1 First Osteosarcoma Reported from a New World Elapid Snake and Review of Reptilian Bony

2 Tumors

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5 Suggested running head: Elapid osteosarcoma

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Abstract

Cancer chiefly occurs in vertebrates. Rare in amphibians, and perhaps common in reptiles, various neoplasms and malignant cancers have been reported with erratic frequency by museums, paleontologists, veterinarians, and pet hobbyists. Unsurprisingly, most herpetofaunal diversity has never been systematically surveyed for the presence of neoplasms owing to the extreme rarity or obscurity of many species. Museum collections can fill these gaps in knowledge, especially when researchers use non-destructive techniques. In this study, we used X-ray computed tomography to discover and characterize an osteosarcoma of the spine in a rare South American coralsnake, *Micrurus ancoralis*. Two spinal vertebrae were completely fused and adjacent vertebrae showed evidence of corruption. The fused vertebrae contained a hollow inner network thought to be vascular tissue. We also review previous reports of tumors in the Elapidae and all bony tumors in non-avian reptiles. The rarely reported technique of X-ray CT for tumor discovery could greatly improve our understanding of the species diversity and perhaps underlying causes of neoplasia.

Keywords: cancer, computed tomography, coralsnake, Elapidae, *Micrurus ancoralis*, neoplasm, osteopathy, tumor

Neoplasms, abnormal cell growths, can grow to large sizes and are often called tumors or cancers (Cooper, 1992; Hernandez-Divers and Garner, 2003). Tumors can be benign or malignant, and chiefly occur in vertebrates (Capasso, 2005). Neoplasms are reported across the entire spectrum of vertebrates (Schlumberger and Lucke, 1948; Stolk, 1958; Capasso, 2005; Rothschild et al., 2012). Amphibians exhibit neoplasms rarely (Capasso, 2005), though there are a few documented cases (Schlumberger and Lucke, 1948; Hill, 1954, 1955; Effron et al., 1977; Hruban, et al. 1992; Rothschild et al., 2012). In contrast, extant reptiles exhibit a diverse range of tumors (Machotka, 1984), and nearly all tumors found in mammals can be found in reptiles plus a few that can't be found in mammals (Effron et al., 1977; Garner et al., 2004; Suedmeyer, 1995; Mauldin and Done, 2006; Rothschild et al., 2012). Our knowledge of reptilian neoplasms is primarily gleaned from systematic reviews from zoos (Hill, 1952–1955, 1957; Cowan, 1968; Ippen, 1972; Effron et al., 1977; Ramsay and Fowler, 1992; Ramsay and Lowenstein, 1996; Catão-Dias and Nichols, 1999; Sykes and Trupkiewicz, 2006), though important contributions have come from the pet trade and veterinary practice (Garner et al., 2004; Mader, 2005; Simard 2016; Christman et al., 2017), private collections (Frye, 1994), and museum collections (Harshbarger, 1969; Machotka and Whitney, 1980).

The frequency of tumors in vertebrates is unclear. A clear historical bias exists in the literature reflecting improved screening and expectations for what animals experience neoplastic growths, and only obvious cases were then reported (e.g., Ohlmacher, 1898; Kalin, 1937). For instance, Peyron (1939) dissected 4,000 snakes and reported no tumors. Similarly, Bergman (1941) noted only one tumor in over 2,200 snakes. The occurrence of specific tumors also changes through time. As one example, Dawe and Harshbarger (1969) explain that reptiles lack leukemias, leukoses, or reticular neoplasms, yet Frye and Carney (1973) report a lymphatic

leukemia in a boa constrictor only a few years later. In 1948, Schlumberger and Lucke presented an impressive review of fish tumors and commented on the state of tumor descriptions in vertebrates. They lamented that previous investigators did a rather poor job at surveying neoplasms in reptiles and this led to a misconception that reptilian neoplasms were rare or absent. Scrutinizing specimens with greater rigor clearly yielded a higher incidence of neoplasia than previously reported. For example, in the same paper they reported over 1,200 examples of renal adenocarcinoma in the frog *Rana pipiens* in a 15 year period (Schlumberger and Lucke, 1948).

