EVALUATION OF THE NORMAL EQUINE PITUITARY GLAND

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(ABSTRACT)

Computed tomography (CT) is becoming more available as a diagnostic tool in the evaluation of the equine skull and brain. Objectives of this study were: 1) refine a CT protocol for evaluating the equine pituitary gland, 2.) define the CT anatomy of the pituitary region, 3.) determine a set of normal values for the pituitary dimensions (length, width, height, volume and weight), 4.) refine CT techniques for measuring pituitary size.

Horses were scanned using 10x10mm, 10x5mm, 4x4mm and 4x2mm slice thickness and interval combinations. The pituitary glands were removed immediately after CT and gross measurements were performed. CT measurements were compared with gross pituitary measurements using analysis of variance (ANOVA) in a randomized block design. Accuracy percentages were also calculated using gross measurements as the known value.

Mean dimensions of the histologically normal pituitary glands were: length 21.07mm, width 21.62mm, height 9.78mm and volume 2.66cm^3. The weights ranged from 1.7g to 3.4g with a mean of 2.6g. Computed tomographic measurement analysis demonstrated that the 10mm slices were the most accurate way to estimate the length of the gland. The 4mm slices yielded the highest accuracy values for width, height and volume of the pituitary gland. The volume was underestimated by all interval and slice

thickness combinations performed by CT. No evidence of an overlap effect was identified for any of the dimensions.

Our findings indicated that contrast-enhanced CT is an accurate technique for estimating pituitary linear dimensions. Three-dimensional CT volumetry may not be an accurate method for estimating pituitary volume.

DEDICATION

This thesis is dedicated to David Robert Fransen, Exxon, Belle, Catfish, Mogollon, Domino, Sandia, Cody, Rococo, Cohloe, Colelia, Ironto, and Stella. Thank you for your love and friendship.

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CHAPTER 1: REVIEW OF LITERATURE

Equine Pituitary Disease

The hypophysis cerebri or pituitary gland is an endocrine organ attached at the ventral midline to the diencephalon. The term pituitary is derived from a historical interpretation by Vesalius concerning the function of this gland as the source of nasal exudate, pituita, or phlegm[1]. This organ plays a major regulatory role in the endocrine system. It is in close communication between the nervous and endocrine systems.

The gland sits within the skull in the hypophyseal fossa, a depression in the dorsal aspect of the basisphenoid bone[2]. When the gland is viewed from a dorsal perspective, the rostral and caudal clinoid processes accentuate the boundaries of the fossa and form a bony complex called the sella turcica. The subarachnoid space does not invest the hypophysis[1]. The pituitary sits in the separation between the inner and outer dural layers. This creates a space with prominent cavernous and intercavernous sinuses surrounding the gland[3].

The gland itself is made up of two major divisions, the adenohypophysis and the neurohypophysis. The adenohypophysis consists of the pars tuberalis (pars proximalis), the pars intermedia, the cavum hypophysis, and the pars distalis. The neurohypophysis consists of the infundibulum (pars proximalis) and the lobus nervosus (pars distalis)[1]. The adenohypophysis is the glandular parenchyma with an extensive blood supply, the neurohypophysis is derived from downgrowth of the hypothalamus[1]. The gland is

suspended from the midline diencephalon at the hypothalamus by a stalk. The stalk is an extension of the median eminence from the hypothalamus and makes up the proximal portion of the neurohypophysis. The pars intermedia of the adenohypophysis is in direct contact with the neurohypophysis.

In the adult dog, the size of the pituitary gland is 1cm in length, 0.7cm in width and 0.5cm in depth. It weighs approximately 0.6grams[3]. In horses, the documented measurements of the normal pituitary gland are variable and sparse. One source says the pituitary measures 2cm in width and 1cm in height with a weight of 1-3grams[4], another source says the gland weights 1-3g, and has measurements of 2x2x0.5cm[5].

The pituitary is an organ of major importance in the endocrine system. The adenohypophysis portion of the pituitary produces several hormones including growth or somatotrophic hormone (GH), gonadotrophic hormones, adrenocorticotrophic hormone (ACTH), thyroid stimulating hormone (TSH), and prolactin. The neurohypophysis releases hormones including oxytocin and vasopressin (antidiuretic hormone, ADH). The pituitary gland of the horse is a source of several other hormones. Some of them have a common precursor, prohormone proopiomelanocortin (POMC) which is contained in both the pars intermedia and the pars distalis. Adrenocorticotrophic hormone in horses is formed in the pars distalis from POMC, the pars intermedia also contains POMC[6]. POMC is an important common source of many substances secreted by the pars

intermedia and the pars distalis. The pars intermedia of horses is also the source of ACTH, melanocyte stimulating hormone (MSH), Beta endorphins, and corticotropin like intermediate lobe peptide (CLIP)[7].

The release or production of hormones from the pituitary is regulated by the hypothalamus[1]. The production of hormones in the pars distalis is mostly controlled by corticotropin releasing factor and arginine vasopressin from the hypothalamus[8,9]. The hormone production in the pars intermedia is more under the influence of dopamine and other neurotransmitters, including serotonin, from the hypothalamus[10]. In most species, pars intermedia secretory control appears to be primarily through tonic inhibition by B-adrenergic and gamma-aminobutyric acid (GABA)[11].

Dysfunction or disease of the pituitary gland can lead to a plethora of clinical syndromes. Trauma, neoplasia, source irradiation (therapy), congenital defects, inflammation and idiopathic conditions can affect the pituitary[12]. While some diseases like pituitary hypofunction (hypopituitarism) lead to a deficiency of production of one or many hormones, others may lead to overproduction or overstimulation of hormones. A syndrome that may be caused by hypopituitarism is pituitary dwarfism, caused by a lack of GH. Neoplasia is an important disease of the pituitary gland. Neoplasia may cause a lack or overproduction of hormones. Tumors can be grouped into functional and nonfunctional neoplasm[12]. Functional tumors include adenomas of the pituitary gland.

Pituitary adenomas may lead to hypersecretion of ACTH and pituitary dependent hyperadrenocorticism (PDH) or (Cushing's disease)[13,14]. Feedback inhibition of excess

ACTH secretion is relatively ineffective, therefore the Cushing's disease evolves[15]. In animals and people, ACTH secretion functions in maintaining plasma cortisol concentrations at levels necessary for homeostasis. Chronic excessive secretion of ACTH results in excess cortisol secretion and eventually adrenocortical hyperplasia[15]. Other hormones besides ACTH may also be affected by a pituitary adenoma. Many of the clinical signs in horses with pituitary adenomas may be a result of over secretion of the POMC peptides as well as increased ACTH secretion. Hypersecretion of ACTH in some but not all horses with pituitary adenoma leads to adrenocortical hyperplasia and oversecretion of cortisol[16]. The secretion of other hormones is also affected [17,18,19,20].

Adenomas can be classified as microadenomas or macroadenomas. . Tumors under 1cm are considered to be microadenomas and are often not visible grossly. Those over 1cm are considered to be macroadenomas[21]. Fifty percent of dogs with PDH have tumors under 3mm in diameter. Those remaining had tumors between 3 and 12mm in diameter[22]. About 15% of dogs have large pituitary tumors (macroadenomas)[23]. The majority of adenomas in the horse appear to be macroadenomas. One study suggests that 30% of equine adenomas were evident only microscopically (microadenomas)[24].

Most dogs (80-85%) with Cushing's disease are affected by pituitary dependent hyperadrenocorticism. The remaining 15% of dogs have hyperadrenocorticism due to adrenal disease[15]. Unlike other animals (in particular the dog), where the adrenal glands can also cause hyperadrenocorticism, the pituitary gland is primarily responsible for this syndrome in the horse[15,25]. Hyperadrenocorticism in the horse has not been

documented other than in association with pituitary adenoma. There is a single case report of a horse with adrenal carcinoma, but endocrine studies were not conducted in that animal[25].

Adenomas in dogs are found in either the pars distalis or the pars intermedia of the adenohypophysis[15]. A small percentage of dogs with PDH have been diagnosed with pituitary hyperplasia. Most dogs with hyperplasia also have pituitary tumors[15]. Functional adenomas or adenomatous hyperplasia of the pars intermedia (of the adenohypophysis) is associated with Cushing's syndrome in the horse[26-28].

Pituitary adenomas are common in older horses[7]. They account for 1.4% of all benign tumors in horses[29]. One report cites an incidence of three to six cases per year in an equine practice[30]. Pituitary adenomas are classically a disease of older horses[29]. The mean age of horses affected with this disease is 21 years[31] with the youngest horse affected recorded at 7 years[18]. Horses are living longer and it has been suggested that 15% of the horse population is currently over 15 years of age[29] This disease may become more prevalent with a larger geriatric horse population.

Cushing's disease is usually suspected based on clinical signs and signalment. This condition is reported in all breeds and in both sexes. However, several recent studies report that it appears to be more common in females [28,32,33,34]. Cushing's horses frequently have a normal complete blood count and equine chemistry panel. Abnormalities may include mild neutrophilia and mild lymphopenia[4]. Hyperglycemia is present in many cases [35]. Clinical signs may arise as a sequel to the excess circulating

glucocorticoids, physical destruction of the pars nervosa, and increased circulating concentrations of POMC peptides [4].

There are a variety of clinical signs demonstrated in horses with Cushing's disease. Clinical signs include: hirsutism, weight loss, chronic laminitis, sole abscesses, hyperhidrosis (excessive sweating), polyuria-polydipsia (PU/PD), muscle wasting, weakness, behavioral change and increased susceptibility to infection[29,36,37,25]. These may be demonstrated individually or in concert. Clinical signs, like PU/PD have a broader list of differential diagnoses making identification of the original etiology more difficult. The most common reported clinical sign is hirsuitism, a long shaggy haircoat that does not shed out in warm weather. Hirsuitism is seen in 94% of the cases reported[16]. The cause of hirsuitism has been suggested to be physical pressure of the pituitary tumor on the thermoregulatory center of the hypothalamus[38]. This is different from PDH in dogs as dogs typically demonstrate alopecia. Polyuria-polydipsea caused by pituitary adenoma has many proposed etiologies, and may be multifactorial. One proposed etiology includes destruction of the pars nervosa by the enlarged pars intermedia, which is suspected to lead to decreased ADH secretion. Hyperglycemia, observed in many Cushing's horses, causes an osmotic diuresis. Cortisol can also directly elevate the glomerular filtration rate[4]. Laminitis may arise secondary to elevated cortisol levels however, it has been proposed that equine Cushing's disease may actually develop secondary to the chronic pain and stress of laminitis [39]. Hyperhidrosis probably has a multifactorial etiology. Equine sweat glands are reported to be entirely

under B-adrenergic control[40], there may be a specific B-adrenergic lesion in the Cushing's horse[4]. Central blindness has been associated with pituitary adenomas in horses[37].

Not all horses with pituitary adenoma have definitive clinical signs of pituitary disease. Some owners may fail to recognize clinical signs. Pituitary adenomas have been reported as incidental findings in 2 of 480 consecutive necropsies[41]. There is usually gross evidence of a pituitary neoplasm on post mortem exam. The tumor appears as a firm, lobulated mass on the ventral aspect of the brain and visual evidence of compression of the overlying hypothalamus, or optic nerves may be evident[25].

There are a variety of tests available to diagnose equine Cushing's disease. However, some sources suggest that there are limitations of standard endocrine tests for investigating Cushing's syndrome in horses[42,43]. Laboratory diagnosis of equine Cushing's disease can be difficult because of the variability in laboratory findings in Cushing's disease in the horse[16]. Standard endocrine tests may not give definitive results of Cushing's disease[42]. Adrenocorticotrophic hormone production by equine pituitary tumors may be quite variable[25] and some pituitary adenomas do not elevate ACTH. Cortisol levels are elevated by exercise, hypoglycemia and surgery [44]. Erroneously high cortisol readings can also be caused by the stress of shipping or hospitalization[45], and by horses unaccustomed to blood sampling[44]. Evaluation of baseline or resting blood cortisol concentration in horses with Cushing's disease is generally indistinguishable from that in normal horses[46] and may be elevated in normal

horses due to the above mentioned reasons. Therefore blood cortisol level evaluation is not a definitive way to diagnose Cushing's disease.

