

Relevance of Companion Animal Exposures to Human Cancer and Aging

Radon Exposures



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He/Him/His



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Speaker Disclosure

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FINANCIAL DISCLOSURE (Active):

Anivive	Advisory board, speaker, honorarium
Boehringer Ingelheim	Advisory board, honorarium, clinical trial
Elanco	Consultant, speaker, advisory board, honorarium
Hill's	Advisory board, honorarium
LifEngine Animal Health	Consultant, own stock
NovaVive	Clinical trial
QBiotics	Consultant, speaker, advisory board, honorarium
VetDC	Clinical trial
Verte Therapeutics	Consultant, honorarium



What you can expect today...

- Background
 - Veterinary oncology market
 - Lung cancer in dogs/cats
- Radon data in dogs/cats
- Future opportunities



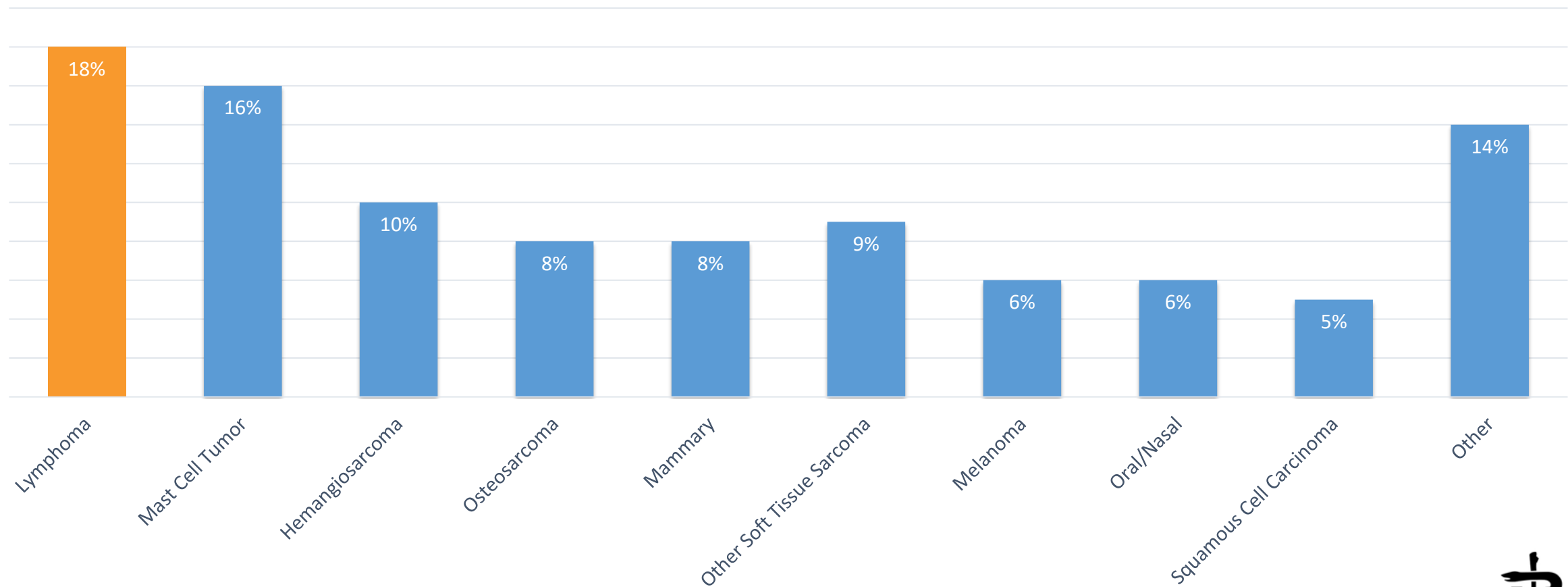


VETERINARY ONCOLOGY MARKET CURRENT STATUS



Canine Oncology: True incidence rates not well established

Percentage of Annual Incidences of Canine Cancer by Tumor Type



Veterinary oncology market growth follows trends in human market

Oncology Therapeutic Companies*

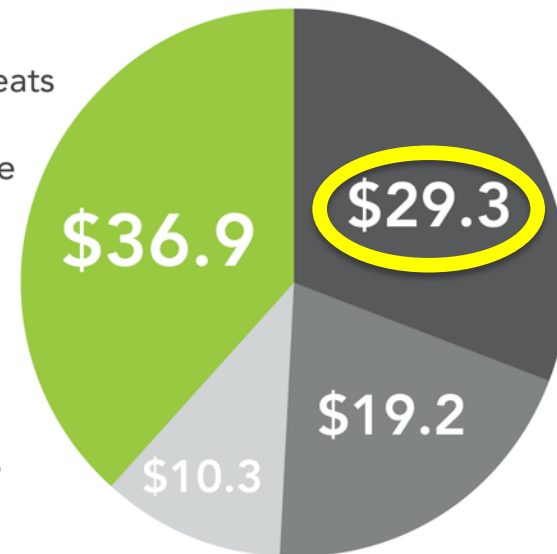
Year	Number
1997	0-1
2002	2
2007	3-4
2012	8-10
2021	~25-30

Actual size and potential of veterinary oncology market not well established

IN 2019, US PET SPENDING
TOTALLED **\$95.7 billion**



- pet food & treats
- veterinary care & products
- supplies, live animals, OTC medicine
- other services



~3% of
dogs/cats
are insured

All numbers measured in billions.
Source: 2019-2020 National Pet Owners Survey, American Pet Products Association

