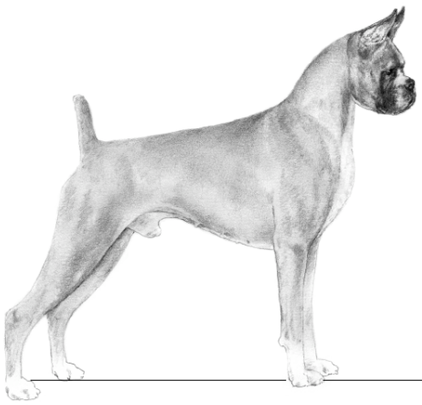

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Boxer Update

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Researchers Aim to Better Understand Brain Tumors in Boxers

Longtime Sunchase Boxer breeder Tracy Hendrickson typically breeds her Boxers when they are from 3 to 6 years old, after they have been tested for breed health conditions. When her foundation bitch, Golden Holly of Norbourne CDX ("Holly"), was diagnosed with a spinal cord tumor at 11 years of age, she was shocked.

A few years later, three Boxer littermates, all with pedigrees listing Holly as their granddam, died from brain tumors between the ages of 9 and 11. Sunchase's Jump Start M' Heart CD ("Joanie") died from complications suffered after surgery for a brain stem tumor. Her brother, Sunchase's Let's Be Frank CD ("Frank"), and sister, CH Sunchase's Razed on Rainbows CD ("Amy"), both experienced sudden-onset seizures. Frank died from complications of radiation therapy, and Amy from a grand mal seizure.

More recently, Hendrickson lost a dam and daughter who also had sudden-onset seizures three to six months before they died. Looking back at these six Boxers who died over the past 25 years, Hendrickson is convinced that they died of malignancies that started as brain tumors.

"The problem is my dogs were bred between the ages of 3 and 6 years, and by the time the brain tumors showed up when they were 9 years old or older, they had already passed on the genetic line," says Hendrickson of Broken Arrow, Okla.

Seizures also were the common sign of a brain tumor in Rhoda Goselin-Brouillette's Boxer "Cher," who died in January 2007 at 8 years of age, three weeks after delivering a litter of two puppies. Goselin-Brouillette can't help but wonder if environmental factors may be to blame since no other Boxers from her breeding have developed a brain tumor.

> "Published data going back 30 to 40 years shows that brachycephalic breeds have more primary brain tumors than other breeds."
>
> *John Robertson, V.M.D., Ph.D., Professor of Veterinary and Comparative Pathology at the Virginia-Maryland Regional College of Veterinary Medicine*

"We have gone to great lengths to test for healthy hearts, hips and thyroids," says Goselin-Brouillette of GRBRG Ranch in Bourbonnais, Ill. "The brain tumor was devastating for us. We just pray there are no others."

Environmental factors could play a role in brain tumors, particularly in predisposed breeds, say investigators studying new treatment techniques for canine brain tumors. Brachycephalic breeds, such as Boxers, Bulldogs and Boston Terriers, for example, are believed to have a higher incidence of brain tumors than other breeds. These short-nosed, short-muzzled breeds are known for having undersized or flattened throat and breathing passages.

Brachycephalic breeds may be at risk due to inherited mutations linked to their breed phenotype, says John Robertson, V.M.D., Ph.D., professor of veterinary and comparative pathology at the Virginia-Maryland Regional College of Veterinary Medicine.

"Published data going back 30 to 40 years shows that brachycephalic breeds have more primary brain tumors than other breeds," he says. "Genetic factors may make these breeds more susceptible to environmental pollutants or radiation causing cancer, but we really have no data to support this hypothesis."

Primary brain tumors, those that grow from cell mutations in the brain or spinal cord versus those that have spread from cancer elsewhere in the body, or tumor metastases, occur in dogs and humans. These tumors are three times more common in dogs, and more than 70 percent of primary tumors in dogs are diagnosed at age 6 or older.

Among the common signs of brain tumors, sudden-onset seizures occur in about 40 percent of dogs. Other signs include behavioral changes such as aggressiveness or withdrawal, blindness, loss of coordination, rear swaying, and circling. Dogs often die within weeks or months of showing signs.

"The location of the tumor determines which signs occur," says John Rossmeisl Jr., D.V.M., DACVIM, assistant professor of neurology and neurosurgery at the Virginia-Maryland Regional College of Veterinary Medicine.

Comparative Research Approach

Ongoing collaborative research among human and canine investigators is focusing on the causes of canine brain tumors and the possibility of improved treatment using novel human therapies. The research, funded by a Wake Forest University Translational Science Institute grant, involves 25 veterinarians, physicians and scientists

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Boxer Owners May Participate in Brain Tumor Research

Owners of Boxers are encouraged to participate in brain tumor research being conducted at Virginia Tech and Wake Forest University. The researchers are seeking DNA samples from Boxers, Boston Terriers, Bulldogs and Briards that are healthy and those diagnosed with brain tumors.