There are a few endocrine tests that are routinely used to diagnose pituitary adenomas. Dexamethasome suppression tests are economical and convenient[29]. This test can be quite helpful in the evaluation of pituitary-adrenocortical function. A normal horse demonstrates 80% depression in plasma cortisol levels 1 hour after injection[47,8,46]. This depression of cortisol persists for approximately 24 hours in normal horses. In horses with pituitary adenomas the response is more modest indicating a lack of response of the pars intermedia to glucocorticoid feedback[46,48] Adrenocorticotrophic hormone- stimulation (a.k.a. ACTH challenge) and basal ACTH concentrations have been used for diagnosis of an adenoma of the pars intermedia of the pituitary gland in horses[31]. Results of ACTH stimulation in normal horses reveal a two to three fold increase in the cortisol levels by 8 hours after injection. If a horse has an active pituitary adenoma the response is very exaggerated and may result in a four-to sixfold increase in cortisol[47,8,49]. The insulin tolerance test has been proposed as a diagnostic test. However this test is typically only useful if the horse is hyperglycemic[4]. Many sources indicate that absolute conformation of a diagnosis of equine Cushing's disease requires post mortem examination to identify pituitary adenomas with histopathologic evidence[25,24].

Currently there are several treatment options available. Supportive care is important. Affected horses require good nutrition, de-worming, preventive hoof care and

routine vaccinations, and dental care. Medical treatment of equine Cushing's disease includes the use of one of two types of drugs; dopamine agonists or seratonin antagonists. Bromocriptine and pergolide are the two most commonly used dopamine agonists[50,51,52,53]. Cyproheptadine, a serotonin antagonist, has also been used with success[7].

Equine Computed Tomography

Computed tomography (CT) creates cross-sectional images using x-rays and computers[54,55]. The CT image is made of the colors black, white and shades of gray assigned to tiny squares called pixels or picture elements. The pixels are two-dimensional representations of tissue. Each pixel represents a block of tissue called the voxel. Voxels are the three dimensional block of tissue. These are determined by the slice thickness set by the scan operator on the computer. [56,54,55]. The CT detectors assign a numerical value based on the density of the tissue in the pixel and the computer processes this into an image. A CT scan consists of a number of slices or images through the area of interest. Computed tomographic images can be manipulated to produce three-dimensional or volume rendered images[57]. This gives superior soft tissue differentiation[56]. Due to the overlying cranial vault, the pituitary can not be visualized

with conventional radiographs. The ability to visualize the pituitary without superimposition of overlying structures is a major advantage of CT [55,58,56]. This makes CT a good tool for evaluating the pituitary gland.

One of the main limiting factors for performing equine CT is patient size. The large weight of the patient makes a special positioning table mandatory[59]. Another limitation is the presence of beam hardening artifacts caused by the large bony prominences of the equine skull. A beam hardening artifact causes dark streaks in areas near high density-low density interfaces [56]. This artifact obscures visualization of structures in it's path. Another inherent limitation of CT is partial volume averaging. Partial volume averaging is a misrepresentation of the data presented in a CT image and is caused by a partial volume effect [56,60]. If two structures in a voxel have a wide variation or difference in density, then the computer averages the density and gives an average CT number. This occurs at the edges of a structure that is curved and may give a false interpretation of the edges or thickness[56].

There are increasing numbers of referral institutions in the United States that have large animal CT capability. Currently, these institutions include Washington State University, University of California Davis, Oklahoma State University, NC State University, and Cornell University. More Universities and private referral institutions, including the Virginia-Maryland Regional College of Veterinary Medicine, are considering the addition of an equine CT table. The cost of a scan is affordable for many equine owners. Equine insurance will cover this procedure in some cases. Equine CT is

a valuable asset in the evaluation of cranial diseases[61] and this technology can only improve the quality of diagnostic procedures available to equine patients.

Designs for CT equipment and protocols for evaluating the equine head have been previously described[62,57]. General anesthesia is needed[62,59]. The horses may be placed in dorsal [59] or lateral recumbency [62]. The normal CT anatomy of the adult horse skull and foal head has been published, however little detailed information on the pituitary region was included in these reports[61,63]. The slice thickness and interval spacing used in equine studies has varied but common protocols include 5mmx5mm slices [63] and 10x10mm slices [36,62]. Specific details on the pituitary gland were not included in these atlases. No reports detailing the CT appearance of the normal adult equine pituitary gland were found.

Computed tomography has been established as a useful technique for evaluating complex problems of the equine skull. These include fractures[57], tooth root abscesses[59], ethmoid hematomas, paranasal cysts and other neoplastic conditions[59]. Previous studies have also found CT to be a valuable tool in evaluating equine brain abscesses and neoplasms[64]. Pituitary tumors in horses have been evaluated using CT by many different investigators[36,42,37,59]. In horses, CT scans allow clear visualization of the equine pituitary gland [42,62]. On computed tomography, the normal human pituitary gland is described as isodense with brain tissue; and enhances uniformly after contrast medium is given because of the gland's incomplete blood-brain barrier [65]. Human pituitary tumors can appear hypodense, isodense or hyperdense in unenhanced scans [66].

The dimensions of equine pituitary tumors (macroadenomas) can vary depending on the case. Gross measurements of different reported adenomas include a tumor with a height of 1.5cm [42] and another tumor 3.5cm in diameter[37]. Gross enlargement of the gland was readily detected and quantified with CT in those horses with pituitary tumors. The linear computed tomographic measurements corresponded closely with actual dimensions of the gland at necropsy[42]. CT has aided in the approaches to treatment and surgical management of lesions by determining the extent of disease and surrounding tissue involvement [67,68]. This technique may also be useful for assisting clinical investigation of new therapeutic agents for the treatment of pituitary adenomas[42]. This has been done for people with pituitary adenomas [69] but no report has been found documenting this use in the equine patient.

In the past, along with hormonal studies, CT scanning was the preferred technique for diagnosis of pituitary tumors in people [36,70]. One report established that CT images obtained with contrast enhancement were able to provide accurate delineation of human pituitary microadenomas [65]. More recently there is some indication that the use of CT to evaluate the soft tissue structures of the human brain may not be as accurate as MRI. According to one study, CT failed to diagnose pituitary lesions in 70% of human patients with pituitary dependent Cushing's disease [71]. Magnetic resonance imaging (MRI) is becoming the predominant tool in the evaluation of the human brain. However, MRI is less available than CT for equine patients. Computed tomography is used frequently in the small animal patient to evaluate head disorders. This includes

assessment of skeletal as well as soft tissue structures. Findings from previous reports indicate that CT can detect canine pituitary tumors [72,15,73].

Future uses of CT include the use of dynamic contrast studies to differentiate tumor types. This application has been promising in people and dogs[74]. Changes in the enhancement pattern of the pituitary gland may allow distinction between abnormalities in the adenohypophysis versus the neurohypophysis. Diagnosis of pituitary microadenomas and/or small macroadenomas may be possible in dogs and people using this technique[74]. It is possible that this may be applicable to equine patients as well.

Computed Tomographic Measurements

Soft tissue structures can be measured using length, width and height values; or by three-dimensional volume. The accuracy of CT measurements may be affected by several factors. First, the window level setting can affect the accuracy of measurements[75]. The window level is the midpoint for the range of the window width values[76]. When a CT scanner creates an image it assigns a value (a number) to the voxel based on tissue density. These values are expressed in Hounsfield units (HU). The CT number (HU) for the brain is between 30 and 42[76]. The window width describes the range of CT values of the gray scale within the image. As CT numbers along edges of anatomical structures are included in or excluded from the numerical range chosen, those edges may appear to shift in position altering the apparent size of the structure[77]. The

window level setting can affect measurement accuracy for cylindrical objects. The shape of the object actually affects the CT number. If the CT number is assigned incorrectly (due to the window level) this could alter the appearance of the object in question, making measurements less precise[75].

A second factor that can effect CT measurement accuracy is partial volume averaging. An object only partially included in the CT slice has less affect on the x-ray transmission data than if it extended completely through the slice[75]. CT numbers are inaccurate for spheres smaller than the CT slice width [75]. The edges of the object of interest may be affected by partial volume averaging. Because the edges are not clearly seen, the measurements may be less precise. Slice thickness and interval spacing may affect measurement accuracy. A report on human craniofacial deformities suggested that thinner slices permit more accurate 3D CT volume measurements [78]. Thinner slices decrease the amount of partial volume averaging artifact and in theory would make measurements more precise. To obtain as precise a measurement as possible, 50% overlap is recommended [79,80].

At the time of this study there was little information about the accuracy of CT measurements with regard to the equine pituitary gland. In previous reports describing CT measurements of equine pituitary tumors, there was no clear description of how measurements were performed [36,42,37]. Accuracy of 2D versus 3D CT volume measurements have not been compared. In one case report of a horse with pituitary adenoma, measurements of the pituitary gland from 2D CT and gross were found to be

similar [42]. However, in studies evaluating canine adrenal glands, differences were found between the gross measurements and the CT measurements [73]. Other literature that has analyzed geometric objects has shown that there is a degree of measurement error present[80,81-83].

Three-dimensional CT volumetry is a newer technique that calculates volume from hand-tracings of the outer margins of a structure in sequential transverse CT images. Three-dimensional CT volumetry has been reported to provide a more accurate representation of facial bones[78] and bone grafts[79]. However, the technique has had variable accuracy for assessing brain tumor size in human studies. One report says that CT volume measurements were accurate for assessing tumor size when compared to autopsy measurements [84]. Another paper found that volume measurements were not accurate in assessing tumor size [85]. No information was found with regard to the use of 3D CT volumetry in the evaluation of the size of the normal or diseased equine pituitary gland.

CHAPTER 2: EVALUATION OF THE NORMAL EQUINE PITUITARY GLAND

Introduction

Pituitary dependent hyperadrenocorticism, or Cushing's disease, is an important endocrine disorder in older horses. Cushing's disease in horses is most often caused by a pituitary adenoma. This is a benign neoplasm located in the pars intermedia of the pituitary gland. Pituitary adenomas account for 1.4% of benign tumors in horses[29]. Affected horses may suffer from weight loss, kidney dysfunction, muscle wasting, increased susceptibility to infection and hirsuitism. The identification of Cushing's disease may be complicated in the horse. The clinical signs can be non-specific. A diagnosis of Cushing's disease may also be difficult with some laboratory procedures. For example, blood cortisol levels can be elevated by other causes such as exercise, hypoglycemia, stress and surgery [44]. Currently, dexamethasone suppression tests are the standard method of laboratory diagnosis.

Computed tomography (CT) is becoming more available as a diagnostic tool in the evaluation of the equine skull and brain. CT is non-invasive and generally cost permissive. This tool may be especially advantageous when a horse has vague clinical signs. CT could also be helpful in monitoring current and/or new treatment protocols. Early detection and treatment of Cushing's disease would benefit horses by helping to reduce organ damage caused by elevated cortisol levels and secondary infections. By

obtaining baseline data on the CT appearance of the normal equine pituitary gland and refining CT techniques for measuring the gland, future researchers and practitioners will be able to more accurately diagnose pituitary adenoma and evaluate response to therapeutic agents. Another advantage of CT is the ability to make volume and linear measurements of structures of interest. In humans, three-dimensional CT is an established technique for measuring the volume of structures, including tumors [79,84]. Traditional length, width and height measurements may also be valuable in ascertaining the boundaries and size of tumors.

At the time of this study, very little information regarding CT anatomy and dimensions of the normal equine pituitary gland could be found in the literature. Objectives of this study were: 1) to refine a CT protocol for evaluating the equine pituitary gland, 2) to define the CT anatomy of the pituitary region, 3) to determine a set of normal values for the pituitary dimensions: (length, width, height, volume and weight), and 4) to refine CT techniques for measuring equine pituitary size and determine which method is the most accurate.

Materials and Methods:

Animal Selection:

Twenty-five horses without clinical signs of pituitary disease were selected for the study. Inclusion criteria consisted of horses over 3 years of age and over 750 pounds (as weighed before euthanasia). All horses were euthanized for reasons unrelated to pituitary disease. The majority of these horses presented for unresolving lameness.

The first two horses were used for the anatomy and CT measurement accuracy studies. The first horse (A) was an 8 year old mixed breed gelding. The second horse (B) was a 13-year-old Thoroughbred mare. The remaining 23 horses were used for the normal values and CT measurement studies.

The remaining 23 horses were used for the CT accuracy and normal dimension portion of the study (Table 1). Seventy percent (16/23) were males, and thirty percent (7/23) were females. These horses ranged in age from 4 years to 27 years. Eighty-three percent (19/23) of the horses were under the age of twenty. The weight range was from 750 pounds to 1250 pounds.

Table # 1 Sample population used for CT of the normal equine pituitary gland.

