

Veterinary Surgical Oncology



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Principles of surgical oncology

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Cancer treatment is a rapidly changing and evolving area involving the use of multiple diagnostic and therapeutic modalities to achieve the most optimal outcome. Surgical intervention remains a pivotal aspect of the treatment of cancer. Surgery cures more cancer than any other single modality. Nonetheless, the optimal treatment pathway for any given animal patient with cancer most often involves several adjuvant treatment modalities. Adjuvant treatments significantly affect the success of surgery, and likewise, surgery affects the outcome of adjuvant treatments. It is widely recognized in human cancer centers that patient outcome is greatly improved when surgery is performed by a surgeon with specialized training in oncologic procedures. These surgeons have expertise in selecting surgical treatment options in combination with other forms of cancer treatment, as well as knowledge of the benefits and risks associated with a multidisciplinary approach beyond that which can be mastered within a 3-year surgery residency training program. This level of expertise requires an understanding of the fundamental biology of cancer, clinical pharmacology, tumor immunology and endocrinology, as well as a thorough understanding of potential complications of multimodality therapy. Veterinary training programs in surgical oncology have been in existence for the last 14 years. With the development of new treatments such as small molecule inhibitors, gene therapy, and new forms of radiation, the role of the surgical oncologist is constantly evolving and changing (O'Reilly et al. 1997; Drixler et al. 2000).

Therapeutic goals (e.g., curative intent, cytoreduction, or palliation) for each case should be established with the pet owners before surgery is initiated. The efficacy of surgical therapy in any patient with cancer is heavily dependent upon the surgeon's global under-

standing of the patient's general health status, lifestyle, and activity level; type and stage of cancer; adjuvant therapies available; alternatives to surgery; and expected prognosis. To maximize effectiveness, the optimal treatment pathway for each case should be strategically assessed before initiating treatment. This planning should always include a frank and thorough discussion with the owner regarding preoperative diagnostic tests, stage of cancer, palliative options, surgical options, adjuvant treatments likely to be needed, costs, postoperative care, and expected function, cosmesis and prognosis including risks of complications. The goal of this discussion is to provide owners with enough information to help them make an informed choice regarding the best treatment plan for their companion. Highly individualized initial planning will allow for the best overall outcome for each patient.

Preoperative Considerations

Signalment

The patient's age, gender, breed, and weight are important factors in the determination of appropriate recommendations. Advanced age is not necessarily a negative prognostic factor. Comorbidities common to geriatric veterinary patients such as renal insufficiency, hepatic disease, or osteoarthritis may limit or change specific treatment recommendations; however, the age of the patient alone should not.

Certain neoplastic diseases are common in a particular gender or breed. The surgical oncologist should always bear in mind the role that gender and breed play in the diagnosis of neoplasia. As an example, the differential list for a flat-coated retriever with a femoral bony lesion noted on radiographs that has been referred

for a suspected diagnosis of osteosarcoma should be expanded to include histiocytic sarcoma; other diagnostics such as an abdominal ultrasound would be recommended to look for other foci of histiocytic disease.

Other portions of the signalment are also important to note, including the patient's weight and body condition. Patients that are morbidly obese or those in poor body condition may not be able to function effectively or may be more severely debilitated by a major surgery. For example, a patient with cancer cachexia can have such profound alterations of their carbohydrate, protein, and fat metabolism that recovery may be compromised (Ogilvie 1998).

Staging and concomitant disease

Staging diagnostics such as a complete blood count, chemistry profile, urinalysis, thoracic radiographs, and abdominal ultrasound are essential components for the preoperative assessment of veterinary oncology patients. While there is debate about the timing of some of these diagnostics (i.e., before or after biopsy), for many patients thorough preoperative staging diagnostics can unmask an underlying condition that may alter the plan or better assist the surgeon to provide a more accurate prognosis. Alternative surgical dose may also be recommended based on the results of staging.

Neoadjuvant therapy

The surgical oncologist is often presented with extremely large tumors or tumors located in difficult anatomical locations. It is important to consider neoadjuvant treatments, if available and warranted, such as chemotherapy and radiotherapy before proceeding with surgery. In some cases, these treatments may decrease the overall surgical dose needed to achieve local control. Most commonly, recommendations about chemotherapy and radiation therapy are made after the grade of the tumor and the surgical margins have been determined. In tumors that are suspected to be sensitive to chemotherapy based on published literature or previous experience, a postoperative protocol can be discussed prior to surgery.

