



Arizona Veterinary Specialists' News

Navigating Through the Mast Cell Tumor Maze: A Surgeon's Perspective

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Dr. Kathy Rowe-Guthrie attended the University of Georgia where she obtained her DVM degree in 2007. Her Masters of Science degree was completed at the University of Wisconsin in 2011. Dr. Rowe-Guthrie completed a small animal medicine and surgery internship at Louisiana State University in 2008. She completed her surgical residency training at the University of Wisconsin July 2014. She moved to Arizona to join Southwest Veterinary Surgical Service, PC in the summer of 2014. Dr. Rowe-Guthrie's areas of special interest include minimally invasive surgery (including arthroscopy), gastrointestinal surgery, and oncologic surgery. She is a member of the Arizona Veterinary Medical Association and the American Veterinary Medical Association.

What do wine and veterinary medicine have in common? February in Napa! I recently returned from the Veterinary Society of Surgical Oncologists (VSSO) conference, held in Napa, CA. The timing of the conference and being asked to write this newsletter article seemed like a nice coincidence, with my renewed enthusiasm and new knowledge of surgical oncology. This was only the third meeting of the society, which was founded in 2005 with the intent to bring together oncologists and surgeons, as well as pathologists and any other specialty involved in the diagnosis and treatment of cancer in veterinary patients. Physicians also participate in the society, bringing a valuable perspective. It is a rapidly growing group of people from all over the world, with a very active listserv, in which I participate. I feel fortunate to be able to communicate with the most brilliant minds in oncologic surgery about my cases.

I have always had a strong interest in oncologic surgery. I love the complexity of the cases, and I love getting rid of cancer, all the while improving the quality of life for our patients. I found the conference to be very stimulating. The approach

is different from other conferences I have attended, with a smaller group of attendees, which encouraged more robust discussion. Topics included specific cancers, as well as what is up and coming with interventional radiology (think stents, tumor embolization), minimally invasive surgery, and personalizing cancer treatment based on genetics. The specific neoplasias covered included osteosarcoma (OSA), melanoma, and mast cell tumor (MCT). We learned how human surgeons approach OSA in children, and about a vaccine for OSA that is being developed. We talked about evaluation of sentinel lymph nodes (SLN) for many tumor types, which involves different methods of determining which lymph node is the first to receive drainage from the tumor, rather than just assuming what lymph node may be affected. We learned about state-of-the-art surgical treatment for melanoma in humans, and ways in which we may apply these skills to our patients.

Despite all the new and exciting advances, the topic that generated the most discussion, some of which was heated, was MCT. Treatment of

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MCT can be extremely frustrating, and I have never walked away from the end of a MCT presentation without feeling more confused than I did at the beginning. After being a part of the discussion in Napa and hearing state-of-the-art presentations on the topic, I wanted to provide you with an updated perspective of mast cell tumors.

Questions that plague the clinician include how do you diagnose it? What margins should you take at surgery? How do you interpret your histopathology results? Which grading scale is most appropriate? When should adjuvant (after surgery) or neoadjuvant (before surgery) treatment be recommended? All of these questions have unclear answers. Why all the controversy and uncertainty? One reason is that we don't have a large amount of literature from the human side from which to gain knowledge. Humans don't develop MCTs-or they are at least exceedingly rare. On the other hand, MCTs make up 11-27% of all malignant skin tumors in small animal patients. Human studies of other cancers include large numbers and are well-funded, with extensive investigation and follow up. We often find similarities between the human and veterinary world with a certain disease, and may therefore take advantage of this large amount of information by extrapolating some of the human findings to our canine and feline patients (whether appropriate or not, but that is a different topic for a different day). We do not have that option with MCTs. Another reason for controversy is that mast cell tumors are unpredictable and have a wide range of initial presentations and biological behaviors. They "disguise" themselves as lipomas, bug bites, cysts, abscesses, skin tags, and a variety of other appearances.