Horse #	Sex	Age (years)	Weight (pounds)	Breed	Reason for euthanasia
1	MC	7	946	Arabian	Lameness
2	F	20	1050	Thoroughbred	EPM
3	MC	5	922	Mix	Laminitis
4	F	4	855	Thoroughbred	Lameness
5	MI	5	1000	Quarter Horse	Colic
6	MC	4	975	Arabian	Lameness
7	MC	27	1000	Quarter Horse	Fibrosarcoma
8	MC	4	1050	Mix	Neurologic (suspect EPM)
9	MC	5	1000	Mix	Navicular
10	F	4	890	Quarter Horse	GI Salmonella
11	MC	19	992	Thoroughbred	Lameness
12	MC	13	984	American Saddlehorse	Lameness (Navicular)
13	F	23	800	Arabian	Uveitis
14	MC	14	1000	Thoroughbred	Lameness
15	F	10	1000	Mix	Ataxia
16	MC	28	1100	Thoroughbred	Lameness
17	MC	12	1200	Thoroughbred	Lameness (tendonitis)
18	MC	4	1200	Mix	Lameness

Horse #	Sex	Age (years)	Weight (pounds)	Breed	Reason for euthanasia
19	MC	14	1250	Mix	Trauma (musculo-skeletal)
20	MC	7	1100	Mix	Lameness
21	F	18	1100	Thoroughbred	COPD
22	MC	6	750	Mix	Laminitis
23	MC	18	1150	Mix	Lameness

Key: MI=male intact, F=Female,MC=male castrated, COPD=chronic obstructive pulmonary disease, EPM= equine protozoal myelitis

Necropsy Preparation:

An indwelling catheter was placed in the jugular vein of each horse. For all horses except horse B (anatomy study), an intravenous injection of iodinated contrast agent[*] was administered immediately before euthanasia. The horses were euthanized with an intravenous injection of barbituate euthanasia solution[†].

The heads were removed at the region of the cranial cervical vertebrae (C1-C2 or C2-C3) within twenty-four hours of euthanasia. The heads were removed by first cutting through the soft tissues and muscles, then sawing through the vertebrae. A waterproof adhesive mixture[‡] was inserted into the opening of the vertebral canal to minimize air intrustion and loss of cerebrospinal fluid. The heads were then placed in a plastic bag in a prone position and transported to the CT room.

Anatomic Correlation and CT protocol:

Two horses, A and B, were used for this portion of the study. For each of the two horses, the head was positioned on a plywood board in a prone position. The board was then placed on the CT table. Lateral and ventrodorsal digital radiographs (pilot views) were made and positioning adjusted as needed to minimize slice plane obliquity (Figure 1). Transverse CT slices were obtained perpendicular to the basisphenoid from the level of the cribriform plate to the foramen magnum using 5mm slice thickness and 5mm slice

[*] Isovue 370mg/ml iopamidol 60ml, Bracco Group. San Raffaele Biomedical Science Park, Milan: horses A, 1,2 and 7.Conray 400mg/ml iothalamate sodium 60ml, Mallinctrodt St. Louis MO, remaining 21 horses.
[†] Fatal-plus. 1cc/10lbs,390mg/ml.
[‡] Nuh-doh. Drummond American, Vernon Hills, Illinois 2inch strip per horse.

spacing[§]. The scan concluded at the occipital condyles. For horse A, scanning was performed using a pelvis protocol [**]and intravenous contrast. For horse B, scanning was performed using an abdomen protocol[††] and no intravenous contrast. Hypodermic needles were inserted into each head specimen at the beginning and ending CT slice locations with guidance by the scanner's laser light marker. Heads were taped on the plywood boards in the exact positioning as that used for scanning and transferred into a freezer. The heads were frozen for several weeks. A bandsaw was used to section the frozen heads, beginning at the first hypodermic needle, into 1cm thick slices. The rostral face of the frozen section corresponded to the first 5mm CT slice, and the caudal face of the frozen section corresponded to the second 5mm CT slice. By continuing these 1cm slices to the occipital condyles (to the caudal hypodermic needle) the entire cranial vault was sectioned to have corresponding CT images.

[§] Picker IQxtra, Fourth Generation Scanner. Marconi Systems, Cleveland, Ohio.
[**] 130 kvP, 330mAs, 400 field size, sharp algorithm and 512 image size
[††] 130 kVp, 262 mAs, 300 field size, smooth algorithm, 512 image size

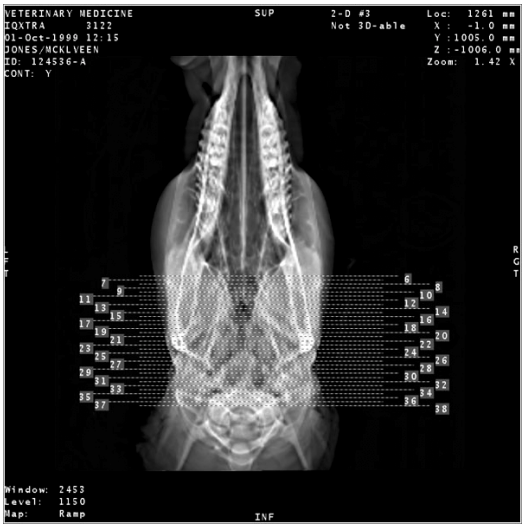


Figure 1A: Ventrodorsal digital radiograph demonstrating CT slice locations for anatomy study

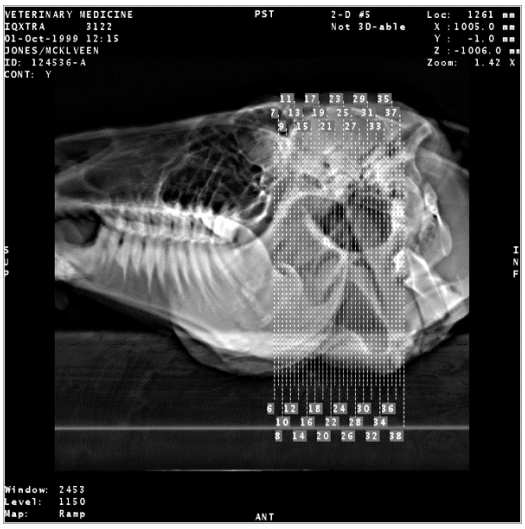


Figure 1B: Lateral digital radiograph demonstrating CT slice locations for anatomy study

Pituitary Measurements:

For the remaining 23 horses, transverse CT slices were obtained from the level of the rostral margin of the temporomandibular joint to the caudal margin of the temporomandibular joint. Heads were also placed in a prone position on the CT table (Figure 2). For each horse, scans were obtained using four different CT slice thickness and interval combinations: 10mm x 10mm, 10mm x 5mm, 4mm x 4mm and 4mm x 2mm. Image data were transferred to a remote workstation where pituitary length, width, height and 3D volume measurements were performed.[#] Pituitary CT measurements were made independently by two observers (TLM and JCJ), who were blinded to the gross measurements. Computed tomographic measurements of the pituitary length, width, and height were obtained from transverse and sagittal reformatted images using an electronic cursor and the workstation's software program for distance calculation. Maximum height and width were measured from transverse CT images. (Figure 3,4). Maximum length was measured from sagittal reformatted CT images (Figure 5). Three-dimensional measurements were obtained using hand-traced outlines of the pituitary gland in sequential transverse images and the computer software for 3D volumetry. (Figure 6). The same window width and level were used for every horse (window width 100, level 45).

[#] Voxel Q Visualization System, Picker International, Cleveland, Ohio.

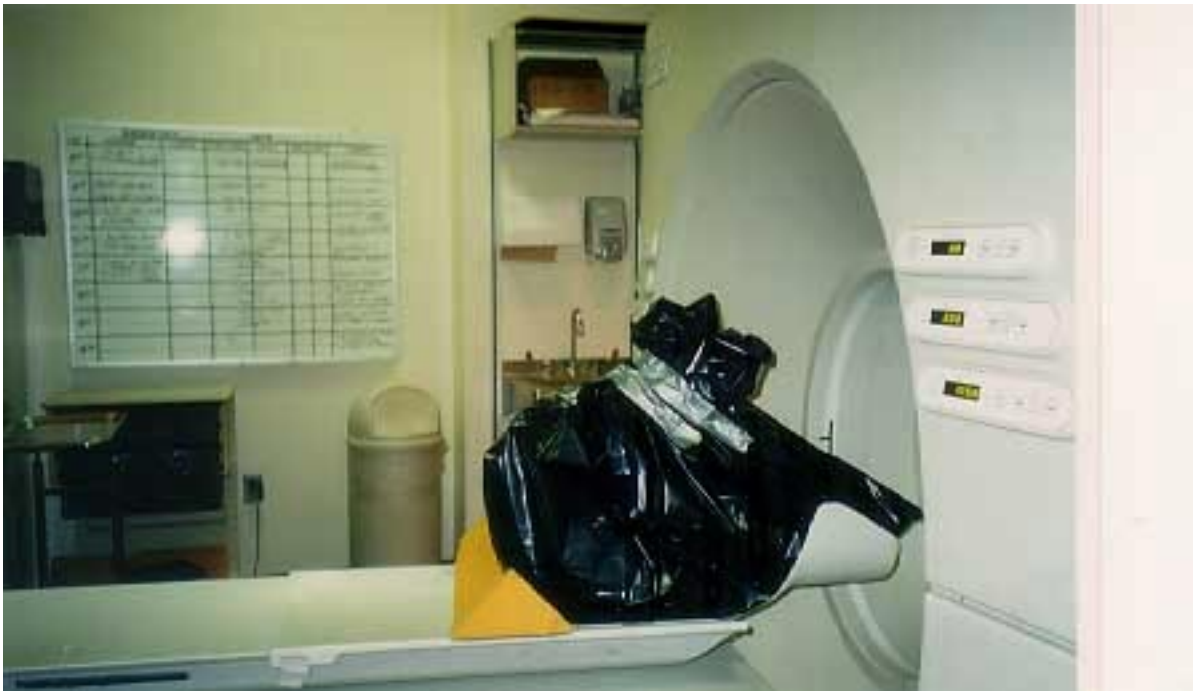


Figure 2: Positioning of patient on CT table. Head is in a prone position with the nose entering the gantry.