Neoadjuvant chemotherapy is rarely pursued in veterinary medicine. However, for certain tumor types, this may prove to be a beneficial adjunct to surgery. In human cases of osteosarcoma, neoadjuvant chemotherapy is commonly used prior to surgery and local tumor response (as measured by percentage of tumor necrosis) has been shown to be associated with increased survival. A recent veterinary study showed that neoadjuvant chemotherapy with prednisone administered to a group of dogs with intermediate grade mast cell tumors resulted in tumor size reduction; surgical excision of very large

mast cell tumors or tumors that were in an anatomical site that precluded wide (3 cm lateral and one facial plane deep) excision was more successful (Stancliff and Gilson 2008). Microscopically complete margins were achieved in many of the pretreated cases. These patients would not likely have had complete surgical margins otherwise (Stancliff and Gilson 2008). Long-term follow-up was not the focus of this study, however, and controversy exists as to the risk of local recurrence in patients where neoadjuvant chemotherapy is used to shrink gross tumor volume to allow a less aggressive surgical margin. Further study is needed to assess the benefit of neoadjuvant chemotherapy in veterinary cancer patients.

Neoadjuvant radiation therapy has also been advocated as a method of treating neoplastic disease to reduce the need for radical surgery (McEntee 2006). Advantages to neoadjuvant radiation therapy include a smaller radiation field, intact tissue planes, better tissue oxygenation, and a reduction in the number of viable neoplastic cells that may be left within a postoperative seroma or hematoma following microscopically incomplete margins. Complications such as poor wound healing may occur more commonly in irradiated surgical sites than in nonirradiated tissue due to the effects of radiation on fibroblasts and blood vessels (Séguin et al. 2005). Even so, surgery in previously irradiated fields can be quite successful provided care is taken to ensure minimum tension, careful surgical technique, and appropriate timing (either before or after acute effects have occurred). Consultation with a radiation oncologist prior to surgery can help the surgeon identify those patients who may be good candidates. Considerations such as whether or not preoperative radiation will diminish the surgical dose and what type of reconstruction will be needed to ensure a tension-free closure in an irradiated surgical field should be discussed at length prior to deciding if neoadjuvant radiation is warranted.

Surgical Planning

Fine-needle aspirate

Fine-needle aspiration is often the most minimally invasive technique for obtaining critical information about a newly identified mass prior to surgery. The accuracy of a fine-needle aspirate depends on many factors, including the tumor type, location, and amount of inflammation. Overall sensitivity and specificity of cytology has been reported to be 89% and 100%, respectively (Eich et al. 2000; Cohen et al. 2003). Imaging tools such as ultrasound and fluoroscopy can increase the chance of obtaining a diagnostic sample.

In most patients, a fine-needle aspirate of cutaneous or subcutaneous lesions can be obtained with no sedation and a minimal amount of discomfort. Fine-needle aspiration has been compared to histopathological samples in several studies. In a recent study of the correlation between cytology generated from fine-needle aspiration and histopathology in cutaneous and subcutaneous masses, the diagnosis was in agreement in close to 91% of cases (Ghisleni et al. 2006). Cytology was 89% sensitive and 98% specific for diagnosing neoplasia (Ghisleni et al. 2006). The goal of fine-needle aspiration is to differentiate between an inflammatory or neoplastic process, and if neoplastic, whether the tumor is benign or malignant. In some cases, the specific tumor type can be determined (e.g., mast cell tumor). In other cases, the class of tumor may be identified (e.g., sarcoma), but the specific diagnosis requires histopathology (e.g., chondrosarcoma versus osteosarcoma). The overall purpose of performing the fine-needle aspiration is to guide the staging diagnostics (where to look for metastasis or paraneoplastic diseases) and surgical dose. For example, a fine-needle aspirate of a mass showing normal adipocytes would indicate that the mass is not inflammatory; rather, it is a neoplastic process and is benign (lipoma). Based on the knowledge of the biological behavior of this tumor we would perform no other staging tests and prescribe a minimal surgical dose (marginal resection). Alternatively, if the fine-needle aspirate of a mass indicated carcinoma cells, we would be prompted to perform more advanced staging (three-view thoracic radiographs, abdominal ultrasound, lymph node aspirates) and would prescribe a larger surgical dose.

Fine-needle aspiration of internal organs can also be performed and may be helpful in guiding diagnostic and treatment choices. Image guidance should be used when obtaining tissue from fine-needle aspirations of masses within a body cavity. Aspirates of lung and other thoracic organs can be performed safely in most cases. In one study, fine-needle aspiration of lung masses had a sensitivity of 77% and a specificity of 100% (DeBerry et al. 2002). The aspiration of cranial mediastinal masses is beneficial, as thymomas can be diagnosed by cytology (Rae et al. 1989; Atwater et al. 1994; Lana et al. 2006). Cytological diagnosis of thymoma requires the presence of a population of unequivocal malignant epithelial cells. The presence of mast cells is also common in thymoma and often supports the diagnosis (Atwater et al. 1994). Flow cytometry is another diagnostic tool that will differentiate thymoma from lymphoma using a fine-needle aspirate sample. Thymomas will contain both CD4+ and CD8+ lymphocytes, whereas lymphoma would typically contain a clonal expansion of one lymphocyte type (Lana et al. 2006).