One early effort to systematically report on vertebrate neoplasms was the annual report from the Zoological Society of London prosector (e.g., Hill 1952–1955, 1957). Here, all London Zoo causes of death were reported. These annual reports included unexpected tumors, thus raising the profile of neoplasms in non-mammals. Recognizing the paucity of data and importance of comparative information of neoplasms in animals, in 1969 the Smithsonian Institution established the Registry of Tumors in Lower Vertebrates (RTLVA) to allow for a common repository for and study of such specimens (Harshbarger, 1969). The Armed Forces Institute of Pathology and the RTLVA were critical in establishing the fact, now widely accepted, that tumors are widespread in vertebrates and are found in nearly all tissue types (Machotka and Whitney, 1980; Frye, 1994; Hernandez-Divers and Garner, 2003).

The question of neoplasm incidence or rate in vertebrates is still the subject of research and varies depending on the context of what incidence rate is being calculated. Among birds and mammals, neoplasms are apparently rare in wild populations, but far more likely in captive animals (Bergman, 1941; Petrak and Gilmore, 1982; Jubb and Kennedy, 1970; Capasso, 2005). Similarly, as previously reported, Bergman (1941) found only one tumor in 2,200 free-ranging

snakes. Effron et al. (1977) provided one of the first modern, authoritative estimates of neoplasia in vertebrates from over 10,000 necropsies at the Zoological Society of San Diego. They reported a 3% rate of neoplasia in mammals and 2% in reptiles and birds. None of the amphibians dissected exhibited neoplasia. A more recent report from an exotic species pathology service hypothesized that, among reptiles, neoplasia may be most common in snakes (Garner et al., 2004). These authors found that neoplasia in snakes are most prevalent in crotalids, followed by viperids, and then boids (including elapids). Simard (2016) recently reported 0.9% of 3995 reptiles available to Ghent University had some kind of neoplasm. Most cases were based on assessment of ante-mortem diagnostics; thus this estimate may be low since only very obvious neoplasms were reported. As reptiles are increasingly owned as pets (Collis and Fenili, 2011), systematic reports from the pet trade and associated veterinary profession will be crucial for expanding our knowledge of the incidence of tumors, at least in captive animals. However, this trend of neoplasm reporting will likely generate a bias towards those animals most commonly kept as pets. Thus, natural history collections will remain useful supplements to study neoplasia, especially in rare and ‘uncharismatic’ species not found in the pet trade (Keck et al., 2011).

In this report, we describe a bony, vascular tumor (osteosarcoma) of the new world elapid coralsnake, *Micrurus ancoralis* (Jan, 1872). Our discovery was made as part of a larger, systematic study of vertebral morphology in elapid snakes using computed tomography (CT). Prior to this report, we are unaware of any published neoplasms in new world elapid snakes (see Schmidt, 1936; Slowinsky, 1995 for phylogeny). Furthermore, this may be the first time that CT has been used as an exploratory tool for finding and describing a tumor in a vertebrate museum specimen. Rosenberg et al. (1995), demonstrated difficult cases for describing osteosarcomas using plain radiographs and supplements known osteopathic cases with tomograms from CT.

Schumacher and Toal (2001) enumerate radiography and ultrasonography techniques for reptile veterinary medicine but discount CT as a routine diagnostic tool. Banzato et al (2013a, b) review veterinary imaging for snakes and lizards and include traditional CT and contrast-enhanced in their review. Cole et al. (2014) used micro CT to describe osteosarcomas in mice injected with an osteosarcoma cell line, confirming that CT can accurately describe osteosarcoma without dissection. We also review known elapid tumors and bony tumors in reptiles.

Methods & Materials

Computed Tomography

The formalin-fixed specimen was CT scanned at UT Arlington's Shimadzu Center for Environmental Forensics and Material Science using a Shimadzu inspeXio SMX-100CT (Shimadzu, Kyoto, Japan). The snake was scanned twice using similar parameters, but with different focal areas. Energy settings were 40kV and 40μA. All slices averaged 6 frames on each of 4 rotations for a total of 1200 views per full rotation. The first, focal scan consisted of 876 slices with 9 μm isotropic voxels. A second, multi-loop section with more vertebrae in focus consisted of 1697 slices with 11 μm isotropic voxels. Each scan lasted about 15 min.