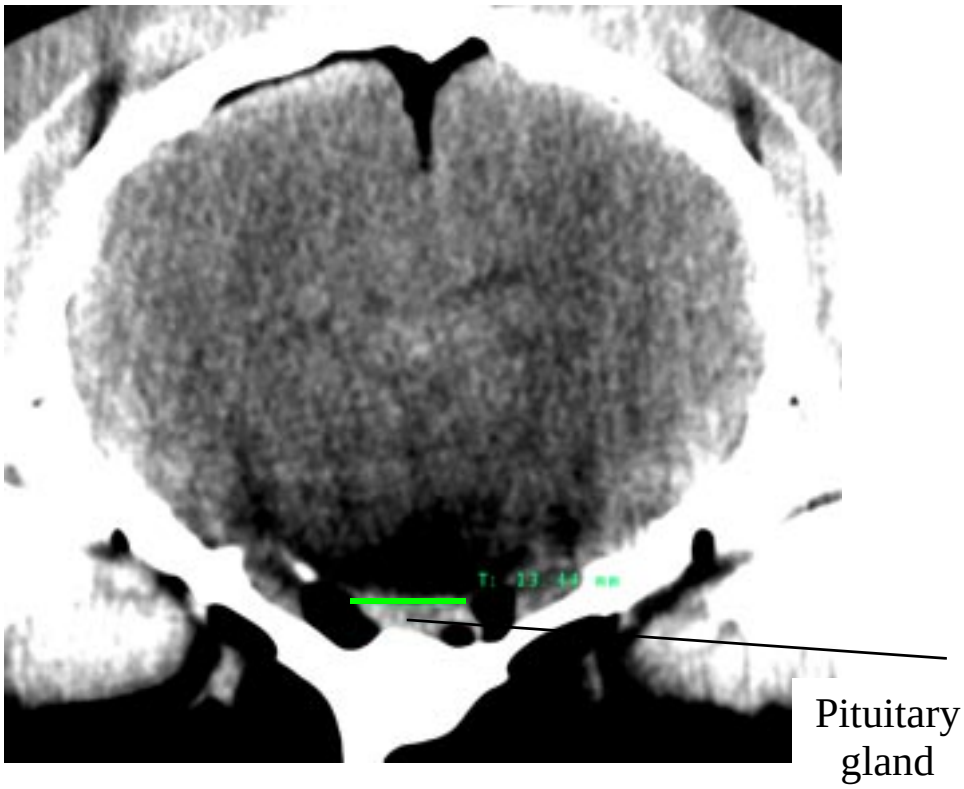


Figure 3: Transverse CT image demonstrating width measurement

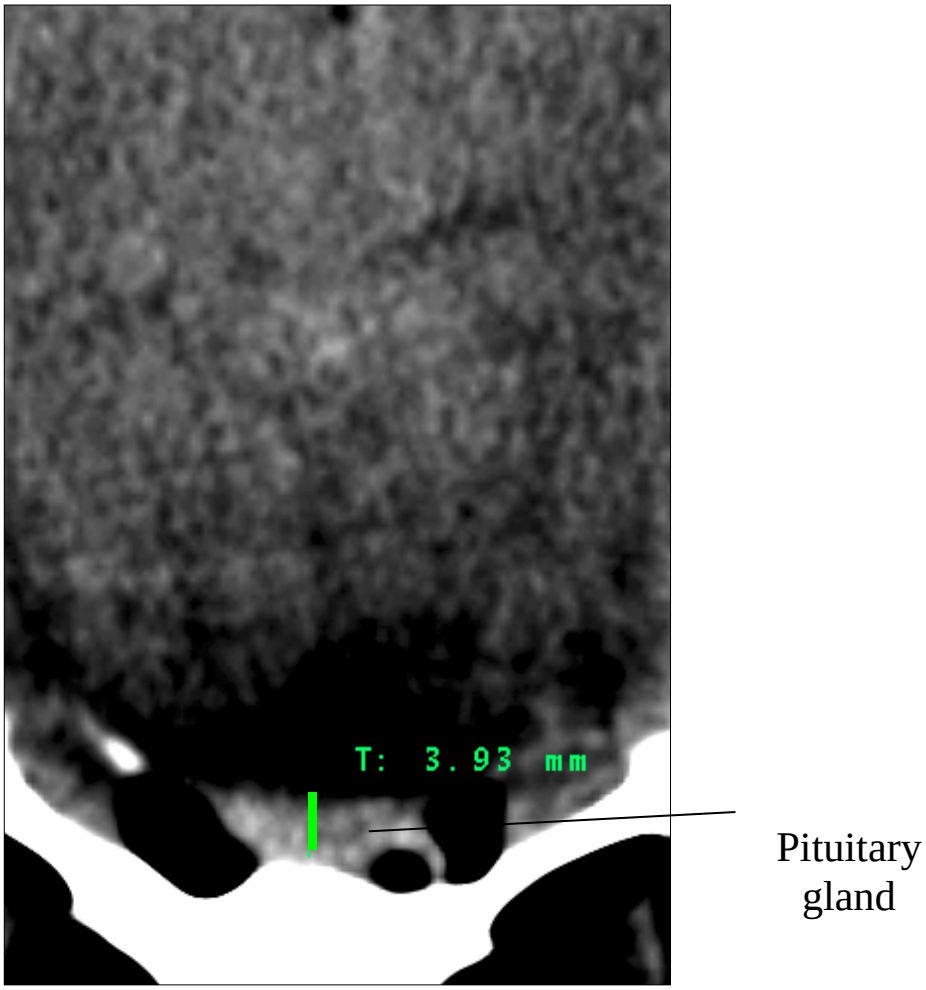


Figure 4: Transverse CT image with a black line over the pituitary gland demonstrating height measurement

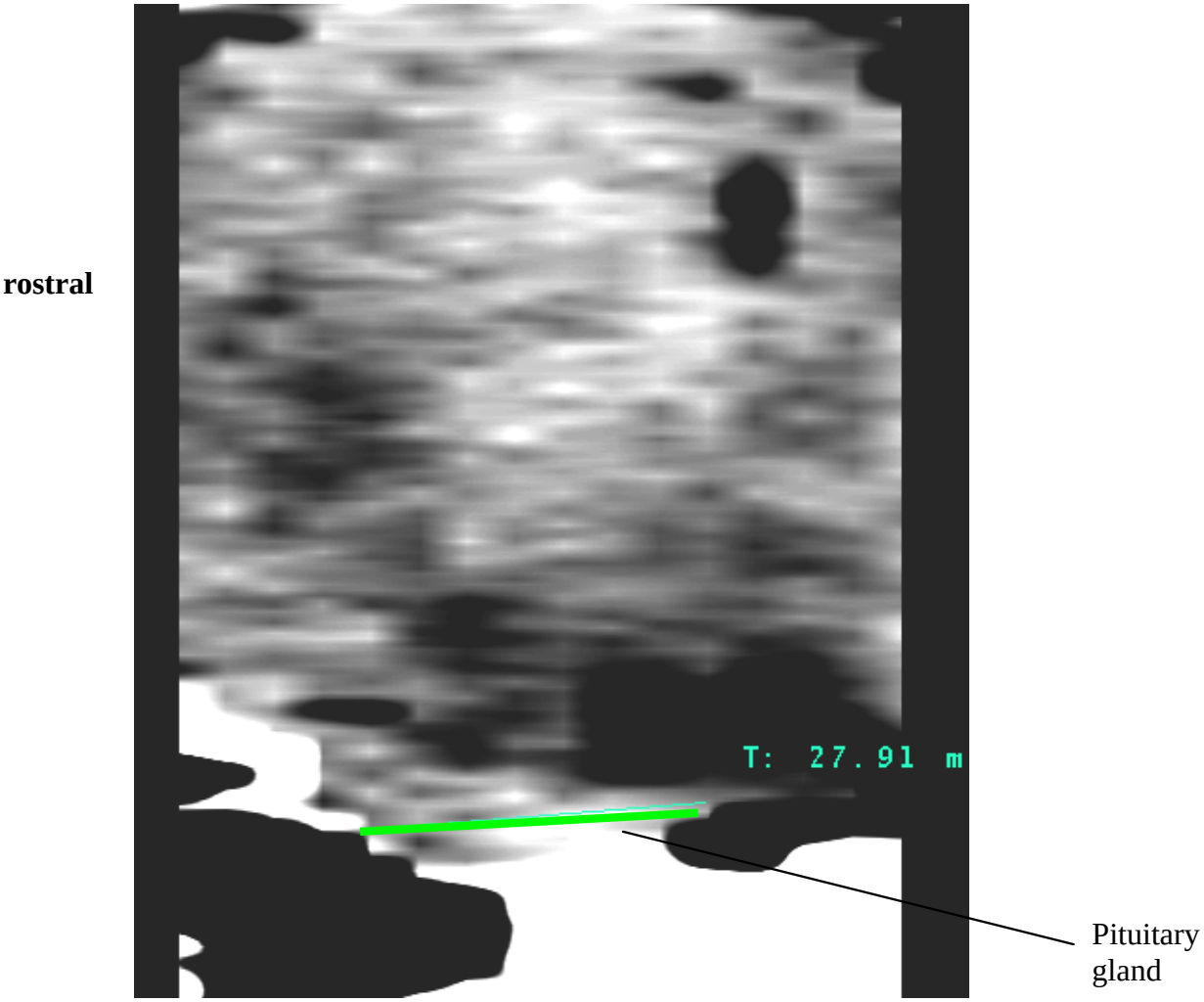


Figure 5: Sagittal CT image demonstrating the technique used to measure the length the pituitary gland

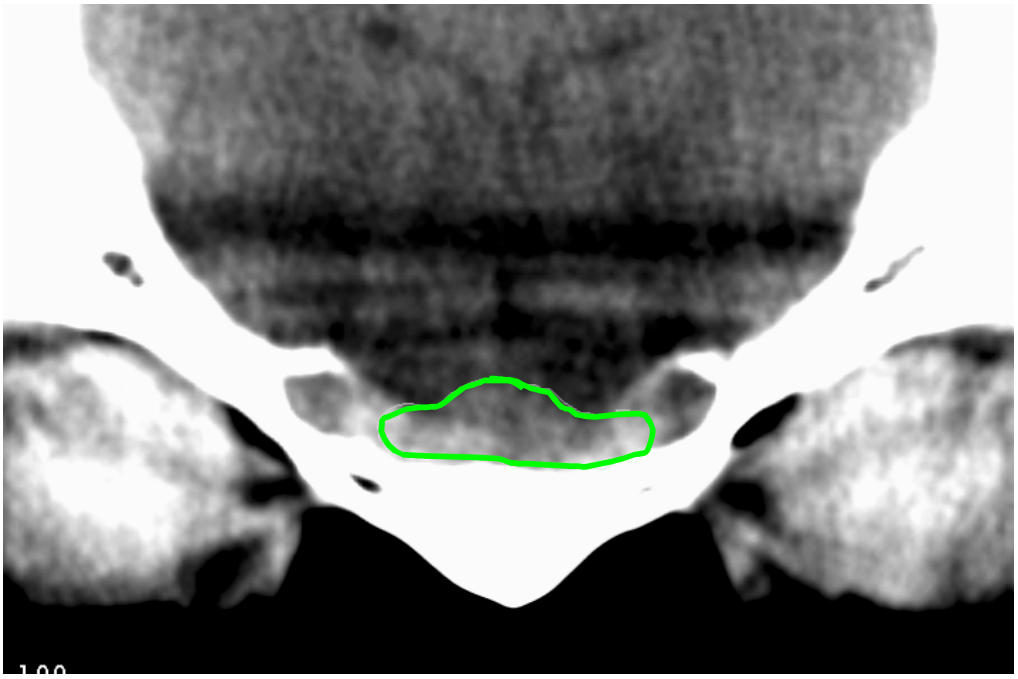


Figure 6: Transverse CT image with hand-tracing of the pituitary gland for volume measurements

The pituitary glands were removed and measured immediately after the CT scans were performed. Gross volume, length, width, height, and weight measurements were made by a pathologist (DPS), who was blinded to the CT measurements. Linear measurements were made with a metric ruler. Gross volume was determined by water displacement. A gram scale was used to determine weight. After measurements were made, the pituitary glands were fixed and stored in 10% neutral buffered formalin. Each pituitary gland was cut sagittally into 4 pieces. Five pieces were cut if the pituitaries were large enough. Then, 4 micron sections were cut from each of the 4 or 5 pieces. Sections were stained with hematoxylin and eosin following routine processing and sectioning of tissue. Histopathologic examination of all pituitary glands was performed by the same pathologist.

Statistical Analysis:

To test for effects of slice thickness and interval combinations and how this affected CT measurements, analysis of variance (ANOVA)[§§] in a randomized block design was performed. The mean measurements (length, width, height and volume) from the two observers were calculated for each horse and each slice thickness/interval setting. The means for each slice thickness and interval were compared to the gross measurements and to each other for each variable (length, width, height and volume). Bias plots were created for each treatment compared to each gross necropsy

measurement. For all tests, a value of $P<0.07$ was used to define significance. Percent accuracy of each slice thickness and interval was calculated using the formula: 100[1-|known-measured|/known]. The known value was the necropsy mean for each measurement and the measured value was the CT measurement.

[§§§§] Proc ANOVA, SAS Corporation, Cary NC

Results

Animals

One of the 23 horses, number 19, had to be excluded due to an error in scanning. Another horse, number 13, did not have gross volume measurements included in the data. Horse number 13 did have length, width, height and weight measurements included in the data analysis. Therefore, the total number of horses used for the gross measurement and CT length, width and height measurement analysis was 22. The total number of horses used in the volume measurement analysis was 21.

Six out of 23 pituitary glands were histologically normal (Table 2). Seventeen horses had small microscopic pituitary cysts, however, the pathologist interpreted these cysts to be of no clinical significance. These cysts were not visible grossly. Horses 3, 13, 16, and 17 had noncompressive nodules consistent with hyperplasia. Horse number 7 was found to have an adenoma in the pars intermedia. The pituitary did not appear grossly abnormal before sectioning and appeared normal on CT. There was no clinical evidence of a pituitary tumor noted on the physical examination. The measurements from the horse with the adenoma were not included in the normal measurements.