Fine-needle aspiration of hepatic and splenic neoplasia has been described in several studies (Osborne et al. 1974; Hanson et al. 2001; Roth 2001; Wang et al. 2004). Successful diagnosis of hepatic neoplasia with fine-needle aspiration is variable. A study has reported diagnostic rates for liver cytology of multiple pathologies (including neoplasia) as high as 80% (Roth 2001); however, another study demonstrated less success with diagnostic rates of 14% in dogs and 33% in cats for fine-needle aspiration of hepatic neoplasia (Wang et al. 2004). In cases of suspected splenic hemangiosarcoma, fine-needle aspiration is generally not recommended, as an accurate diagnosis is unlikely due to the abundance of blood-filled cavities. Additionally, complications may include severe bleeding from the aspiration site. Fine-needle aspiration of splenic neoplasia such as lymphoma and mast cell tumors is often diagnostic (Hanson et al. 2001).

Other tumors in which fine-needle aspiration has been used to obtain diagnostic information include gastrointestinal tumors and bony tumors. The accuracy of fine-needle aspiration in the diagnosis of gastrointestinal neoplasia is often dependent on the type of neoplasia present. For instance, fine-needle aspiration of gastrointestinal lymphoma tends to have a higher sensitivity than aspiration of gastrointestinal carcinoma/adenocarcinoma or leiomyoma/leiomyosarcoma (Bonfanti et al. 2006). The specificity of the diagnosis is similar among these neoplastic diseases with fine-needle aspiration (Bonfanti et al. 2006). In a recent report, ultrasound-guided fine-needle aspiration of osteosarcoma lesions was found to have a sensitivity of 97% and specificity of 100% for the diagnosis of a sarcoma (Britt et al. 2007). Another study found that cytology after fine-needle aspiration agreed with incisional and excisional biopsies of bony lesions in 71% of cases (Berzina et al. 2008).

As with any procedure, fine-needle aspirates are not without risk. In certain cases, bleeding or fluid leakage can be problematic, especially within a closed body cavity where it cannot be easily controlled. Tumor seeding and implantation along the needle tract is a rare occurrence but in certain tumors has been reported more frequently. Localized tumor implantation following ultrasound-guided fine-needle aspiration of transitional cell carcinoma of the bladder has been reported (Nyland et al. 2002) and should be a consideration when deciding on methods for diagnosing bladder masses. Fine-needle aspiration of mast cell tumors can cause massive degranulation, and clinicians should be prepared to treat untoward systemic effects following aspiration of a suspicious or known mast cell tumor. Despite the risks associated with fine-needle aspiration,

it remains an effective, inexpensive, and valuable tool in the preoperative planning process.

Biopsy

Clinicians often use the term *biopsy* as a nonspecific description of obtaining a tissue sample for histopathological interpretation. For this reason, we will designate biopsy procedures into two major categories: pretreatment biopsy (tissue obtained before treatment initiation) or posttreatment biopsy (tissue obtained at the time of definitive tumor resection). We will also give examples of specific biopsy techniques. All biopsy procedures, whether pretreatment or posttreatment, should be carefully planned with several factors in mind. These factors include known patient comorbidities, anatomical location of the mass, differential diagnoses, biopsy technique, eventual definitive treatment, and any neo-adjuvant or adjuvant therapies that may need to be incorporated.

Pretreatment biopsy

Needle core biopsy

This technique is commonly used for soft tissue, visceral, and thoracic masses (Osborne et al. 1974; Atwater et al. 1994; deRycke et al. 1999). Image guidance is recommended when using this technique in closed body cavities. Most patients require sedation and local anesthesia but do not need general anesthesia.

Instrumentation includes a needle core biopsy instrument (automated or manual), no. 11 scalpel blade, local anesthetic, and a 22-gauge hypodermic needle. To perform the procedure, the area surrounding the mass is clipped free of fur and prepared with aseptic technique. If intact skin is to be penetrated and the animal is not anesthetized, the skin overlying the area to be penetrated is anesthetized with lidocaine or bupivacaine. A 1–2 mm stab incision is made over the mass to allow for placement of the needle core biopsy instrument. The instrument is oriented properly and fired, and the instrument is withdrawn. The 22-gauge needle can be used to gently remove the biopsy from the trough of the needle core instrument. This identical procedure is performed for masses within a body cavity; however, it is necessary to use image guidance for proper placement of the instrument within the desired tissue. Imaging can be used to determine the depth of penetration and to safely avoid nearby vital structures.

