Kubanda Cryotherapy

Mammary Tumors 101

Practical Assessment and Treatment Guidelines for Dogs and Cats

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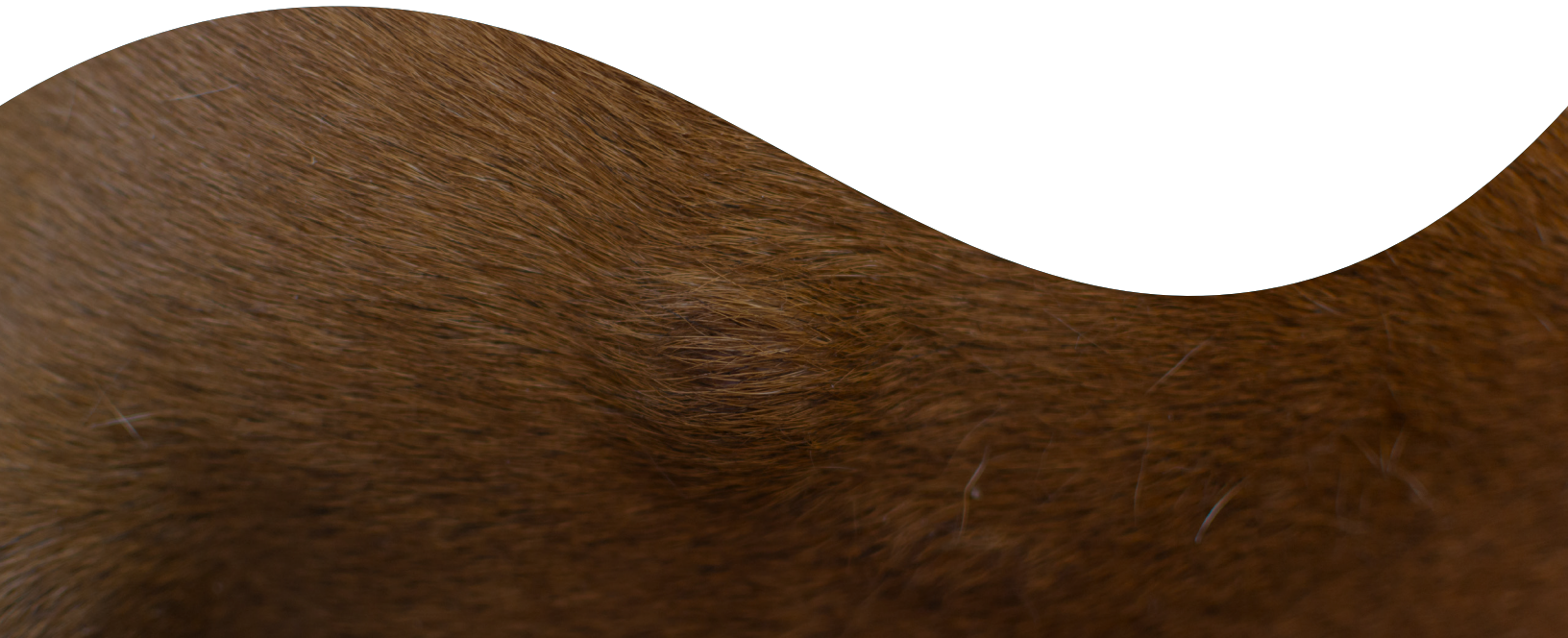