Table 2: Histopathology results

Horse number	Histopathology Results
1	Normal
2	Few small cysts
3	Few small cysts, tiny noncompressive nodule in the pars intermedia
4	Normal
5	Normal
6	Few small cysts
7	Compressive nodule (adenoma) with cysts in the pars intermedia
8	Normal
9	Few small cysts in the pars intermedia
10	Normal
11	Several small and intermediate cysts
12	Several small cysts
13	Small noncompressive nodule in the pars distalis, few small cysts
14	Small cysts in the pars intermedia
15	Small cysts in the pars intermedia
16	Several small cysts in the pars intermedia, large cyst in the pars distalis, few small noncompressive nodules in the pars distalis with few small mineralized foci
17	Several small cysts in the pars intermedia, single compressive nodule in pars intermedia
18	Normal
19	Small cysts in pars intermedia and pars distalis
20	Few small cysts in the pars distalis
21	Small cysts in the pars intermedia
22	Small cysts in the pars intermedia
23	Small cysts in pars distalis

Specimen Preparation:

Use of waterproof adhesive in the vertebral canal opening was partially effective. All of the specimens had air in variable quantities within the cranial vault. This air was seen within the subarachnoid space, the venous sinuses, or both. We were unable to find a specific way to remove the head and place the adhesive that significantly reduced the amount of air. Approximately 10 horses had marked air intrusion.

In horse B, the absence of intravenous contrast made the pituitary gland very difficult to distinguish (Figure 7A). Contrast administration improved visualization of the pituitary gland in most of the other horses (Figure 7B). In several of the horses, margins of the pituitary were obscured even with administration of intravenous contrast. Iopamadol was discontinued, after attempting to use it in 3 horses, due to crystallization of the medium. An attempt was made to use a 60 degree hot water bath to make the crystals go back into solution. This was time consuming and not always effective. Use of iothalamate sodium for the remaining horses did not appear to effect the degree of enhancement seen on CT images.

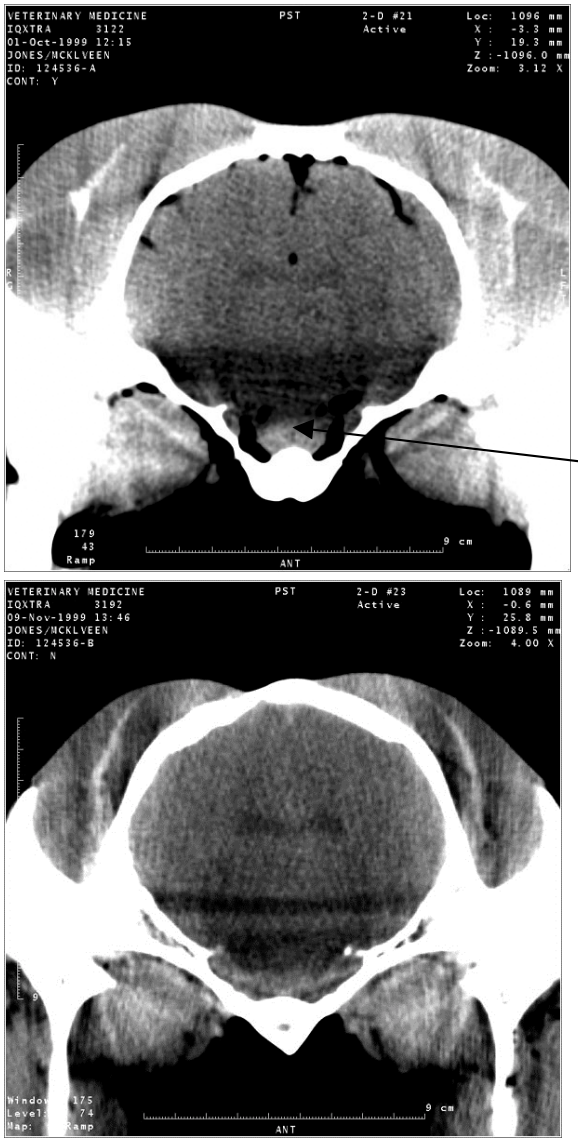


Fig 7: Transverse CT images with (top) and without (bottom)contrast enhancement of the pituitary gland

Anatomic Correlation:

The imaging protocol selected was the pelvis protocol. This allowed better visualization of the margins of the pituitary gland. The temporomandibular joint (TMJ) was well visualized in both horses. The TMJ is a condylar joint on the left and the right side with articular surfaces provided by the mandibular fossa of the skull (formed by the squamous temporal bone), and the condylar process of the mandible. In CT images, the TM joints appeared as paired oblong bony structures lateral and slightly caudal to the pituitary gland. The joint space was visible as a curved lucency positioned between the mandibular fossa of the skull and the condylar process of the mandible (Figures 8,9,10).

The hypophysis or pituitary gland was well visualized after contrast enhancement. This gland appeared as a rounded, isodense, markedly enhancing soft tissue structure in the hypophysial fossa in the floor of the cranial vault. Connective tissue, vascular tissue and a venous (cavernous) sinus surrounded the gland. Since the pituitary was located between the left and right TM joints, the scan could be limited to that area.

The dorsal bones of the braincase included the frontal and the parietal bones. The frontal bone was identified as a thin, rounded plate rostral to the pituitary gland. The parietal bone was similar in appearance and located dorsal to the pituitary. It was difficult to determine the line of demarcation between the basioccipital (caudal) and the basisphenoid (rostral) bones. Both of these bones were ventral to the pituitary. The sphenopalatine sinus was identified was a somewhat square, air filled space surrounded by bone rostal to the pituitary gland and ventral to the optic chiasm (Figure 11). The soft tissue structures of the brain were not as easily discriminated as the skeletal structures. The cerebrum and cerebellum were noted but specific anatomic features were not well

visualized. The lateral ventricles were poorly visualized. Differentiation between gray and white matter was not evident. A round, isodense, non-enhancing soft tissue structure was discernible ventral to the cerebrum and dorsal to the sphenopalatine sinus. This was the optic chiasm. It was important to note that the optic chiasm was rostral to the temporomandibular joint so that it would not be confused with the pituitary gland.

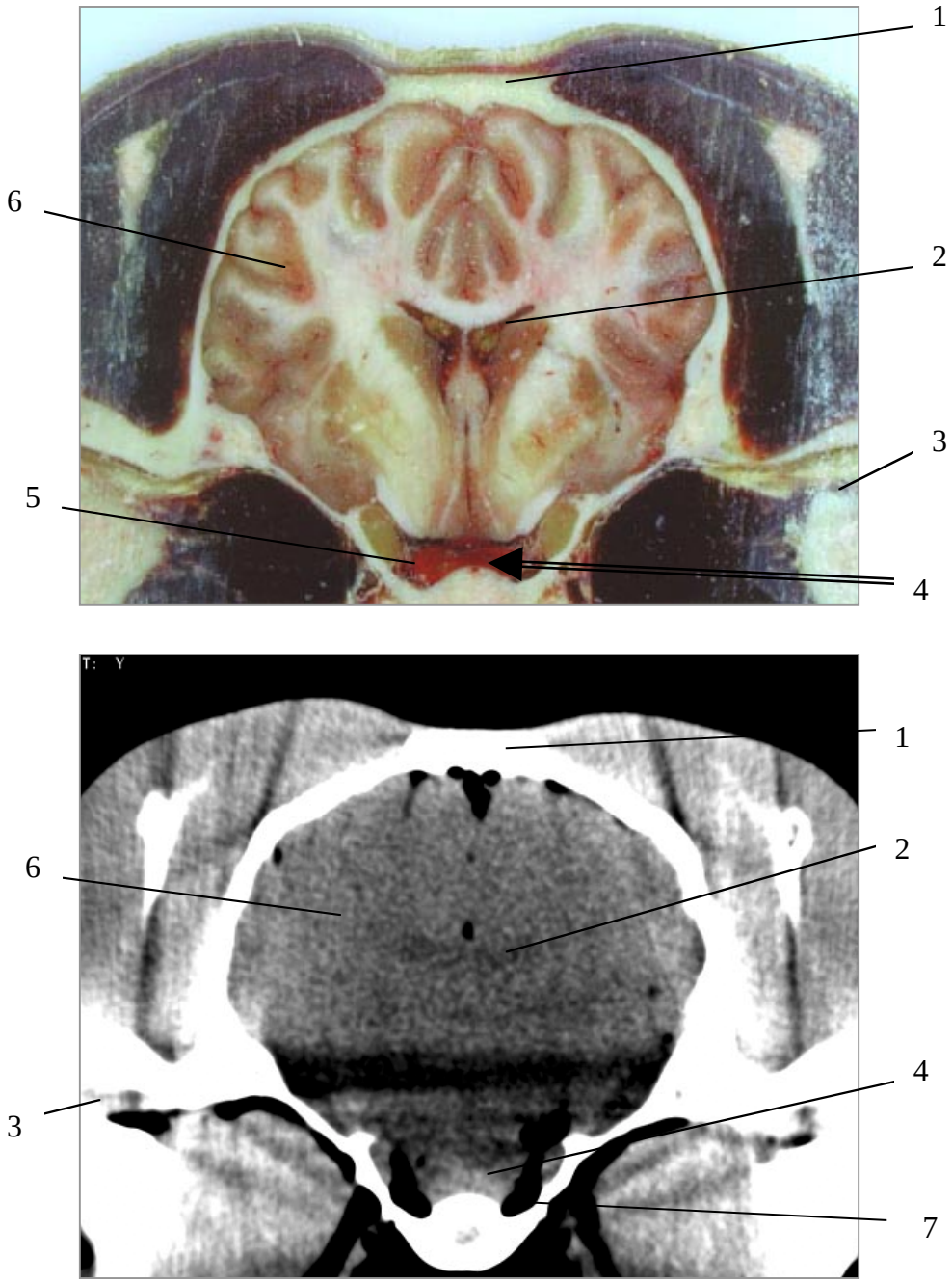


Figure 8: Corresponding transverse gross and CT slices: 1-parietal bone, 2-lateral ventricle, 3-temporomandibular joint, 4-rostral pituitary gland, 5-soft tissue surrounding pituitary, 6-cerebrum, 7-air in venous sinus

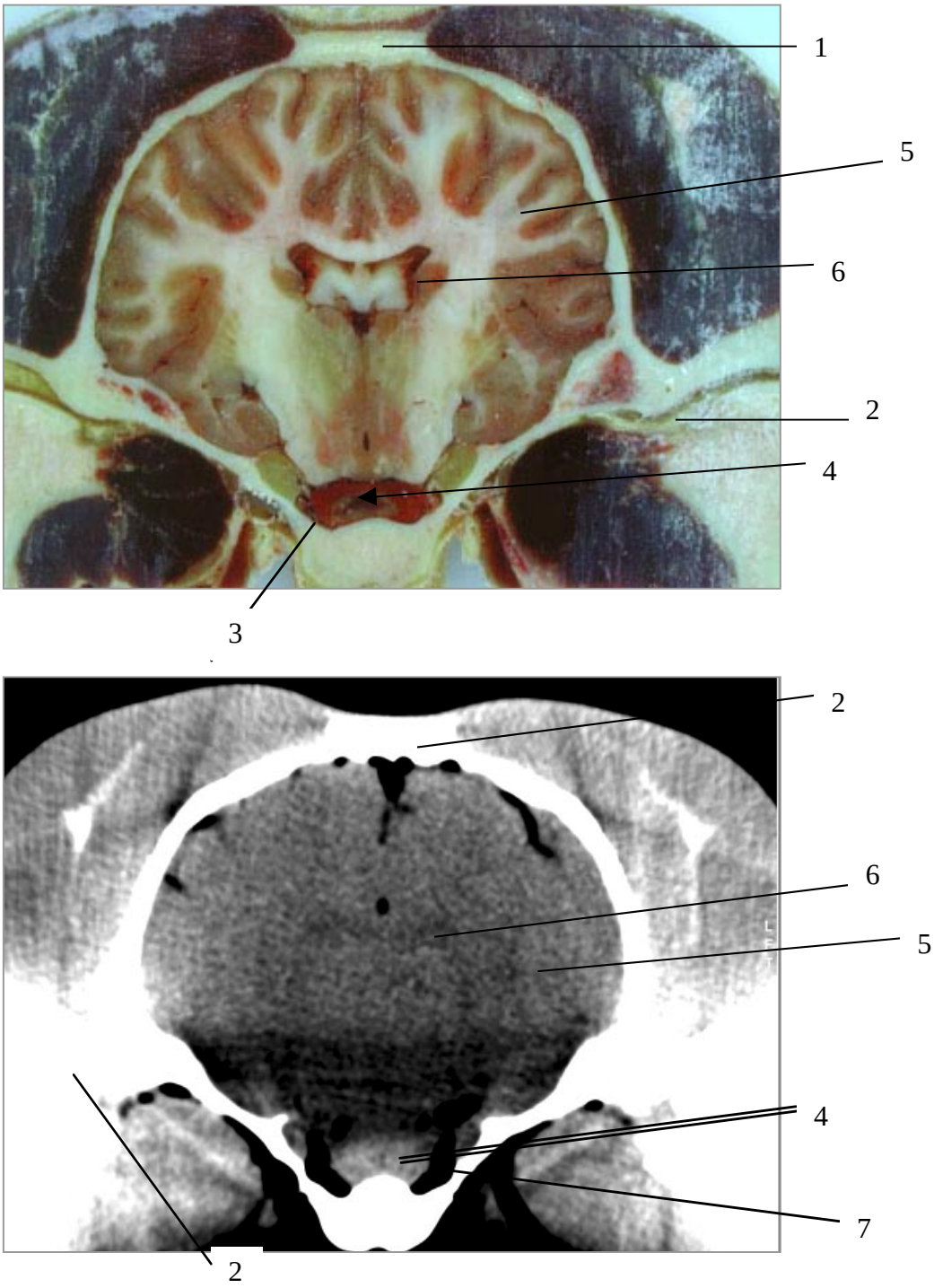


Figure 9: Corresponding transverse gross and CT slices: 1-parietal bone, 2-temporomandibular joint, 3-soft tissue surrounding pituitary, 4-middle of the pituitary, 5-lateral ventricle, 6-cerebrum, 7-air in venous sinus