Raw X-ray data were reconstructed using Shimadzu's inspeXio software and exported as 1024 x 1024 16-bit TIFF. Each stack of 16-bit TIFF images was rotated and cropped in ImageJ and imported into Thermo Scientific™ Avizo™ Software 9.5 (Thermo Fisher Scientific, Waltham, MA, US). As a volume, each data set was resampled to align better with the X axis, cropped, filtered using ring-artifact correction, passed through a non-local means filter, and then filtered using unsharp masking. This combination of filters retained fine features and smoothed the majority of artifacts found in all computed tomography data. Multiloop scans in cone beam CT inherently experience distortion at the periphery of each component scan, and this is slightly

noticeable in the final, filtered data. Vertebrae were segmented in Avizo following Hall et al. (2018). In the multi-loop scan, pores in the fused vertebrae were segmented out using a combination of thresholding and manual editing. The raw CT data, videos of each data set (Vids. S1-S3), and label data are available on a MorphoSource project: http://www.morphosource.org/Detail/ProjectDetail/Show/project_id/625. Additionally, raw CT data are archived at the University of Texas at Arlington Amphibian and Reptile Diversity Research Center digital image collection.

Literature Reviews

We sought to generate two reviews of neoplasms in snakes: one specific to the snake family Elapidae, and another for all bony tumors in non-avian reptiles. We compiled a list of elapid neoplasms from a thorough literature search using relevant search terms in English, Spanish, German, French, and Dutch. This included searches with combinations of all genera of Elapid snake (reconciled between Campbell and Lamar [2004] and Uetz [2018]), the terms “elapid,” “elapinae,” or “Elapidae,” and “tumor,” “cancer,” “neoplasm,” or “sarcoma” etc. Similarly, we searched for bony tumors – defined as neoplasms of osteoids, periosteum, skeletal cartilage, and adjacent supporting tissues in the case of metastasis – in combination with common and scientific names for orders and family names of reptiles, per Uetz (2018). In each review, we examined all literature that cited relevant articles and also the references cited within. We did this regardless of whether these secondary articles could be found in the searches laid out above. Given the historical utility of the RTLA (e.g., Harshbarger, 1969), we contacted their current curatorial home to check for any unreported, relevant neoplasms for these reviews. For internal consistency, we updated common and scientific names throughout this report to match The Reptile Database (Uetz 2018).

Results

Computed Tomography

Two cervical vertebrae were fused together in bone and vasculature (Fig. 1C,D; Vids. S1, S3). The dorsal region of these two vertebrae was porous and resembled trabecular bone. Fusion of the vertebrae increased from the ventral to dorsal aspect. The surface and interior of the neural arch was entirely fused between the two vertebrae and its surface was porous. In contrast, the surface of cervical vertebrae elsewhere in the same specimen were smooth and not porous (Fig. 1A,B, Vid. S2). The condyle of the anterior fused vertebra and the adjacent cotyle were fused with some porosity. Unaffected vertebrae exhibit a uniform gap. Similarly, the postzygapophyseal and prezygapophyseal articular facets of the affected vertebrae were fused with some porosity. Unaffected vertebrae had a uniform gap (Fig. 1A, Vids. S1, S2). The anterior aspect of the neural spine of the posteriorly adjacent vertebra was split in a Y-shape and porous. The neural spines of the two anteriorly adjacent vertebrae were porous, dorsolaterally blunted, and enlarged on the anterior aspect. The surface of the inside of the neural canal in fused vertebrae was rougher and more porous than unaffected vertebrae. The hypapophyses of fused vertebrae were not visibly different compared to unaffected vertebrae. Canals, thought to be blood vessels, ran chaotically through each affected vertebra and seamlessly crossed the two vertebrae (Fig. 1D, Vid. S3). By contrast, blood vessels in unaffected bones only ran through the center of each lateral vertebral process, condyle, cotyle, and hypapophysis (Fig. 1B).