The week before I left for Napa, I performed surgery on an older male neutered Labrador retriever named Luka. The owner had brought him in for a subcutaneous mass on his ventral abdomen that had been there for about

a year without any change. It was a soft, approximately 6-cm diameter mass and the owner was becoming more concerned about it. I recommended a fine-needle aspirate, as I recommend for any cutaneous or subcutaneous mass. I always send the samples to a pathologist unless I am convinced that it is a lipoma (only greasy fat seen on the slides, without blood or evidence of other cells). Upon aspirating this mass from several locations and angles, only fat was noted on the slides, which was consistent with a lipoma. The owner wanted the mass removed, so I performed a marginal excision and submitted the tissue for histopathology (as I always do for any mass that I remove-remember the nagging professor in vet school telling you "if it's worth taking off, it's worth sending in"? They were right). The results were waiting for me when I returned from California: grade II (low grade according to the two-tier system) MCT, narrowly excised (with only 1 mm margins). I also knew there was no deep margin taken, as I had not removed fascia. I silently cursed mast cell tumors for being masters of disguise, and was irritated by the lack of diagnosis on FNA (this was the first time I did not diagnose a MCT on an FNA). What if I had done a biopsy? At least I would have known it was a MCT, but grading is not always accurate with an incisional biopsy, as the grade is determined by the most active/aggressive region of the entire tumor, which is potentially missed with a biopsy. Additionally, with an incisional biopsy there are risks of histamine release from degranulation, as well as uncontrollable bleeding. The question could also be raised if the increased expense and morbidity of performing a biopsy on every soft subcutaneous mass suspected to be a lipoma is justified?

I was now faced with the dilemma of what to do with this case. Should I perform a second surgery? Should I refer the patient to an oncologist for radiation and/or chemotherapy? Do we wait and see if it recurs? Will it metastasize while we are waiting? The

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oncologic surgeon in me said, “operate again, with appropriate wide and deep margins! Get all the cancer out!” The “first do no harm” surgeon in me asked if that was really necessary. A second, more aggressive surgery would cause more morbidity, with a larger incision, more pain, and a greater risk of infection and dehiscence. Then there are the risks of anesthesia to consider, along with expense for the client. Further, I thought it was reasonable that the dog could pass away from something else before the tumor recurred, if it recurred. So I considered the evidence, the things we do know about MCTs.

We know that low-grade mast cell tumors (grade I and the majority of grade II tumors using the three-tiered system) generally have a good prognosis with surgical excision, with a median survival time of about 2 years (versus 4 months for high-grade tumors). Luka’s tumor was indeed classified as a low-grade tumor. But we also know that a certain number (25% of dogs with grade I tumors in one study) of dogs with low-grade tumors will have lymph node metastases (stage II). The prognosis significantly decreases with stage II disease regardless of tumor grade, with a median survival time of 0.8 years, versus 6.2 years without lymph node metastases. Finding a metastatic lymph node, if it exists, is not straightforward, however, since palpation of regional lymph nodes is neither sensitive nor specific. Any enlarged and firm lymph nodes should be aspirated and excised if positive, but there is a high rate of false negatives with simple palpation (as well as a high rate of false positives, thinking a node is metastatic when it isn’t). The goal is to identify the SLN, which is the first node to receive lymph fluid from the tumor, as mentioned above. The SLN cannot be accurately predicted based on location of the tumor, but must be detected using contrast or dye studies. These studies often use radioactive isotopes and a gamma camera, which are not widely available in veterinary hospitals, although they are available at Arizona Veterinary Specialists. The alternatives to the use of radioactive materials are expensive and time-

consuming. Simply using methylene blue dye intraoperatively, which is neither expensive nor time-consuming, sometimes may be useful, but only if your sentinel node is within your surgical field (and usually it is not with cutaneous tumors). So I couldn’t use lymph node status to help with the recommendations for Luka. One thing we did know, however, was that chemotherapy would not be recommended without confirmed stage II disease.

