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Variability in tumor margin reporting for soft tissue sarcoma and cutaneous mast cell tumors in dogs: A systematic review

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Abstract

Objective: To identify which classification systems have been used for tumor margin reporting and to determine whether factors (publication year, tumor type, and specialty of the contributing authors) influenced trends in margin reporting within literature describing canine soft tissue sarcoma (STS) and cutaneous mast cell tumors (MCT).

Study design: Systematic literature review.

Methods: Eligible articles were identified through electronic database searches performed for STS and MCT. Data abstracted from relevant studies included publication year, author list, specialty of contributing authors, criteria used to report the planned surgical margins, and the status of histologic margins. Categorization of papers was based on the classification systems used to report surgical and histologic tumor margins.

Results: Fifty-three articles were included, 11 on STS, 37 on MCT, and five that included both tumor types. Criteria for classifying the planned surgical margins were described in only 50.9% of studies. Articles that listed a veterinary surgeon as a contributing author ($P = .01$) and STS articles compared to MCT papers ($P = .01$) were more likely to report surgical margins. Most (56.6%) studies reported the status of histologic margins dichotomously as "complete" or "incomplete." Although a previously published consensus statement recommended that quantitative criteria be used to report histologic margins, only 7.5% of articles used quantitative methods.

The abstract from this study was presented at the American College of Veterinary Surgeons Surgery Summit; October 17-19, 2019; Las Vegas, Nevada.

Conclusion: Classification systems used for reporting tumor margins were highly variable among studies.

Clinical significance: The findings of this review provide evidence that a standardized classification system for reporting surgical and histologic tumor margins is required in veterinary medicine. A universal system may support more consistent reporting of neoplastic biopsy specimens and allow for more meaningful comparisons across research studies.

1 | INTRODUCTION

Mast cell tumors (MCT) and soft tissue sarcomas (STS) are the most frequently encountered cutaneous and subcutaneous malignancies in dogs.[1] A characteristic behavior shared by both tumor types is for microscopic extension of tumor cells to exist beyond the main tumor bed.[2] As a consequence of this predictable behavior, the mainstay of treatment is wide surgical excision with the goal of obtaining complete tumor excision with an adequate margin of tumor free tissue resection.[3]

However, defining the adequate resection margin required to achieve local tumor control is not a straightforward endeavor. In general, it is well accepted that the status of surgical margins in many types of locally invasive tumors can have prognostic implications for the animal related to local recurrence and overall survival. Case series[3,4] as well as a recent systematic review and meta-analysis[5] on canine STS have provided evidence that the completeness of surgical excision is protective against local tumor recurrence. Conversely, researchers[3,6-11] who have evaluated cutaneous MCT in dogs have reported conflicting results regarding whether completeness of surgical excision is predictive of local recurrence and overall survival. The findings from these studies are affected not only by small sample populations and confounding variables but also by the lack of uniformity in how tumor margins are reported in veterinary medicine, making it impossible to compare results across publications in which risk factors for tumor recurrence, metastasis, and overall survival after surgery have been evaluated.

Furthermore, a distinct difference exists between the extent of surgery performed and the method for assessing margin status. This is an important consideration when the literature for margin evaluation in dogs with STS and cutaneous MCT is interpreted because the type of margin tested for association with a particular oncologic outcome (eg, local recurrence or survival time) may differ on the basis of the operational definition and classification scheme selected by the investigators. For example, some researchers[12,13] have related outcomes to the surgical dose used (ie, the planned surgical margins), while others[8,14] have evaluated the histologic status of the excised tumor (ie, the histologic margins). The residual tumor (R-classification) system,[15] which is the universally accepted system for tumor margin reporting in human surgical oncology, integrates both the clinical and pathologic assessment of tumor margins. According to this system, an R0 margin is defined as being free of malignancy (ie, surgical and histologic margins are negative for tumor cells); an R1 margin has microscopic tumor cells present at the cut edge of the specimen (ie, positive histologic margins); an R2 margin refers to an intralesional tumor resection (ie, grossly positive surgical margins).[16] Although the American Joint Committee on Cancer (AJCC) has recommended the use of the R-classification system in reporting tumor margin results throughout the human literature since 1978,[15] to the best of the authors' knowledge, this classification system has not been used in the veterinary literature.

Several classification schemes have been used to categorize or describe the surgical intent (or the planned surgical margins) in veterinary oncologic surgery. Common methods include reporting a prescribed metric distance away from the tumor, which may be considered a quantitative system, or use of the Enneking system,[17] which classifies the intent of surgery as either an intralesional, marginal, wide local, or radical excision. Similarly, several systems described in the veterinary literature have been used to categorize the microscopic status of tumor margins or the histologic margins. The simplest systems use dichotomous terminology to describe histologic margins, in which the presence or absence of tumor cells at or near an inked margin designates a "positive" or "negative" margin, respectively. Reporting histologic margins trichotomously includes a "close" or "narrow" margin category in addition to the positive and negative margins. Conversely, quantitative reporting systems represent histologic margin data as a continuous variable by providing metric measurements (millimeters) of the distance between tumor cells and the margin edge.