Literature Reviews

We found 38 cases of neoplasia in the snake family Elapidae, all from old world species (Table 1). Of 13 cases when sex was reported, four were male and nine were female. 23 (60%) of cases reported were from the genus *Naja*, with the second most cases from *Aspidelaps* (four;

10.5%) and then third most from *Ophiophagus* (three; 7.9%). Kidney-related neoplasms were the most reported (nine; 23.7%; Keck et al. 2011). Despite the limited number of reported elapid neoplasms, reports covered many cell types and locations (Table 1), including three bony tumors in *Naja* species. Our review of bony tumors in reptiles revealed 58 cases (Table 2). This included 49 squamates, 5 turtles, and 4 crocodylians. Six of ten cases with known sex were female and four were male. We found several varieties of bony neoplasms, including osteoma (bone cell neoplasm), osteosarcoma (malignant bone cell tumor), osteochondroma (bony, cartilage covered exostoses), chondroma (cartilage cell neoplasm), and chondrosarcoma (malignant cartilage cell tumor). *Varanus* and *Pantherophis* each included eight cases of bony tumors (16.3% of squamates). We note very few bony tumors of the head or face: only one report of osteoma of the skull from a male *Caiman crocodilus* (Kalin 1937).

Currently, the RTLA resides at Experimental Pathology Laboratories in Virginia. Jeffrey Wolf, current curator of the RTLA, knew of only one bony tumor in the Elapidae from their collection: a metastatic vertebral osteochondrosarcoma in *Naja nigricolis* (RTLA case #2474). Wolf noted no tumors in the collection within the genus *Micrurus*. Additionally, Wolf reported the following elapid neoplasms in the RTLA archive: six renal adenocarcinomas, two hepatocarcinomas, two lymphomas, one fibrosarcoma, one nasal carcinoma, one leiomyosarcoma, one Sertoli cell tumor, and one adrenal adenoma.

Discussion

There are few alternative explanations for the displayed osteopathy. One alternative is osteoperiostitis. There is a precedent for this condition in two female Black Iguanas (*Ctenosaura similis*) and a female Chinese Stripe-tailed Snake (*Elaphe taenura*; Cowan, 1968). In each case, the bone and adjacent soft tissue became indistinct, softened, and exhibited exotosis. The periosteum of the laminae was affected, but not the intervertebral or apophyseal joints. Microscopically, the periosteum separated the new growth from the original bone, as new growth arose from the mesenchymal tissue on the surface of the periosteum. Cowan (1968) compared these osteopathic growths to virally induced osteoperiostitis (i.e., osteopetrosis) in chickens (Sanger et al., 1966). Compared to osteoperiostitis, as reported by Cowan (1968), the specimen in this study had fused intervertebral (i.e., condyle and cotyle) and apophyseal joints. Additionally, the growth occurred, it seems, inside of existing bone and not on top of the periosteum.

A second alternative is the possibility of infection of the bone or its supporting tissues (Rothschild et al., 2012). These authors exhaustively review and in some cases re-evaluate osteopathological conditions reported in the herpetological literature and rule several cases to be due to bone infection (Rothschild et al., 2012). In this study, infection cannot be ruled out, but there is clear evidence for neoplastic growth: low anisotropy of the bone, fused bones, and absence of bony growth on and in the periosteum. Furthermore, the scarcity of this specimen led the respective curator to disallow destructive histopathology.

Tumor vasculature becomes interesting in this study since we could easily segment it from the specimen's micro CT data (Figure 1D). Generally speaking, solid tumors are more vascularized than healthy tissues (Forster et al., 2017), but their chaotic growth results in chronic

and acute hypoxia due to poor circulation (Siemann, 2011; Forster et al., 2017). Among the earliest comments on vasculature of bony tumors in reptiles is Hill's (1957) report of a vascular osteoid osteoma in a Common Water Monitor (*Varanus salvator*). Hill (1957) briefly notes that reptile osteomas (at least in snakes) may be synonymous with exotoses found in human osteomas. Interestingly, Stolk (1958) reports several osteomas in the caudal vertebrae of a female European Green Lizard (*Lacerta viridis*) that exhibited normal vasculature. The discrepancy in vasculature may be due to a different origin for the neoplastic growth in the *Lacerta*, as Stolk (1958) hypothesized the tumors to have originated from the marrow of the caudal long bones. Fitting with the generally chaotic nature of tumor vasculature, Cowan et al. (2011) reported an osteosarcoma in a Woma Python (*Aspidites ramsayi*) that was characterized by disorderly arrangement of osseous trabeculae. They also noted that mesenchymal cells surrounded an eosinophilic osteoid matrix.

