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The use of sniffer dogs for early detection of cancer: a One Health approach

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ABSTRACT
This review, which is part of the "Currents in One Health" series, describes and evaluates the current research on the utilization of trained medical scent detection, aka "sniffer" dogs for the detection of diseases, with particular emphasis on neoplasia, both within human and veterinary patients. A recent study by the authors that used sniffer dogs to detect differences in saliva from dogs diagnosed with various neoplastic processes compared with healthy control dogs is described. The concept of One Health is explored by the description of previous studies that have utilized sniffer dogs in the detection of human neoplasia (focusing on lung, prostate, and breast cancer) and veterinary neoplasia and demonstrating that further research in this arena can benefit multiple species. Future avenues of research and utilization of these findings are outlined. The companion Currents in One Health by Ungar et al, JAVMA, January 2024, addresses the use of sniffer dogs to detect human COVID-19 infections.

Keywords: cancer, scent detection, sniffer dog, early detection, tumor

In the companion Currents in One Health article by Ungar et al,[1] *JAVMA*, January 2024, the concept of using trained dogs for scent detection of disease in humans and animals is introduced. The article describes the use of trained scent dogs to detect COVID-19 (C19) infections in individuals. The results of that article revealed that 2 scent-trained dogs were able to detect whether an individual was infected with C19 with 94–96% accuracy and a detection time of 5–10 seconds. Evidence suggests that trained scent dogs can detect a variety of diseases in both humans and animals accurately and often earlier than many existing screening tools. This is a perfect illustration of the concept of One Health, whereby advancing the use of scent-detection dogs can have benefits for all species.

It is well established, and described in the JAVMA companion article,[1] that dogs have a significantly more sensitive sense of scent compared with humans, with their ability reported as 100,000 times that of the average human.[2] Due to these abilities, scent-detection dogs have been used for decades to locate drugs, explosives, toxic waste, cadavers, and more. Utilizing their abilities for human health, scent dogs have been trained to alert for seizures, hypoglycemia related to Diabetes mellitus, and to screen for viruses, bacterial infections, and numerous cancers (mammary, prostate, lung, ovarian, colorectal, and melanoma).[3–6]

The commonality behind the detection of these seemingly different disease processes is the presence of volatile organic compounds, or VOCs. VOCs are low molecular weight compounds of cellular origin that are produced by an afflicted individual's immune system and are unique to each illness, from endocrine to inflammatory to neoplastic diseases.[7] VOCs have been detected in exhaled breath, urine, blood, and colon contents[8] and have been identified in human cancer patients utilizing gas chromatography/mass spectroscopy.[9] Changes in biogenic volatile organic compound concentrations can be used to mirror metabolic or pathophysiological processes in the body.[8] Dogs can discriminate between volatile organic compounds at extremely low concentrations, as small as 1 part per trillion.[10]

The companion Currents in One Health by Ungar et al, JAVMA, January 2024, outlined the utility of sniffer dogs to detect viral infection, which was especially useful during the C19 global pandemic. In this study, 2 dogs were trained to detect C19 infections via positive reinforcement. They were able to detect infections in real-time by alerting their handlers when exposed to infected individuals, needing approximately 5–10 seconds per individual for detection. The dogs' findings were highly accurate when compared with PCR testing, with 94–96% agreement. It was also noted that the dogs could detect infection in some individuals 2 to 3 days before symptoms started. This potential for early detection of the disease could be utilized across disciplines but is especially attractive in the field of both human and veterinary oncology, where early detection is critical and techniques such as liquid biopsy continue to be an area of attractive research.[11]

The first indications that dogs' amazing sense of scent could be utilized in cancer detection came from anecdotal reports of companion animals alerting their owners to the presence of dermatologic malignancies.[12] Extrapolating from these experiences, over the past 2 decades, researchers have evaluated the use of dogs to detect differences in samples taken from human patients with various cancers. A recent systematic review article indicates that 226 dogs have participated in various disease detection projects and of those studies, 68% focused on cancer detection, with the top 3 cancers included in the review being lung, prostate, and breast.[13] Multiple different sample types have been used, ranging from exhaled breath, sweat, and saliva to urine, fecal material, and blood.[13-20] The range of cancers tested with sniffer dogs include primary lung tumors, urothelial tumors, breast, ovarian, colorectal, and prostate tumors, as well as others.[3–5,13–30] Unfortunately, not every study has shown positive results[2,13,19,23] with large variations in sensitivity and specificity[13] and potentially confounding factors such as the presence of concurrent, noncancerous diseases, or the use of certain medications by individuals.[18] However, the common conclusion is that dogs exhibit an amazing odor detection capability that with further refinement may provide a noninvasive method for early detection of various cancers.