The terminology regarding tumor margins is not well defined in the veterinary literature, and this has been hampered, in part, by the lack of a common classification scheme for margin reporting.[18] An attempt was made by the American College of Veterinary Pathologists' Oncology

Committee in 2011 that set forth guidelines recommending a standardized approach to the assessment of histologic margins.[19] The consensus guidelines, published by Kamstock et al,[19] discouraged the use of subjective terminology (eg, clean, dirty, close, and narrow), advocated for histologic margins to be reported as objective measurements of distance from the margin edge to the closest neoplastic cell, and encouraged reporting margin quality (eg, fat, fascia, bone, etc). An example of a pathology report adhering to these guidelines may read, "clusters of neoplastic cells are within 5 mm of the deep margin which consists of adipose tissue (4.5 mm) and muscle (0.5 mm)." However, whether this consensus has influenced the methodology for margin reporting in veterinary publications is currently unknown. To the best of the authors' knowledge, an evaluation of the trends in margin reporting across the veterinary literature has not been previously investigated.

The objective of this study was to systematically evaluate the current evidence within the veterinary literature to identify which classification systems have been used for reporting surgical and histologic margins for canine STS and cutaneous MCT. In addition, we sought to determine whether factors such as publication year, tumor type (STS vs MCT), or specialty of the contributing authors influenced trends in margin reporting.

2 | MATERIALS AND METHODS

2.1 | Database search

A systematic search of digital bibliographic databases (including PubMed [1950 to present], Web of Science [1900 to present], Medline [1950 to present], and CAB Abstracts [1973 to present]) was conducted. Separate literature searches for MCT and STS were performed in September 2017. Search terms were identified in the MeSH (Medical Subject Headings) database, and the specific search strings used are provided for reference (Appendix). Two authors (A.B.P. and L.E.S.) screened the titles and abstracts to identify relevant articles.

The citations retrieved from each search were stored in Endnote online reference management software (Clarivate Analytics, Philadelphia, Pennsylvania). Duplicate citations were identified by electronic and hand scanning of the resultant citation library, and only the most complete citation was retained.

2.2 | Study selection

Articles were screened, and citations that were not relevant to the review were removed. Primary research studies published in peer-reviewed journals that reported on outcome after surgical treatment of cutaneous MCT or STS in dogs were considered eligible. The following criteria were used to exclude articles during the screening process: (1) research conducted in man; (2) articles that could not be retrieved; (3) case reports or nonoriginal studies, such as reviews or opinion papers; (4) articles that included animals with other tumor types in which results for STS and MCT were not specifically reported; (5) articles pertaining to MCT not arising from the skin (eg, subcutaneous, intramuscular, visceral, etc); (6) articles that did not report at least one of the following oncologic treatment outcomes: local recurrence, disease-free survival/disease-free interval, or overall survival; (7) articles that did not report tumor margin data; and (8) articles in which the margin classification scheme was not explicitly defined in the methodology or outlined in the results.

Relevance screening was carried out in two stages. Stage 1 of the relevance screening involved two authors (A.B.P. and L.E.S.) independently reviewing each title and abstract. Citations progressed to the second stage of review when both reviewers agreed that the citation either described primary research assessing the outcome of surgical treatment for STS/MCT or did not contain enough information to determine eligibility. Any disagreements were resolved by discussion and consensus between the reviewers. Stage 2 of relevance screening was conducted independently by three authors (B.E.A., L.E.S., and A.B.P.) and involved evaluation of the full manuscript by using the same inclusion and exclusion criteria. During review of each full manuscript, article reference lists were hand searched, and relevant articles that had not been captured by electronic searches were added to the citation library on the reference management software. Any disagreements were resolved via consensus.

2.3 | Data extraction

One reviewer (B.E.A.) extracted relevant information from manuscripts that passed through both stages of relevance screening. To determine accuracy and completeness, a second reviewer (L.E.S.) assessed the compiled data. Data captured from individual studies included the study population, number of animals treated with surgery, terminology used for reporting the planned surgical margins and the status of histologic margins, author list, publication year, specialty of the primary author (if any), and whether a veterinary surgeon was listed as a contributing author.

For the purposes of this systematic review, the term *surgical margin* was used to refer to the macroscopic

boundaries of a planned surgical resection measured by the surgeon or the prescribed surgical dose related to the surgical resection of a solid tumor. The term *histologic margin* was used to refer to the microscopic assessment or status of the resected margin edges performed by the pathologist.

Publications were categorized by the classification system used to report the surgical margins or surgical dose as *Enneking* when the surgical margins were reported to have used Enneking[17] criteria: intralesional, marginal, wide local, or radical excision; *modified Enneking* when the surgical margins were categorized by using ≥2 Enneking[17] criteria and the remaining criteria were either defined by using different nomenclature or included additional categories not defined in the original criteria (eg, narrow[20]); *quantitative* when the surgical margins were reported as a distance (centimeters) measured from the gross tumor; or *other* when the surgical margins were described by using a unique methodology system not previously published in the literature.