Punch biopsy

The punch biopsy technique is most effective for cutaneous lesions as well as intraoperatively for biopsies of masses within organs such as the liver, spleen, and

kidney. Subcutaneous lesions can be biopsied using this method, but it is best to incise the skin overlying the mass and then obtain the sample using the biopsy instrument.

Instrumentation includes a punch biopsy instrument, no. 11 scalpel blade, local anesthetic, Metzenbaum scissors, forceps, and suture. The area containing the mass is clipped free of fur and prepared with aseptic technique. If intact skin will be penetrated and the animal is not anesthetized, the skin overlying the lesion is anesthetized with lidocaine or bupivacaine. For cutaneous masses, an incision is not necessary. For subcutaneous masses, make an incision in the skin over the mass to allow a better sample to be procured. The skin incision should be large enough for the punch biopsy instrument to be placed and allow it to be twisted without engaging skin. Twist the punch biopsy instrument until the device is embedded into the mass to the hub. The punch biopsy instrument is then withdrawn from the mass to expose the tissue sample. Gently grasp the sample with forceps, use Metzenbaum scissors to sever the deep aspect of the sample from the rest of the tissue, and remove the sample. A single suture is generally sufficient to close the incision. The same procedure can be performed on visceral organs.

Incisional (wedge) biopsy

The incisional biopsy technique is effective for masses in all locations and generates a larger sample for histopathological evaluation as compared to the needle core biopsy. The location of the incision should be carefully planned, as the biopsy incision will need to be removed during the definitive treatment. Care should be taken to avoid dissection and prevent hematoma or seroma formation as these may potentially seed tumor cells into the adjacent subcutaneous space. Although the junction of normal and abnormal tissue is often mentioned as the ideal place to obtain a biopsy sample, one should take care to avoid entering uninvolved tissues. Obtaining a representative sample of the mass is the most important principle to consider. It is also important to obtain a sample that is deep enough and that contains the actual tumor, rather than just the fibrous capsule surrounding the mass. Incisional biopsy has a higher potential for complications such as bleeding, swelling, and infection due to the increase in incision size and dissection.

Instrumentation includes a no. 11 or no. 15 scalpel blade, local anesthetic, Metzenbaum scissors, forceps, suture, and hemostats. A gelpi retractor or similar self-retaining retractor aids in visualization if the mass is covered by skin. If the skin is intact and moveable over the mass, a single incision is made in the skin. Once the tissue layer containing the tumor is exposed, two parallel

incisions are started superficially and then meet at a deep location to form a wedge. The wedge is then grasped with forceps and removed. If the deep margin of the wedge is still attached, the Metzenbaum scissors can be used to sever the biopsy sample free of the parent tumor. The wedge site is then closed with suture.

Posttreatment biopsy (excisional biopsy)

The approach to an excisional biopsy varies based on location, goal of surgery, and predetermined adjuvant therapy. An excisional biopsy has the advantage of being both a diagnostic technique as well as a treatment modality. A great deal of caution should be exercised in cases where the diagnosis is unclear. At a minimum, a fine-needle aspirate should be obtained to discern if a given mass is inflammatory or neoplastic, and if neoplastic, whether benign or malignant. This information is imperative in order to determine surgical dose.

There are cases where an excisional biopsy may be a reasonable option if doubt remains after fine-needle aspiration, depending on the size and location of the tumor. In these instances, the surgeon must contemplate if an excisional biopsy will compromise the ability to enact a cure by using a wide excision. If it is deemed that an excisional biopsy can be performed while leaving this option, an excisional biopsy may be considered.

Once an excision is performed, the local anatomy is forever altered; both deep and wide tissue planes to the tumor are invaded, providing the opportunity for tumor cells to extend and seed deeper and wider into tissues. For this reason, the best chance for complete excision is at the time of the first surgical excision. In order to perform a curative surgery, the surgeon must take the appropriate margin of tissue for the tumor type. In some cases (e.g., lipoma), this margin is minimal or even intralesional. In other cases (e.g., soft tissue sarcoma), the margin should be much more extensive. Unless the tumor type is known at the time of excision, the surgeon may compromise the patient by doing too little or too much surgery.