Introduction

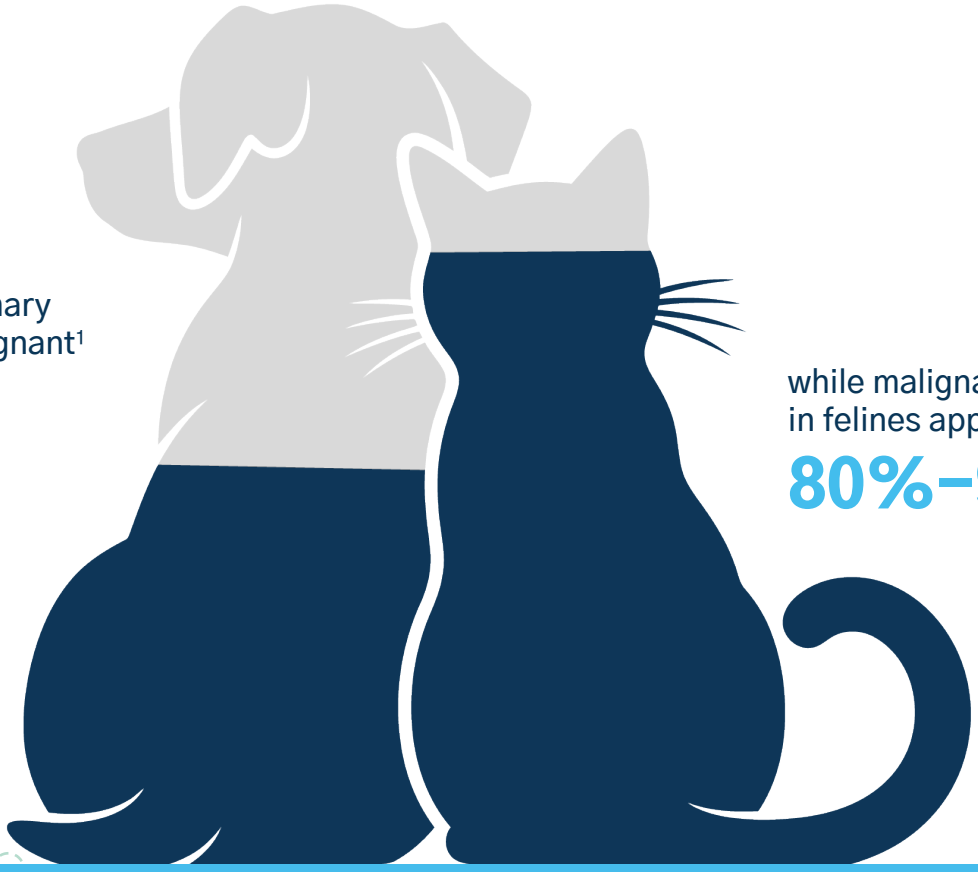
Mammary tumors

are among the most common tumor types in cats and dogs, occurring most frequently in unspayed females.

Approximately

50%

of canine mammary tumors are malignant[1]



while malignancy rates in felines approach

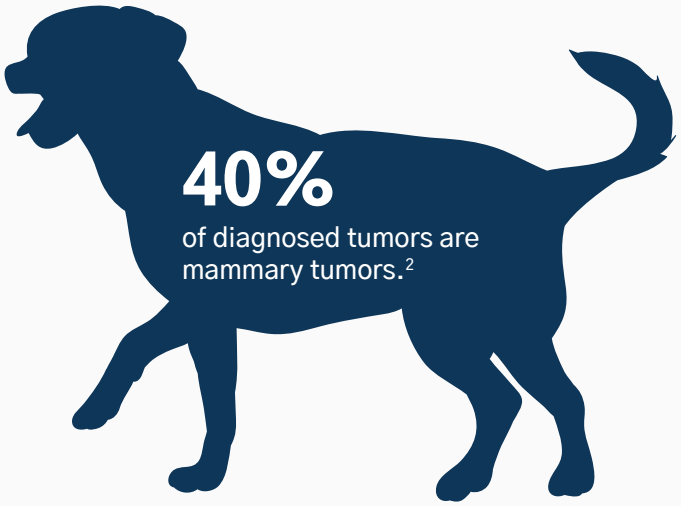
80%–90%[1]

Current treatment strategies focus largely on surgical resection and are most effective when tumors are identified and addressed early. **Intratumoral cryoablation**, a minimally invasive modality used in the management of many common tumor types, may also play a role in the treatment of mammary tumors in both cats and dogs. Depending on tumor size, staging, and malignancy, cryotherapy may be used as a standalone treatment or alongside other therapeutic approaches to improve overall treatment outcomes, particularly in canines.