Articles were also allocated into one of the following classification schemes according to the criteria used to report the status of histologic margins. Studies were classified as *dichotomous* when histologic margins were categorized simply as complete or incomplete; analogous terminology for a complete margin included "negative," "clean," "histologically tumor free," among others; equivalent terminology for an incomplete margin included "positive," "dirty," infiltrated," "histologically non–tumor-free," among others. Studies were classified as *trichotomous* when histologic margins were categorized into three groups: "complete," "close," and "incomplete" or when equivalent terminology was used; q*uantitative* when histologic margins were reported as the distance measured from the cut edge to the nearest neoplastic cell; or o*ther* when histologic margins were described by using a unique methodology system not previously published in the literature.

The specialty affiliation of the first author was categorized as surgery, pathology (including clinical or anatomic pathology), medical oncology, radiation oncology, internal medicine, or none. The author list for each publication was evaluated, and articles that had a veterinary surgeon as a contributing author were identified and separated from those that did not list a surgeon. When the specialty credentials of authors were not specifically listed in the full text version of the manuscript, a web search was performed in February 2019 to identify whether the author had since been awarded diplomate status by a recognized veterinary specialty organization.

To further evaluate whether the Kamstock guidelines[19] influenced how histologic margins were reported, articles were categorized as those published prior to 2011 vs in 2011 or after.

2.4 | Statistical analysis

Categorical variables were expressed as frequencies and percentages. Fisher's exact test was used to assess the association between having a surgeon as primary or contributing author and reporting of surgical margins. Fisher's exact test was also used to evaluate the association between publication year (before 2011 vs 2011 or after) and methods for reporting histologic margins. $P < .05$ was considered statistically significant. Statistical analyses were performed in SAS version 9.4 (SAS Institute, Cary, North Carolina).

3 | RESULTS

Using the previously described search techniques, we identified 1068 records (MCT, n = 772; STS, n = 296). Stage 1 screening of titles and abstract review excluded 903 studies. Stage 2 screening of full manuscripts subsequently excluded 118 articles, and hand searching identified six studies. The article exclusion process resulted in 53 eligible articles—37 on MCT, 11 on STS, and five that included both MCT and STS (Figure 1). Among the 53 reports that discussed tumor margins and evaluated at least one oncologic outcome, the earliest publication year was 1995.

3.1 | Reporting of surgical margins

Criteria for classifying surgical margins were reported in only 50.9% of the studies overall; quantitative methods (17/27 [63%]) were the most frequent system used (Table 1). Among the 37 MCT papers, surgical margins were described infrequently (14/37 [37.8%]). Quantitative criteria were used most often (11/14 [78.6%]) in MCT studies in which surgical margins were reported, and the measured lateral margin for surgical excision of MCT varied between 0.5 cm[21] and 3 cm[8] across papers. Researchers in one MCT study[22] used Enneking criteria, and researchers in the remaining two studies[23,24] used unique criteria to report the planned surgical margins (Table 2).

Conversely, surgical margins were more consistently reported in the STS literature (9/11 [81.8%]). When STS papers were compared to MCT papers, a difference in the proportion of authors that reported surgical margins was noted ($P = .01$). Most authors of STS articles used a quantitative system in which the lateral surgical margins ranged between 0.5 cm[14] and 3 cm.[25] The remaining researchers used Enneking, modified Enneking, or both modified Enneking and quantitative criteria (Table 1).

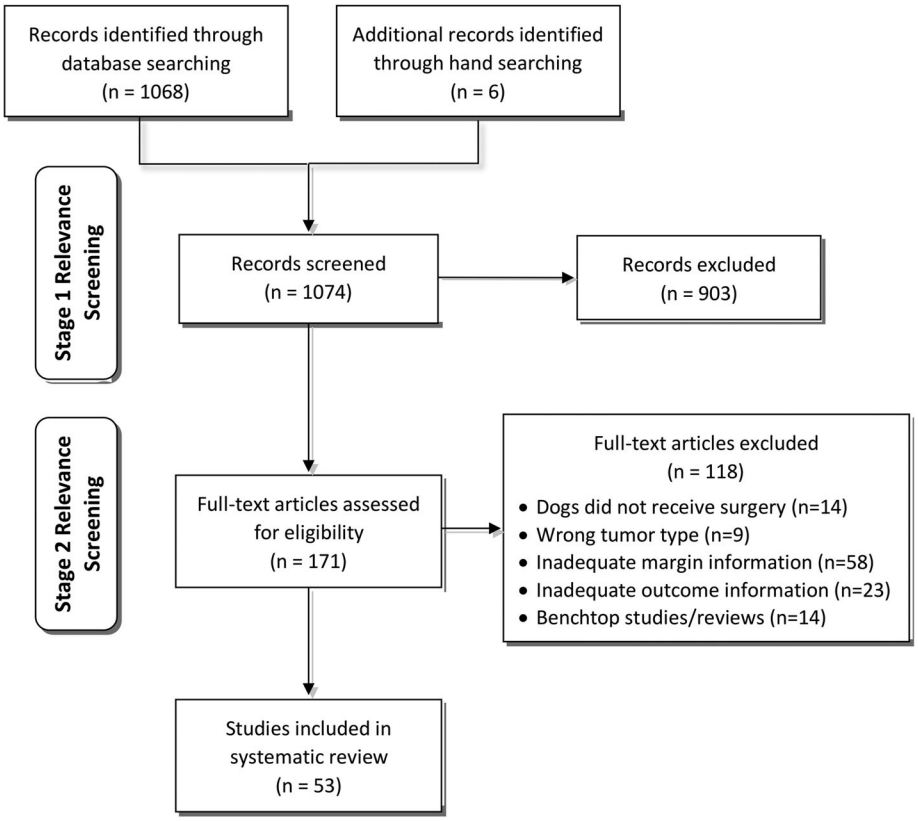

FIGURE 1 Flow diagram of study selection process conducted for systematic review evaluating classification schemes used for margin reporting in canine mast cell tumor and soft tissue sarcoma literature

The few articles that included both STS and MCT frequently contained reports of surgical margins (4/5 [80%]). A similar proportion of researchers used quantitative and Enneking systems for reporting the planned surgical margins (Table 1).