Specific biopsy techniques

Bone biopsy

The clinician performing the bone biopsy procedure should consider the eventual definitive treatment that is likely to be pursued for each case. The biopsy tract or incision needs to be in a location that can be removed during the definitive treatment. A reactive zone of bone exists in the periphery of most bone tumors, and samples taken from this region are more likely to result in an incorrect diagnosis (Wykes et al. 1985; Liptak et al. 2004). The surgeon should target the anatomical center

of the bony lesion. Two radiographic views of the involved bone should be available during the procedure as this will aid in optimal sampling. The majority of bone biopsies are performed using either a Michele trephine or a Jamshidi needle (Wykes et al. 1985; Powers et al. 1988; Liptak et al. 2004). A trephine instrument provides a large sample and has been associated with 93.8% diagnostic accuracy (Wykes et al. 1985). The disadvantages of the trephine technique include increased likelihood of fracture as compared to other techniques, requirement of a surgical approach, and a more lengthy decalcification time prior to sectioning (Wykes et al. 1985; Ehrhart 1998).

Michele trephines are available in variable diameters. As a small surgical approach is required, a simple surgical pack is needed for the procedure. The biopsy site is clipped free of fur, and the patient is prepared with aseptic technique and draped. A 1–3 cm incision is made over the bony lesion, and the soft tissues are dissected from the surface of the tumor. The trephine is then seated into the tumor using a twisting motion. The trephine is advanced through the *cis* cortex. An effort should be made to not penetrate both the *cis* and *trans* cortex as fracture of the bone is more likely (Liptak et al. 2004). Once the trephine is within the medullary cavity, the trephine is rocked back and forth to loosen the sample and then removed. A stylet is introduced into the trephine to push the sample out of the trephine onto a gauze square.

The Jamshidi needle technique is considered a less invasive means of obtaining a bone biopsy as compared to a Michele trephine. A small stab incision is necessary to introduce this device and fractures are unlikely. In approximately 92% of cases, a correct diagnosis of tumor versus nontumor is achieved when using a Jamshidi needle (Powers et al. 1988).

Instrumentation includes a no. 11 scalpel blade and a Jamshidi needle. The surgical site is clipped free of fur, and the patient is prepared with aseptic technique and draped. A 1–2 mm stab incision is made over the bony lesion. The Jamshidi needle is introduced into the stab incision and pressed onto the bony lesion. The stylet is then removed from the needle, and the needle is twisted until the *cis* cortex is penetrated. The Jamshidi needle is rocked back and forth to loosen the sample and then removed. The stylet is reintroduced into the needle in the opposite direction of the initial location. As the stylet is moved through the Jamshidi needle, the biopsy will be ejected from the base of the Jamshidi needle.

Lymph node biopsy

Treatment and biopsy of lymph nodes in neoplastic disease remains controversial (Gilson 1995). Removing

a lymph node or performing an incisional biopsy of a lymph node can aid in staging the patient and assist in determining prognosis or treatment options. The surgical oncologist should have a thorough knowledge of the anatomical location of the probable draining lymph node for a mass in a particular location. The excisional biopsy of superficial lymph nodes such as the mandibular, prescapular, axillary, inguinal, or popliteal lymph nodes is described below. For removal of lymph nodes within the thorax or abdomen, an exploration of that body cavity is performed, and the lymph nodes are removed by careful dissection and maintenance of hemostasis.

Instrumentation includes a no. 10 or no. 15 scalpel blade, Metzenbaum scissors, forceps, suture, and suture scissors. The surgical site is clipped free of fur, and the patient is prepared with aseptic technique and draped. An incision slightly larger than the palpable lymph node is made parallel to the axis of the lymph node. The superficial tissue overlying the lymph node is bluntly and sharply dissected. The lymph node capsule is then grasped with the forceps and blunt or sharp dissection is performed around the lymph node to free it from the surrounding tissue. Vessels that are encountered may need to be ligated. The lymph node is then removed, and the subcutaneous tissue and skin are closed.

Endoscopic biopsy

Esophagoscopy, gastroscopy, duodenoscopy, and colonoscopy are routinely performed in veterinary medicine as minimally invasive techniques to attain biopsy tissue from the gastrointestinal tract. Biopsies attained during these procedures are generally smaller than that which can be achieved with an open procedure; however, the biopsies are often diagnostic, and the morbidity associated with these procedures is reduced over open procedures (Magne 1995; Moore 2003).

Laparoscopy and thoracoscopy are still relatively underused modalities, but successful procurement of kidney, bladder, liver, spleen, adrenal gland, pancreas, stomach, intestine, and lung biopsies have been described by use of these procedures (Rawlings et al. 2002; Lansdowne et al. 2005; Vaden 2005; Barnes et al. 2006). Case selection is essential when considering these minimally invasive alternatives, as cases that have excessively large tumors or other potential contraindications should undergo an open procedure.