*Johannes estimates; does not include compounding pharmacies



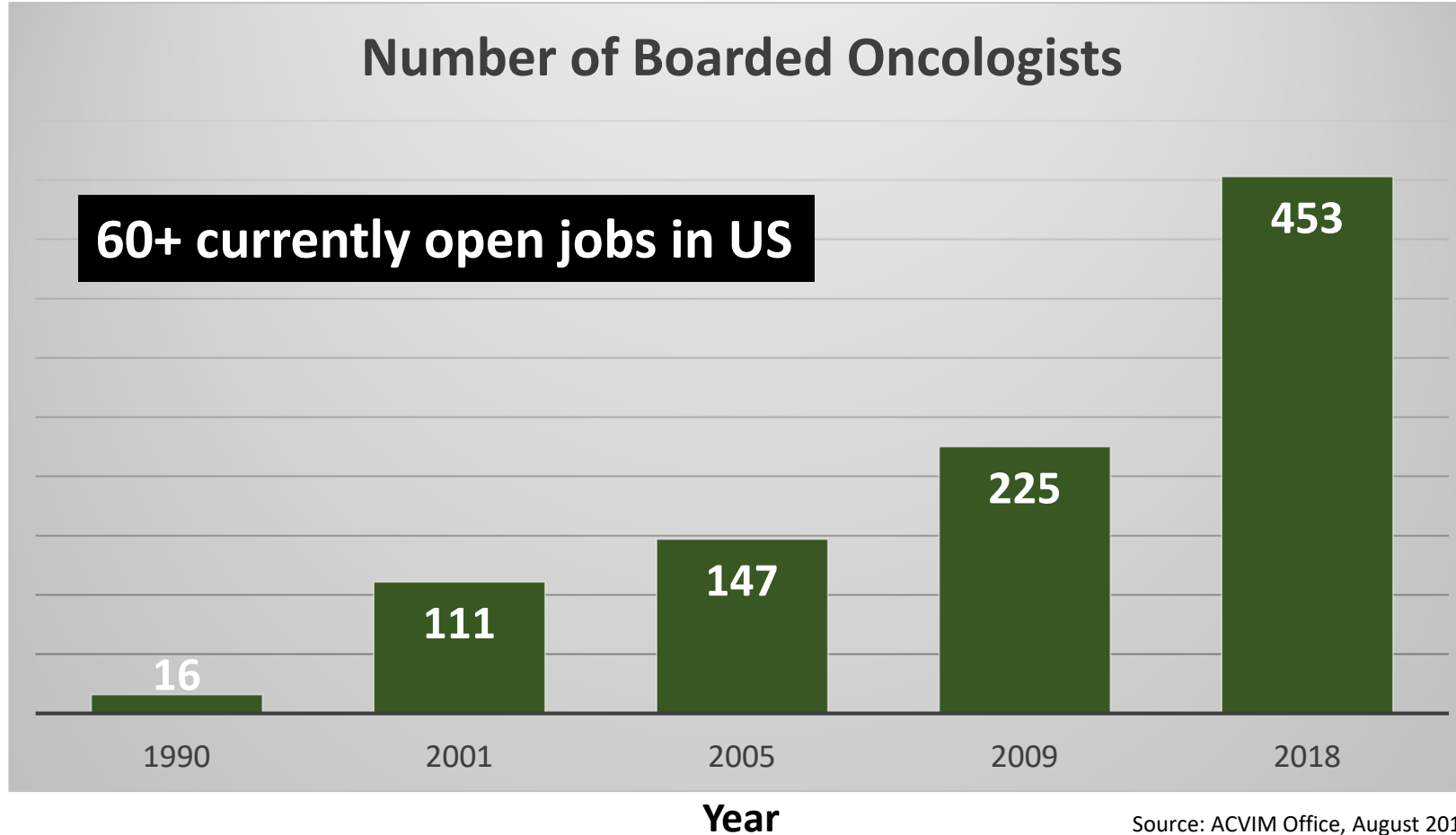
Canine Oncology Therapeutics

Commercially Available – US, Canada, EU (2021)

Trade Name	Compound Name	Company	Indication	Regulatory Status	Available?
N/A	Canine lymphoma vaccine, DNA	Merial/BI	B-cell lymphoma	USDA Conditional License (2015)	No
Immunocidin®	Mycobacterium cell wall fraction	NovaVive	Mammary tumors	USDA Licensed	Yes (US, CA)
Laverdia™-CA1	Verdinexor	Anivive	Lymphoma	FDA Conditional Approval (2021)	Yes (US)
Masivet®	Masitinib	AB Science	Mast cell tumor	EMA Approved	Yes (EU)