The specialties of the first authors included surgery (24/53 [45.3%]), medical oncology (12/53 [30.2%]), and pathology (9/53 [17%]) and one each of radiation oncology and internal medicine. Two primary authors were not specialists (Table 2). Although surgical margins criteria were infrequently described in the literature, having a surgeon as the first author of the publication was associated with an increased likelihood of surgical margins being reported (63.1% vs. 26.9%; $P = .02$), and having a surgeon as a contributing author of the paper was associated with a higher chance that a study provided methodology for defining surgical margins (77.8% vs. 53.9%; $P = .01$).

3.2 | Reporting of histologic margins

Methods for classifying the status of histologic margins were provided in all 53 publications. Dichotomous, trichotomous, or quantitative criteria were used to describe histologic margins in most (51/53 [96.2%]) articles, and, in the other two papers,[23,24] authors established unique systems wherein four categories for classifying histologic margins were defined (Table 2). Overall, most (30/53 [56.6%]) papers reported histologic tumor margins by using dichotomous criteria, many (17/53 [32.1%]) papers reported histologic tumor margins by using trichotomous systems, and very few (3/53 [5.6%]) papers reported histologic tumor margins by using quantitative or both quantitative and trichotomous criteria (1/53 [1.9%]; Table 1).

In the MCT literature, dichotomous reporting (23/37 [62.2%]) was the most common classification scheme used, followed by trichotomous (11/37 [29.7%]) and quantitative reporting systems (2/37 [5.4%]). Authors of one MCT article[26] used categorization not reported elsewhere (Table 2).

Among STS publications, the same number of publications reported dichotomous (5/11 [45.5%]) and trichotomous (5/11 [45.5%]) criteria to report the status of histologic margins. Authors of one STS article[27] used both quantitative and trichotomous methods. No predominant classification system was found in the five studies in which both tumor types were evaluated (Table 1).

No trend was found in the proportion of articles that reported histologic margins by using dichotomous, trichotomous, or quantitative methods prior to 2011 vs 2011 or after (Figure 2). Overall, the number of articles in which quantitative methods were used to report histologic margins was limited (4/53 [7.5%]). An interesting,

TABLE 1 Summary of the classification systems used to report the surgical and histologic margins in 53 articles on surgical excision of cutaneous MCT and STS in dogs

Surgical margins	n (%)	Histologic margins	n (%)
MCT articles	14	MCT articles	37
Quantitative	11 (78.6)	Dichotomous	23 (62.2)
Other	2 (14.3)	Trichotomous	11 (29.7)
Enneking	1 (7.1)	Quantitative	2 (5.4)
		Other	1 (2.7)
STS articles	9	STS articles	11
Quantitative	4 (44.5)	Dichotomous	5 (45.5)
Enneking	2 (22.2)	Trichotomous	5 (45.5)
Modified Enneking & Quantitative	2 (22.2)	Trichotomous & quantitative	1 (9.1)
Modified Enneking	1 (11.1)		
Articles with MCT & STS	4	Articles with MCT & STS	5
Quantitative	2 (50)	Dichotomous	2 (40)
Enneking	2 (50)	Trichotomous	1 (20)
		Quantitative	1 (20)
		Other	1 (20)
All articles	27	All articles	53
Quantitative	17 (63)	Dichotomous	30 (56.6)
Enneking	4 (14.8)	Trichotomous	17 (32.1)
Modified Enneking	4 (14.8)	Quantitative	3 (5.6)
Modified Enneking & Quantitative	2 (7.4)	Trichotomous & quantitative	1 (1.9)
		Other	2 (3.8)

Abbreviations: MCT, mast cell tumor; STS, soft tissue sarcoma.

albeit subjective, observation was that all except one of these articles were published in 2011 or later, after publication of the Kamstock guidelines.[19] The other study in which quantitative and trichotomous criteria were used concurrently was published in 2004.

3.3 | Operational definitions for close margins and complete margins

Twenty-one studies included a close or narrow margin category in the classification system used to report histologic margins. The exact operational definition of a close margin varied substantially across papers. In most (5/21 [23.8%]) studies, a close margin was defined as having neoplastic cells within 1 mm of the cut edge. However, others considered this threshold distance that defined a close histologic margin as extending anywhere from 2 mm[3,10] to 10 mm,[28,29] depending on the study (Table 3).