What do we know about recurrence? Most of the recurrence statistics are based on MCTs that have been incompletely excised, as they are the tumors that we know are more likely to recur. Does our tumor count as incomplete? That is a controversy of its own, about whether “narrow” excision is as bad or nearly as bad as “dirty”, or incomplete, excision. For the purposes of Luka, I assumed incomplete excision, with the margins so narrow and no appropriate deep margin. Statistically speaking, 77% of dogs with incomplete excision of their MCT will suffer recurrence. Rates for grades I and II tumors are even more promising, with a range between 7-23%. So at least 75% of dogs with Luka’s histopathology results do not experience recurrence of their MCTs. But what if he is in the minority? Are there ways to predict recurrence? The short answer is yes; although I will leave details to the medical oncologists, there are proliferation markers Ki-67, AgNOR, and PCNA, which when elevated, predict a higher likelihood of recurrence. Performing those tests on the histopathology for Luka was discussed with the owner.

What about staging? Thoracic radiographs may be indicated, although we know that MCTs rarely metastasize to the lungs, particularly low-grade tumors. An abdominal ultrasound would be a more appropriate diagnostic test, although only 2% of dogs with grade II tumors have evidence of mast cell disease with FNA of the liver and spleen (the most likely places for metastasis other than the SLN).

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In the end, the owners opted to simply monitor Luka for any recurrence of his MCT. It is unfortunate that I did not detect mast cells on the cytology sample prior to surgical excision. Ideally, I plan for 3-cm margins laterally (measured from the edge of the tumor, not the center) if the tumor is in a location amenable to wide margins. I always use a sterile marking pen and flexible ruler to accurately outline the measurements on the patient at the start of surgery. One of the major arguments at the conference was whether we could recommend 2-cm margins for tumor excision. There is evidence that 2-cm margins are adequate for grades I and II MCT, judged by lack of recurrence. However, a small percentage of grade II tumors are not completely excised with 2-cm margins, therefore I still stick with 3-cm margins when feasible. In a location where closure would be difficult with such wide margins, I consider reconstructive techniques such as skin flaps. If the owners do not want to be that aggressive, I will take as wide of margins as possible and hope for a low-grade tumor on histopathology. Regardless of lateral margins, I

always take a fascial plane deep to the tumor. What about those huge, ugly, ulcerated MCTs that you know in your gut are high-grade? Prognosis is poor, but treatment is still possible. We know that regardless of how widely the tumor is excised, recurrence is highly likely (although more likely with incomplete excision). Excision with as wide of margins as possible is recommended (up to 4 cm laterally if the tumor diameter is 4 cm or greater). If excision does not seem possible, neoadjuvant chemotherapy with vinblastine may help to decrease the tumor size. Prednisone may decrease inflammation and appear to shrink the tumor, but it is not clear if it actually destroys tumor cells by inducing apoptosis. Tumor recurrence after neoadjuvant prednisone was noted to be similar to recurrence rates without pre-operative prednisone treatment in one study. Radiation therapy is nearly always indicated following excision of high-grade/grade III tumors. Together, excision and radiation therapy can provide some palliation for the patient by removing the painful, infected lesion and delaying tumor recurrence. Stage II disease is very common with these cases, and chemotherapy will almost always be recommended as well.

We know that for any MCT, excisional biopsy is the least effective course of action. This is most routinely performed in lieu of an FNA, and once histopathology results are back, the case is referred to a surgeon for a second surgery. This situation is frustrating for clients, and increases morbidity for the patient. The second surgery nearly always has to be more aggressive than the initial surgery would have been, if done appropriately with adequate margins. An FNA does not always give you the answer, but it's always the first diagnostic test with any skin or subcutaneous mass that needs to be excised. The first photo shows the type of marking pen and ruler I use, and the rest of the photos show a large MCT on the lateral aspect of an elbow (courtesy of VSSO).