Oncept®	Canine melanoma vaccine, DNA	Merial/BI	Melanoma	USDA Licensed (2010); EMA Approved	Yes (US, EU, CA)
Palladia®	Toceranib phosphate	Zoetis	Mast cell tumor	FDA Approved (2009); EMA Approved	Yes (US, EU, CA)
Stelfonta®	Tigilanol tiglate	QBiotics/ Virbac	Mast cell tumor	FDA Approved (2020); EMA Approved	Yes (US, EU)
Tanovea®	Rabacfosadine for injection	VetDC/ Elanco	Lymphoma	FDA Approved (2021)	Yes (US)



Oncology specialty experiencing exceptional growth



Source: ACVIM Office, August 2018

*CAGR – Compound Annual Growth Rate



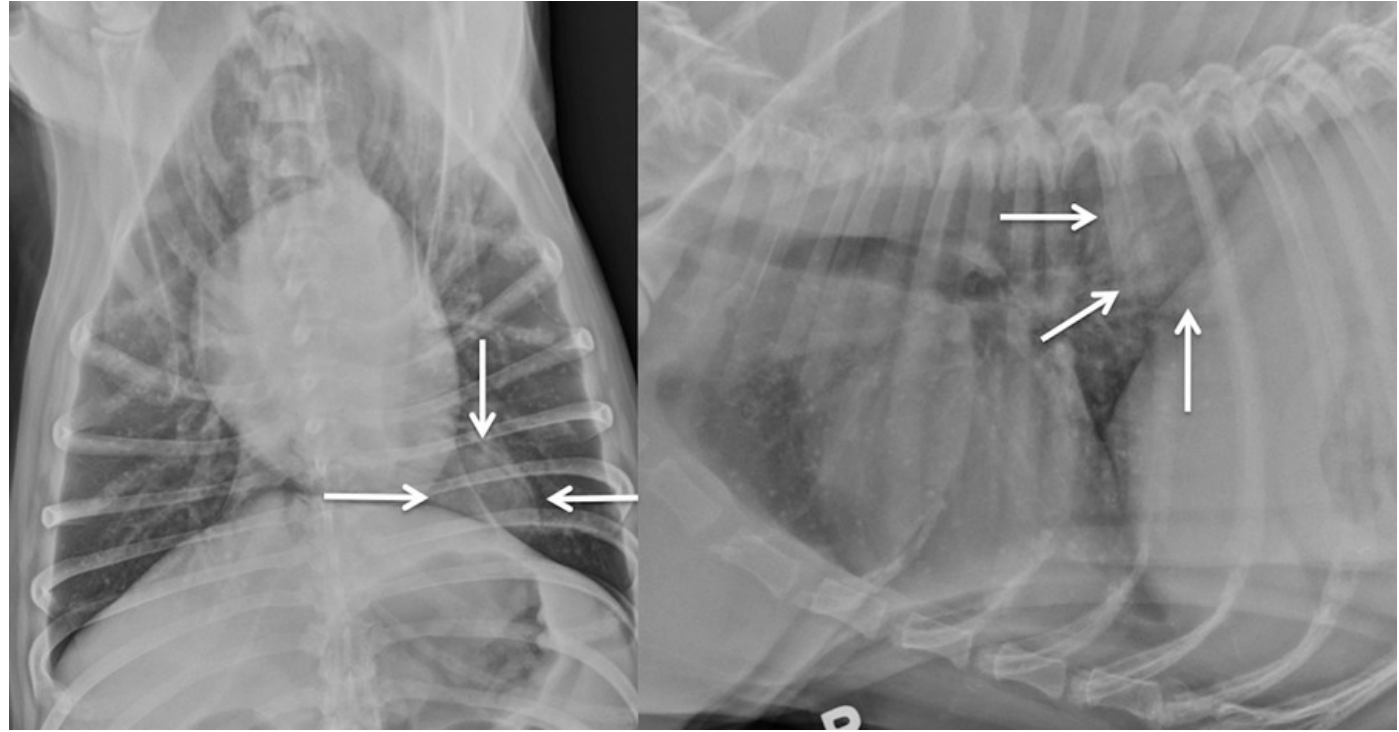
The corporatization of vet med...

