Dynamic computed tomographic evaluation of the pituitary gland in healthy dogs

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Objective—To determine the contrast enhancement pattern of the pituitary gland in healthy dogs via dynamic computed tomography (CT).

Animals—17 dogs.

Procedure—With each dog in sternal recumbency, transverse CT scans were made perpendicular to the skull base from the rostral clinoid processes to the dorsum sellae. At the position of the image that contained the largest cross section of the pituitary gland, a series of 9 to 11 scans was made during and after IV injection of contrast medium (dynamic CT scans). The contrast enhancement pattern of the pituitary gland and surrounding arteries was assessed visually and by use of time-density curves.

Results—After strong enhancement of the maxillary arteries, the intracavernous parts of the internal carotid arteries, and the communicating arteries of the arterial cerebral circle, there was a strong enhancement of the central part of the pituitary gland followed by enhancement of its peripheral part. On the last images of the dynamic series of the pituitary gland, the central part was hypodense, compared with the peripheral part. Time-density curves confirmed an early, strong enhancement of the central part and a delayed, less strong enhancement of the peripheral part of the gland.

Conclusions and Clinical Relevance—The difference in enhancement between the central and peripheral parts of the pituitary gland was attributable to a difference in vascularization of the neurohypophysis and adenohypophysis, respectively. Distortion or disappearance of the strong central enhancement (pituitary flush) may be used for the detection and localization of pituitary abnormalities in the adenohypophysis. (Am J Vet Res 2004;65:1518–1524)

Naturally occurring pituitary-dependent hyperadrenocorticism (PDH) is one of the most frequently occurring endocrinopathies in dogs. The characteristics of PDH in dogs are similar to those of PDH (Cushing disease) in humans, but this form of hyperadrenocorticism is much more common in dogs than it is in humans. In dogs, treatment for PDH can be medical (eg, administration of an adrenocorticolytic agent such as mitotane) or surgical (eg, via bilateral adrenalectomy or transphenoidal hypophysectomy). For hypophysectomy, detailed information about the size of the pituitary gland and its exact location in relation to the surgical landmarks is required. Information regarding the size and expansion of pituitary lesions also has prognostic implications. Therefore, PDH is the most frequent indication for evaluation of the pituitary gland in dogs by use of advanced imaging techniques.

Contrast-enhanced computed tomography (CT) is used in humans and dogs to evaluate pituitary tumors. Large pituitary tumors with suprasellar expansion are readily diagnosed. However, microadenomas that do not affect the size and shape of the pituitary gland may not be detected because of isointensity of the adenoma tissue and the surrounding unaffected pituitary tissue.

In humans, microadenomas have been identified by use of dynamic CT. Dynamic contrast-enhanced CT includes a series of scans of identical slice thickness at the same slice position through the center of the pituitary gland during and after IV injection of a bolus of contrast medium. During dynamic CT in humans, enhancement of the internal carotid artery is observed followed by enhancement of the central part of the secondary capillary bed of the adenohypophysis, which has been called the pituitary tuft. Finally, there is a centrifugal enhancement of the pars distalis of the adenohypophysis. Microadenomas may cause a deviation or distortion of the secondary capillary bed (the so-called tuft sign).

There are important anatomical differences between human and canine pituitary glands. In humans, the axis of the pituitary gland is vertical, whereas in dogs, the axis of the pituitary gland is more horizontal. In humans, a transverse CT imaging section includes either the anterior lobe or the posterior lobe; in dogs, both parts of the pituitary gland are visible in a transverse section, in which the neurohypophysis appears in the center, partly enveloped by the adenohypophysis. Therefore, the enhancement patterns obtained via transverse dynamic CT of the pituitary glands of dogs and humans may be different.

The enhancement pattern of the normal canine pituitary gland during dynamic CT has been reported. In 3 of the 4 dogs of that study, an early intense enhancement of the central portion of the pituitary gland was observed, which was followed by a peripheral rim enhancement. However, a time-density curve for the complete pituitary gland was plotted in that particular study, and differences in enhancement pattern between the central and the peripheral part of the pituitary gland were not specified. The purpose of the study reported here was to determine the dynamic CT enhancement pattern of the pituitary gland in healthy dogs. Changes in the enhancement pattern within the
contours of the pituitary gland were monitored by use of separate time-density curves.