Human Lung Cancer

In a study by Junqueira et al,[20] 4 Beagle dogs were clicker trained with serum samples taken from human patients with newly diagnosed and treatment naïve nonsmall cell lung cancer (NSCLC) compared with control, healthy patients. After 8 weeks of training, during which 1 dog was removed from the training program due to lack of food motivation, the remaining 3 dogs were exposed to new serum samples in a double-blind manner with a ratio of control to positive (cancer samples) of 40:10. During the trial, dogs were exposed to serum samples housed within a canister for 5–10 seconds. A positive result was indicated by the dog sitting in front of the sample. The overall sensitivity and specificity were 96.7% and 97.5%, respectively, with a positive predictive value (PPV, the proportion of patients with lung cancer whose samples were accurately detected by the dogs) of 90.6% and a negative predictive value (NPV, the proportion of patients without lung cancer whose samples were declared negative by the dogs) was 99.2%. A recent study by Feil et al[21] examined the use of a sniffer dog for the detection of lung cancer using breath and urine samples. After a 1-year training program, in a double-blind clinical trial, the dog was able to detect lung cancer using breath samples and urine samples with an overall detection rate of 97.6%. Used alone, the detection rates were 78% for breath and 87.8% for urine. Conversely, another study[22] found that a team of trained sniffer dogs (n = 6) were able to detect lung cancer using exhaled breath with increased sensitivity and specificity as compared with urine samples. Dogs underwent 3 stages of training. In the first stage, the dogs were trained to recognize the target odor using 3 sample types (exhaled breath, urine, and tumor tissue). During stage 2, after training using lung cancer tissue, detection rates on breath and urine were examined. For stage 3, detection rates on breath and urine samples were examined after training using breath samples. Of special interest, training the dogs using breath samples resulted in higher detection rates than training the dogs using cancer tissue samples. This perhaps demonstrates that VOCs are not preserved in the neoplastic tissue as well as they are in the breath samples.

Human Prostate Cancer

One study examined the potential of dogs to detect breast or prostate cancer in urine samples from human patients.[23] A group of pet dog trainers trained their own dogs at home to discriminate between urine from individuals with and without 1 of the 2 cancer types. Six dogs were trained for breast cancer and 4 for prostate cancer. After training 2 to 7 times per week over 12–14 months, testing of the dogs indicated performance results no better than chance. Similar results were found by Elliker.[19] Inadequacies in the training and testing protocols were suggested as contributing factors to the poor results with suggestions on how to improve success rates in future studies. Several other groups of researchers have had greater success in the utilization of scent detection dogs for odor discrimination of prostate cancer in urine samples with sensitivities and specificities over 90%.[24-26] Furthermore, results of 1 study indicated that trained dogs (previously trained for explosive detection) could detect the biochemical recurrence of prostate cancer in urine after radical prostatectomy, correlating with patient prostate-specific antigen (PSA) levels.[27]

Human Breast Cancer

A study by McCulloch et al[14] utilized breath samples from adults who had recent biopsy-confirmed breast (n = 31) or lung (n = 55) cancer, as well as 85 control patients without cancer. Samples were collected before the initiation of chemotherapy as there was consideration that this could change the VOCs/scent profile. The sniffer dog team consisted of 5 dogs between the ages of 7 and 15 months obtained from a local guide-dog training program, or dogs kept as companion animals with "basic obedience training." After the positive reinforcement training period, the double-blind experiments resulted in accurate detection with a sensitivity of 88% for breast and 99% for lung, and a specificity of 98% and 99%, respectively. The results were similar across all stages of both cancers. Other studies have evaluated the detection of breast cancer utilizing skin secretions[28] and urine samples[29] with high sensitivity (90.3–100%) and specificity (100%). Finally, an interesting study[30] examined whether dogs trained to detect an odor from 1 type of cancer could discriminate odor samples from cancer of a completely different type. Two dogs were trained using liquid cell culture samples from murine mammary carcinoma and murine colorectal carcinoma cell lines. Each dog was initially trained on a specific cell line (either mammary or colorectal carcinoma), then during the final phase of testing were introduced to the opposite cell line than that which they were trained. Results indicated that sensitivity and specificity of odor discrimination were over 90% regardless of which cell line the dog was trained on, demonstrating that the dog trained with mammary carcinoma samples was able to detect colorectal carcinoma samples and vice versa.

Studies in Veterinary Patients

After studies with human patients demonstrated the potential of canine scent detection in human disease, it seemed only natural that the potential for "sniffer dogs" to benefit their own species should be investigated. The first veterinary study to investigate sniffer dogs and canine cancer analyzed urine samples from dogs with urinary transitional cell carcinoma.[31] In this study, 4 dogs underwent 3 phases of training using urine samples from dogs diagnosed with transitional cell carcinoma confirmed via cytology and imaging. Control urine samples were taken from dogs with normal urination, as well as those with noncancerous urinary diseases such as urinary tract infections and incontinence. Only 1 sniffer dog successfully underwent all 3 phases of training, but in the final double-blind evaluation when presented with 2 urine samples from dogs with transitional cell carcinoma vs 6 urine samples from control dogs, this dog was unable to successfully identify the positive tumor samples. Dorman and colleagues offered several plausible explanations for this negative result, including the impact of other medications, sample preparation, and the training regime. It is also well known that many animals, including dogs, communicate with each other via pheromones in urine, so perhaps these other messages clouded the ability to detect the presence of cancer.[32]