- 28,000-32,000 veterinary practices (US)
- Corporately owned:
 - Primary care: 10%
 - Referral/specialty: 50%
 - Total: 20%



30 years in the making, the pace of corporate acquisition of practices has accelerated recently.





BACKGROUND



Primary pulmonary neoplasia (PPN) in dogs

- **Incidence rates (dogs)**

85% bronchoalveolar in origin

- <1% at time of necropsy
- 4.2/10,000 per year (US); 15/100,000 per year (UK)
- 8.8% in closed beagle colony

- **Population dynamics**

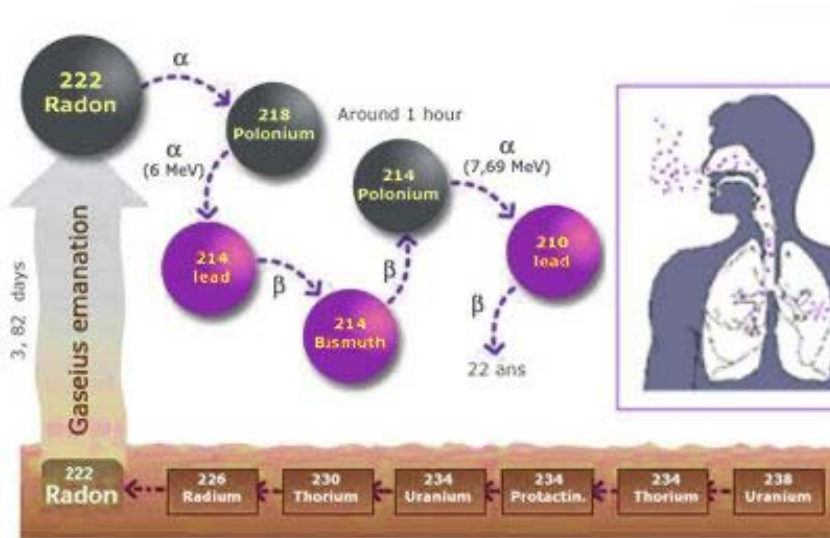
- 11 years = avg age at dx
- Breeds overrepresented: Boxer, Doberman, Australian shepherd, Irish setter, BMD