Materials and Methods

Dogs—Seventeen healthy dogs (12 Beagles and 5 cross-breed dogs) were included in the study. The dogs were 2 to 10 years of age (median age, 4 years) and body weights ranged from 11.5 to 18.1 kg (median weight, 15 kg). Normal pituitary function was confirmed in all dogs on the basis of results of a pituitary function test that consisted of a combined IV injection of 4 hypothalamic hormones (coritocritropin-releasing hormone, growth hormone-releasing hormone, gonadotropin-releasing hormone, and thyrotropin-releasing hormone) and measurements of plasma adrenocorticotropic hormone, cortisol, growth hormone, luteinizing hormone, and prolactin concentrations, as described. The experimental protocol was approved by the Ethical Committee of the Utrecht University.

Anesthesia—Food was withheld from all dogs for 18 hours prior to CT evaluations. After premedication with medetomidine (50 μg/kg, IV), anesthesia was induced by IV administration of propofol (1 to 2 mg/kg). The trachea was intubated and inhalation anesthesia was maintained in a semiclosed system with a mixture of isoflurane, nitrous oxide, and oxygen. Continuous monitoring during anesthesia consisted of electrocardiography, capnography, and pulse oximetry, and a stable plane of anesthesia was maintained during CT examination and injection of the contrast medium.

CT—Evaluation via CT was performed by use of a third-generation CT scanner. With each dog in sternal recumbency, transverse scans of the skull were made (perpendicular to the skull base) from the rostral clinoid processes to the dorsum sellae. By use of a 9-second scanning time and a 22-second interslice delay, 2-mm-thick contiguous slices were made with 120 kV and 220 mA. The image that contained the largest cross section of the pituitary gland (usually the most caudal image just rostral to the dorsum sellae) was selected, and at the position of this image, a series of 9 to 11 scans was made with 120 kV and 220 mA (dynamic series of scans). One scan was made before (unenhanced scan) and 8 to 10 scans were made during and following the rapid IV bolus injection of an iodine-containing contrast medium (sodium meglumine ioxithalamate containing 380 mg of iodine/ml). The contrast medium was injected through an 18-gauge IV catheter placed in the cranial branch of the lateral saphenous vein of the hind limb. All contrast material was injected by hand by an experienced anesthesia technician, and injection was completed within 12 seconds. Because of a preparation delay inherent to the scanner used, the start of the first of the 8 to 10 scans was 5 seconds after the start of the injection. Three scanning protocols were used: in 3 dogs, the dynamic series of scans was made with a 2.8-second scanning time and an interscan time of 11.2 seconds (760 mg of iodine/kg was administered); in 6 dogs, the dynamic series of scans was made with a 2.8-second scanning time and an interscan time of 11.2 seconds (760 mg of iodine/kg was administered); and in 8 dogs, the dynamic series of scans was made with a 4.5-second scanning time and an interscan time of 9.5 seconds (760 mg of iodine/kg was administered).

After completion of the dynamic series of scans, the region from the rostral clinoid processes to the dorsum sellae was rescanned (spatial series of scans) by use of the same protocol (9-second scanning time and 22-second interslice delay) as that used for the precontrast series of scans. The dogs that underwent the first and third scanning protocols received an additional dose of 380 mg of iodine/kg. The dogs that underwent the second scanning protocol received no additional contrast medium. The spatial series of scans was performed to obtain a contrast-enhanced complete view of the pituitary gland from the rostral to caudal extents and to identify its exact location and relation to the bony landmarks of the skull base.

Image analysis—For all dogs, the enhancement patterns of the arteries and the pituitary gland on the dynamic series of scans were assessed visually by the same observer (RHV). The computer software used enabled different settings of window width (contrast) and level (brightness) and image subtraction to identify the borders of the pituitary gland and outline the difference in enhancement between the central and peripheral parts of the pituitary gland in 1 CT image. Unsynchronized density measurements were made of one of the maxillary arteries and of the central and peripheral part of the pituitary gland. Densities were measured in Hounsfield units (HU) on all images in the same regions of interest (Figure 1). The location of the regions of interest was set to be a reliable representation of the structures to be measured. In each dog, the moment of maximum enhancement of the maxillary artery was the moment after the contrast medium injection (in the series of dynamic scans) at which the highest density of the maxillary artery was measured. This moment was designated as time 0 (synchronization). Synchronized density measurements of the central and peripheral part of the pituitary gland were made on the unenhanced image at the moment of maximum enhancement of the maxillary artery (time 0) and on the subsequent images of the dynamic series. Mean and SD values of density were calculated, and time-mean density curves were calculated for the maxillary artery and for the central and peripheral part of the pituitary gland for the different groups of dogs.