Laparoscopy and thoracoscopy may have a role in the staging of veterinary patients as the use of these techniques increases. In cases where lymph node evaluation and biopsy would assist in predicting outcome or determining treatment, these procedures could be per-

formed by minimally invasive techniques (Fagotti et al. 2007).

Surgical considerations for curative-intent surgery

Certain surgical technical principles will improve the chance of success and minimize the risk of local or distant seeding of tumor cells. The tumor should be draped off from the rest of the surgical field. Surgeons should avoid contact with ulcerated or open areas of tumor with gloves or instruments. Sharp dissection is preferred over blunt dissection when possible, as this will decrease the likelihood of leaving neoplastic cells within the patient and decrease the risk of straying from the preestablished margin. Tension on skin closures should be avoided whenever possible, especially in cases that have undergone radiotherapy. Proper knowledge of tension-relieving techniques such as tension-relieving sutures and flaps can assist in closure (Soderstrom and Gilson 1995; Aiken 2003). If an indwelling drain is deemed necessary in a tumor resection site, the drain should be located in an area that can be resected during a subsequent surgery or in an area that will not compromise radiation therapy and can easily be included in the radiation field. Lastly, control of hemostasis and prevention of seroma or abscess development due to dead space is encouraged. Seromas or hematomas following an incomplete resection allow tumor cells to gain access to areas beyond the surgical field as these fluids may be widely dispersed throughout the subcutaneous space during movement.

To decrease the risk of recurrence after tumor resection, there are several techniques the surgeon should practice. For tumors that have been previously biopsied or for which a drain has been placed, the biopsy tract and/or drain hole need to be removed en bloc with the tumor. Similarly, adhesions should be removed with the tumor, when possible. Leaving any of these can result in an increased risk of tumor recurrence. Additionally, when establishing a margin during surgical dissection, this margin must be maintained around the periphery of the tumor down to the deep margin. Straying from this may result in an incomplete resection. Similarly, the pseudocapsule present around a tumor should not be penetrated, as this pseudocapsule is constructed of a compressed layer of neoplastic cells (Soderstrom and Gilson 1995). Seeding of these cells will likely result in recurrence, and healing may be inhibited. Lastly, it is essential that a new set of instruments, gloves, and possibly drapes be used for closure of a wound created by tumor removal or reconstruction of a wound. This principle applies to the removal of subsequent tumors on the

same patient as these items should not be transferred from one surgical site to another.

Defining and evaluating surgical margins

The evaluation of surgical margins of an excised specimen is an essential component to appropriate care in a cancer patient. A surgical margin denotes a tissue plane established at the time of surgical excision, the tissue beyond which remains in the patient. Excised masses should be submitted in their entirety for evaluation of the completeness of excision. The surgeon should indicate the margins with ink or some other method prior to placing the specimen in formalin to aid the pathologist in identifying the actual surgical margin. Because the larger tumor specimen is trimmed by a technician to fit on a microscope slide, the pathologist may not be oriented as to what represents a surgical margin versus a sectioning “margin”. Tissue ink on the surgical margin allows orientation throughout sectioning. The ink is present throughout the processing of the tumor specimen and is visible on the slide. If tumor cells are seen at the inked margin under the microscope, the surgical margin is by definition “dirty” or incomplete.

The surgical techniques used to remove tumors define the type and magnitude of intended surgical margin. When tumors are removed using an intracapsular technique, dissection occurs within the dimensions of the tumor and residual microscopic disease always remains (Soderstrom and Gilson 1995). Marginal excision refers to tumors excised with a 1 cm or less cuff of normal tissue surrounding the mass. Marginal excision may be quite appropriate for certain tumors such as lipomas but is often not sufficient for malignant tumors (Ehrhart and Powers 2007). Wide excision refers to tumors removed with 1–3 cm of normal tissue in all directions, including a deep margin. To achieve wide excision, the mass needs to be removed en bloc and the pseudocapsule and reactive zone should be completely contained within a cuff of normal tissue. Because dissection for a wide excision is intracompartmental, it is distinguished from a radical excision. A radical excision is considered an excision of normal tissue surrounding the mass of greater than 3 cm or the entire anatomical compartment (e.g., amputation). Extracompartmental excision is defined by a plane of excision beyond the anatomical compartment considered to have a cancer-resistant tissue barrier (Soderstrom and Gilson 1995).