- **Environmental risk factors (potential)**

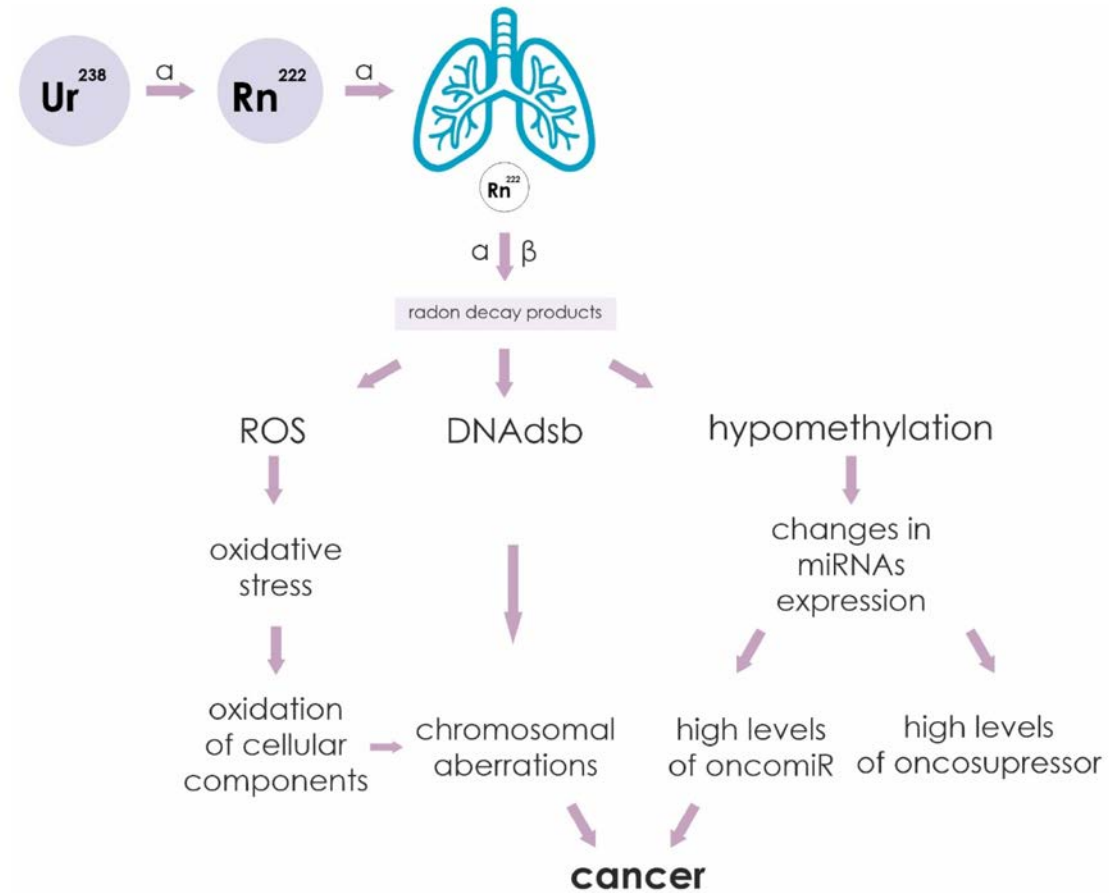
- Urban living, second-hand tobacco exposure, polluted air
- **Experimental radiation (plutonium)** exposure - research dogs



Radon – role in lung cancer development



<https://theoarp.com/What-Is-Radon>



<https://www.mdpi.com/1422-0067/21/6/2154/htm>



Radiation-related gene mutations in dogs

Evaluated p53, erbB-2, K-ras gene alterations in canine lung tumors

- $^{239}\text{PuO}_2$ exposed beagles (n=80); spontaneous/non-exposed (n=37)
- 16/116 (14%) elevated nuclear accumulation of p53 protein
 - 94% of all tumors with p53 abnormalities = adenosquamous/squamous cell
- **p53 and K-ras gene abnormalities are infrequent events**



Tierney LA, et al. *Radiat Res*, 1996;145(2):181-7.



Advantages of dogs/cats in studying role of radon

- Shorter lifespan
- Majority are primarily/solely indoors
 - Less mobile/same household for lifetime
 - Majority of day/time spent in house
- No occupational exposure



Is lifetime radon exposure in dogs/cats a predisposing factor to development of PPN?

Potential model for role of radon in human lung cancer development?





RADON DATA IN DOGS/CATS



Lung tumors more common in high radon zones?

DOI: 10.1111/jvim.15936

STANDARD ARTICLE

Journal of Veterinary Internal Medicine

Open Access

ACVIM
American College of
Veterinary Internal Medicine

Ecological level analysis of primary lung tumors in dogs and cats and environmental radon activity