Blood samples especially from family lines with a history of brain tumors and from dogs 8 years or older are needed. The researchers also are interested in receiving brain tissue samples from dogs that have died from brain tumors.

For additional information, you may visit this link on the Virginia-Maryland Regional College of Veterinary Medicine information Web site: *www.vetmed.vt.edu/vth/sa/clin/trials.asp*. You also may contact Dr. John Robertson, project coordinator, at (540) 231-7666 or drbob@vet.edu.

Brain Tumors in Boxers

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at Wake Forest University School of Medicine in Winston-Salem, N.C., and Virginia Tech in Blacksburg, Va.

Robertson, project coordinator and director of the Center for Comparative Oncology at Virginia Tech, says three breeds — Boxers, Boston Terriers and Bulldogs — are part of the research that has been under way for four years.

"Potentially, this work may yield information about genetic mutations causing this disease," Robertson says.

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As the dog genome is quite similar to the human genome, the investigators are optimistic that genetic discoveries could benefit both humans and dogs. "We are looking to identify the presence of molecular markers that have already been identified in human tumors," says Waldemar Debinski, M.D., Ph.D., co-principal investigator and director of the Wake Forest University Brain Tumor Center of Excellence. "We will compare DNA from highly susceptible breeds to those with low-incidence rates and to breeds that develop other forms of cancer."

Already three proteins and protein receptors have been identified in human brain tumor cells that are not in normal tissue. New anti-cancer therapies are being tested on these protein molecules to determine their effectiveness in treating brain tumor cells.

"We place a lot of hope in new, experimental human therapies that are coming in the next decade," says Debinski, whose research in this area has been supported by National Cancer Institute grants. "We believe because of the molecular similarities we will have similar success in treating dogs."

"Data on dogs with brain tumors is currently not very informative," says Rossmeisl, co-principal investigator. "We aim to document statistical incidence, breed-related risk factors, disease progression and prognosis of specific types of brain tumors. We also plan to biopsy tumors to confirm tumor type and help us determine the most effective treatment for an individual dog."

Two types of highly aggressive brain tumors are recognized: gliomas and malignant meningiomas. Gliomas begin in connective tissue and quickly spread to surrounding areas, making tumors difficult to completely remove. The two most common types of gliomas are astrocytomas and oligodendrogliomas. These tumors "develop within the substance of the brain," Robertson explains. "They are extremely difficult to remove. We need to find better ways to treat these tumors."

On the other hand, meningiomas form on the brain's surface, where there is a better chance of surgical removal. Meningioma surgery followed by radiation has shown the best success rate in dogs, even increasing life expectancy several years, Rossmeisl says.

In contrast, "brain stem tumors, which can be meningiomas, gliomas or other types, are much harder to remove," he says. "Brain stem tumors are like playing Russian roulette in areas that control essential functions like breathing."

Traditional treatments for canine brain tumors have included neurosurgery, radiation and chemotherapy, often used in combination. Prognosis typically depends on tumor type, location and size. Only about half of dogs diagnosed with brain tumors are referred for surgical treatment, the investigators estimate. Part of this may be due to the fact that brain surgery is risky and can have complications such as brain swelling.

Surgery without subsequent radiation increases the odds of cancer recurring because there is "almost always microscopic cancer cells left behind," says Rossmeisl. "We don't know enough about brain tumors. All we know for sure is that if we do nothing with a glioma, a patient dies in a few weeks to six months."

Testing Novel Therapies

Two novel therapies first used in humans are being studied. Gamma-ray therapy provides an alternative to neurosurgery using multiple beams of gamma radiation to successfully destroy brain tumors. Beams of radiation focus on one target without exposing and subsequently harming surrounding tissue.

"Unlike traditional radiation in which small doses of radiation are given daily over the course of several weeks, gamma-ray therapy gives one huge shot of radiation at once," Rossmeisl says. "With this method, radiation is delivered with pinpoint accuracy."

Recombinant cytotoxins provide a second novel treatment option. "This involves using modified cellular toxins specifically targeted at brain tumor cells," explains Debinski. "We have identified several molecular targets and several cytotoxins that will kill cancer cells at very low concentrations."

An innovative technique, called convection enhanced delivery (CED), allows researchers to bathe the tumor cell cavity with cytotoxins once the tumor is removed. Unlike traditional chemotherapy or radiation following surgery, CED applies cytotoxins directly to the tumor site via catheters. Cytotoxins effectively kill any remaining cancer cells without harming normal tissue.

"We want to know if the same experimental treatments we're offering humans are verified in dogs," Debinski says. "Potentially CED will prove to be a breakthrough treatment for invasive gliomas and meningiomas."

Though canine brain tumors are complex and as fast-growing as those that occur in humans, this research offers promise that one day novel therapies might be available to help dogs diagnosed with brain tumors. Early tumor detection and identification of dogs with a genetic predisposition are other ways that research may benefit affected dogs. ■

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