Special focus is usually placed on mast cell tumors and soft tissue sarcomas when considering surgical margins. These tumor types generally have a bulky mass that is easily palpable; however, microscopic projections

of tumor cells extend out from the main tumor bed (Séguin et al. 2001; Murphy et al. 2004; Ehrhart 2005). These tendrils of tumor cells need to be considered preoperatively so that a proper surgical dose can be determined. Historically, 3 cm margins were recommended for excision of mast cell tumors and soft tissue sarcomas. Recently, though, studies have shown that 2 cm margins are sufficient for complete excision of 91%–100% of grade 2 mast cell tumors (Simpson et al. 2004; Fulcher et al. 2006). Recommendations for surgical margins around soft tissue sarcomas, however, continue to be at least 3 cm (Aiken 2003; Ehrhart 2005; Liptak and Forrest 2007).

In many cases, the deep margin of a tumor excision can be less than 2–3 cm from the tumor if removal of one tissue plane deep to the last tissue plane the tumor touches is achieved. For example, if the tumor is freely moveable in the subcutaneous tissue of the thigh, removal of the fascia lata as the deep margin will often be sufficient to achieve a clean margin. On the other hand, if the tumor is attached to the fascia lata, a muscle plane deep to this layer must be removed to achieve a clean margin. Unfortunately, the true definition of a “fascial plane” is lacking in medicine, and specific guidelines remain elusive (Fasel et al. 2007). While to some authors the definition of fascia has included adipose tissue, this concept is not universally supported (Fasel et al. 2007). A current definition of fascia is considered “sheaths, sheets, or other dissectible connective tissue aggregations visible to the unaided eye” (Wendell-Smith 1997; Fasel et al. 2007). Furthermore, fascia can be “considered as gross structures enveloping and/or supporting other formations” (Fasel et al. 2007). These definitions support the removal of a deep layer of connective tissue (not including adipose tissue) when considering a deep margin.

When an incomplete margin is noted on histopathological evaluation, the surgeon must decide on the next appropriate course of action. Options include intensive monitoring for recurrence, reexcision, and chemotherapy and radiation therapy. Both human and veterinary studies support early reexcision of a surgical wound bed when an incomplete margin is achieved during the primary surgery (Raney et al. 1982; Gibbs et al. 1997; Bacon et al. 2007). The goal during a reexcision surgery is to achieve tumor-free margins. Therefore, the entire wound bed must be treated as a dirty site and must be completely removed with a margin of normal tissue around it so that all tumor cells and microscopic extensions previously left in the patient will be removed. This always requires a more extensive surgery than the original surgical attempt.

Palliative and cytoreductive surgery

The decision to perform a palliative or cytoreductive surgery is often a difficult one, and the surgeon needs to educate the client and referring veterinarian about the risks and benefits of such surgery. Piecemeal removal (debulking) of a mass should generally only be performed when the mass is physically causing obstruction or altering function. There is little advantage to debulking otherwise, unless the removal results in only microscopic amounts of disease left behind. Palliation of symptoms caused by obstructive masses by removing most of or portions of large masses can temporarily improve quality of life in some cases. This should be performed only when necessary as excessive bleeding can often occur and dehiscence is very common.

Postoperative Considerations

Tissue marking

As discussed above, following an excisional biopsy, the surgical margins of the mass should be clearly indicated in some way so that the histopathologist can accurately evaluate the mass for complete excision. Several methods have been proposed to do this, including specialized sectioning techniques, suture markers, inking, and the submission of adjacent tissue as a separate sample (Rochat et al. 1992; Mann and Pace 1993; Seitz et al. 1995). Inappropriate sectioning can result in neoplastic cells being noted at the cut margin, and a false-positive result can occur. Sutures can be used to mark a particular area of interest or for tumor orientation, but sutures need to be removed before sectioning to prevent microscopic artifact (Mann and Pace 1993). A sample of tissue surrounding the surgical wound can also be submitted for evaluation. However, this increases the size of the wound bed, and added expense may be seen due to the submission of extra biopsy samples.

In general, the marking of tumor margins with inks or dyes is recommended. Several types of inks and dyes have been evaluated, including merbromin, laundry bluing, India ink, alcian blue, typists' correction fluid, commercial acrylic pigments, and artists' pigment in acetone (Rochat et al. 1992; Mann and Pace 1993; Seitz et al. 1995; Chiam et al. 2003). Alcian blue has been shown to be the best marking material; however, India ink and commercial kits (Davidson Marking System, IMEB Inc., San Diego, CA) are reasonable alternatives (Seitz et al. 1995). One of the benefits of the commercial kits is that multiple colors are provided. When using these kits, all the margins can be marked in different colors, but at a minimum, the lateral margin can be marked in one color and the deep margin in a different color. Yellow, black, and blue are considered the best

colors to use, whereas red and green are less ideal (Seitz et al. 1995).