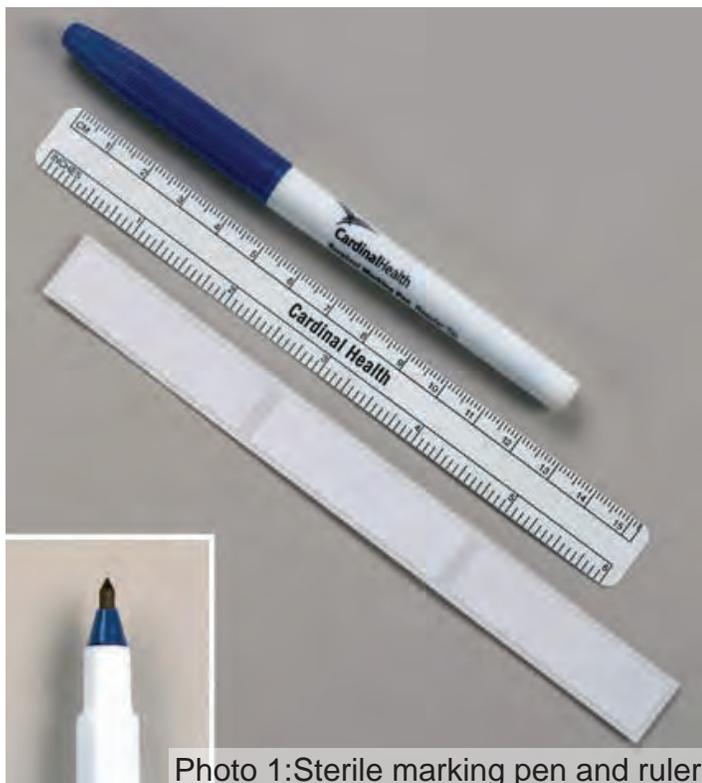
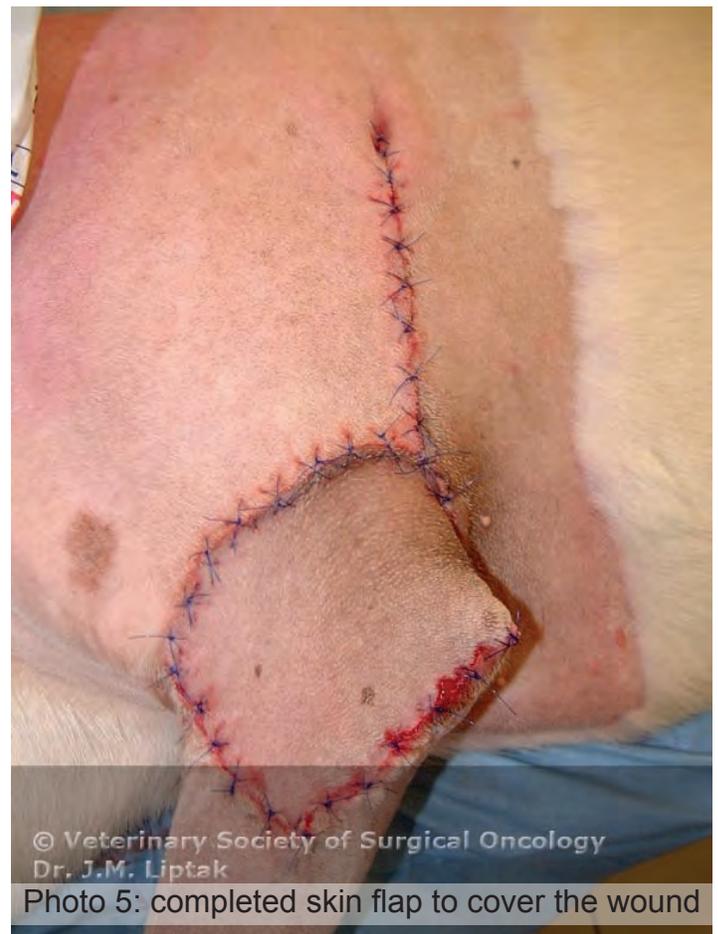
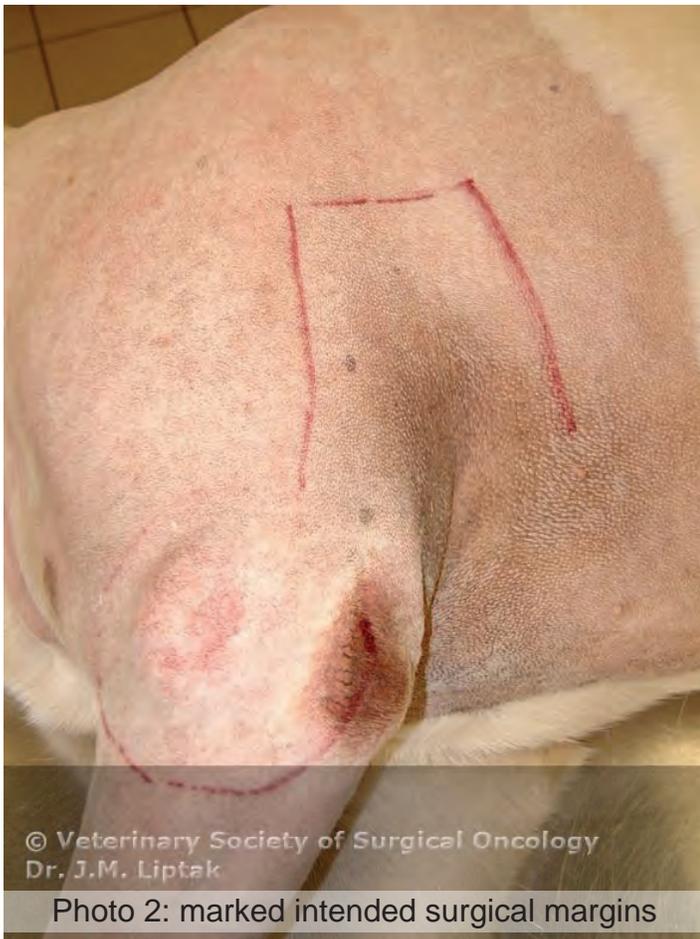