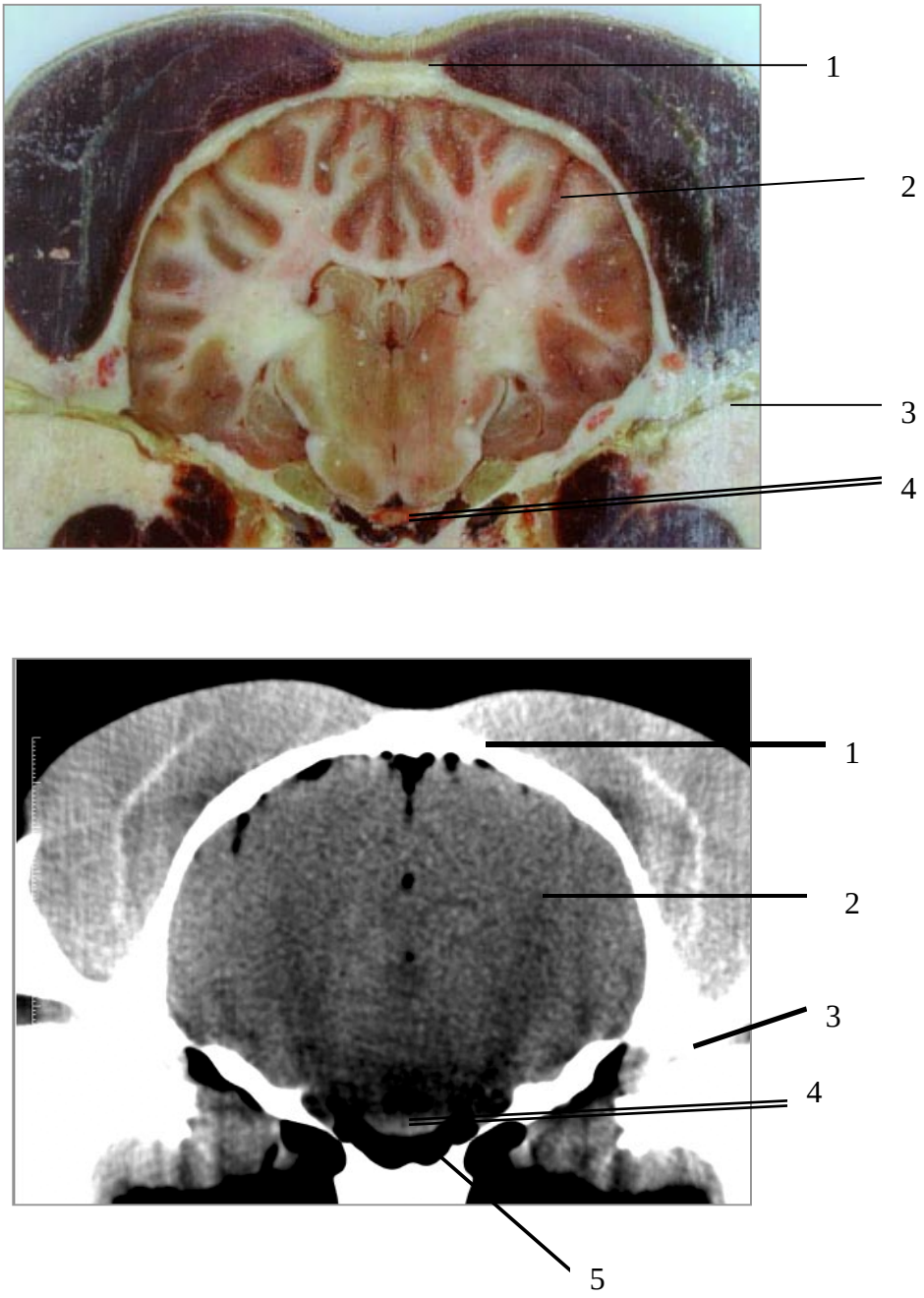


Figure 10: Corresponding transverse gross and CT slices: 1- parietal bone, 2-cerebrum, 3-temporomandibularjoint, 4-caudal pituitary, 5-air in venous sinus

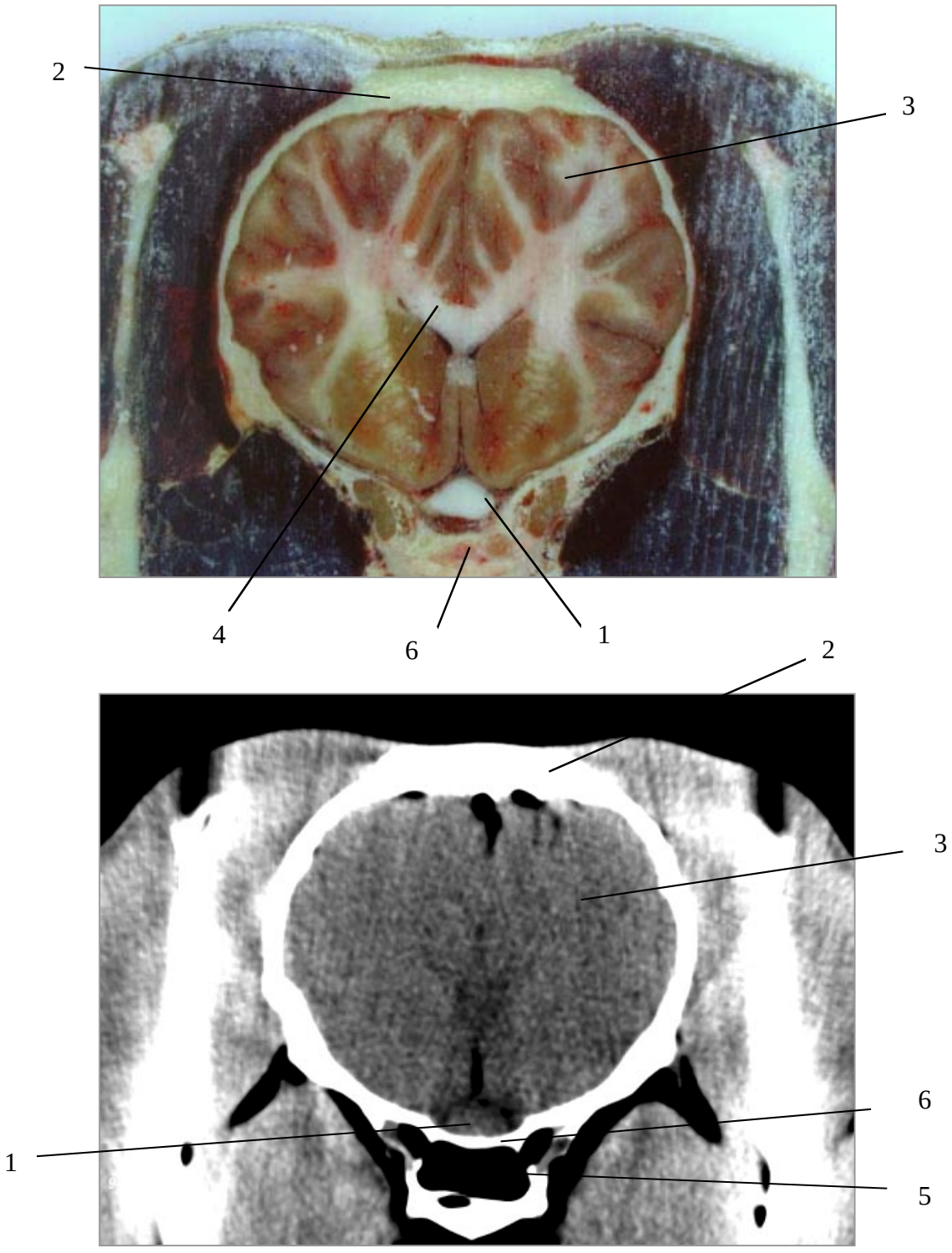


Figure 11: 1-optic chiasm, 2-frontal bone,3-cerebrum,4-corpus callosum, 5-sphenopalatine sinus, 6-basisphenoid bone

Gross Measurement:

Gross measurement means and ranges were calculated for the histologically normal glands (Table 4) and those microscopic cysts or hyperplasia. Horse number 7 was excluded from mean calculations due to the presence of a subclinical pituitary adenoma. The measurement of the adenomatous gland was 1.8cm length, 1.4cm width, 1.0cm height and 2.6cm^3 volume. The weight of the neoplastic gland was 2.5grams. Therefore, all measurements for the adenomatous gland were within our normal limits.

Table 4: Gross measurement means and ranges for equine pituitary glands with no histologic evidence of neoplasia.

Measurements	Mean (number of horses)	Range
Length (cm)	2.1 (22)	1.6-2.5
Width (cm)	2.2 (22)	1.3-2.6
Height (cm)	1.0 (22)	0.5-1.6
Volume (cm^3)	2.7 (21)	1.8-3.5
Weight (grams)	2.6 (22)	1.7-3.4

CT Measurements :

Length measurements performed from the 10mm slices did not differ from the gross measurements (Table 5). There was no significant difference between mean lengths measured from 10x10mm versus 10x5mm slices (p value < 0.06). Measurements performed from 10mm slices underestimated the length while those performed from 4mm slices overestimated the length (Figure 12). The accuracy was determined to be 97%, 99%, 89%, and 88% for the 10x10mm, 10x5mm, 4x4mm and 4x2mm slices respectively.

All CT scanning techniques caused the width of the pituitary to be underestimated (Figure 13). CT measurements performed using 4mm slices did not differ significantly from the gross measurements of width. There was no difference between mean widths measured from 4x4mm and 4x2mm slices ($p < 0.05$). The accuracy of the width measurements from 10x10mm, 10x5mm, 4x4mm and 4x2mm were 81%, 85%, 92% and 92% respectively.

All slice thickness and interval combination mean values underestimated the height measurements (Figure 14). Mean CT measurements from all techniques were statistically different from the gross measurements ($p < 0.07$). The mean measurements obtained from 4x2mm slices was the closest to the mean height assessed by gross measurement. The accuracy of the measurements was 58%, 61%, 69% and 71% for the 10x10mm, 10x5mm, 4x4mm and 4x2mm slices respectively.

The different CT slice thickness and interval combinations all underestimated the mean volume of the gross pituitary determined by water displacement (Figure 15). Mean

CT measurements from all techniques were statistically different from the gross measurements ($p < 0.07$). The measurements obtained from 4mm slices were closest to the gross volume. There was no significant difference between the 4x4mm and the 4x2mm slices. The accuracy was determined to be 41%, 48%, 68% and 61% for the10x10mm, 10x5mm, 4x4mm and 4x2mm slices respectively.

