The general rule of thumb for the excision of a malignancy is that 3cm lateral margins and a fascial plane deep are required for complete tumor excision. Although this dogma is widespread, there is not a great deal of evidence available in the literature to determine its origin. In veterinary medicine, some research has been done in this area with mast cell tumor excision. In a study evaluating the margins after excision of mast cell tumors at 1, 2 and 3cm margins, Simpson et al showed that margins of 2cm were all that were required. This was put into practice by the same research group in a second study that utilized 2cm margins to remove grade I and II MCT. In that study by Fulcher et al, the rate of dirty margins was 2/19 for grade II tumors, suggesting that 2cm is not an adequate margin in all cases. Although it is likely that more than 2cm margins for mast cell tumors is likely overkill for low-grade mast cell tumors, the problem is that usually the grade is unknown for most mast cell tumors prior to excision. Even with preoperative grading, the grade of an incisional biopsy may not be accurate, compared to when the pathologist has the entire mass to evaluate. The crux of the issue is that the small mast cell tumors are not difficult to remove with 2 or 3cm margins, and likely they require less resection. The larger tumors are more difficult to resect and likely require larger margins of excision. A recent study by Donnelly et al evaluating margins in mast cell tumor using the two-tier grading system reported that in 90 cases with complete margins, the high grade tumors were 13.7X more likely to recur than the low grade tumors, suggesting that grade may trump clean margins in local recurrence.

In soft tissue sarcoma in humans, a definite association between the completeness of excision and prognosis has been reported in multiple publications. In the veterinary literature, reexcision of scars after incomplete excision of soft tissue sarcomas has led to long survival times and low recurrence rates. (Bacon) A recent study evaluating the use of reexcision or radiation of dirty mast cell tumor scars compared with no treatment has shown a significant survival advantage with additional local therapy after incomplete excision. (Kry)

When working with the pathologist evaluating your samples, it is important to use ink and to communicate well with the pathologist about the tissues that you are submitting. When the margins are reported, the radial margins should be reported as a metric margin. The deep margin is more appropriately reported with the quality of the tissue that is intervening between the tumor and the inked edge. One millimetre of fascia is a clean margin, whereas 1cm of subcutaneous tissue and fat may not be. It is important that the deep margin is inked and evaluated carefully, as this area is at risk for an incomplete resection. A major downfall of classical margin assessment in veterinary margin is that it is not possible to assess margin in its entirety, especially with large tumors. This means that a dirty margin is dirty and a clean margin is likely clean, but a foci of tumor cells may exist along a margin that was not evaluated. The clean but close margin is another problem that exists in veterinary medicine and in general, the close margin should be treated as a dirty margin and/or request for further recuts by your pathologist to more fully evaluate the margins should be made.
A question that arises in the surgical planning for complete margins of excision is whether or not neoadjuvant therapy is worthwhile pursuing prior to excision. The most common tumor type in veterinary medicine where neoadjuvant therapy has been attempted for local downstaging is mast cell tumors. The use of neoadjuvant therapies remains somewhat controversial and the use of preoperative therapies may depend to some extent on the goals of surgical therapy. The use of corticosteroids will likely shrink the tumor and may facilitate excision. However, the primary effect of corticosteroids is most likely to be anti-inflammatory, rather than cytotoxic. This may result in a decrease in tumor size, but the continued presence of tumor cells in the tumor periphery. This approach is warranted if the goal is cytoreduction and primary closure, followed by radiation therapy or, in adjuvant chemotherapy in cases with metastasis beyond a lymph node. It may, however, give the surgeon a false sense of security if a curative intent excision is part of the treatment plan. Chemotherapy such as vinblastine or palladia, may be effective as a tool to downstage mast cell tumors prior to wide surgical excision because of their cytotoxic effects. However, this remains to be reported in the veterinary literature. In general, if a mast cell can be removed with clean margins with a wide excision, it is recommended by the author to excise the tumor without downstaging first, with downstaging reserved for cases where a curative excision is not possible or not possible without unacceptable morbidity to the patient. In these cases, adjuvant radiation therapy may also be a necessary part of treatment.

In the human literature, the most classic use of neoadjuvant chemotherapy is for downstaging prior to limb salvage surgery. Historically, this was done to allow therapy to be initiated while custom-made prostheses were developed for limb salvage. It has also allowed for evaluation of the efficacy of the neoadjuvant chemotherapy through the assessment of the percentage necrosis of the tumor. With newer implants being used, the wait for a custom prosthesis is not as long and is not generally a reason for neoadjuvant chemotherapy to be pursued. There is also an emerging theory that the use of neoadjuvant chemotherapy may actually contribute to chemoresistance. It may be that this convention in human orthopedic oncology is now based on the belief that limb salvage is facilitated by down staging with chemotherapy, rather than evidence that it is beneficial. This area requires further evaluation in both human and veterinary surgical oncology. It is, however, a difficult area to study and definitively prove whether or not there is a clinical benefit.

Classical margin evaluation with a metric radial margin and a fascial plane deep to the tumor must be adjusted in the assessment of margins for solid carcinomas such as thyroid carcinoma, anal sac adenocarcinoma and thymic carcinoma. If these tumors are marked with tissue ink and submitted for histopathology, it is possible that a pathologist may report a metric margin and that this margin, if 0-2mm, may be interpreted as a dirty margin. More work in the reporting of the margins of these tissues is required, with very little information available in the veterinary literature. In human evaluation of thyroid carcinoma, the focus is on whether or not there is extracapsular extension of the tumor. This is a more appropriate way to evaluate the completeness of excision in solid carcinomas. For any of the solid carcinomas listed above, an en bloc excision with 3cm margins and/or a true fascial plane surrounding the tumor is not feasible. However, without extracapsular extension, the rate of recurrence in these tumor types is low, with failure more commonly due to metastatic disease.
In the future, real time optical fluorescence in surgery or molecular markers of tumor cells in the margins may be employed to assess margins of excision in real time and with great accuracy. These techniques are just starting to be employed in human surgical oncology and may assist with overcoming some of the obstacles that exist in veterinary and human pathological margin assessment.

References