Prevalence and Malignancy Rate

Mammary Tumor Prevalence in Dogs

In dogs, approximately **4 out of 10** diagnosed tumors are mammary tumors,making mammary tumors more common in female dogs than in humans.[2]

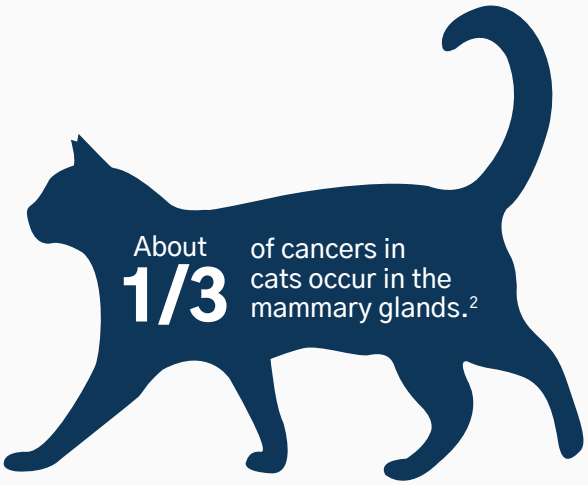


Malignancy Rate in Dogs

Approximately 50% of canine mammary tumors are malignant, while the remaining half are benign.

Mammary Tumor Prevalence in Cats

Mammary tumors represent approximately one-third of all cancers in cats and are the third most common type of cancer in felines.[2]



Malignancy Rate in Cats

Compared to dogs, mammary tumors in cats are much more likely to be malignant (more than 80%), with upwards of 85% of these tumors classified as adenocarcinomas.[2] 50%–90% of feline mammary tumors will cause metastasis, most frequently to the lymph nodes, lungs, liver, or other mammary glands.

Early ovariohysterectomy, performed prior to sexual maturity, is the most effective preventive strategy for mammary tumors in both canines and felines.

Diagnosis, Classification, Grading, & Staging

Diagnosis

Physical Exam

Diagnosis typically begins with a thorough physical examination, including palpation of both mammary chains and assessment of lymph nodes, tumor size, fixation, and ulceration. Blood work and urinalysis may also be performed.

Biopsy

Histopathologic evaluation via biopsy is the gold standard for definitive diagnosis, allowing for tumor classification and grading. These findings are essential for treatment planning and prognosis.

Classification & Grading

Canine

The World Health Organization has categorized canine mammary tumors into eight broad categories. This classification system was proposed by the WHO in 1999 and has been updated several times through 2019 to include the following[4,5,6,7]:

- Hyperplasia/dysplasia of the mammary gland
- Hyperplasia/dysplasia of the teat
- Benign epithelial neoplasms (including complex adenomas and mixed mammary tumors, and ductal–associated benign tumors)
- Malignant neoplasms (including simple, non–simple, and ductal carcinomas)
- Malignant epithelial neoplasms of special type (squamous cell carcinoma, adenosquamous carcinoma, mucinous, secretory, and spindle cell carcinomas, and malignant myoepithelioma)
- Malignant mesenchymal neoplasma (sarcomas)
- Carcinosarcomas
- Neoplasms of the teat (benign and malignant ductal–associated neoplasms of the teat and Paget–like disease (Carcinoma with epidermal infiltration)

The most frequently used grading system used for canine mammary tumors is the Goldschmidt M, et al. Classification and grading of canine mammary tumors system. This system considers tubule formation, nucleus variation, and mitotic count when classifying a tumor as low, intermediate, or high grade.[5,8]

Feline

An updated, comprehensive classification system for feline mammary tumors, based on the WHO system for dogs, was reported by Zappulli et al. in 2019, including[7]:

- Hyperplasia/Dysplasia
- Benign epithelial neoplasms
- Malignant epithelial neoplasms
- Malignant epithelial neoplasms—special types
- Malignant mesenchymal neoplasms of the mammary gland
- Carcinosarcoma
- Hyperplasia/Dysplasia of the teat
- Neoplasms of the teat

The mitotic modified Elston and Ellis (MMEE) grading system is often used for feline mammary tumors. This system considers tubule formation, nucleus variation, and mitotic count when classifying a tumor as low, intermediate, or high grade.[9]

The Cassali classification system (2023) is another system used in conjunction with the World Health Organization Classification system, utilizing cell arrangement and differentiation in an effort to standardize nomenclature and increase the accuracy of prognosis for appropriate treatment planning.[10]

Newer strategies for classification of both canine and feline tumors can include genetic mutation and molecular profile, and histopathological evaluation of mitotic count, cellular differentiation, and necrosis, in an attempt to better predict biological behavior of the tumor.