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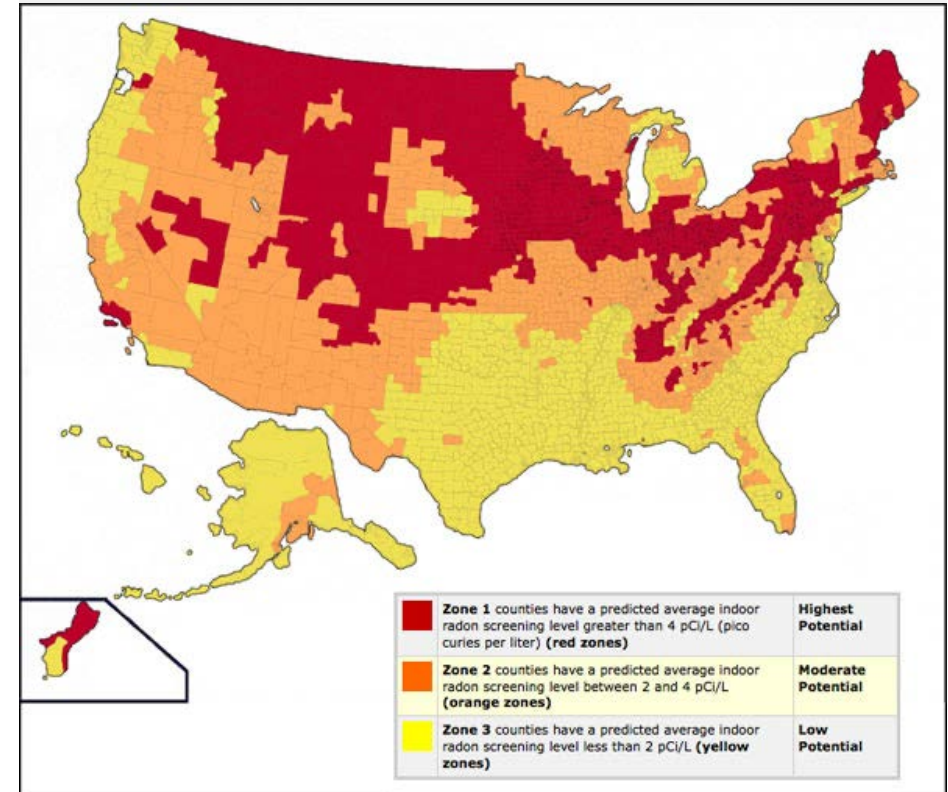


Data from 10 institutions (2010-2015)

Dogs (n=690)

EPA radon zone	Veterinary college	Cases per college per zone		
		ERL >4 pCi/L (zone 1)	ERL 2-4 pCi/L (zone 2)	ERL <2 pCi/L (zone 3)
1	Colorado State University	186	11	5
	Cornell University	62	18	2
	Iowa State University	124	0	0
	Purdue University	47	19	1
2	North Carolina State University	1	7	29
	University of Georgia	2	15	3
3	Mississippi State University	2	18	25
	Oklahoma State University	1	2	18
	Oregon State University	0	3	24
	University of Pennsylvania	32	21	12

EPA Radon Geographic Zones

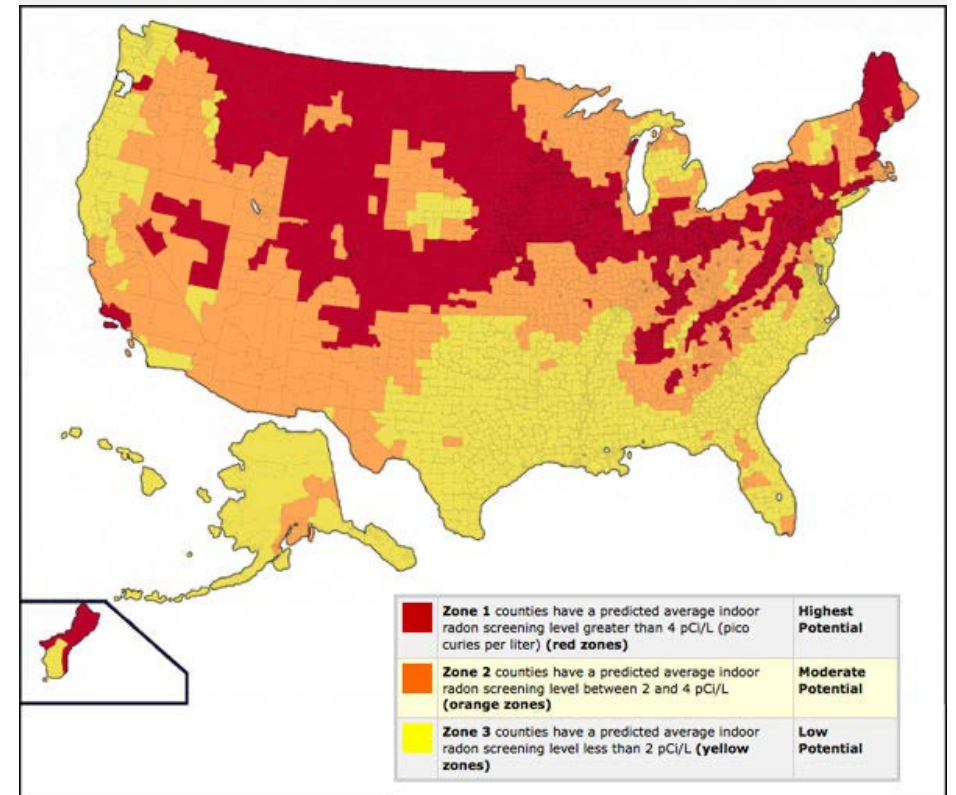


Data from 10 institutions (2010-2015)

