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**ULTRASONOGRAPHY AND PATHOLOGY OF GENITAL TRACT LEIOMYOMAS  
IN CAPTIVE ASIAN ELEPHANTS:  
IMPLICATIONS FOR REPRODUCTIVE SOUNDNESS**

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**Introduction**

Leiomyomas (leiomyomata, fibroleiomyomas, fibroids, myomas) are benign spindle-cell tumors of smooth muscle origin that arise from the involuntary muscle layers usually of hollow viscous organs. In humans, leiomyomas are the most common tumor of the tubular genital tract in 20% of woman over 30 years of age often associated with

infertility, menorrhagia and/or dysmenorrhea (ADASHI et al., 1996, Porter et al., 1995). In domestic animals, genital tract leiomyomas are most common in the bitch, and are rarely encountered in most other domestic species including goats, ewes, sows, cows and mares.

In a post mortem study between 1975 and 1995 of approximately 30,000 exotic mammal cases at the Institute for Zoo Biology and Wildlife Research (IZW) Berlin,

Table 1: Necropsy Prevalence of Leiomyomas from Mammal in Selected US and European Zoos  
(From HILDEBRANDT et al., 1995)

Species	# of ♀ with leiomyomas	# of ♀ with necropsied	Prevalence	Distribution/Location of leiomyomas
Asia elephant, <i>Elephas maximus</i>	27	27	100%	multiple/uterus
Indian Rhinoceros, <i>Rhinoceros unicornis</i>	4	5	80%	multiple/uterus, cervix, vagina
Bactrian camel, <i>Camelus bactrianus</i>	1	23	4%	solitary/vagina
Clouded leopard, <i>Panthera nebulosa</i>	4	23	17%	multiple/uterus, cervix
Asian Lion, <i>Panthera leo persica</i>	3	24	12%	multiple/uterus, cervix
Leopard, <i>Panthera pardus</i>	4	9	44%	multiple/uterus
Bengal tiger, <i>Panthera tigris tigris</i>	2	27	7%	solitary/uterus, cervix
Lesser Grison, <i>Galictis cuja</i>	2	2	100%	multiple/uterus
Giant panda, <i>Ailuropoda melanoleuca</i>	1	1	100%	multiple/uterus
Maned wolf, <i>Chrysocyon brachyurus</i>	1	11	9%	solitary/vagina
Opossum, <i>Monodelphis domestica</i>	2	25	8%	solitary/uterus
Rock cavy, <i>Kerodon rupestris</i>	1	22	4%	multiple/uterus
Pere David's deer, <i>Elaphurus davidianus</i>	1	31	3%	multiple/uterus
Guinea pig, <i>Cavia porcellus</i>	1	48	2%	solitary/uterus

and the Smithsonian Institution, Washington DC, (HILDEBRANDT et al., 1995) leiomyomas were found in the uterus, cervix, and vagina in 14 species of exotic mammals (Table 1). These animals originated from the Smithsonian's National Zoological Park (NZP) and from multiple zoos in Europe. This study indicated a very high necropsy prevalence of genital tract leiomyomas in Asian elephants as compared to other species.

Asian elephants are considered endangered by the International Union for the Conservation of Nature and Natural Resources (IUCN) and are the focus of intensive global captive management programs for species survival purposes. Asian elephants are difficult breeders, and establishing conditions for successful reproduction has been difficult. One reason may be the common persistence of leiomyomas in their reproductive tracts which are usually subclinical but may cause interference or signify abnormalities with reproductive mechanisms.

In humans, the etiology and symptomatology of genital leiomyomas are still not fully understood but are believed to be related to dysharmonia of the ovarian steroid hormones; consequently, clinical management of these tumors in women patients has not been consistent.

The purpose of this paper is to describe some newer aspects of transrectal ultrasonographic imaging techniques in female Asian elephants that were used to detect leiomyomas of their reproductive tracts by correlative pathological examinations. Recent surveys of genital tract leiomyomas in elephants kept in North American and European zoos are also described and compared with reported cases of genital tract leiomyomas in other species and in women, emphasizing the potential impact of these tumors on reproduction.