Staging

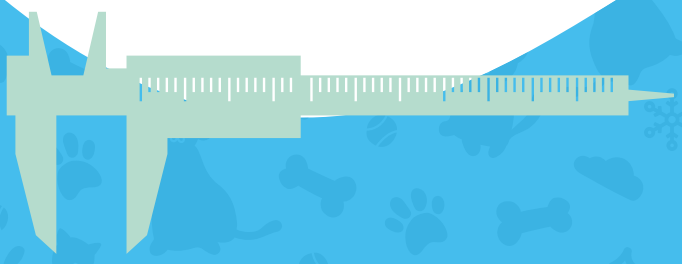
Staging for both canine and feline mammary tumors is based on a modified version of the TNM (Tumor, Nodes, Metastasis) system from the World Health Organization (WHO).

Canine[11]

Stage	Tumor Size (T)	Lymph Node (N)	Metastasis (M)
I	≤ 3 cm (T_1)	N_0	M_0
II	3 to 5 cm (T_2)	N_0	M_0
III	> 5 cm (T_3)	N_0	M_0
IV	Any size	N_1	M_0
V	Any size	N_0 or N_1	M_1

Feline[12]

Stage	Tumor Size (T)	Lymph Node (N)	Metastasis (M)
I	< 2 cm (T_1)	Negative (N_0)	Negative (M_0)
II	2–3 cm (T_2)	Negative (N_0)	Negative (M_0)
III	> 3 cm (T_3) ≤ 3 cm (T_1–T_2)	Negative or positive (N_0 or N_1) Positive (N_1)	Negative (M_0) Negative (M_0)
IV	Any T	Any N	Positive (M_1)



Tumor size is a strong prognostic factor and should be measured with calipers after surgical resection for proper grading.

Status Quo Treatment Options

Treatment of mammary tumors in dogs and cats is guided by tumor type, size, location, biologic behavior, and the presence of metastatic disease. A multimodal approach is often required, particularly for malignant tumors.

Surgical Excision

Surgical removal remains the primary treatment for most mammary tumors and may range from regional to radical mastectomy, depending on tumor size and margins. Complete excision with histopathologic evaluation is a key prognostic factor in both species.

Chemotherapy, Radiotherapy, and Immunotherapy

In canines, other interventions, including chemotherapy and radiation therapy, may be considered for malignant or high–risk tumors, incomplete surgical margins, or metastatic disease. Immunocidin is a USDA–approved immunotherapy and can be used for treatment of canine adenocarcinomas. Several bacterial, viral, or virus–like particle immunotherapeutics are under clinical investigation. In felines, there is currently little to no evidence that chemotherapy significantly impacts survival.[4]

Emerging Approaches

Minimally invasive options may be appropriate as an adjuvant, or for select patients when surgery is contraindicated, declined, or cannot be performed with adequate margins. Learn how intratumoral cryotherapy is being used to expand treatment options on the next page.

The Role of Intratumoral Cryotherapy

Cryotherapy has traditionally been used to treat topical lesions and other dermatological conditions. It can also be used subcutaneously to effectively treat many common tumors – often referred to as cryoablation.

During cryoablation, tissue is supercooled to lethal temperatures and ultimately frozen as pressurized cryogenic gas flows through a closed-system probe that is inserted in the neoplastic tissue. The iceball that forms around the inserted probe causes intra- and extracellular ice crystals to form. During the freeze and thaw cycles, those ice crystals and osmotic processes induce and localize enzymatic and structural damage to targeted cells, resulting in tumor cell necrosis and apoptosis. It can be used independently for small tumor management and as a well-tolerated neoadjuvant therapy with surgical resection, chemotherapy, or radiation therapy.

In human medicine, cryoablation has been FDA-approved for numerous types of cancers for decades and favorably evaluated and determined to be just as effective as surgical resection for early-stage low-grade breast cancer in clinical trials.

With the introduction of the first and only subcutaneous cryoablation device specifically designed for veterinary use, this modality is now available as a treatment option for canine and feline mammary tumors.