Looking backwards through time, bony tumors do occasionally show up in the reptile fossil record (Moodie, 1917, 1923). A well-known example is Moodie's (1918) description of an osteoma in a mosasaur (see also Moodie, 1923). In this case, however, Rothschild et al. (2012) reassessed this paleontological osteopathy as a hamartoma (i.e., not considered neoplasia). Our review also includes bony neoplasms in an extinct turtle, *Syllomus aegyptiacus* (Weems, 1974), and an extinct crocodile, *Leidyosuchus formidabilis* (Sawyer and Erickson, 1998). The fossil record, obviously, is sparse and uneven across time, and the condition and taphonomy of fossils complicates their accurate osteopathological diagnosis (Moodie, 1917; Rothschild et al., 2012). Computed tomography, especially from a synchrotron light source, may assist properly diagnosing suspected fossil neoplasms, as histology is typically ruled out.

Prior to this report, we are unaware of any published neoplasms in new world elapid snakes (Table 1), likely reflecting their general absence in private collections and zoos compared to other species (Keck et al., 2011). Large, charismatic venomous cobras of the old world are relatively common in zoos throughout the world (e.g., Ramsay et al., 1996; Catão-Dias and Nichols, 1999; Collis and Fenili, 2011) and would thus be expected to be necropsied more often (Table 1). Compared to the hundreds of tumors reported for other families of snakes (Garner et al. 2004), even the RTLA (similar to other collections and reports), likely reflects the historical bias against including elapid snakes in zoo and private collections (Keck et al., 2011; Wolf J, pers. comm.). The relative obscurity of new world elapids (Schmidt, 1936), especially in captivity (Collis and Fenili, 2011), thus requires focused effort investigating specimens in natural history collections to understand their neoplasms. Another obvious omission in the neoplasm literature is a comparative phylogenetic study of tumors across reptiles and birds. Machotka and Jacobson (1989) provided the most recent phylogenetically organized treatment of neoplasms in this group; however, this study was entirely descriptive. Furthermore, our knowledge of comparative phylogenetics (e.g., Freckleton et al., 2002) and the reptile phylogeny has since vastly improved (Reeder et al. 2015, Streicher and Wiens, 2017). A comparative phylogentic test of neoplasia prevalence across the Sauria would reveal unexpected neoplasm absences and focus future study of natural history collections on these groups. Our report demonstrates that studying neoplasms is sometimes possible without dissecting valuable, rare specimens.

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Table 1. Neoplasms found in the snake family Elapidae.

Scientific Name	Common Name	Neoplasm	Reference
<i>Acanthophis antarcticus</i> ♀	Common Death Adder	Lymphosarcoma, leukemic	Effron et al., 1977
<i>Aspidelaps l. lubricus</i>	Cape coral snake	Tubular carcinoma (kidney)	Keck et al., 2011 (unpublished)
<i>Aspidelaps l. lubricus</i> ♀	Cape Coral Snake	Renal adenocarcinoma	Keck et al., 2011
<i>Aspidelaps l. lubricus</i> ♀	Cape coral snake	Renal adenocarcinoma	Keck et al., 2011
<i>Aspidelaps l. lubricus</i> ♂	Cape Coral Snake	Renal adenocarcinoma	Keck et al., 2011
<i>Acanthophis madagascarensis</i> (92-SnN-75)*	??	Squamous cell carcinoma	Frye, 1994
<i>Dendroaspis polylepis</i>	Black Mamba	Biliary adenocarcinoma with sarcomatous desmoplasia	Ramsay et al., 1996
<i>Naja atra</i>	Chinese Cobra	Carcinoma (pancreas?)	Machotka and Whitney, 1980
<i>Naja haje</i> (87-B-51)	Egyptian cobra	Papillary adenoma	Frye, 1994
<i>Naja melanoleuca</i>	Black-and-white Cobra	Venom gland carcinoma	Hill, 1952
<i>Naja melanoleuca</i>	Black Cobra	Osteochondrosarcoma (spinal column)	Wadsworth, 1954a, b
<i>Naja melanoleuca</i> (?)	“African Black Cobra”	Osteochondroma (dorsal aspect of spinal column)	Wadsworth, 1954b
<i>Naja melanoleuca</i> ♂	Black Cobra	Ductular adenocarcinoma (pancreas)	Sykes and Trupkiewicz, 2006
<i>Naja naja</i>	Indian Cobra	Biliary adenoma	Ramsay et al., 1996
<i>Naja naja</i>	Indian Cobra	Renal adenoma	Ramsay et al., 1996
<i>Naja naja</i>	Indian Cobra	Adrenal adenoma	Ramsay et al., 1996
<i>Naja naja</i>	Indian Cobra	Bile duct adenoma	Cowan, 1968
<i>Naja naja</i>	Indian Cobra	Ganulosa cell tumor	Ramsay et al., 1996
<i>Naja naja</i>	Indian Cobra	Pancreatic carcinoma	??
<i>Naja naja</i>	Indian Cobra	Granuloma (head and neck)	Wadsworth, 1956