Similarly, the definition of a complete or negative margin fluctuated across publications. Among the 42 studies in which a definition for a complete margin was provided, 14 of 42 (33.3%) defined a complete margin as the absence of tumor cells at the cut edge. The distance between the cut edge and the nearest neoplastic cells that defined a complete excision in other studies varied between 1 mm[9,11-13,30-34] and 10 mm[26,28,29] (Table 3).

4 | DISCUSSION

This systematic review offers a comprehensive summary of the classification systems used to report surgical and histologic margins in the canine STS and cutaneous MCT literature. To the best of the authors' knowledge, this is the first report to provide a quantitative evaluation of how tumor margins are reported in the veterinary literature. Among the articles included in this systematic review, the most common classification system used to report surgical margins was quantitative criteria. Although Enneking criteria were used in both canine MCT and STS literature, this system for reporting planned surgical margins was used more commonly in STS papers. Half of the articles did not provide a

TABLE 2 Characteristics of the articles in the systematic review of surgical and histologic margin reporting within the canine cutaneous MCT and STS literature

Article	Specialty of first author	Surgeon contributing author	Surgical margins system	Surgical margin details	Histologic margins system	Histologic margin details
MCT studies						
Baginski,[35] 2014	Surgery	Yes	None		Dichotomous	
Berlato,[30] 2015	Med Onc	No	None		Trichotomous	
Brocks,[21] 2008	Surgery	Yes	Quantitative	Lateral: 0.5 cm	Dichotomous	
Cahalane,[36] 2004	Surgery	Yes	None		Dichotomous	
Camus,[10] 2016	Clin Path	No	None		Trichotomous	
Cooper,[37] 2009	Med Onc	No	None		Dichotomous	
Donnelly,[11] 2015	Med Onc	No	None		Quantitative	
Fulcher,[13] 2006	Surgery	Yes	Quantitative	Lateral: 2 cm	Dichotomous	
Grier,[38] 1995	Surgery	Yes	Quantitative	Lateral: 1.5-2 cm	Dichotomous	
Hayes,[26] 2007	Med Onc	No	None		Other	Clean, acceptable, narrow, or dirty
Hosoya,[39] 2009	Rad Onc	No	None		Dichotomous	
Hume,[40] 2011	Med Onc	No	None		Dichotomous	
Kry,[41] 2014	Surgery	Yes	Quantitative	Lateral: 0.5-3 cm, scar revision	Trichotomous	
Lejeune,[42] 2015	Med Onc	No	None		Dichotomous	
Michels,[8] 2002	Clin Path	No	Quantitative	Lateral: 3 cm; deep: 3 cm	Dichotomous	
Miller,[43] 2016	IMed	No	None		Trichotomous	
Mullins,[44] 2006	Med Onc	Yes	None		Dichotomous	
Murphy,[6] 2004	Surgery	Yes	None		Trichotomous	
Murphy,[45] 2006	Surgery	Yes	None		Trichotomous	
Northrup,[46] 2004	Med Onc	No	None		Dichotomous	
O'Connell,[47] 2013	Med Onc	Yes	None		Trichotomous	
Ozaki,[48] 2007	Pathology	No	None		Dichotomous	
Pratschke,[31] 2013	Surgery	Yes	Quantitative	Lateral: distance = tumor diameter	Dichotomous	
Schultheiss,[7] 2011	Pathology	No	Quantitative	Lateral: 0.1-2 cm	Quantitative	
Seguin,[32] 2001	Surgery	Yes	Quantitative	Lateral: 2-3 cm	Trichotomous	
Seguin,[9] 2006	Surgery	Yes	None		Dichotomous	
Sfiligoi,[49] 2005	Med Onc	No	None		Dichotomous	
Simpson,[12] 2004	Surgery	Yes	Quantitative	Lateral: 3 cm; deep: 1 fascial plane	Trichotomous	
Smith,[50] 2017	Med Onc	Yes	None		Dichotomous	
Stanclift,[33] 2008	Surgery	Yes	Quantitative	Lateral: 3 cm	Trichotomous	
Thamm,[23] 1999	Med Onc	No	Other	Marginal or appropriately aggressive surgery with no histologic evidence of tumor cells at margin	Dichotomous	

(Continues)

TABLE 2 (Continued)