Photo 1: Sterile marking pen and ruler

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The second photo shows the marked intended surgical margins, the third photo shows the incision, the fourth photo shows the wound bed with the deep margin of fascia excised as well,



and then the fifth photo shows the completed flap to cover the wound.

In two years I plan on attending the fourth VSSO conference (hopefully on a beach!), and look forward to sharing the latest information on oncologic surgery with you. Until then, feel free to contact me if you have any questions about any of your surgical cases!



LEADERS IN SPECIALTY CARE

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Arizona Veterinary Specialists, LLC
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- ◆ Root canals
- ◆ Nasal disease treatment
- ◆ Oral disease treatment
- ◆ Oral surgery
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- ◆ Maxillofacial surgery
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- ◆ Fractured teeth treatment
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- ◆ Crown therapy
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- ◆ Telephone radiographic consultation
- ◆ Bite evaluation

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Radiation Oncology

- ◆ Conventional Radiation Therapy
- ◆ Stereotactic Radiosurgery
- ◆ I-131 radioactive iodine treatment

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- ◆ Chemotherapy
- ◆ Immunotherapy
- ◆ Cryotherapy
- ◆ Oncologic surgery
- ◆ Clinical trials

Desert Veterinary Medical Specialists

Internal Medicine

- ◆ Endoscopy
 - Bronchoscopy
 - Bronchoalveolar lavage
 - Colonoscopy
 - Cystoscopy
 - Foreign body retrieval
 - Gastroduodenoscopy
 - PEG tube placement
 - Rhinoscopy
- ◆ Endocrine disorders
- ◆ Emergency consultations
- ◆ Blood and plasma transfusions
- ◆ Gastrointestinal diseases
- ◆ Genitourinary disorders
- ◆ Hepatic diseases
- ◆ Infectious diseases
- ◆ Intensive care treatment
- ◆ Immune-mediated diseases
- ◆ Nutrition consultations
- ◆ Oxygen therapy
- ◆ Pancreatic diseases
- ◆ Pulmonary diseases
- ◆ Renal disease
- ◆ Respiratory diseases
- ◆ Second opinion examinations
- ◆ Ultrasonography
- ◆ Tracheal and urethral stenting