To expand along this line of research, the current authors recently completed a study[33] evaluating the ability of trained dogs to detect differences in saliva samples obtained from dogs diagnosed with a variety of cancers compared to healthy control dogs. Saliva samples were taken from dogs via cheek swabbing, at least 1 hour separated from food or water consumption. Samples were taken from 139 dogs, diagnosed with a variety of cancers including sarcomas, lymphoma, mast cell tumors, melanoma, or various carcinomas. Diagnosis of cancer was confirmed by histopathology or cytology and ancillary testing as appropriate. All samples from patients diagnosed with cancer were collected in the setting of "gross disease," that is, measurable and observable cancer within the body and before treatment with radiation, surgery, or chemotherapy. Samples were collected from 161 control dogs who were deemed healthy based on physical examination and clinical history; this population was also younger (under the age of 6) when neoplastic or other diseases were less likely to occur. After collection, samples were stored at a temperature of 2 to 8 °C within 30 minutes, then shipped on ice to a storage facility where they were maintained at a temperature of −24 °C until use in training or testing.

Six dogs were trained to distinguish between samples from dogs with cancer vs controls in a positive reinforcement manner **(Figure 1)**. Various apparatuses and scent activities were used to train the dogs **(Supplementary Video S1)**. After successfully completing the training program, dogs were tested on novel samples with handlers blinded to sample location. The results of our study showed that dogs could distinguish between saliva samples from cancer and control dogs with high accuracy **(Table 1)**. Mean sensitivity for all dogs was 90%, with a range of 80–100%; mean specificity was 98%, with a range of 91–100%. Both the positive and negative predictive values were 95%.

Our group is currently conducting a similar study evaluating feline cancers, such as squamous cell

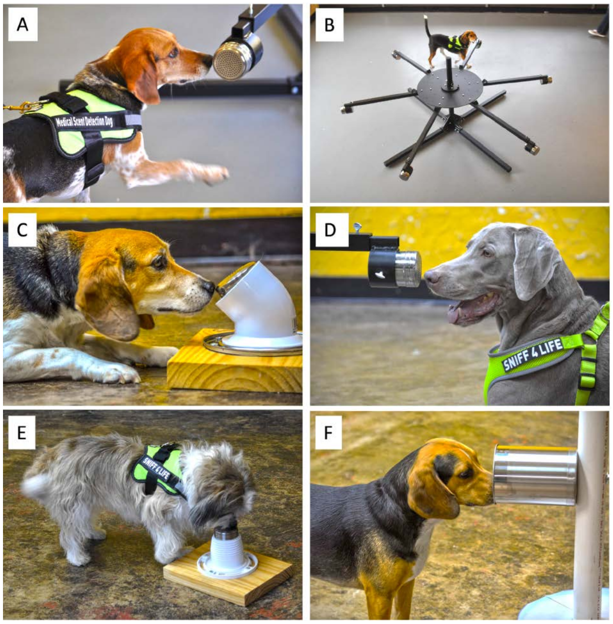

Figure 1—Six dogs were trained to distinguish between samples from dogs with cancer vs controls in a positive reinforcement manner.

Table 1—Results of testing indicating the ability of the MSD dog team in discriminating between cancer vs healthy samples by odor.

Dog ID	True positives (A)	False positives (B)	False negatives (C)	True negatives (D)	Sensitivity (%)	Specificity (%)	Positive predictive value	Negative predictive value
A-CC	9	0	1	22	90	100	100	96
B-CC	8	1	2	21	80	95	89	91
C-CC	9	0	1	22	90	100	100	91
D-CC	9	0	1	22	90	100	100	96
E-CC	9	2	1	20	90	91	82	95
F-CC	10	0	0	22	100	100	100	100
Mean	—	—	—	—	90	98	95	95

MSD = Medical scent detection.

carcinoma, mammary carcinomas, sarcomas, and lymphomas, evaluating differences between specific types of tumors, as well as various tumor stages, and the impact that treatment has on scent detection in future directions of research is warranted.

Future Directions

Preliminary research continues to show that the remarkable scent detection of dogs can be utilized to advance the health and welfare of humans, as well as various animal species. Additional research is needed with attention to details such as dog selection and training, sourcing of samples for training and testing, storage conditions, ensuring discrimination not memorization of samples, training protocols and scent configuration, preservation, and optimization of VOCs available for odor discrimination.[13] Thus far, results in this growing and exciting field of study suggest that the detection of viral infection and cancers can occur rapidly and with high accuracy. While dogs are increasingly being utilized in the human healthcare system, typically for cognitive or mental-health therapy,[34] in the future one could imagine a clinic sniffer-dog utilized for disease screening. This approach would be limited by health and safety regulations, as well as training and availability of the sniffer dogs. A more practical future application could be the collection of samples from both human and veterinary patients, either in their homes or in a clinic setting, with these samples then sent to a research or commercial laboratory where sniffer dogs screen the samples. Regardless of how future utilization plays out, as demonstrated here and in the companion Currents in One Health article by Ungar et al, *JAVMA*, January 2024,[1] these talented and capable scent-detection dogs deserve a larger role in public health protection.

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Supplementary Materials

Supplementary materials are posted online at the journal website: avmajournals.avma.org.