Article	Specialty of first author	Surgeon contributing author	Surgical margins system	Surgical margin details	Histologic margins system	Histologic margin details
Thamm,[24] 2006	Med Onc	No	Other	Marginal or appropriately aggressive surgery with no histologic evidence of tumor cells at margin	Dichotomous	
Trumel,[51] 2005	Clin Path	No	Quantitative	Lateral: 3 cm	Dichotomous	
Webster,[52] 2008	Pathology	No	None		Dichotomous	
Weishaar,[22] 2014	Med Onc	Yes	Enneking	Marginal or wide local	Dichotomous	
Weisse,[53] 2002	Surgery	Yes	None		Dichotomous	
STS studies						
Bacon,[14] 2007	Surgery	Yes	Quantitative	Lateral: 0.5-3 cm, scar revision	Trichotomous	
Baez,[54] 2004	Med Onc	No	Modified Enneking	Incisional biopsy, marginal, or Wide	Dichotomous	
Banks,[27] 2004	Surgery	Yes	Quantitative	Lateral: 3 cm	Quantitative/ trichotomous	
Bray,[34] 2014	Surgery	Yes	Modified Enneking/ quantitative	Marginal, local (<3 cm around tumor), wide (≥3 cm around tumor), or radical	Dichotomous	
Chase,[20] 2009	Surgery	Yes	Modified Enneking/ quantitative	Marginal, narrow (<3 cm around tumor), wide (≥3 cm around tumor), or radical	Dichotomous	
Kuntz,[4] 1997	Surgery	Yes	Enneking		Dichotomous	
McSporran,[55] 2009	Pathology	No	None		Trichotomous	
Prpich,[56] 2014	Surgery	Yes	Quantitative	Lateral: 2 cm	Dichotomous	
Selting,[29] 2005	Med Onc	Yes	None		Trichotomous	
Stefanello[57] 2008	Surgery	Yes	Enneking		Trichotomous	
Stefanello,[25] 2011	Surgery	Yes	Quantitative	Lateral: 3 cm	Trichotomous	
Studies including both MCT and STS						
Baker-Gabb,[58] 2003	DVM	Yes	Enneking		Trichotomous	
Eward,[59] 2013	Surgery	Yes	Enneking	Wide or radical	Dichotomous	
Monteiro,[60] 2011	DVM	Yes	Quantitative	Lateral: 3 cm; deep: 1 fascial plane	Dichotomous	Incomplete/close or complete
Russell,[61] 2017	Pathology	Yes	Quantitative	Lateral: 0.3-7 cm; deep: 0-2 fascial planes	Quantitative	
Scarpa,[3] 2012	Pathology	Yes	None		Other	Clean, close, focally infiltrated, or diffusely infiltrated

Abbreviations: Clin-Path, clinical pathology; DVM, Doctor of Veterinary Medicine; IMed, internal medicine; MCT, mast cell tumor; Med-Onc, medical oncology; Rad-Onc, radiation oncology; STS, soft tissue sarcoma.

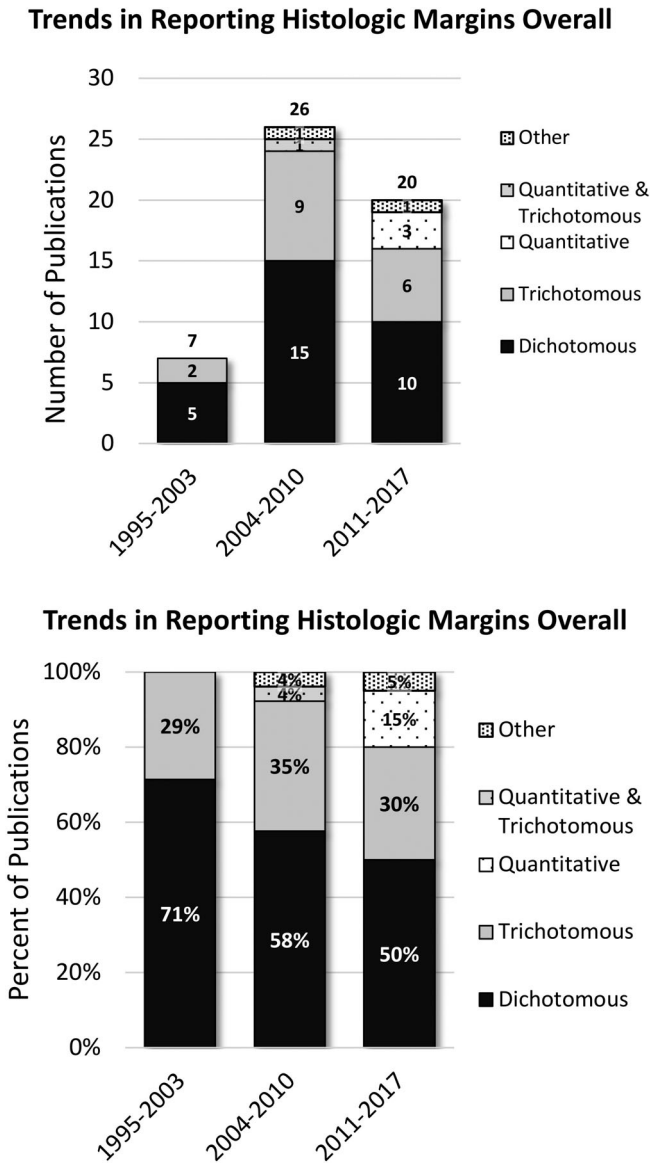

FIGURE 2 Bar graphs, presented as both the number and percentage of total papers, illustrating the use of various histologic margin classification schemes over time. Despite publication of a consensus statement in 2011 in which consistent use of quantitative methods for reporting histologic margins was recommended, a significant trend in the proportion of publications that reported histologic margins by using dichotomous, trichotomous or quantitative methods was not found over time

description of the planned surgical margins. However, studies in which a veterinary surgeon was listed as a contributing author and those in which canine STS (compared to MCT) was reported were more likely to provide surgical margin details. Most papers reported the status of histologic margins dichotomously as complete or incomplete, and, despite publication of the American College of Veterinary Pathologists consensus statement that set guidelines for histologic margin reporting within veterinary medicine, a trend in research studies in which quantitative criteria were used to report the status of histologic margins was not found.