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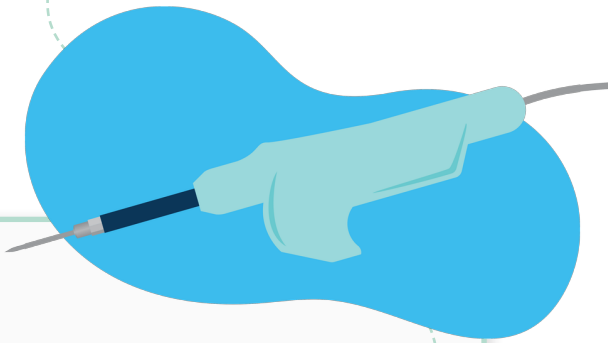
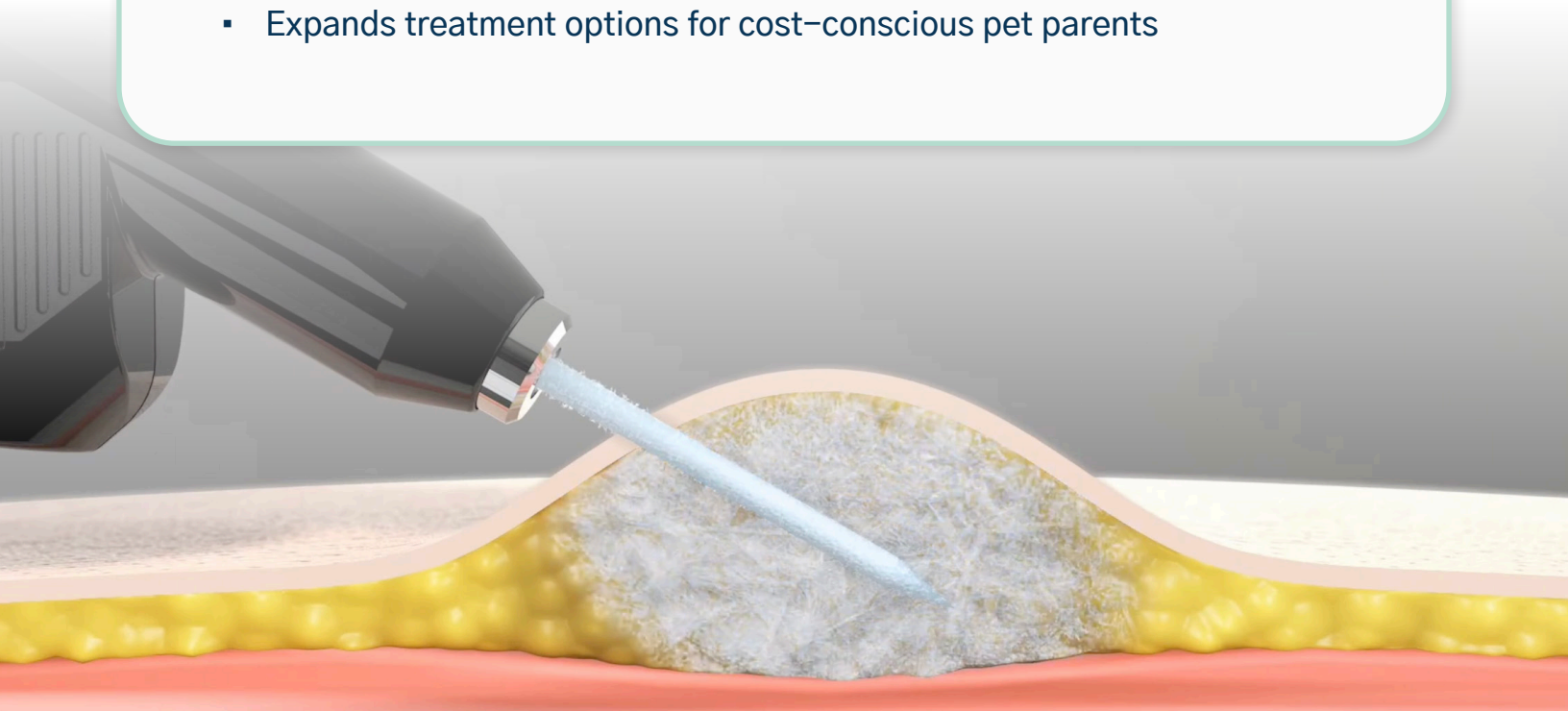
Reach out to learn more about the results of a recent study comparing the effectiveness of the Kubanda CO_2 intratumoral cryotherapy device to a human-grade, argon-powered device.