Cats (n=205)

EPA radon zone	Veterinary college	Cases per college per zone		
		ERL >4 pCi/L (zone 1)	ERL 2-4 pCi/L (zone 2)	ERL <2 pCi/L (zone 3)
1	Colorado State University	42	1	0
	Cornell University	23	5	0
	Iowa State University	35	0	1
	Purdue University	14	5	0
2	North Carolina State University	2	11	6
	University of Georgia	0	3	1
3	Mississippi State University	0	3	6
	Oklahoma State University	1	0	7
	Oregon State University	0	1	8
	University of Pennsylvania	11	7	12

EPA Radon Geographic Zones



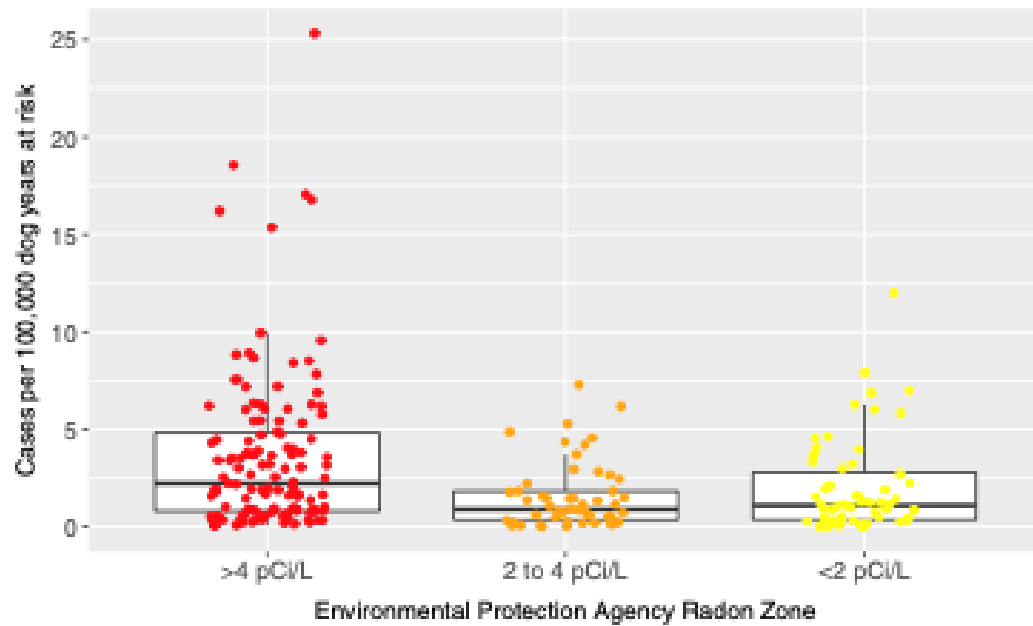
PPN diagnoses in dogs & cats



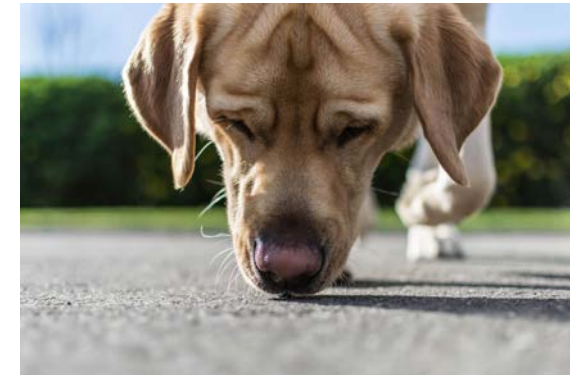
	DOG (n = 431)			CAT (n = 110)		
	Surgical biopsy	Cytology	Necropsy	Surgical biopsy	Cytology	Necropsy
Bronchoalveolar carcinoma	80 (18.6%)			18 (16.4%)		
	42	28	31	7	1	10
Bronchogenic carcinoma	16 (3.7%)			6 (5.5%)		
	1	15	1	0	6	0
Histiocytic sarcoma	50 (11.6%)			1 (0.9%)		
	16	29	14	0	1	0
Pulmonary adenocarcinoma	102 (23.7%)			26 (23.6%)		
	69	44	28	6	8	16
Pulmonary carcinoma	136 (31.6%)			51 (46.4%)		
	33	94	29	11	38	14
Squamous cell carcinoma	11 (2.6%)			5 (4.5%)		
	7	4	3	0	2	3
Other	36 (7.9%)			3 (2.7%)		
	11	13	16	0	2	1