The most common methods to describe the planned surgical margins in the MCT and STS literature were quantitative systems. When a solid tumor is surgically treated, important, clinically relevant information is determining what the minimum width of grossly normal tissue around a tumor is required to resect to prevent local recurrence. The finding that quantitative methods were used in most of the studies in this review to report surgical margins may reflect the priorities of investigators in seeking to answer this question for canine MCT and STS.

The observation that the Enneking criteria was regularly used to report surgical margins in canine STS papers is in line with the Enneking criteria's original application as a classification system developed for use in the human sarcoma margin literature. Although the Enneking system has classically been used in the human literature in reference to musculoskeletal sarcomas, this review illustrated how veterinary medicine has adapted this classification system for use in both canine MCT and canine STS papers.

Only half of the articles included in this review provided a description of the planned surgical margins. We found that papers that listed a surgeon as either a primary or contributing author were more likely to provide surgical margin details. It makes sense that surgeons would be motivated to investigate and subsequently report surgical margins compared with other specialists. When excision of a tumor is planned, the effect that surgical dose has on the patient's ultimate function and outcome directly influences a surgeon's approach and clinical decision making.

The fact that STS papers described the planned surgical margins more often than MCT articles (81.8% vs 37.8%, respectively) may relate to the respective prevalence of these tumor types in man. Cutaneous MCT, or mastocytomas, are relatively rare tumors in man. Consequently, a margin classification system does not exist for mastocytomas. This is in contrast to the human sarcoma literature, in which several surgical margin schemes have been described, including Enneking,[17] R-classification,[15] and Toronto margin context[62] classification systems, among others. Because veterinary studies often replicate methods and standards that have been established in the human literature, the lack of a margin classification system for human mastocytomas may have contributed to the disparity in margin reporting observed between canine STS and MCT papers.

In contrast to the Enneking criteria, a margin classification system that abandons the use of compartmental

TABLE 3 Summary of the various operational definitions of a histologically close and complete margin within the canine cutaneous MCT and STS literature

	Close margin (mm)	Complete margin (mm)
MCT studies		
Baginski,[35] 2014	Na	≥2
Berlato,[30] 2015	<1	≥1
Brocks,[21] 2008	Na	0
Camus,[10] 2016	<2	≥2
Davies,[28] 2004	1-10	≥10
Donnelly,[11] 2015	Na	≥1
Fulcher,[13] 2006	Na	≥1
Grier,[38] 1995	Na	0
Hayes,[26] 2007	Acceptable: 5-10 narrow: ≤5	>10
Hosoya,[39] 2009	Na	0
Hume,[40] 2011	Na	0
Kry,[41] 2014	<3	≥3
Lejeune,[42] 2015	Na	≥5
Michels,[8] 2002	Na	0
Miller,[43] 2016	Not explicitly defined	Not explicitly defined
Murphy,[6] 2004	<5	>5
Murphy,[45] 2006	<5	>5
O'Connell,[47] 2013	1-5	>5
Ozaki,[48] 2007	Na	0
Pratschke,[31] 2013	Na	>1
Seguin,[32] 2001	<1	≥1
Seguin,[9] 2006[9]	Na	≥1
Simpson,[12] 2004[12]	<1	≥1
Smith,[50] 2017[60]	Na	>5
Stanclift,[33] 2008	<1	≥1
Thamm,[23] 1999	Na	0
Thamm,[24] 2006	Na	0
Trumel,[51] 2005	Na	0
Webster,[52] 2008	Na	0
Weishaar,[22] 2014	Na	0
Weisse,[53] 2002	Na	>1-2
STS studies		
Bacon,[14] 2007	<3	≥3
Baez,[54] 2004	Na	0
Banks,[27] 2004	<5	≥5
Bray,[34] 2014	Na	>1
Kuntz.[4] 1997	Na	0
McSporran,[55] 2009	No pseudocapsule or < 1 mm beyond	≥1 mm beyond pseudocapsule
Prpich,[56] 2014	Na	0
Selting,[29] 2005	1-10	>10

TABLE 3 (Continued)

	Close margin (mm)	Complete margin (mm)
Stefanello,[57] 2008	1-3	>3
Stefanello 2011[25]	1-3	>3
Studies including both MCT and STS		
Baker-Gabb,[58] 2003	Not explicitly defined	Not explicitly defined
Monteiro,[60] 2011	1-5	>5
Scarpa,[3] 2012	≤2	>2

Abbreviations: MCT, mast cell tumor; Na, not applicable; STS, soft tissue sarcoma.

anatomy to describe resections may be more clinically applicable. An example of one such system used by human surgical oncologists is the R-classification system.[15] Unlike other margin classification systems that differentiate surgical margins from histologic margins, the R-classification system incorporates both clinical and pathologic findings. The AJCC has recommended use of the R-classification system in result reporting since 1978.[15] Universal acceptance and application of the system was established in 1987 after international collaboration between the AJCC and the International Union Against Cancer that led to the revised and unified the formulation of the TNM Classification of Malignant Tumors.[63] The prognostic value of the R-classification system has not only been demonstrated in human STS[64-67] but it has also been validated in enumerable other tumor types.[68-71] Because of this system's uniform utility, its applicability to most tumor types, and the fact that its prognostic ability has been repeatedly validated, it may be worthwhile to consider clinically validating the R-classification system in animals with cancer.