## Material and Methods

**Ultrasonographic Imaging work:** The reproductive health and aspects of the sexual cycle were assessed in 33 captive, non-sedated Asian Elephants from European Zoos by transrectal ultrasonographical examination of the uterine tracts. Ultrasonographic equipment used was an S 9100 Oculus, Ecoscan with a 3.5 MHz probe and a specially designed 7.5 Mhz ultrasound probe for transrectal use in elephants to enlarge the examiners field of exploration and to achieve better sonographic coupling. (HILDEBRANDT and GÖRITZ, 1995; GÖRITZ et al., 1995). Post mortem transrectal sonograms of the genital tracts were performed on five additional European Zoo Asian elephants that died or were euthanized for humane reasons unrelated to reproductive tract abnormalities. The sonograms were correlated with pathologic examinations of the elephants' reproductive tracts carried out right after the ultrasonography. Video recordings of all ultrasonographic examinations underwent detailed retrospective analysis.

**Pathology studies:** Necropsy findings in the reproductive tracts of the five captive Asian elephants from Europe,

together with pathology data from a survey obtained from North American Zoos (via co-author E. RAMSAY) from the reproductive tracts of 18 female Asian and eight African elephants 20 years and older that died between 1985 and 1995 were analyzed, compared and collated. Specimens taken from selected genital tract masses described in many of the cases were routinely processed in paraffin and determined to be uterine leiomyomas by histopathological examination.

## Results

**Ultrasound studies:** Masses consistent with leiomyomas (as determined by the correlative post mortem ultrasonographic and necropsy studies in the five captive elephants from Europe) were evident within the uteruses of 10/33 Asian elephants examined by transrectal ultrasonography. The masses were characterized as spherical, structures with hyperechogenic borders (Fig. 1). Up to 20 masses were distributed throughout the uterus and ranged from 2 to 20 cm in diameter; in a few cases masses were limited to the body and posterior segment of the uterine horns. Changes of leiomyomas in size and echostructure attributed to the sexual cycle were also noted; during estrus tumors appeared larger and more hypoechogenic. Other abnormalities of the uterus by ultrasono-



Fig. 1: Sonogram of a uterine leiomyoma in an Asian elephant



Fig. 2: Gross appearance of a uterine Leiomyoma in cross-section

Table 2: Results of Transrectal Ultrasound Examinations in 33 Asian Elephant Cows from European Zoos with and without Imaging Evidence of Uterine Masses

ID	age (years)	reproductive status	sexual cycle	Leiomyomas		
				presence	severity	location
<b>Asian elephant</b>						
24Mü	~7	nulliparous	no	no	-	-
27Sp	~14	pregnant	no	no	-	-
12Ro	~15	pregnant	no	no	-	-
13Ro	~15	pregnant	no	no	-	-
1HH	~17	primiparous	yes	no	-	-
23Se	~16	nulliparous	yes	no	-	-
26Mü	~19	nulliparous	yes	no	-	-
22Se	~20	nulliparous	yes	no	-	-
20Wo	~20	nulliparous	yes	no	-	-
9	~20	nulliparous	?	no	-	-
11	~20	nulliparous	?	no	-	-
14DC	~20	primiparous	yes	no	-	-
32Sp	~22	nulliparous	yes	no	-	-
16St	~22	aborted	yes	no	-	-
17St	~22	nulliparous	irregular	no (cystic)	-	endometrium
28Sp	~22	nulliparous	no	no	-	-
15St	~25	primiparous	no	no	-	-
7	~28	primiparous	yes	no	-	-
8	~28	nulliparous	no	no	-	-
18Wo	~29	aborted	yes	no	-	-
31Sp	~31	pluriparous	yes	no	-	-
33Sp	~32	nulliparous	yes	no	-	-
6	~35	primiparous	yes	no	-	-
10	~21	nulliparous	?	yes	2+	uterine body
2	~27	nulliparous	yes	yes	2+	entire uterus
5	~28	nulliparous	yes	yes	3+	entire uterus
19Wo	~28	nulliparous	irregular	yes	3+	entire uterus
4	~30	nulliparous	yes	yes	3+	entire uterus
34Mü	~30	nulliparous	yes	yes	2+	uterine horns
21Se	~30	nulliparous	yes	yes	2+	uterine horns
3	~31	nulliparous	yes	yes	2+	entire uterus
29Sp	~32	nulliparous	yes	yes	2+	uterine horns
30Sp	~46	nulliparous	yes	yes	4+	entire uterus

Key grade	#of tumors	diameter (cm)
1+	≤ 5	≤ 3
2+	≥ 5 ≤ 10	4 – 6
3+	≥ 11 ≤ 20	7 – 12
4+	≤ 21	13 – 20
5+	≥ 21	21 – 25

graphy in elephants with the masses were not evident. The elephant cows with these uterine masses ranged in age from 21 to 46 years old. The 23 elephants without uterine masses were from seven to 35 years old and with the exception of one cow with a cystic endometrium, other abnormalities were not evident. Parity and status of sexual cycle of each animal are noted in Table 2.