<i>Naja naja</i> (80-68452)	Indian Cobra	Seminoma	Frye, 1994
<i>Naja naja</i> (RTLA 560)	Indian Cobra	Leiomyosarcoma	Machotka and Whitney, 1980
<i>Naja naja</i> ♀	Indian Cobra	Hepatocellular carcinoma (liver)	Catão-Dias and Nichols, 1999
<i>Naja naja</i> ♀	Indian Cobra	Hepatocellular carcinoma (liver)	Catão-Dias and Nichols, 1999
<i>Naja nigricollis</i> (90-SB-63)	Black-necked Spitting Cobra	Renal, Tubular adenoma	Frye, 1994
<i>Naja nigricollis</i> ♀	Black-necked Spitting Cobra	Lymphosarcoma	Effron et al., 1977
<i>Naja nigricollis</i> ♂	Black-necked Spitting Cobra	Bile duct adenoma	Cowan, 1968
<i>Naja nigricollis</i>	Black-necked Spitting Cobra	Osteochondrosarcoma (Metastatic to Spleen and Kidney)	Machotka and Jacobson, 1989
<i>Naja nivea</i> ♂	Cape Cobra	Bronchogenic adenocarcinoma	Effron et al., 1977
<i>Naja sp.</i> (93-SnN-82)	Cobra	Hepatoma, malignant	Frye, 1994
<i>Naja sp.</i> (haje?)	Egyptian cobra	Lymphosarcoma (heart and liver)	Cowan, 1968
<i>Ophiophagus hannah</i>	King Cobra	Lymphoma	Willette et al., 2001
<i>Ophiophagus hannah</i> ♀	King Cobra	Tubular adenoma (kidney)	Catão-Dias and Nichols, 1999
<i>Ophiophagus hannah</i> ♀	King Cobra	Chondrosarcoma (vertebra)	Vico et al., 2016
<i>Pseudechis porphyriacus</i> ♀	Red-bellied Black Snake	Papillomas of skin; adenomatous proliferation of intrahepatic bile ducts	Effron et al., 1977
<i>Pseudechis sp.</i>	Black Snake	Fibrosarcoma	Wadsworth, 1956
<i>Walterinnesia aegyptia</i>	Sinai Desert Cobra	Renal adenocarcinoma	Frye, 1991a
<i>Walterinnesia sp.</i> (88-N-01)	Black Desert Cobra	Renal tubular adenoma	Frye, 1994
“Elapid”	Cobra (?)	Adenocarcinoma (Pancreas)	Ratcliffe, 1943

¹Possibly *Acrantophis madagascariensis*, which is not an Elapid.

Table 2. Summary of bony neoplasms reported in non-avian reptiles.