Cardiology

- ◆ Echocardiography
- ◆ Electrocardiogram (ECG)
- ◆ Chest radiographs
- ◆ Blood pressure
- ◆ Pericardiocentesis
- ◆ Cardiology breed certification
- ◆ Holter monitoring
- ◆ Event monitoring
- ◆ Non-surgical PDA repair
- ◆ Balloon valvuloplasty
- ◆ Pacemaker implantation
- ◆ Invasive blood pressure measurements
- ◆ Angiography

- ◆ Implantable ECG Loop Recording

Radiology

- ◆ Outpatient and inpatient ultrasound
- ◆ Radiology Rounds
- ◆ Digital radiography
- ◆ Helical CT scanning
- ◆ Fluoroscopic urinary, GI, and tracheal studies
- ◆ Nuclear imaging
 - GFR scans
 - Bone scans
 - Thyroid scans
 - Splenic scintigraphy
- ◆ Radiographic interpretation
- ◆ CT and MRI interpretation

Dermatology for Animals, PC

Dermatology

- ◆ Allergy testing (skin testing) and immunotherapy
- ◆ CO₂ laser for ablation of skin tumors
- ◆ Testing for food allergies and hypoallergenic diets
- ◆ Ear disease diagnosis and treatment
- ◆ Bacterial and fungal skin disease diagnosis and treatment
- ◆ Cytological smears and microbiologic examinations
- ◆ Ectoparasite identification and treatment
- ◆ Immune-mediated and hormonal skin disease diagnosis and treatment
- ◆ Treatments of nail and nail bed disorders
- ◆ Skin biopsy sampling and histopathology interpretation

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Southwest Veterinary Surgical Service, PC Surgery

- ◆ Abdominal surgery
- ◆ Airway surgery
- ◆ Angular limb deformity surgery
- ◆ Arthroscopy
- ◆ CT Scans
- ◆ External skeletal fixation
- ◆ Fracture repair
- ◆ Laparoscopy and Thoracoscopy
- ◆ Neurologic surgery
- ◆ Oncologic surgery
- ◆ Oral surgery, such as maxillofacial surgery and oral fractures
- ◆ Orthopedic surgery
- ◆ Otologic surgery
- ◆ Perineal surgery
- ◆ Reconstructive surgery
- ◆ Ring fixators
- ◆ Soft Tissue surgery
- ◆ Thoracic surgery
- ◆ Tibial Plateau Leveling Osteotomy (TPLO)
- ◆ Triple Pelvic Osteotomy (TPO)
- ◆ Total Hip Replacement (THR) both cemented and cementless procedures available
- ◆ Tracheal Stenting
- ◆ Tibial Tuberosity Advancement (TTA)

Anesthesia and Pain Management

- ◆ Anesthetic management of high risk and critical care patients
- ◆ Extensive anesthesia monitoring
 - Blood pressure, both direct and indirect
 - Pulse oximetry
 - Electrocardiogram
 - Capnography
 - Body temperature
 - Ventilator therapy
- ◆ Pain patches
- ◆ Chronic pain management consultations