With the images of the spatial series of scans displayed at the same window settings (window width, 250; window length, +80), the shape and enhancement of the pituitary gland were assessed visually. The height of the pituitary gland was measured from the image that contained the largest cross section of the pituitary gland. On the same image, the edges of the brain were traced and the enclosed area was calculated by the computer. The ratio of the pituitary gland height (mm) to brain area (mm²) × 100 was calculated (designated the P:B ratio), as described. All measurements were performed by use of a trackball-driven cursor and CT computer software.
Figure 2—Representative transverse dynamic CT images through the pituitary fossa in a healthy Beagle. The dotted line delineates the brain and pituitary gland from the bone of the skull base. A—Unenhanced (UE) image. B—Image obtained at 33 seconds (synchronized as time 0 [sec]) after IV injection of contrast medium illustrating the arterial phase, including contrast enhancement of the maxillary artery (black arrow), the intracavernous part of the internal carotid artery (arrowhead), and the arterial cerebral circle (white arrow). C—Image obtained at 47 seconds (synchronized time, 14 seconds) after IV injection of contrast medium. Notice the contrast enhancement of the central part of the pituitary gland (i.e., the neurohypophysis [arrow]) and of the remaining parts of the cavernous sinuses (arrowhead). D—Image obtained at 75 seconds (synchronized time, 42 seconds) after IV injection of contrast medium. Notice the homogeneous enhancement of the pituitary gland as a result of decreased enhancement of the central part (neurohypophysis) and increased enhancement of the peripheral part (i.e., the adenohypophysis). E—Image obtained at 89 seconds (synchronized time, 56 seconds) after contrast medium injection. Notice the hypodense appearance of the central part of the pituitary gland (arrow), compared with the appearance of the peripheral part of the pituitary gland. F—Subtraction image derived from images in panel C and E. Notice the difference in enhancement between the central (arrow) and peripheral part (white rim) of the pituitary gland. In all panels, R represents the right side of the dog; scale bar = 3 × 1 cm.
Results

The dynamic series with short scanning time (2.8 seconds) and incomplete rotation of the x-ray tube resulted in poor image quality. A scanning time of 4.5 seconds, coupled to a 360° rotation of the x-ray tube, resulted in a better image quality.

On the subsequent images of the dynamic series of scans, the same enhancement pattern was detected in all dogs (Figure 2). Following strong enhancement of the maxillary arteries, the intracavernous parts of the internal carotid arteries, and the communicating arteries of the arterial cerebral circle, there was strong enhancement of the central part of the pituitary gland, followed by enhancement of the peripheral part of the pituitary gland. On the last images of the dynamic series, the central part of the pituitary was hypodense, compared with the peripheral part of the pituitary gland. Especially during the enhancement phase that followed the pituitary flush, it was difficult to differentiate the homogeneously enhanced pituitary gland from the surrounding bone. To improve the differentiation of the enhanced pituitary gland, the window width and level were adjusted; subtraction images outlined the difference in enhancement of the central and peripheral part of the pituitary gland and emphasized the enhancement patterns.

The mean ± SD moment of maximum enhancement (unsynchronized) of the maxillary artery following the start of the injection of contrast medium was 35.5 ± 10.2 seconds (range, 19 to 61 seconds). The degree of enhancement of the maxillary artery varied among individual dogs, and the degree of enhancement achieved with the dose of contrast medium that provided 380 mg of iodine/kg was less than that achieved with the dose of contrast medium that provided 760 mg of iodine/kg (226 ± 34.4 HUs and 539.8 ± 122.0 HUs, respectively; Figure 3). The mean precontrast values for the central and peripheral parts of the pituitary gland were 52.2 ± 7.5 HUs and 70.9 ± 34.7 HUs, respectively. After synchronization of the maximum enhancement of the maxillary artery to time 0, the maximum enhancement of the central part of the pituitary occurred at 13.2 ± 6 seconds (range, 6 to 28 seconds) and the maximum enhancement of the peripheral part of the pituitary gland occurred at 50.2 ± 14.9 seconds (range, 14 to 70 seconds; Figure 4). The mean maximum enhancement for the central and peripheral parts of the pituitary was 201.7 ± 65.3 HUs and 180.7 ± 52.4 HUs, respectively.