Scientific name	Common name	Neoplasm	Reference
Squamata			
<i>Aspidites ramsayi</i>	Woma Python	Osteosarcoma	Cowan et al., 2011
Colubrid sp. (5)	-	Chondrosarcoma	Garner et al., 2004
Crotalid sp.	-	Osteosarcoma (vertebra)	Garner et al., 2004
Crotalid sp. (2)	-	Chondrosarcoma	Garner et al., 2004
<i>Crotalus ruber</i> (RTLA 984)	Red Diamond Rattlesnake	Undifferentiated sarcoma (dorsal and lateral to spinal column)	Harshbarger, 1975 (contributed by E. A. Holzinger)
<i>Cyclura cornuta</i>	Rhinoceros Iguana	Chondro-osteofibroma	Jacobson, 1981, Machotka, 1984
<i>Cyclura cornuta</i>	Rhinoceros Iguana	Osteochondrosarcoma, fibrosarcoma (legs and pelvis)	Rodhain, 1949
<i>Cyclura cornuta</i>	Rhinoceros Iguana	Osteochondrosarcoma, fibrosarcoma (pelvis)	Rodhain, 1949
<i>Cyclura nebula</i>	Cuban Lizard	Osteochondroma (humerus, femur, other)	Ippen, 1966
<i>Dendroaspis polylepis</i>	Black Mamba	Osteochondrosarcoma	Wadsworth, 1954a, b
Elapid sp.	Cobra (?)	Osteosarcoma (extraskeletal)	Garner et al., 2004
<i>Gekko gecko</i>	Tokay Gecko	Mineralized carcinoma in endolymphatic sac	Sander et al., 2015
<i>Gerrhosaurus sp.</i>	Plated Lizard	Chondrosarcoma (humerus)	Garner et al., 2004
<i>Iguana iguana</i> ♀	Common Green Iguana	Osteosarcoma	Dietz et al., 2015
<i>Iguana iguana</i>	Common Green Iguana	Osteochondroma (legs)	Ippen, 1966
<i>Iguana iguana</i> ♀	Common Green Iguana	Osteosarcoma (fibroblastic)	Dietz et al., 2015
<i>Lacerta viridis</i>	Emerald Lizard	Osteosarcoma (multiple)	Jacobson, 1981
<i>Lacerta viridis</i> ♀	European Green Lizard	Osteomas (tail vertebrae)	Stolk, 1958
<i>Naja melanoleuca</i>	African Black Cobra	Osteochondrosarcoma (spinal column)	Wadsworth, 1954b

<i>Pantherophis guttatus</i>	Corn Snake	Chondrosarcoma (mandible)	Schmidt and Reavill, 2012
<i>Pantherophis guttatus</i>	Corn Snake	Chondrosarcoma	Mauldin and Done, 2006
<i>Pantherophis guttatus</i>	Corn Snake	Chondrosarcoma (vertebra)	Dawe et al., 1980
<i>Pantherophis guttatus</i>	Corn Snake	Chondrosarcoma (vertebra)	Garner and Collins, 1995
<i>Pantherophis guttatus</i>	Corn Snake	Chondrosarcoma	Hoff et al., 1984
<i>Pantherophis guttatus</i>	Corn snake	Chondrosarcoma	Harshbarger, 1974
<i>Pantherophis guttatus</i> ♀	Corn snake	Osteosarcoma (ribs)	Simard, 2016
<i>Pantherophis obsoletus</i>	Black Rat Snake	Undifferentiated sarcoma with osseous metaplasia (Abdominal cavity and liver)	Machotka and Whitney, 1980 (contributed by R. S. Wilhelm)
<i>Pantherophis obsoletus obsoletus</i>	Western Rat Snake	Chondrosarcoma (vertebra)	Honour et al., 1993
<i>Pogona vitticeps</i>	Central Bearded Dragon	Osteosarcoma (fibroblastic)	Dietz et al., 2015
<i>Python bivittatus</i>	Burmese python	Osteosarcoma (mandible)	Frye, 1991a
<i>Rhamphiophis rostratus</i>	Rufous-beaked Snake	Osteosarcoma (spine)	Hill, 1955
<i>Uromastix dispar maliensis</i>	Sudan Mastigure	Periosteal chondroma (juxtacortical bone)	Gál et al., 2007
<i>Varanus acanthurus</i> ♂	Spiny-tailed Monitor Lizard	Chondroblastic osteosarcoma	Needle et al., 2013
<i>Varanus acanthurus</i> ♂	Spiny-tailed Monitor Lizard	Chondroblastic osteosarcoma	Needle et al., 2013
<i>Varanus bengalensis</i>	Bengal Monitor	Osteochondroma (neck)	Frye, 1991b
<i>Varanus bengalensis nebulosus</i> (juv.)	Bengal Monitor	Osteocartilaginous exostoses	Frye, 1991a
<i>Varanus dracoena</i>	Indian Monitor	Enchondroma (multiple bones)	Bland-Sutton, 1885
<i>Varanus griseus</i>	Desert Monitor Lizard	Osteochondrosarcoma	Schönbauer et al., 1982
<i>Varanus salvator</i>	Common Water Monitor	Chondromatous enlargement on hyoid	Hill, 1957
<i>Varanus salvator</i> ♀	Common Water Monitor	Osteoid osteoma (vascular)	Hill, 1957
Viperid sp.	-	Osteosarcoma (vertebra)	Garner et al., 2004