Guidelines for fixation of surgical tissue specimens

Small biopsy samples should be placed in fixative immediately to prevent drying of the sample. Early fixation will initiate changes in the sample that will prevent autolysis and bacterial alteration of the sample (Stevens et al. 1974). In large biopsy submissions, the sample should be sliced evenly to allow more complete fixation (Dernell and Withrow 1998; Ehrhart and Withrow 2007). Many fixatives, including formalin, Bouin's fluid, chilled isopentane, Zenker's fluid, and glutaraldehyde have been described in veterinary medicine (Osborne 1974; Stevens et al. 1974), but in general, 10% buffered formalin is sufficient for almost all biopsies. A biopsy sample should be fixed in formalin in a 1:10 solution of tissue to formalin (Ehrhart and Withrow 2007).

Frozen sections

The use of frozen sections is common in human medicine. (Lessells and Simpson 1976; Kaufman et al. 1986). Frozen sections generate an accurate diagnosis in greater than 97% of human biopsy samples (Lessells and Simpson 1976; Kaufman et al. 1986). The process requires highly trained personnel and equipment specific to the procedure, and thus veterinary facilities that have the capability are limited (Ehrhart 1998). In one veterinary study, the accuracy of frozen sections in determining a specific diagnosis was 83% (Whitehair et al. 1993). In that same study, frozen sections were able to make a determination between neoplastic and non-neoplastic diseases in 93% of cases (Whitehair et al. 1993).

Wound healing

The veterinary oncology patient has several risk factors that may increase the frequency of complications associated with wound healing (Cornell and Waters 1995). Nutritional compromise and concomitant disease can be treated to improve the outcome of wound healing, but other factors such as tumor type and completeness of surgical excision have to be considered as well. Neo-adjuvant and adjuvant therapies such as chemotherapy, radiotherapy, and antiangiogenic medications have also been documented to impair wound healing (Devereux et al. 1979; Cornell and Waters 1995; te Velde et al. 2002; Séguin et al. 2005).

Proper surgical technique as described above can be employed to decrease the chance of wound complications. Regular communication with the patient's owner

both before and after surgery will help to preemptively prepare for complications or aid in rapid identification and intervention when complications arise. Prevention of self-trauma should be routinely discussed with the owner, and methods of prevention such as bandaging or having the patient wear an Elizabethan collar should be included in the postoperative care.

Adjuvant therapy

The time to discuss the potential need for adjuvant therapy in a tumor patient is prior to any surgical intervention. This allows owners to make informed choices and to better prepare for the financial burden, time required, and potential complications associated with this type of therapy. Failing to properly prepare the client for these additional treatments and the benefits and challenges unique to each one may leave the patient's owner feeling overwhelmed, underinformed, and may expose the patient to unnecessary morbidity or delay in treatment.

Chemotherapy in the adjuvant setting is generally administered after wound healing has been completed. Experimentally, it has been shown that administering certain types of chemotherapy before or at the same time as surgery may retard wound healing (Shamberger et al. 1981; de Roy van Zuidewijn et al. 1986; Lawrence, Talbot et al. 1986; Lawrence, Norton, et al. 1986). By the time a patient is ready for suture or staple removal, a wound is generally healed sufficiently, and chemotherapy may be administered. The results of the biopsy will also be accessible at a similar time, and these can help to guide chemotherapeutic recommendations.

Radiation therapy may be administered preoperatively or postoperatively. In general, radiation therapy will slow wound healing. In cases where radiation is administered either before or after surgery, it is important to ensure that there is minimal tension on the wound closure. This requires careful planning prior to and during the initial surgery. In some cases, if local flaps require extensive dissection in areas away from the tumor bed and outside the proposed radiation field, it may be better to delay primary closure until it is known if tumor margins are clean. This will help prevent seeding of tumor cells along the dissection planes where the flap will be raised. In postoperative patients who require radiation therapy but have wound complications such as infection or dehiscence, it is often better to try to manage the wound complication before beginning radiation. This may not always be possible, as tumor remaining in the wound may prevent wound healing. In these cases, it may be necessary to go forward with radiation in an open wound setting. In many cases, once acute effects have resolved, the wound can be closed. In these

cases, strict adherence to the "no skin tension" rule is imperative.

While certain basic concepts of surgery will remain static for the treatment of neoplasia, pursuit of better options for our patients will require that the surgical oncologist be able to adapt. It is hoped that the desire for improved outcomes will continue to improve the lives of our patients as well as their owners. Prolonging a quality of life for veterinary patients and advising their owners appropriately about the options that we have to offer should remain our goal as advances in therapy occur.

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