BluePearl Veterinary Partners, PLC Emergency and Critical Care

- ◆ In house diagnostic tests
 - STAT laboratory blood tests
 - * Complete Blood Count (CBC)
 - * Serum biochemical analysis
 - * Blood gas analysis
 - * Urinalysis
 - * Blood lactate measurement
 - * Coagulation testing
 - * Ethylene glycol (Antifreeze) testing
 - * Parvovirus testing
 - Digital x-rays
 - * Radiologist interpretation
 - Scanning ultrasound
 - Gastrointestinal endoscopy
- ◆ Specialized Therapies
 - Intravascular volume expansion/shock therapy
 - Blood component therapy
 - Rattlesnake antivenom therapy
 - Oxygen
 - Short and long term ventilator therapy
 - Anesthetic ventilator
 - Pain medication delivery via constant rate infusion
 - Nutritional support
 - Feeding tube placement
 - Peritoneal dialysis
 - Continuous suction for chest and other drains
 - Central and peripheral IV catheter placement
 - CPR with advanced life support
 - Electrical defibrillation & emergency cardioversion
 - Anesthesia for high-risk critical patients

- ◆ Soft tissue emergency surgical procedures performed by our emergency veterinarians (included, but not limited to):
 - Wound repair
 - Emergency tracheostomy
 - Chest tube placement
 - Abdominal surgeries
 - Gastric Dilatation Volvulus (GDV) or bloat surgery
 - GI foreign body removal
 - C-section
 - Splenectomy
 - Bladder stone removal
- ◆ Intensive monitoring
 - Electrocardiogram (EKG)
 - Blood pressure (direct arterial and indirect)
 - Urinary catheter placement and measurement of urine output
 - Pulse oximetry (Oxygen saturation)
 - Capnography (End Tidal CO₂)
 - Central venous pressure
 - Arterial and venous blood gas measurement

Eye Care for Animals, dba Ophthalmology

- ◆ Biomicroscopy
- ◆ Indirect ophthalmoscopy
- ◆ Electroretinography
- ◆ Ultrasonography
- ◆ Applanation tonometry
- ◆ Fluorescein angiography
- ◆ Glaucoma treatment
- ◆ Cataract surgery
- ◆ Corneal reconstructive surgery
- ◆ Treatment of eyelid abnormalities

AVS Specialty Practices

Southwest Veterinary Surgical Service, PC

- ◆ Bradford C. Dixon, DVM, MS
Diplomate, American College of Veterinary Surgeons
- ◆ Jeffrey A. Steurer, DVM, MS
Diplomate, American College of Veterinary Surgeons
- ◆ Kathleen M. Rowe-Guthrie DVM, MS
Diplomate, American College of Veterinary Surgeons
- ◆ Rachel Seibert, DVM, CCRP
Diplomate, American College of Veterinary Surgeons
- ◆ Megan Schaible, DVM
(Practice Limited to Surgery)

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- ◆ Chris Visser, DVM
*Diplomate, American Veterinary Dental College
Diplomate, European Veterinary Dental College*
- ◆ Curt Coffman, DVM
Diplomate, American Veterinary Dental College
- ◆ Michael Balke, DVM
(Practice Limited to Dentistry and Oral Surgery)

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*Diplomate, American College of Internal Medicine
(Medical Oncology)*
- ◆ Rachel Venable, DVM, MS
*Diplomate, American College of Internal Medicine
(Medical Oncology)*

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- ◆ Raegan Wells, DVM, MS
Diplomate, American College of Veterinary Emergency and Critical Care
- ◆ Katherine Smith, DVM
Diplomate, American College of Veterinary Emergency and Critical Care

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Diplomate, American College of Veterinary Dermatology
- ◆ Rebecca Mount, DVM
Diplomate, American College of Veterinary Dermatology
- ◆ Carine Laporte, VMD
(Practice Limited to Dermatology)
- ◆ Samantha Lockwood, DVM
(Practice Limited to Dermatology)
- ◆ Stephanie Schwartz, DVM
(Practice Limited to Dermatology)

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- ◆ Lisa M. Felchle, DVM
Diplomate, American College of Veterinary Ophthalmology
- ◆ Paul M. Barrett, DVM
Diplomate, American College of Veterinary Ophthalmology

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(Cardiology)*
- ◆ Melissa Riensche, DVM
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