Table 5: Mean pituitary dimensions and percent accuracy values [***]

Dimension	Necropsy mean +/- SEM	CT Technique	CT mean +/-SEM	Accuracy (%)
Length (mm) N=22	21.07 +/- 0.787[a]	10 x 10	20.53 +/- 0.802[a]	97 %
		10 x 5	20.90 +/- 0.802[a]	99 %
		4 x 4	23.36 +/- 0.802[b]	89 %
		4 x 2	23.54 +/- 0.802[b]	88 %
Width (mm) N=22	21.62 +/- 0.709[c]	10 x 10	17.55 +/- 0.721[a]	81%
		10 x 5	18.46 +/- 0.721[ab]	85%
		4 x 4	19.89 +/- 0.721[bc]	92%
		4 x 2	19.95 +/- 0.721[bc]	92%
Height (mm) N=22	9.78 +/- 0.42[d]	10 x 10	5.69 +/- 0.430[a]	58%
		10 x 5	5.97 +/- 0.430[ab]	61%
		4 x 4	6.71 +/- 0.430[bc]	69%
		4 x 2	6.99 +/- 0.430[c]	71%
Volume (cm3) N=21	2.66 +/- 0.134[d]	10 x 10	1.08 +/- 0.135[a]	41%
		10 x 5	1.28 +/- 0.135[ab]	48%
		4 x 4	1.80 +/- 0.135[c]	68%
		4 x 2	1.63 +/- 0.135[bc]	61%

[***] For each dimension, means having the same letter superscript did not differ (p>0.07)

Figure 12: Bias plots of the distribution of CT length measurements compared to gross measurements

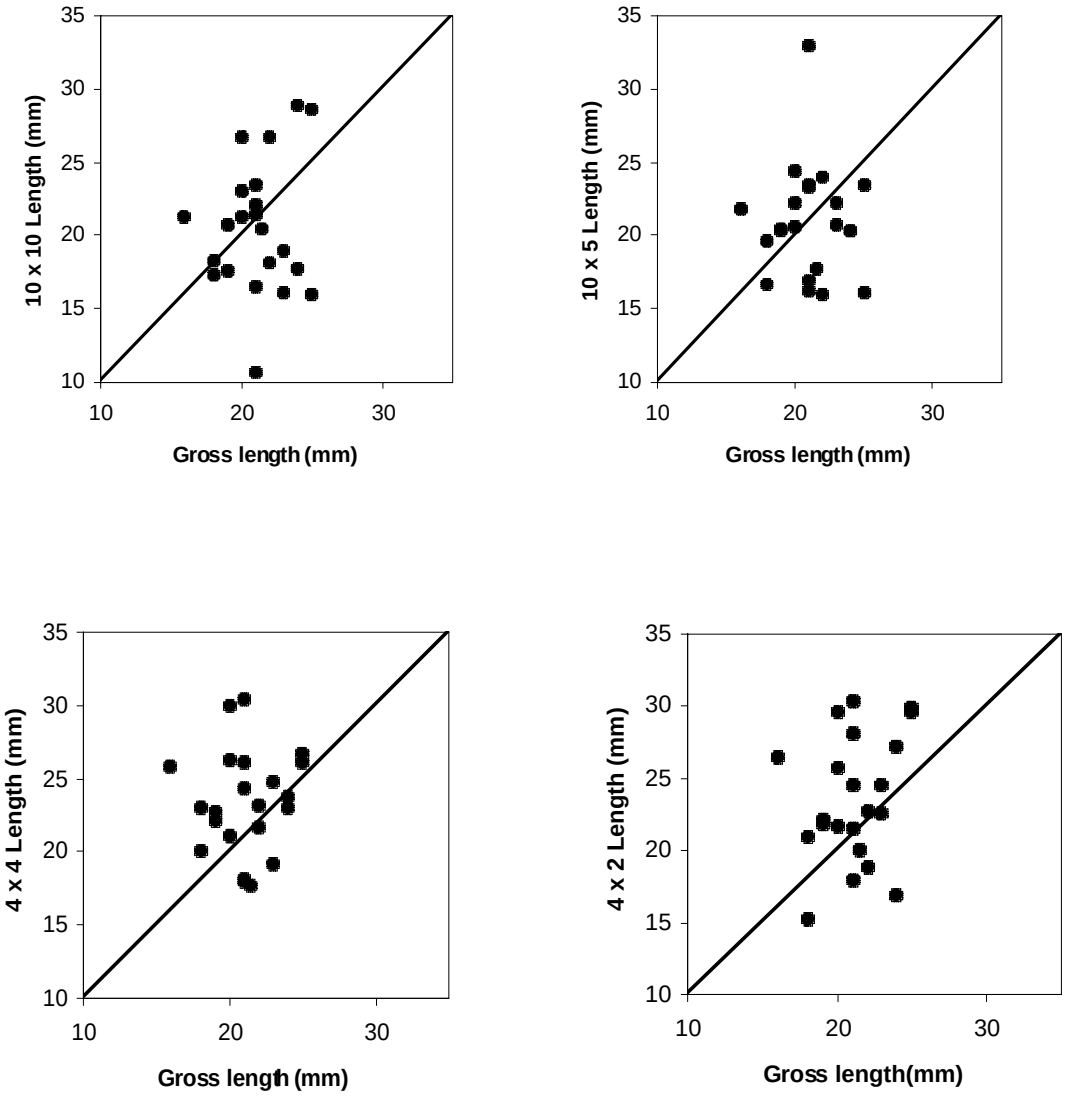
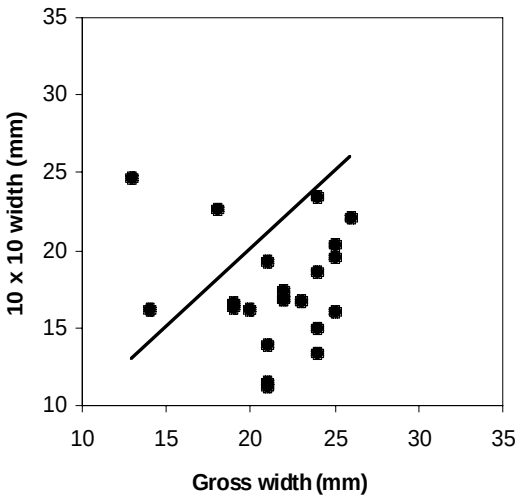
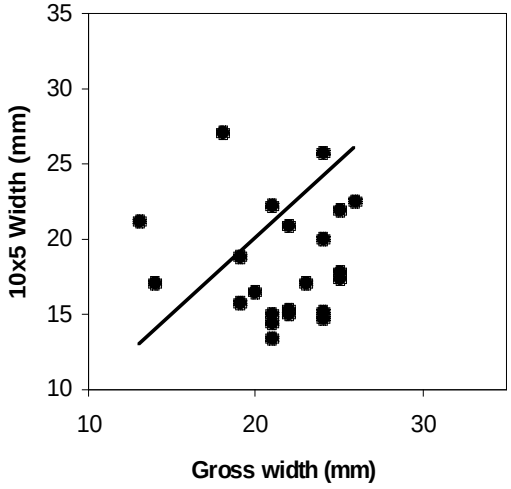
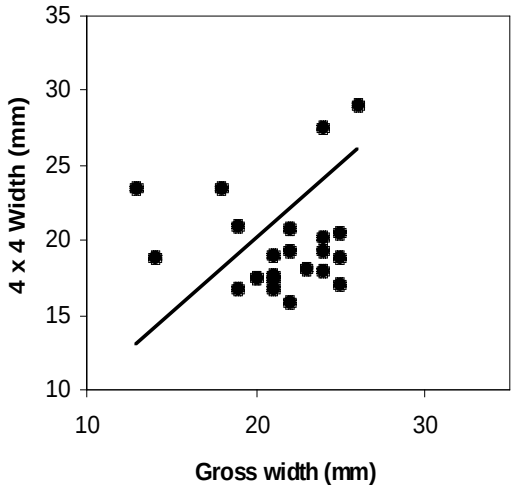


Figure 13: Bias plots of the distribution of CT width measurements compared to gross measurements







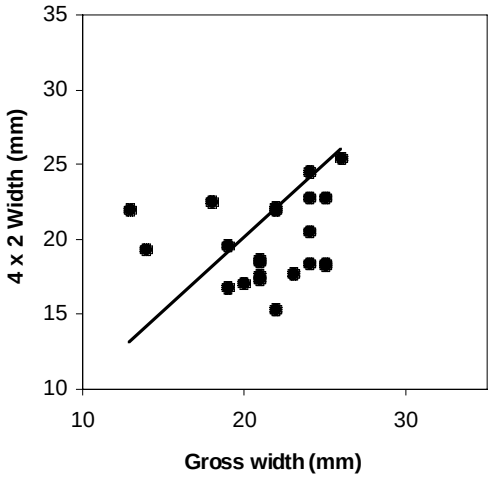


Figure 14: Bias plots of the distribution of CT height measurements compared to gross measurements

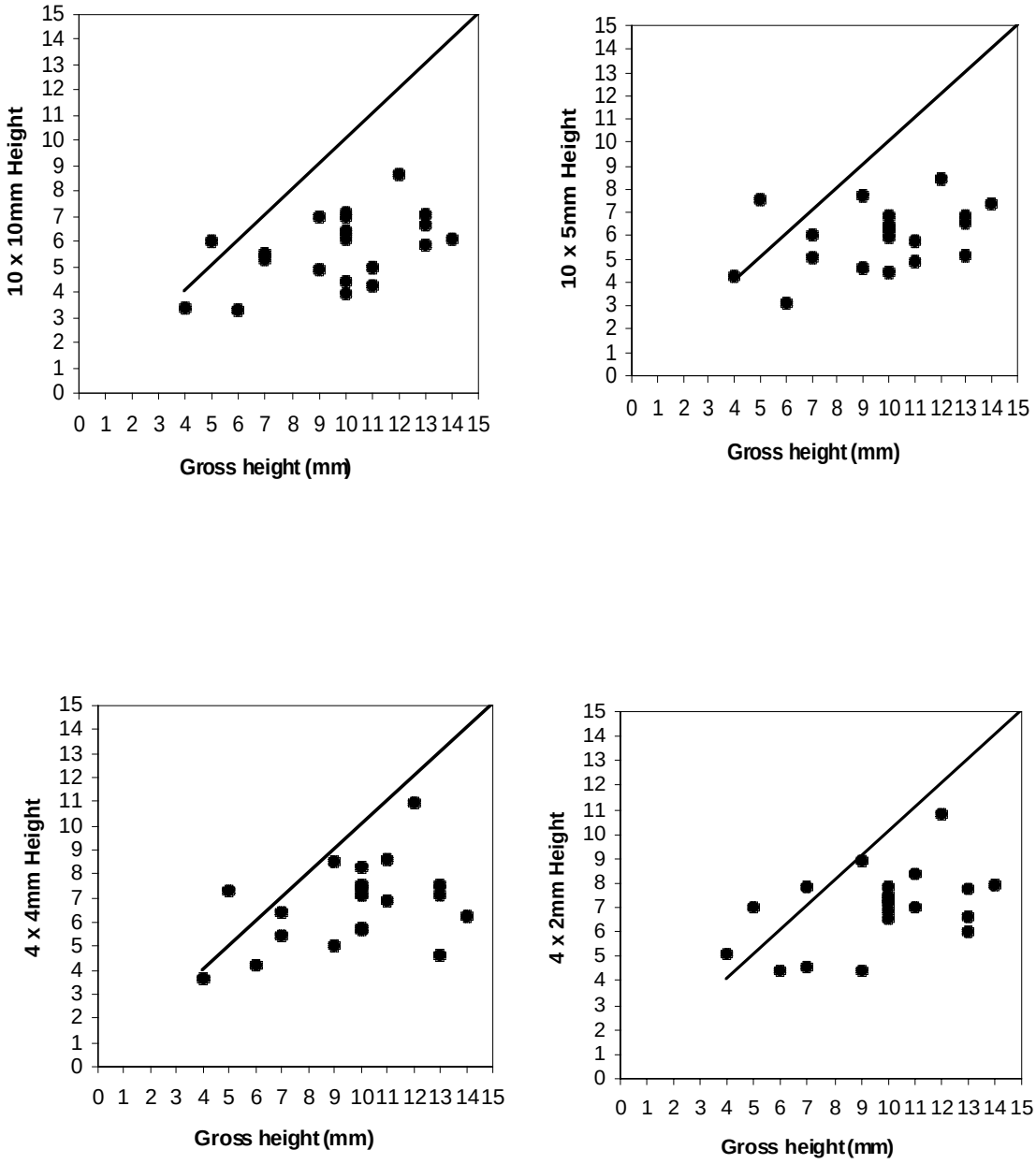
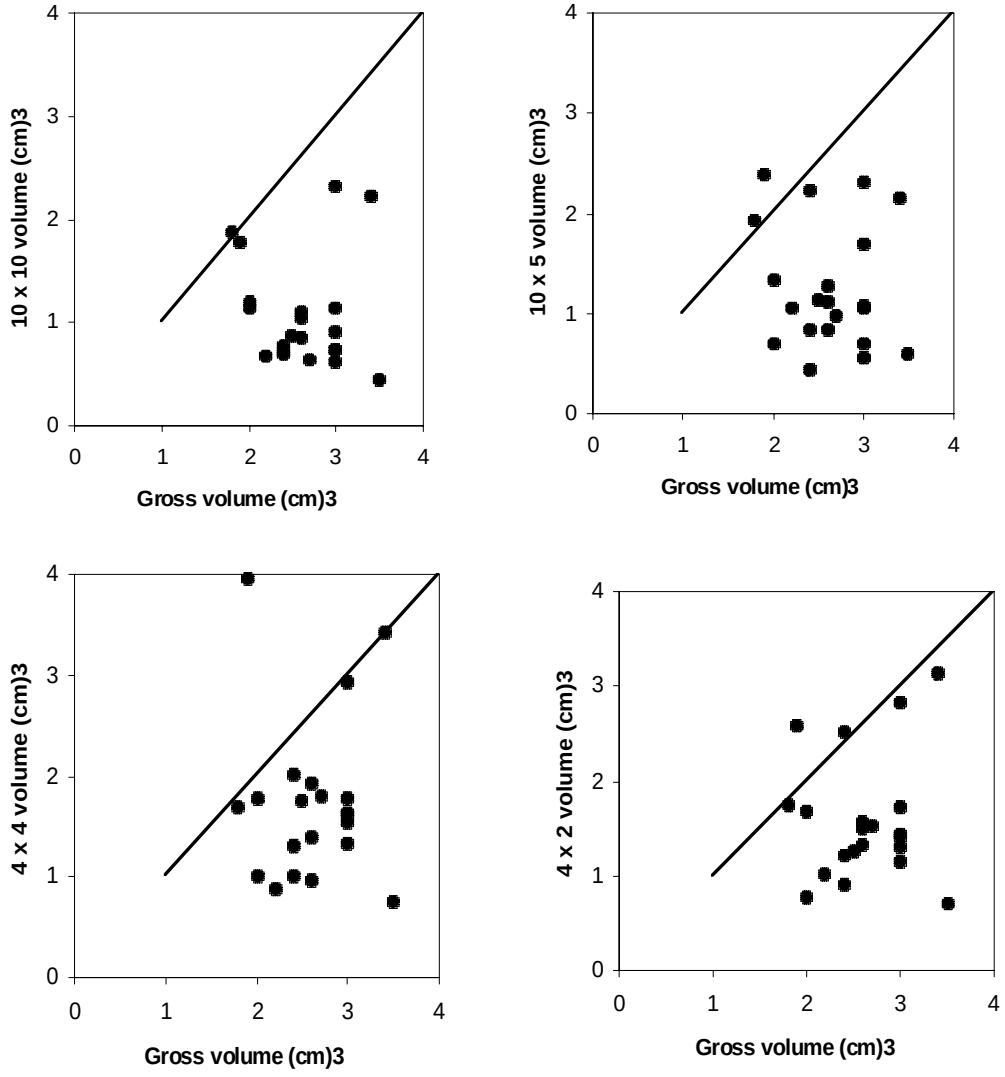


