

Primary and Metastatic Lung Cancer: Incidence and Biomarker Detection

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Abstract

(Revised) Lung cancer is the deadliest form of cancer in people, and new models are currently being used in veterinary medicine to assist in diagnosis and treatment of this disease. Dogs are useful because they share our environment, are immunocompetent, and represent a stable, outbred population that we can work with.

Since primary lung cancer is relatively rare in dogs, I conducted a multi-institutional retrospective study to develop a knowledge base of primary lung cancer.

To investigate a novel method of noninvasive detection of lung cancer, we collected breath samples from dogs, called exhaled breath condensates (EBC).

Our aims were therefore to document and characterize the incidence and behavior of primary lung cancer in dogs, and to collect EBC samples from dogs to screen for biomarkers of primary and metastatic lung cancer.

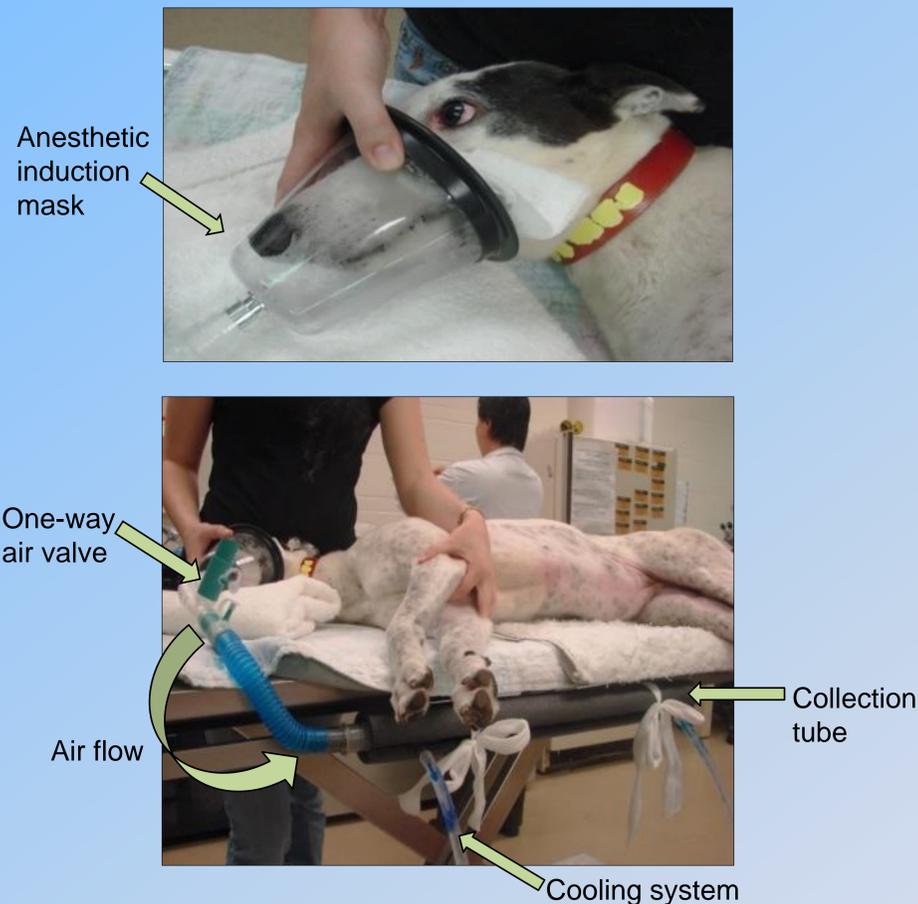
Background Information

- Based on current literature, lung cancer in dogs is rare. The most common forms of lung cancer in dogs are adenocarcinomas, squamous cell carcinomas, and bronchioalveolar carcinomas.
- Therapy consists of surgery and chemotherapy with drugs like vinorelbine. Inhalant chemotherapy is another hot trend in this field.
- Diagnostic testing of lung cancer is invasive requiring thoracotomy to obtain tissue, and known prognostic factors are few. However, thyroid transcription factor-1 has been correlated with lung cancer when samples are histochemically stained.
- Our goal is to find new non-invasive biomarkers for lung cancer. Markers found in EBC samples may reflect pathological processes occurring in the diseased lungs, and could lead to earlier detection and improved monitoring of dogs with lung cancer. These findings may be translated to humans as well.