A predominant classification system for reporting the status of histologic margins was identified. Across the papers reviewed, one of three primary classification systems (dichotomous, trichotomous, or quantitative) was used in all but two studies to report the status of histologic margins. Most of those papers reported the status of histologic margins dichotomously as complete or incomplete. The simplicity and reproducibility of using dichotomous criteria could be selected by authors and pathologists to reduce the opportunity to introduce more variability, which may lend itself to making comparisons across studies. Although an incomplete margin was most often defined as the presence of neoplastic cells at histologic evaluation of the resected margin, considerable variability existed in how a complete margin was defined. Similarly, when a close or narrow margin was considered, a standard definition was not apparent throughout the literature. This heterogeneity and lack of uniformity in operational definitions impedes the ability to compare results across studies in which tumor margins and oncologic outcomes have been evaluated.

Although the proportion of papers in which quantitative methods were used for reporting histologic margins subjectively increased after publication of the Kamstock guidelines, a statistically significant trend was not found. While the scope of this study was not to evaluate which classification system is best suited for margin reporting, following the recommendations of the American College of Veterinary Pathologists consensus statement by Kamstock et al[19] for consistent histologic reporting of specimen margins with objective measurement may assist future endeavors to determine a histologic safety margin for MCT and STS. Determination of a histologic safety margin, which is defined as the histologically tumor free margin distance required to decrease or eliminate the odds of local recurrence, in canine MCT and STS remains to be elucidated. A prospective randomized trial, perhaps with stratification by tumor grade, for both MCT and STS would be ideal.

A limitation of this study was that margin reporting data were specific to canine STS and cutaneous MCT literature. Therefore, the observations made from these results are limited to the context of these tumor types within this particular species. In addition, studies that may have otherwise met the criteria for inclusion in this systematic review may have been missed during the initial database searches as a result of the delay in time between manuscript acceptance and publication.

The findings of this study provide evidence that a universal system of margin reporting is required. Following a consensus for margin evaluation reporting may generate standardized data that will improve data uniformity, thereby allowing comparison of results across studies so that larger, more robust animal populations can be evaluated for prognostic variables. This may lead to more reliable information that will ultimately result in improved animal care.

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collection, data cleaning and interpretation, drafting the manuscript, and approval of the final manuscript; Ruple A, DVM, MS, PhD, DACVPM, MRCVS: Design of the study, data interpretation, drafting the manuscript, and approval of the final manuscript; Wavreille V, DMV, MS, MRCVS, DACVS-SA, ACVS Fellow - Surgical Oncology: Design of the study, data interpretation, drafting the manuscript, and approval of the final manuscript; Selmic LE, BVetMed (Hons), MPH, DACVS-SA, DECVS, MRCVS, ACVS Founding Fellow - Surgical Oncology: Conceptualization and design of the study, data analysis and interpretation, drafting and revising the manuscript, and approval of the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this report.

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APPENDIX A

SEARCH STRATEGY OF MeSH STRINGS USED TO PERFORM SYSTEMATIC REVIEW

For MCT the complete search string utilized was:

("mast cells"[MeSH Terms] OR ("mast"[All Fields] AND "cells"[All Fields]) OR "mast cells"[All Fields] OR ("mast"[All Fields] AND "cell"[All Fields]) OR "mast cell"[All Fields]) AND ("tumour"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "tumor"[All Fields]) AND ("dogs"[MeSH Terms] OR "dogs"[All Fields] OR "dog"[All Fields]) mast cell tumor dog surgery and ("surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "surgery"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields]). For STS, the complete search string utilized was ("sarcoma"[MeSH Terms] OR "sarcoma"[All Fields] OR ("soft"[All Fields] AND "tissue"[All Fields] AND "sarcoma"[All Fields]) OR "soft tissue sarcoma"[All Fields]) AND ("fibrosarcoma"[MeSH Terms] OR "fibrosarcoma"[All Fields]) AND ("surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "surgery"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields]) AND ("dogs"[MeSH Terms] OR "dogs"[All Fields] OR "dog"[All Fields]).

Second strategy:

MCT: ("mast cells"[MeSH Terms] OR ("mast"[All Fields] AND "cells"[All Fields]) OR "mast.

cells"[All Fields] OR ("mast"[All Fields] AND "cell"[All Fields]) OR "mast cell"[All Fields]).

AND ("tumour"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR.

"tumor"[All Fields]) AND ("dogs"[MeSH Terms] OR "dogs"[All Fields] OR "dog"[All Fields])).

STS: ("sarcoma"[MeSH Terms] OR "sarcoma"[All Fields] OR ("soft"[All Fields] AND "tissue"[All Fields] AND "sarcoma"[All Fields]) OR "soft tissue sarcoma"[All Fields]) AND.

("fibrosarcoma"[MeSH Terms] OR "fibrosarcoma"[All Fields]) AND ("dogs"[MeSH Terms] OR.

"dogs"[All Fields] OR "dog"[All Fields]).