

New Study Aims to Better Treat Head and Neck Cancer in Dogs and Humans

A collaboration between the University of Colorado Cancer Center and Colorado State University explores canine sinonasal carcinoma with the aim of better treatment options for humans — and our canine companions.

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A study is underway at [Flint Animal Cancer Center](#) in Fort Collins that has implications for human head and neck cancer. Funded by an administrative supplement for the Dog Oncology Grant Supplement (DOGS) Program issued by the National Cancer Institute (NCI) from the University of [Colorado Cancer Center Head and Neck Cancer Specialized Programs of Research Excellence \(SPORE\)](#), researchers speculate this study's findings may improve outcomes for dogs and humans.

[Keara Boss](#), DVM, PhD, CU Cancer Center member and veterinary radiation oncologist at Colorado State University (CSU), is using SPORE funding to study radiation therapy in dogs with sinonasal carcinoma, a type of [head and neck cancer](#). A subset of the dogs will receive radiation and a repurposed drug combination they believe can optimize the immune system's response to fight tumors.

A link between canine and human carcinomas

In humans, sinonasal cancers are rare, serious, and understudied. Little evidence of effective therapies exist, making this an important area of study globally. Sinonasal cancer is linked to occupational exposure due to inhalation of industrial and environmental fumes. Unfortunately, limited effective, durable treatment options exist for people diagnosed with sinonasal cancer.

Boss and her research team have been studying the shared characteristics between human and canine cancers through a K01 career development award from the National Institutes of Health, with mentorship from CU and CSU faculty members.

Boss believes studying naturally occurring canine cancer can serve as a model for the human form. Radiation therapy is used in both dogs and people to treat sinonasal cancer. Dogs develop sinonasal carcinoma at a higher incidence than people do. Though it's not known why, Boss wonders whether, like in people, it's related to what they inhale.

Optimizing the immune system response

Boss says radiation therapy is excellent at killing tumor cells, but local tumor recurrence following radiation therapy remains an issue for human and canine sinonasal cancer patients. During the process of tumor irradiation and cell killing, an immune response is also stimulated. This can bring in helpful immune cells to both the site that's been irradiated and throughout the body. But there's also a downside.

"The flip to that is that radiation can also bring in immune cells that are suppressive to a positive immune response," Boss says.

She aims to optimize the immune response.

"It's tricky in cancer. The immune system is doing its best, but tumors hijack the process and trick the immune cells to back off and not fight the cancer."

She hypothesizes that the introduction of immunotherapy or immunomodulatory drugs will "tip the balance" toward a stimulated immune response by weakening the cells that would otherwise dampen the immune system.

Repurposing blood pressure medications

The study uses two blood pressure medications, propranolol and losartan.

Propranolol is a beta blocker that regulates heart rate, blood pressure, and blood flow. It's also been shown to help bring in positive immune cells and "clear out" suppressive immune cells in the tumor microenvironment.

Losartan is an angiotensin receptor blocker that relaxes blood vessels to allow for better blood flow. It has been shown to introduce immune modulatory properties, reducing the ability of white blood cells called monocytes to infiltrate tumors. When monocytes enter a tumor, they become macrophages. Macrophages typically dampen positive immune responses, and losartan has been shown to prevent the suppressive effects of monocytes and macrophages within the tumor and throughout the body.

Losartan may also improve the oxygenation of tumors. Better oxygenation of tumors may allow for a better response to radiation.

"Radiation alone does crazy things to tumor blood vessels, so we're thinking the drug combination will help irradiated tumors stay more perfused and may improve responses," Boss says.

High-dose radiation increases immune response

The study uses stereotactic body radiotherapy (SBRT), a targeted, high-dose intensity administration of energy via X-rays. Traditionally, radiation therapy for head and neck cancer patients uses small, daily doses of radiation given over the course of six weeks, which has not been associated with a robust, positive immune response. This study aims to maximize the immune response and will include three sequential large doses of radiation. The SBRT protocol used for the canine sinonasal cancer patients is similar to SBRT protocols used for human head and neck cancer patients.

The study is examining CT scans before and after radiation, looking at how blood flows to the tumors. The team will compare the differences between tumors treated with radiation alone and tumors treated with radiation and the drug combination.

Boss says having the subset of dogs getting the radiation alone will add to the literature on stereotactic radiation for head and neck cancer. The subset of dogs receiving radiation and the repurposed drug combination adds to the study's potential in understanding the degree of possible immunomodulation.

"Our hypothesis is that we'll see improved outcomes with improved immune responses in the dogs treated with the immunomodulatory drug combination," she says.

A team effort

The study is funded for one year, with the potential for extension if needed. Currently 11 dogs have been enrolled, all of whom were previously diagnosed with cancer, and funding has been received to enroll an additional 14 dogs.

Boss credits the importance of the CU Cancer Center team in this project, recognizing her colleagues at CSU, [Steven Dow, DVM, PhD](#), and [Dan Regan, DVM, PhD](#). She also recognizes the instrumental role of [Sana Karam, MD, PhD](#), professor of Radiation Oncology at the CU School of Medicine.

"We would have never been given this opportunity had it not been for everyone's collaboration in making this happen," Boss says.

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