Intratumoral cryotherapy may be considered for patients with benign or small malignant mammary tumors, or as an adjuvant for complex cases. This technique allows for targeted destruction of neoplastic tissue and offers many unique benefits.

Benefits of Cryoablation for Mammary Tumors



- Minimally invasive targeted tumor destruction
- An attractive complement to surgery or other therapies
- Tissue type agnostic
- Option for patients with comorbidities
- Can be used alone for small tumors, as a neoadjuvant therapy with surgery, chemotherapy, or radiation, or as an adjuvant for surgical resection with presumed close margins
- Well-tolerated with generally low complication rates
- Supports tumor debulking prior to surgical resection for larger masses
- Treatment may invoke an adaptive immune response
- Expands treatment options for cost-conscious pet parents



Case Study – Bori

14 yo | Female | Maltese | 7.92 lbs

Patient

14-year old 8-lb female Maltese dog, Bori, was inherited by her present owner in 2022 and presented with (unknown duration of a history) a 7-cm tri-lobulated mammary mass at the level of the 2nd mammary glands, spanning the midline. Fine-needle aspiration (FNA) of this mass in Fairfax, VA showed a mammary gland epithelial cell proliferation of either a benign neoplasm or carcinoma. Thoracic radiographs were obtained and revealed multiple (3) nodules of soft-tissue opacity within the lungs, suggestive of pulmonary metastases.

The owner had recently adopted Bori from a deceased family member. The owner is a student in medical sciences with extremely limited financial resources. Although initially hesitant, given the size of the mass compared to the size of the dog, the lung metastases, and the dog's age, the referring veterinarian agreed to a planned two-step approach to palliate Bori's cancer. First, cryoablation was performed at CIGAT at Johns Hopkins with the intent of debulking the tumor and potentially invoking an immune response against the pulmonary tumors. Three weeks later, surgical resection of the mammary mass was performed to eliminate the expected remaining tumor tissue. Informed consent was obtained, and the owner understood and accepted the challenges with Bori's very large mass and pulmonary status.

Methods

After pre-surgical bloodwork, thoracic radiographs, and FNA, Bori was presented for cryoablation in April 2023. She was sedated and placed under general anesthesia (isoflurane). Bori was sterilely prepped and draped. A stab incision was made in the distal portion of the mass for insertion of the cryoprobe. One 8:20 freeze- 7:00 minute thaw – 8:25 minute freeze cycle was performed using the Kubanda Cryotherapy system at the Center for Image-Guided Animal Therapy at Johns Hopkins Hospital, Baltimore, MD. One staple was used to close the wound site. Bori was discharged with NSAIDs (carprofen) for pain management and antibiotics (Cefpoderm) per protocol.

Clinical findings

The owner noted that Bori had no signs of discomfort and underwent all daily routines with normal energy and enthusiasm. There was a small area of skin tissue necrosis at the location of the stab incision that began on Post-Cryoablation Day 7 and had sloughed and mostly resolved by Post-Cryoablation Day 18.

Bori underwent bilateral radical mastectomy, that was planned prior to enrollment in the CIGAT study, in lieu of wide excision of her tumor on Post cryoablation Day 21. Her owner requested the bilateral mastectomy to eliminate any potential for future mammary tumors. She was sedated and placed under general anesthesia by Dr. Salaat and her team, a specialist veterinary surgeon from Lazar Veterinary Surgeons at Fairfax Veterinary Hospital. The surgical resection involved the removal of both entire mammary chains. Bori was discharged home the same day with Gabapentin, carprofen, and tramadol for pain management and Clavamox antibiotics. The owner noted that she was uncomfortable the first night at home but became more comfortable after approximately 24-36 hours at home with oral pain medications. Bori recovered uneventfully and had her sutures removed on Postop Day 16.

Images show the mass pre- cryoablation treatment (left) and then (middle) 19 days post cryoablation, with some reduction of volume in the mass and less taut skin, especially on the bottom lobe. The right photo is post-bilateral mastectomy with compression bandage in late May 2023.