The pituitary gland was identified in all dogs on the images of the spatial series of scans. The pituitary gland had a triangular or round shape on the most rostral image that contained a part of the gland and a round or oval shape on the caudal images. The dorsal margin was convex in all dogs. The height of the pituitary gland ranged from 3.7 to 5.5 mm (mean height ± SD, 4.1 ± 0.5 mm), and the brain area ranged from 1,368.5 to 1,799.2 mm² (mean area, 1,561.5 ± 148.4 mm²); the P:B ratio ranged from 0.22 to 0.31 (mean value, 0.26 ± 0.03). The pituitary gland was enhanced uniformly on the images of the spatial series in 10 dogs (of which 5 dogs received a total of 760 mg of iodine/kg and 5 dogs received a total of 1,140 mg of iodine/kg). In 7 dogs (of which 4 dogs received a total of 760 mg of iodine/kg and 3 dogs received a total of 1,140 mg of iodine/kg), the central part of the pituitary gland was somewhat hypodense, compared with the peripheral part of the gland.

Figure 3—Time-mean density curves obtained during dynamic CT imaging of the maxillary artery (A) and the central (B) and peripheral (C) parts of the pituitary glands of 17 healthy dogs receiving 1 of 3 imaging protocols. Protocols used to complete the dynamic series included IV administration of contrast medium equivalent to a dose of 380 mg of iodine/kg, after which scans were made with scanning time of 2.8 seconds and interscan time of 11.2 seconds (3 dogs; black diamond); IV administration of contrast medium equivalent to a dose of 760 mg of iodine/kg, after which scans were made with scanning time of 2.8 seconds and interscan time of 11.2 seconds (6 dogs; open square); or IV administration of contrast medium equivalent to a dose of 760 mg of iodine/kg, after which scans were made with scanning time of 4.5 seconds and interscan time of 9.5 seconds (8 dogs; open triangle). The bar at each data point represents the SD value. HUs = Hounsfield units. UE = Value obtained from unenhanced imaging. Time 0 = Moment of maximum enhancement of the maxillary artery.
lobe) in humans cannot be observed in the same transverse lobe) and neurohypophysis (posterior or neural lobe) and neurohypophysis. In humans, the strong and early enhancement of the neurohypophysis and its subsequent hypodense appearance, compared with the adenohypophysis, has been detected by use of dynamic CT in an axial scan plane. In humans, blood reaches the arterioles of the neurohypophysis earlier than it does the sinusoids of the adenohypophysis. In humans, the pituitary gland lies in a more horizontal position, with the infundibular process oriented dorsally and the neural lobe embedded in the pars distalis ventrally. The enhancement of the secondary capillary bed of the adenohypophysis in transverse CT images in humans has been called the pituitary tuft, and displacement or distortion of this tuft (called the tuft sign) has been used to identify pituitary microadenomas. To avoid confusion with the term pituitary tuft, the term pituitary flush has been used to describe the enhancement of the neurohypophysis in dogs with PDH. The adenohypophyseal tuft was not detected in dogs, probably because of the smaller dimensions and peripheral distribution of the adenohypophysis and the overwhelming central neurohypophyseal flush.

In the study reported here, a strong and early enhancement of the central part of the pituitary gland followed by enhancement of the peripheral part of the pituitary gland was observed in all 17 dogs. Similar findings were reported for 3 of 4 dogs included in a study conducted by Love et al.

The difference in the timing of enhancement between the central and peripheral parts of the pituitary gland may be explained by a different blood supply of the neurohypophysis and adenohypophysis in dogs. In the caudal distal region where the adenohypophysis does not completely invest the pars distalis neurohypophysis, distinct arterioles termed the caudal hypophyseal arteries (branchings of the caudal intercarotid artery, itself a branch of the internal carotid artery) enter the parenchyma of the pars distalis neurohypophysis and distribute as capillaries. Through these caudal hypophyseal arteries, the neurohypophysis (central part of the pituitary gland) has a direct arterial blood supply, in contrast with the pars distalis adenohypophysis (peripheral part of the pituitary gland), which receives its blood supply from veins; the latter are the hypophyseal portal vessels that connect the primary capillary network in the median eminence of the hypothalamus (supplied by the rostral hypophyseal arteries) with the secondary blood capillary network that forms the sinusoids of the adenohypophysis. In humans, blood reaches the arterioles of the neurohypophysis earlier than it does the sinusoids of the adenohypophysis. On transverse dynamic CT images in humans, there is also a strong enhancement in the center of the pituitary gland, but this has been explained by the sudden filling of the secondary capillary bed of the adenohypophysis and not by enhancement of the neurohypophysis. In humans, blood reaches the arterioles of the neurohypophysis earlier than it does the sinusoids of the adenohypophysis. In humans, the pituitary gland lies in a more horizontal position, with the infundibular process oriented dorsally and the neural lobe embedded in the pars distalis ventrally.