Materials and Methods

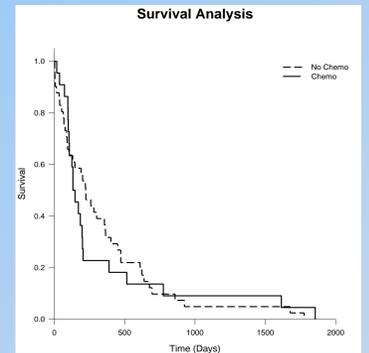
Retrospective study: A multi-institutional study was initiated via the ACVIM Oncology listserv. Data was abstracted from records of dogs with primary lung cancer and included tumor and patient variables, treatment details and case outcome.

Pilot investigation of EBC: To obtain EBC samples, we used a glass condensation system. An outer tube circulates cold water to condense the air, and the inner tube houses the breath sample. After 20 minutes of breathing, samples were collected in cryotubes and stored at -80 C. Plasma samples were collected from each dog to examine cell-free DNA content. High-resolution NMR and proteomics via SELDI-TOF technique were used to analyze the metabolites and proteins found in the EBC, respectively.



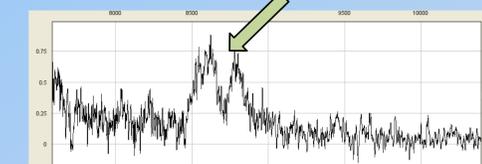
Results

Retrospective study: To date, a total of 126 cases were recruited from 9 institutions and clinics. There were 52 FS, 71 MC, and 1 MI, with many different breeds represented. Most dogs were treated with surgical excision chemotherapy. Kaplan Meier Survival Analysis showed no difference between treatment groups (223 d vs. 132 d, P=0.787):

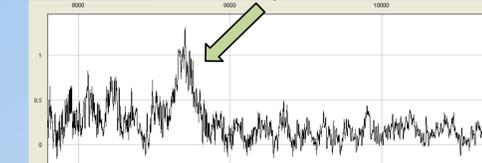


EBC

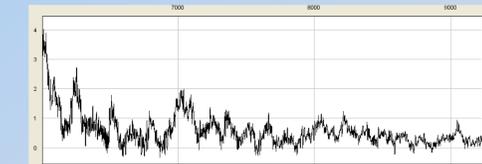
Proteomics



Metastatic mammary adenocarcinoma

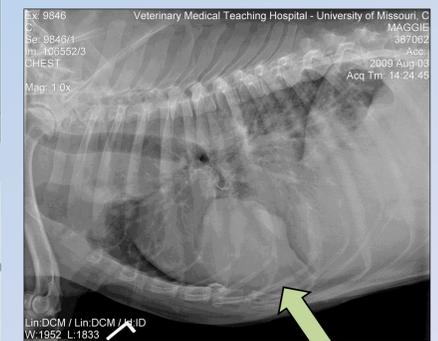
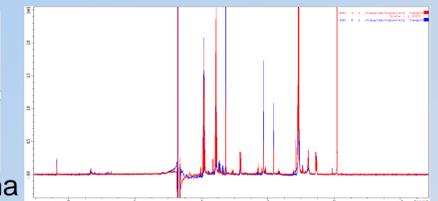


Metastatic thyroid tumor



Control

Metabolomics



Conclusions

The main conclusions from this study are: Lung cancer in dogs is rare and can be aggressive. The addition of chemotherapy may not improve survival. EBC is relatively simple to collect and may provide a non-invasive method to diagnose and monitor lung cancer.

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