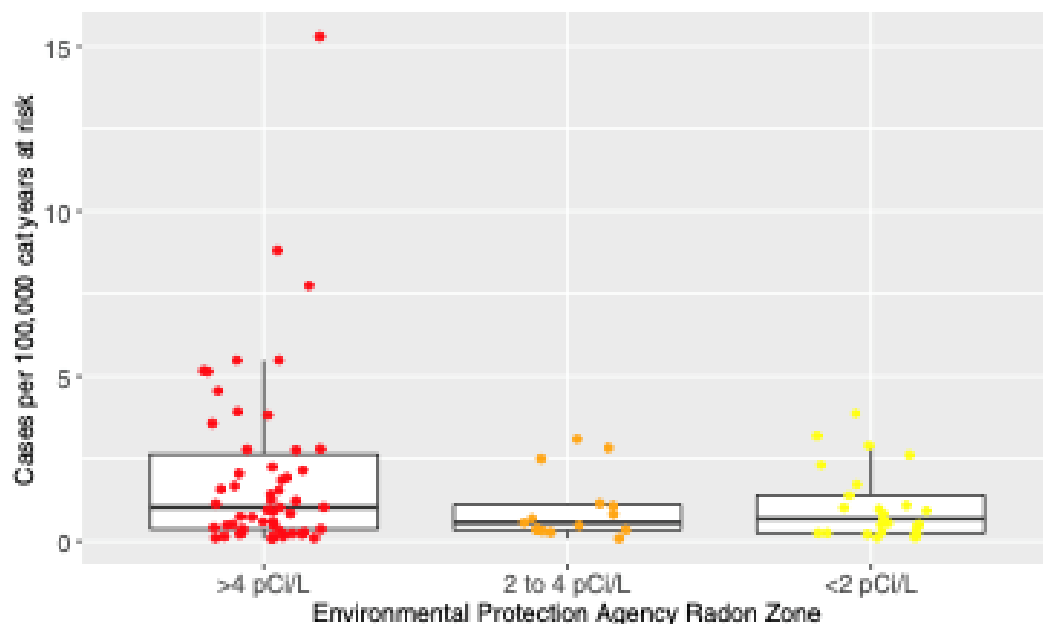
Radon zone and incidence of PPN in dogs (n=690)



	EPA designated radon zone (numerator)	EPA designated radon zone (denominator)	Rate ratio (95% confidence interval)
Definitive and suspect cases			
Dogs, all counties	1	2	2.49 (1.56-4.00)
	1	3	2.29 (1.46-3.59)
	2	3	0.92 (0.53-1.59)



Radon zone and incidence of PPN in cats (n=205)



	EPA designated radon zone (numerator)	EPA designated radon zone (denominator)	Rate ratio (95% confidence interval)
Definitive and suspect cases			
Cats, all counties	1	2	2.13 (0.95-4.79)
	1	3	1.81 (0.90-3.61)
	2	3	0.85 (0.33-2.15)



Summary/key findings...

- Incidence rate of PPN higher in regions with **higher environmental radon levels** for both dogs & cats
- Findings **similar to several human studies**
- Dog/cat data better able to capture **entire lifetime radon exposure?**
- Differences seen in cats:
 - True lower incidence vs fewer annual DVM visits
- **Skewed patient population** due to referral hospital data source





FUTURE OPPORTUNITIES



Achievable next steps?

- Improve data on **canine/feline cancer incidence**
- Similar ecological level evaluation of **canine sinonasal tumors**
- **Radon exposure/tissue deposition analysis** in dogs & cats
 - Biomarkers
- Observational cohort studies
 - **Include dogs** w/ human studies

Public/corporate partnering opportunities...



Questions?



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