Viperid sp. (2)	-	Chondrosarcoma	Garner et al., 2004
?	“Lizard”	Chondrosarcoma	Hernandez-Divers and Garner, 2003
?	“Unidentified snake”	Osseous metaplasia (Subcutis)	Ramsay et al., 1996
Chelonia			
<i>Chelonoidis</i> sp. (TAMU 219609)	Galapagos Tortoise	Osteoma	Christman et al., 2017
<i>Cyclenys dentata</i>	Asian Leaf Turtle	Adenocarcinoma (femur)	Gál et al., 2010
<i>Gopherus agassizii</i>	California Desert Tortoise	Chondroma (carapace)	Roskopf, 1986
<i>Pseudemys rubriventris</i> ♀	Northern red-bellied turtle	Mucinous melanophoroma (humerus)	Bielli et al., 2015
<i>Syllomus aegyptiacus</i>	[Extinct species]	Osteoma (or osteoblastoma)	Weems, 1974; Rothschild et al., 2013
Crocodylia			
<i>Caiman crocodilus</i> ♂	Spectacled Caiman	Osteosarcoma (vertebra)	Kalin, 1937
<i>Caiman crocodilus</i> ♂	Spectacled Caiman	Osteoma (skull, shoulder)	Kalin, 1937
<i>Crocodylus porosus</i> ♀	Saltwater Crocodile	Osteoma and osteosarcoma (hands and radius)	Kalin, 1937
<i>Leidyosuchus</i> (= <i>Borealosuchus</i>) <i>formidabilis</i>	[Extinct species]	Osteoma, chondroma	Sawyer and Erickson, 1998

Figure Legends

Figure 1. Vertebral osteosarcoma in a new world elapid snake, *Micrurus ancoralis* (UTA R-55945). Pairs of vertebrae from unaffected (A, B) and pathologic (C, D) regions of the spine as shown with micro-computed tomography. Blood vessels (in red) and ligament and cartilage (in blue) are shown (B and D) for each pair. Chaotic vasculature is shown in green for pathologic vertebrae (D). From left to right, views are cranial, caudal, dorsal, ventral, and both lateral angles. Scale bars are 1 mm.

Video S1. Section of vertebrae surrounding a vertebral osteosarcoma in *Micrurus ancoralis* (UTA R-55945). Available from MorphoSource:

http://www.morphosource.org/Detail/MediaDetail/Show/media_id/34110.

Video S2. Pair of normal vertebrae in *Micrurus ancoralis* (UTA R-55945). Blood vessels are shown in red and connective tissues are shown in blue. Available from MorphoSource:

http://www.morphosource.org/Detail/MediaDetail/Show/media_id/34108.

Video S3. Fused pair of pathologic vertebrae in *Micrurus ancoralis* (UTA R-55945). Blood vessels are shown in red, chaotic vasculature is shown in green, and connective tissues are shown in blue. Note the blunted and nearly absent neural spine and indistinguishable nature of the two vertebrae. Available from MorphoSource:

http://www.morphosource.org/Detail/MediaDetail/Show/media_id/34109.