The variation in moment and degree of maximum enhancement of the maxillary artery among the dogs in our study may be explained by differences in injection volume, rate of contrast medium injection, body weight, blood viscosity, blood pressure, cardiac output, 

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and heart rate. To get a better overview of the enhancement pattern of the canine pituitary gland, the maximum enhancement of the maxillary artery was synchronized in all dogs. The shape of the time-density curve of the complete pituitary gland as reported by Love et al. is mainly influenced by the early and strong enhancement of the central neurohypophysis and resembles the arterial time-density curves of other organs. In our study in dogs, the separate time-density curves of the central and peripheral parts of the pituitary gland illustrated the difference in blood sup-
Computed tomographic imaging of the pituitary gland in dogs with PDH that may undergo hypophysectomy should include a conventional contrast-enhanced series of scans, which enables assessment of the size of the pituitary gland tumor and its precise localization in relation to the surgical landmarks. Single-slice dynamic CT imaging of the pituitary gland provides useful additional information. The displacement or distortion of the pituitary flush (i.e., the neurohypophysis) has been reported in dogs with PDH and was used to detect microadenomas of the adenohypophysis in the same way as the tuft sign has been used in humans. Dynamic CT was performed in 55 dogs with PDH that underwent hypophysectomy, and in 36 of those dogs, a distinct contrast enhancement of the neurohypophysis was detected. In 24 of the 36 dogs, the pituitary flush was displaced, which indicated the presence of an adenoma. In 18 of those 24 dogs, this diagnosis was confirmed grossly during surgery and histologically. In the 19 dogs in which no pituitary flush was detected, the contrast-enhancement pattern was diffusely abnormal and diffusely abnormal tissue was confirmed histologically in all 19 dogs. It was concluded that the use of dynamic CT imaging in dogs with PDH provided useful additional information, such as the identification of an adenoma (pituitary flush displaced) or a diffusely abnormal pituitary gland (no pituitary flush). Single-slice dynamic CT may give indirect evidence of the presence of a microadenoma when it is captured within the scan slice volume and when the adenoma is of sufficient size to displace or distort the neurohypophysis. Dynamic CT examination of the total volume of the pituitary gland (eg, with the use of spiral CT) may generate a 3-dimensional pituitary flush that enables localization of microadenomas in the complete pituitary gland in a single session.

In adult humans, the upper aspect of the normal pituitary gland appears most often flat or concave, whereas the dorsal margin of the pituitary gland in healthy dogs is convex. In healthy dogs, the size of the pituitary gland varies among different breeds and among individual dogs of the same breed. With an increase of body weight, there is an absolute increase in pituitary gland size but a decrease in proportion to increase of body weight. In a study of 47 dogs, the P:B ratio in dogs with PDH, the ratio between the height of the pituitary gland and the area of the brain appeared to provide good discrimination between enlarged and nonenlarged pituitary glands. The P:B ratio in dogs with nonenlarged pituitary glands is ≤0.31, and the P:B ratio in dogs with enlarged pituitaries is > 0.31. In the dogs of our study, the shapes, heights, and P:B ratios indicated that the pituitary glands were not enlarged. Evaluation of our study reveals certain weaknesses and strengths. The use of hand injection rather than pressure injection may have introduced variability in the contrast enhancement pattern among dogs. Furthermore, variation in arterial blood CO₂ concentration and peripheral blood pressure may also have provided additional sources of variability. However, all contrast medium injections were completed within 12 seconds, and density measurements for the pituitary gland were synchronized to the maximal enhancement of the maxillary artery. Also, if there were additional sources of variability, then these were similar for all dogs. All examinations, assessments, and measurements were performed by 1 observer. The major strength of our study was that we demonstrated the separate assessment of the adenohypophysis and neurohypophysis with a simple, single-slice CT scanner. The direct arterial vascularization of the neurohypophysis (which explains the pituitary flush during dynamic CT) has been confirmed by findings of histologic examination of normal canine pituitary glands reported previously by one of the authors.

Our data have indicated that the difference in timing of enhancement between the central and peripheral parts of the adenohypophysis is a consequence of a difference in vascularization of the neurohypophysis and the adenohypophysis, respectively. For dynamic CT imaging of the pituitary gland of dogs, it is recommended to make a series of 2-mm-thick scans with a scanning time of 4.5 seconds and an interscan time of 9.5 seconds after IV injection of contrast medium to provide a dose of 760 mg of iodine/kg. Displacement, distortion, or disappearance of the strong central enhancement (pituitary flush) may be used for the detection and localization of pituitary abnormalities in the adenohypophysis such as microadenomas in dogs with PDH.

References