Thank you for passing on comments on our manuscript 'The impact of extirpation of non-palpable/normal-sized regional lymph nodes on staging of canine cutaneous mast cell tumours: A multicentric retrospective study" published in the December 2018 issue of Veterinary and Comparative Oncology (pp. 505-510).<sup>1</sup>

The aim of our study was to assess the metastatic rate of non-palpable or normal-sized regional

lymph nodes (RLNs) in newly-diagnosed canine mast cell tumours (MCTs). We have documented that approximately 50% of non-palpable or normal-sized RLNs are metastatic at first presentation. The impact of RLN metastasis on outcome was beyond the aim of the study and no outcome data were reported. Conversely, several studies have already documented the potential negative prognostic role of RLN metastasis and the presence of loco-regional metastasis is still listed as a negative prognostic factor in MCTs.<sup>2-8</sup> Furthermore, Patnaik-grade II MCTs with lymph node metastasis are often considered as "high-risk" tumours requiring adjuvant treatment.<sup>9-12</sup>

Unfortunately, in many retrospective studies the impact of RLNs metastasis is possibly biased by the absence of complete and standardized staging procedures with a possible underestimation of the disease extension in some cases, or by addressing some form of treatment (extirpation and/or radiation and/or adjuvant chemotherapy) to the metastatic RLNs, thus possibly masking the negative effect of loco-regional metastasis.<sup>7,10,13-16</sup>

In the study of Bagiski and colleagues (2014) it was concluded that there was no significant difference in median survival time between dogs with grade II MCTs with and without RLN metastasis. However, the authors also reported "This should be interpreted with caution due to the differences in adjunctive therapy between groups. However, dogs with a metastatic LN lived longer if it was removed. Given the difference in survival time between dogs with and without removal of the metastatic RLNs, extirpation of the draining lymph node is recommended in cases where it is

clinically feasible." To reinforce this paradigm, the therapeutic role of the extirpation of metastatic

RLN was recently confirmed.<sup>17</sup>

Similarly to human medicine, also veterinary oncologists are increasingly oriented on the early

detection of loco-regional metastasis. While the uncertain prognostic role of occult metastasis

cannot be denied (especially if histologically described as pre-metastatic or early metastatis), future

efforts are greatly needed to address this issue, so that a more precise prognosis can be formulated,

and an adequate treatment started.

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