**Pathological Studies:** As noted in Table 3 a total of ten uterine leiomyoma cases (five from European post mortem cases and five from North American survey) were identified from 23 necropsied Asian elephants. The necropsy prevalence of these benign genital tract neoplasms in female Asian elephants ranged from 100% (5/5 reproductive tracts examined) in the European cases, to 28% (5/18 reproductive tracts examined) in the

Table 3: Combined post mortem findings of 10 Asian Elephant cows from European and US Zoos with Uterine Leiomyomas

ID	age (years)	reproductive status	sexual cycle	Leiomyomas		
				presence	severity	location
<b>Elephants from Europe</b>						
P1	~60	primiparous	no	yes	1+	uterine bifurcation
P2	~34	nulliparous	yes	yes	4+	entire uterus
P3	~38	nulliparous	yes	yes	3+	entire uterus
P4	~34	nulliparous	yes	yes	5+	entire uterus
P5	~54	nulliparous	yes	yes	5+	entire uterus
<b>Elephants from North America</b>						
Suzie	~47	nulliparous	yes	yes	2+	entire uterus
Maya	~51	nulliparous	yes	yes	4+	entire uterus
Lucki	~50	?	yes	yes	3+	entire uterus
Marie	~42	nulliparous	yes	yes	4+	entire uterus
Pumi	~34	?	?	yes	present	entire uterus

(key same as for Table 2)

North American Zoo survey for a combined necropsy prevalence of 43%. Leiomyomas were not found in any of the eight African elephants from the North American survey. The tumors usually appeared as well circumscribed sessile masses within the wall of the uterine components. Tumors were often multicentric, ranged from 2 cm up to 25 cm in diameter and were distributed throughout the uterus (Fig. 2). In a few cases the tumor masses were limited to the body and posterior segment of the uterine horns. The cut surfaces of the tumor masses were yellowish-white and had a fibrous appearance. Some of the larger masses had liquid, hemorrhagic and/or necrotic centers. Histologically the tumors consisted of well-differentiated, smooth muscle-like cells that formed whorls and interlacing patterns. In a few of the leiomyoma cases, cystic changes in the ovaries and endometrium were also described and a malignant cervical tumor occurred in one of the Asian elephants without uterine leiomyomas.

## Discussion

As noted in the results, Asian elephants appear to have a high prevalence of uterine leiomyomas based on correlative post mortem findings and ultrasonographic examination. Masses observed post mortem by transrectal ultrasonographic imaging in the 5 elephants from European Zoos were compatible with the size and distribution of uterine leiomyomas identified later at necropsy in the same 5 elephants and were proven as benign tumors of smooth muscle origin by histopathological examination. As noted in Table 2, trends coincident with these leiomyomas in Asian elephants include increased tumor involvement and severity with aging, a functioning sexual cycle, and no consistent association with any other anatomical reproductive tract abnormalities.

This high prevalence in Asian elephants may exceed the 20 – 25% incidence of uterine leiomyomas (fibroids) in women of reproductive age, 40% of whom have a history of infertility (ADASHI et al., 1996). The exact mechanism of leiomyoma formation in women is unclear but is thought to be related to hyperestrogenic states either from abnormal physiologic responses to estrogen or increased estrogen receptor sites with hyperstimulation of the putative smooth muscle tumor cells. The role of estrogen as a causative factor has been experimentally supported by estrogen responsiveness (PORTER et al., 1995) and subsequent inhibition by tamoxifen (a non-steroidal anti-estrogen) of an Eker rat leiomyoma-derived cell line *in vitro*, and a nude mouse xenograft of leiomyoma tumor cells *in vivo* (HOWE et al., 1995; EVERITT et al., 1995).