Figure 15: Bias plots showing the distribution of CT volume measurements compared to gross measurements



Discussion

We chose the age and weight range of our sample population based on literature evidence that pituitary disease is more commonly seen in adult horses. Our goal was to develop an age-matched set of control data for future studies. Twenty-three out of the twenty-five horses used were under the age of 20. However, to increase our sample population we did include a few horses between the ages of 20 and 27. All horses were evaluated by a board-certified equine medicine specialist and determined to have no clinical evidence of pituitary adenomas. To determine if some horses may have had subclinical disease, we also performed histopathologic evaluation of the glands. One horse did have a pituitary adenoma confirmed by histopathology. This was a 27 year-old Quarter horse gelding that presented for euthanasia due to a fibrosarcoma. This was an incidental finding as there was no clinical evidence of a pituitary neoplasm. Interestingly, measurements obtained from this horse did not skew the data. The gross measurements of the pituitary gland from the horse with the adenoma fell within the normal ranges obtained.

The adhesive material we used to occlude the vertebral canal has been used with success in a previous study involving dogs[86]. Information on how other investigators attempted to prevent the loss of CSF and minimize air intrusion was not found in other postmortem reports in horses[37,61] Despite our efforts, some of the horses in our study had significant air intrusion into the subarachnoid and vascular spaces. Air intrusion around the pituitary gland may have caused the margins to be more clearly seen than in vivo. Loss of CSF may also have made the ventricles appear smaller. It is possible that

the plastic material was not placed quickly enough, due to the cumbersome size and weight of the heads.

We used CT and anatomic slice thickness settings similar to those described in a recently published atlas of the head of the foal[63]. In that study, CT slices were also 5mm thick and anatomic slices were 10 mm thick. This allowed the photograph of the cranial face of the anatomic slice to be compared with the first CT slice and the photograph of the caudal face of the anatomic slice to be compared with the second CT slice. In another study, frozen slices varied in width from 1.5-3cm and CT slices were 5x5mm thick[61]. A paper describing scanning techniques in horses[62] makes mention of using slice widths from 8-13mm, or as low as 1-2mm. The slice thickness and interval combinations chosen for evaluating intracranial diseases in the horse have varied. For example, in one study, 10x10mm slices were used in scans for evaluation equine pituitary disease[36]. In another study, 5x5mm slices were used [37]. Little information about the use of overlapping slices was found with regard to scanning of the horse brain or head.

The anatomic correlation study was quite helpful in this project. At the time we initiated the study, no detailed description of normal pituitary region anatomy could be found. In order to insure that our measurements were made correctly, we needed to document the anatomic landmarks and surrounding features. We also wanted to identify external landmarks that could be used for slice planning. The goal was to develop a way to minimize anesthesia time in future studies, by scanning just the area of interest. The temporomandibular joint proved to be a readily recognized external feature that corresponded well to the boundaries of the pituitary gland. The other important

information obtained from the correlation study was that the optic chiasm is located just rostral to the pituitary gland. This structure may be confused with the pituitary gland, as it is ventrally located, round, and fairly easily distinguished from surrounding tissue. The optic chiasm was located dorsal to the sphenopalatine sinus, rather than at the level of the temporomandibular joints. The optic chiasm also differed from the pituitary gland in that it did not enhance with intravenous contrast.

Computed tomography is becoming more affordable and available to the equine patient and clinician. With this advanced technology more readily utilized, we felt that some issues and questions needed to be addressed. Developing a range of normal values for the equine pituitary dimensions is important because some horses with Cushing's disease may have vague clinical signs. Precise measurements of individual equine pituitary glands were previously published, but no range of normal values was found[5]. One report indicated that the normal gross equine pituitary gland is 2x2x.05cm[5], but it was unclear how many horses were used to make this determination. Our mean value for height was 1cm, with a range of 0.05cm to 1.6cm. The high end of our normal measurements were a length of 2.5cm, width 2.6cm and height of 1.6cm. One study indicated that a horse with a confirmed adenoma had pituitary dimensions of 2.5x2.25x1.5cm[36]. These measurements are within our range of normal measurements. One horse in our study had a pituitary adenoma and the measurements were within our normal range. The adenomatous gland measured 1.8x1.4x1.0cm. We included horses with microscopic cysts and hyperplasia as these glands did not appear grossly abnormal

and they did not skew our data. The gross weight range from our study correlated well with previously described weights of normal glands.

Literature pertaining to the accuracy of CT measurements indicates that thinner slices are more accurate when determining the dimensions of a structure[78]. Also, overlapping slices are recommended[79,80]. Volumetric calculations have been established as a good way to assess the dimensions of irregularly shaped structures[81,82,83]. Based on this information, we chose 4 different slice thickness and spacing combinations that we felt were most clinically feasible for equine pituitary scanning. We expected to find that thinner slices with more overlap were the most accurate way to determine the dimensions when compared to the gross dimensions. We also expected to find that the volume calculations would be the most precise way to measure the gland when compared to gross volume. Our results did not consistently support these assumptions.

The length measurements were the most accurate of all the measurement techniques. Surprisingly, we found that the 10mm slices resulted in more accurate estimates of length than did the 4mm slices. A tapering caudal soft tissue structure the same density as the gland was more easily visualized on thinner slices. This soft tissue made it difficult to determine the caudal boundary of the gland. Since we were not able to visualize this tissue as clearly on the thicker slices, it is possible we were more accurate in estimating the caudal boundary of the gland.

The height, width and volume were all underestimated by CT when compared to the gross measurements. This may have happened because of several factors. First, two

different evaluators assessed the size of the gland. Averaging these two measurements may have affected the accuracy. However, our plots of observer data did not demonstrate a consistent trend for underestimation or overestimation by one observer. Second, partial volume averaging may have made the margins of structures difficult to visualize. Even with the thinner slices, some partial volume effects were seen. Third, surrounding anatomic structures were sometimes indistinguishable from the pituitary gland. The pituitary gland is surrounded by a venous sinus and connective tissue. Both the gland and the surrounding venous sinus exhibited contrast-enhancement. This sometimes made it difficult to distinguish pituitary margins from vascular margins. However, we tended to include all enhancing tissue in our measurements, so this would have caused us to overestimate. Lastly, our window level setting may have affected our measurements. We chose window level settings consistent with that used to visualize brain tissue. We did not investigate the accuracy of measurements when changing the window setting.

It was surprising to find that volume was the least accurate of our four measurement methods. The volume measurements were all significantly different from the gross measurements by ANOVA. Error factors previously described for linear measurements may have also contributed to volume estimate inaccuracies. Another factor may have been the choice to round our gross measurements off to the nearest 0.1 cm^3. The CT volume measurements were calculated to the nearest 0.01 cm^3. To measure the length, width and height, we chose sagittal or transverse slices where the gland appeared largest. To measure the volume, we hand-traced what we perceived to be

pituitary margins in each sequential transverse slice. It is possible that the tapering shape of the pituitary gland impaired our ability to perceive the rostral and caudal margins. We may have failed to incorporate all of the pituitary tissue in our tracings. The most likely reason for the error in volume measurements is the fact that our volume calculation software was designed for a spiral CT scanner. We have a single slice scanner. In fact, after performing a study on a phantom model, we found that our scanner significantly underestimated the 3-D volume for the phantom at all different thickness and interval combinations.

Conclusions:

Our findings indicated that contrast-enhanced CT is an accurate technique for estimating pituitary linear dimensions. Thinner slices yielded the best results for height, width and volume estimates. Thicker slices yielded the best results for length estimates. For all slice thickness and spacing combinations, three-dimensional CT volume estimates differed from gross measurements. This suggests that three-dimensional CT volumetry may not be an accurate method for estimating pituitary tumor volume. However, due to our software problem, we can not conclude that volume measurements would not be accurate in other studies of the pituitary. Further analysis using software that has been tested on phantom objects would be needed. Future studies of 3D CT volume accuracy using a spiral scanner and phantoms of known dimensions would also be helpful. Also, we were unable to identify a small adenoma that occurred in one of our horses. Dynamic contrast studies in live horses may be helpful for distinguishing these smaller pituitary adenomas in the future.

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VITA

Tori Leigh McKlveen (3/2/70) grew up in Tempe, Arizona. Her father John McKlveen was a professor of nuclear engineering at Arizona State University until his death in 1991. He would be extremely proud to know that she chose a career path that included nuclear medicine. Her mother Jackie currently works for the military, stationed near a NATO base in the Netherlands. Other family members include a sister Holly in Tucson, Arizona, two stepbrothers, a stepmom, and a stepfather.

In 1988 Tori moved to Fort Collins, Colorado. She received her undergraduate degree in Microbiology in 1992 from Colorado State University. During her undergraduate education she worked at the Centers for Disease Control in the Department of Immunochemistry. From 1992-1993 she worked as a research associate in a microbiology lab. In 1993, Tori began veterinary school at Colorado State University. She graduated cum Laude in 1997. After graduation Tori moved to Albuquerque, New Mexico and worked in a small animal hospital. She met her fiancé Robert Fransen in Albuquerque in 1997. In 1998 Tori moved to Blacksburg, Virginia to do a residency in radiology at the Virginia-Maryland Regional College of Veterinary Medicine. This was a great move professionally and personally as she was close to her grandmother Lou, and her Aunt Janice in Maryland.

Tori's hobbies include playing the piano. She started piano lessons at the age of three, and in 1995 performed at the Colorado Music Festival. Besides classical music, other hobbies include horseback riding (combined training) and collecting rocks.