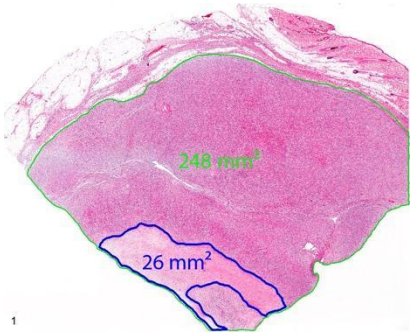
Introduction: Necrosis is used in multiple tumor grading systems (see below).[1] This is because, theoretically, the greater the amount of necrosis, the more aggressive the tumor, but data to support this theory are not definitive. Currently there are no standardized methods for trimming tumors or estimating and reporting percent of necrosis in tumors. Authors and editors must ensure that the methods used to assess tumor necrosis are described in such detail that others can replicate and validate results. Colleagues are encouraged to read the full guideline on necrosis[2] and consult specific references therein for details not included here. Guidelines will be updated as we receive feedback from colleagues and as peer-reviewed literature provides data. Please send comments and/or suggestions to Emily Corbin (emcvetpath@gmail.com). Currently we recommend the following methods when assessing necrosis; some of these recommendations are based on published data (cited) and some are based on consensus of the authors (asterisks).

Recommendations for Evaluating Tumor Necrosis:

1. Use histologic assessment only rather than gross and histologic assessment of necrosis.*
2. For trimming: There is currently no standard method to trim tumors; future investigations should identify best practices for trimming tumors.
    a. Record if areas of necrosis were purposefully avoided during trimming.*
    b. One reference suggests 1 section per 2cm of tumor in its longest dimension, consider implementing this method.[3]
3. Use one of the following methods to determine percent necrosis:
    a. Whole slide imaging (WSI) with drawing software: Outline tumor circumference (X, green line), outline area(s) of necrosis (Y, blue line), calculate % necrosis for that section = (Y/X) x 100. Example: Y/X is 26mm^2 / 248mm^2 ≈10%.[2]
    b. Microscope or WSI without drawing software: Visually estimate the amount of necrosis in each section.



4. Report an average of necrosis from all the evaluated sections rather than selecting one section.*
5. Avoid necrosis caused by factors such as fine needle aspiration, incisional biopsy, chemotherapeutic or radiation therapy, ulceration, or mucinous or hyaline change.[2,3]
6. Record the amount of necrosis as a percentage:
    a. Diagnostic pathology:

   i. If a published grading system for the specific tumor type exists, consider using the reported necrosis thresholds.[1]
   ii. If no published grading system is available for the specific tumor type, consider using thresholds of 0%,<50%, or ≥50%.*

b. Research studies:
   i. Consider reporting percent of tumor necrosis in 10% or smaller increments. Tumor necrosis of >10% has been correlated with tumor behavior in some human tumors[4] and has been reported to correlate with a nearly threefold increased risk of death in canine soft tissue tumors/sarcomas (STT/STS) in one study[5], but this requires clarification and validation.

*Statements with asterisks are based on consensus of the authors and require validation.

Necrosis in Selected Tumor Grading Systems in Veterinary Medicine:

The tumors listed below have published grading systems that use necrosis as a criterion, with necrosis thresholds listed. These grading systems are not necessarily widely accepted or endorsed; they are included here as a resource.[1]

- Canine STT/STS: 0%, <50%, or ≥50%; however, consider including a 0-10% threshold as dogs with tumors with >10% necrosis may be ~2.7 times more likely to die of tumor-related causes[5]
- Canine splenic hemangiosarcoma: 0%,<25%, 25-50%, or >50%
- Feline injection site sarcoma (FISS): 0%,<50%, or ≥50%
- Canine multilobular tumor of bone: Absent or present
- Canine osteosarcoma (2 published grading systems): 0%, <15%, 15-50%, or >50%; or <25%, 25-50%, or >50%
- Feline osteosarcoma: <25%, 25-50%, or >50%
- Canine mast cell tumor (3 tier system, 1984): Necrosis and edema assessed as minimal, diffuse areas, or common
- Canine pulmonary carcinoma: 0%, 1-20%, 21-50%, or >50%
- Canine gliomas: high grade gliomas have necrosis and/or one or more of several other diagnostic criteria

SELECTED REFERENCES:

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3. Roccabianca P, Schulman FY, Avallone G, et. al. *Surgical Pathology of Tumors of Domestic Animals Volume 3: Tumors of Soft Tissue*. Gurnee, IL: Davis-Thompson Foundation; 2020.
4. Vayrynen SA, Vayrynen JP, Klintrup K, et. al. Clinical impact and network of determinants of tumour necrosis in colorectal cancer. *Br J Cancer*. 2016;114**:** 1334-134.
5. Kuntz CA, Dernell WS, Powers BE, Devitt C, Straw RC, Withrow SJ. Prognostic factors for surgical treatment of soft-tissue sarcomas in dogs: 75 cases (1986-1996). *J Am Vet Med Assoc*. 1997;211**:** 1147-1151.