Use of synthetic gonadatropin releasing hormones (GnRH), e.g., leuprolide acetate, (Lupron Depot, TAP Pharmaceuticals, Inc., Deerfield, IL 60015) an analog of luteinizing hormone releasing hormone (LHRH) apparently abolishes estrogen stimulation. Lupron has been used therapeutically in women to reverse uterine leiomyomas in order to improve fertility and to diminish injurious effects primarily by shrinkage of the large tumor masses. GnRH analogs have also been used in male elephants to control musth and one type, (Dekapeptyl®) has also been employed therapeutically in an Asian rhinoceros (*Rhinoceros unicornis*) with uterine leiomyomas with promising results (HILDEBRANDT and GÖRITZ, 1995). Therefore, GnRH analogs may be useful as a treatment for uterine leiomyomas after further research and a better understanding of this neoplastic condition in Asian elephants.

One other interesting comparative observation is the lack of any incidence of genital tract leiomyomas in African elephants in the North American survey and from other documented observations (HILDEBRANDT and

GÖRITZ, 1995; GÖRITZ et al., 1995). Routine assays for monitoring the sexual cycle of both Asian and African elephants have indicated no major differences in the sex steroids and metabolites between the two species (Personal communication, 1997, Dr. Janine BROWN, National Zoological Park, Front Royal, VA USA). It may be a species difference perhaps based on genetic factors. However, more in depth endocrinological studies are required to address these differences between Asian and African elephant species.

A similar tumor relationship exists between Asian and African rhinoceroses in that some Asian rhinoceros species are prone to leiomyomas of the tubular genital tract but this does not appear to be a problem in the African species. Leiomyomas were previously reported in the vaginal, cervical and uterine segments of four older adult Indian rhinoceroses (*Rhinoceros unicornis*) to which infertility was attributed (MONTALI et al., 1982). Several small uterine masses visualized by transrectal ultrasonography were considered as possible leiomyomas in two Sumatran rhinoceroses (*Dicerorhinus sumatrensis*), (SCHAFFER et al., 1994); whereas, to our knowledge, incidences of such tumors by ultrasonography or at necropsy have not been identified in any African species of rhinoceroses.

The high prevalence of genital tract leiomyomas in Asian elephants appears to be a very significant finding particularly in light of the negative effect these tumors have on fertility in women and other megavertebrates. Ultrasonographic studies have elucidated some very important preliminary findings in this study in Asian elephants. Further in depth work with ultrasonic imaging of the entire reproductive tract is required in elephants to correlate with endocrinological monitoring of the sexual cycle, breeding activities, and careful pathological examinations.

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## Summary

### Ultrasonography and Pathology of Genital Tract Leiomyomas in Captive Asian Elephants: Implications for Reproductive Soundness

Asian elephants in zoos from Europe and North America were found to have a high prevalence of uterine leiomyomas. This was based on ultrasonographic studies using a customized transrectal imaging instrument. Uterine masses were observed in 10/33 Asian elephants examined and correlated with post mortem sonograms and pathologic findings of leiomyomas in the reproductive tracts of five additional Asian elephants. Uterine leiomyomas were not found in any African elephant examined. As with women and female Asian rhinoceroses, the leiomyomas are considered detrimental to reproductive soundness in Asian elephants.

## Zusammenfassung

### Sonographie und Pathologie von Leiomyomen im Genitaltrakt von in Menschenhand lebenden Asiatischen Elefanten: Auswirkung auf den reproduktiven Zustand

Asiatische Elefanten europäischer und nordamerikanischer Zoos zeigten eine hohes Vorkommen uteriner Leiomyome. Hierzu durchgeführte sonographische Untersuchungen erfolgten mittels eines speziell angefertigten, transrektalen Ultraschalladapters. Strukturveränderungen der Gebärmutter konnten in 10 von 33 untersuchten Asiatischen Elefanten beobachtet werden und korrelierten mit post mortal erstellten Sonogrammen sowie pathologischen Befunden von Leiomyomen im Genitaltrakt fünf zusätzlich untersuchter Tiere. Bei keinem der untersuchten Afrikanischen Elefanten konnte ein Vorkommen von Leiomyomen beobachtet werden. Vergleichbar zur Frau und zu Asiatischen Nashornarten, scheinen Leiomyome einen negativen Einfluß zu haben auf den reproduktiven Zustand Asiatischer Elefanten.

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