Conclusion

Bori was diagnosed with both a benign mixed mammary tumor, which had some cartilage cells in the lobules, as well as Grade 1 Mammary Adenocarcinoma in situ with multiple adenomas in the bottom part of the tumor. Both findings were from within the same tri-lobulated mass pictured above. Pathological evaluation of submitted stained slides revealed necrosis from cryoablation.

Because Bori presented with pulmonary metastases, repeat chest X-rays were taken 3 months after her bilateral mastectomy and were reviewed by a board-certified veterinary radiologist. There was variable progression in the size of the previously reported lung nodules, with a 0.4 cm increase in the right deepest lung lobe nodule that is positioned towards her back. The lung nodule in the right middle lung lobe, more towards her belly, remained the same size. There was one new small nodule on her left lung.

12-month follow-up chest x-rays on March 1, 2024, noted the static appearance of her four masses with no noted progression of the pulmonary disease. Her physical exam was unremarkable.

As of January 2026, her last follow-up interval, Bori is enjoying an excellent quality and active life with her family.

Clinical Significance

There have been no new external masses noted since resection and Bori has a very good quality of life. She is energetic, walks daily, and is doing well per her owner's report in January 2026 and her physical exam from March 2024. Regarding the lung nodules that were present at the time of study enrollment, after the initial changes between cryoablation and her 3-month follow-up appointment, her pulmonary disease is stable, and the size of the nodules remains the same. At 34 months post cryoablation, she is an active dog with an excellent quality of life. Bori's case and her survival and excellent quality of life have ignited further interest in the utility of cryoablation for debulking large tumors and its potential long-term immunological effects. Formal clinical trials observing immune activation and potential abscopal effect are in process at an American veterinary school.

Prognosis & Follow-Up Care

Prognosis

Outcomes for canine and feline mammary tumors depend on tumor type, grade, stage, and overall patient health. A greater percentage of canine patients with malignant mammary tumors will achieve longer overall survival when compared with feline patients, due to feline propensity of aggressive disease and early metastasis. Early detection and appropriate treatment – including surgery, adjunctive therapies, or combinations thereof – are associated with the best prognosis.

Cryoablation Follow-Up Care:

Post-treatment surveillance

The skin around the probe insertion area should be kept clean and dry. A scab is expected to form at the probe insertion site. Patients should not be permitted to lick the treated area during healing.

- Some darkening of the skin in the area may be expected and peeling of this skin and/or scab, 8–14 days after treatment, is not uncommon.
- Shrinking or remodeling of masses is a slow process and usually begins within 1–2 weeks following cryoablation.
- Routine physical examination and diagnostic imaging as indicated to monitor for local recurrence or distant metastasis is recommended.

Histopathologic assessment

Ongoing management should be informed by pathology findings, when appropriate.

Therapy integration

Coordinate follow-up and additional interventions if recommended (e.g., retreatment, surgery, chemotherapy, radiation, or other adjuvant modalities) based on treatment response/disease progression.

Case reassessment

Periodic reevaluation of treatment strategy is recommended, particularly in cases of recurrence, incomplete margins, or progressive disease.

About Kubanda Cryotherapy

Kubanda Cryotherapy lets you treat lumps, bumps, and tumors in your office by providing an easy-to-use, minimally invasive, point-of-care solution to pet parents looking for better treatment options.

Kubanda's cryotherapy system uses extreme cold to deliver high-quality, targeted tumor treatment at a fraction of the cost of surgery. Our custom-designed cryosystem consists of a cryoprobe and a gas-control module that fits perfectly into the general veterinary workflows.

Treatment is done with mild sedation, and the short recovery time and low cost means cryotherapy is a great choice for happy vets, pets, and pet parents. Kubanda Cryotherapy can be used in all areas of tumor management (cancer, cosmesis, palliation, and debulking) as a versatile addition to the veterinary tool box.

We allow vets to trade a knife for a needle and provide state-of-the-art tumor treatment in the primary care setting with a versatile, adaptable tool suitable for both benign and cancerous masses.

> Kubanda's simple procedure really made a difference in our dog's quality of life. We are beyond grateful.
>
> – Victor, Pet Owner

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