Thin-slice three-dimensional gradient-echo magnetic resonance imaging of the pituitary gland in healthy dogs

Roselinda H. van der Vlugt-Meijer, DVM, MSc; Björn P. Meij, DVM, PhD; George Voorhout, DVM, PhD

Objective—To evaluate thin-slice 3-dimensional gradient-echo (GE) magnetic resonance imaging (MRI) of the pituitary gland in healthy dogs.

Animals—11 healthy dogs.

Procedures—By use of a 0.2-Tesla open magnet, MRI of the skull was performed with T1-weighted GE sequences and various protocols with variations in imaging plane, slice thickness, and flip angle before and after administration of contrast medium; multiplanar reconstructions were made. The pituitary region was subjectively assessed, and its dimensions were measured. Image quality was determined by calculation of contrast-to-noise and signal-to-noise ratios.

Results—Best-detailed images were obtained with a T1-weighted GE sequence with 1-mm slice thickness and 30° flip angle before and after administration of contrast medium. Images with flip angles > 50° were of poor quality. Quality of multiplanar reconstruction images with 1-mm slices was better than with 2-mm slices. The bright signal was best seen without contrast medium. With contrast medium, the dorsal border of the pituitary gland was clearly delineated, but lateral borders were more difficult to discern.

Conclusions and Clinical Relevance—MRI of the canine pituitary gland with a 0.2-Tesla open magnet should include a T1-weighted GE sequence with 1-mm slice thickness and flip angle of 30° before and after administration of contrast medium. The neurohypophysis was best visualized without contrast medium. The MRI examination permitted differentiation between the pituitary gland and surrounding structures. (Am J Vet Res 2006;67:1865–1872)

Detailed imaging of the pituitary gland in dogs has diagnostic and therapeutic planning value. Several techniques have been described, among which CT is most commonly used. Computed tomography gives information about the size of the pituitary gland and the exact location of the pituitary gland in relation to the bony surgical landmarks required for transsphenoidal hypophysectomy in dogs with PDH. In addition, dynamic CT, which comprises a series of transverse scans through the center of the pituitary gland during and after rapid IV injection of contrast medium, may indirectly reveal the site of the microadenoma in dogs with PDH by visualization of the displacement or distortion of the neurohypophyseal flush.

The imaging modality of choice for the evaluation of the pituitary gland in humans is MRI, which allows for superior differentiation of soft tissue structures in all scan planes. Furthermore, the pituitary bright signal, a hypertensive signal on T1-weighted images representing the neurohypophysis, can give additional anatomic and functional information. In dogs, MRI has been used to diagnose pituitary gland macrotumors and to evaluate the pituitary gland in dogs with PDH. There are 2 reports on MRI of the pituitary gland in healthy dogs performed with a 1.5-Tesla machine and SE sequences with 3-mm and 5-mm slice thickness. Normal pituitary gland anatomic features, including the appearance of the pituitary bright signal, were described in one report. The contrast enhancement pattern during dynamic MRI has also been described. In the other report, pituitary gland dimensions were related to the size of the dog.

Microadenomas in dogs with PDH do not change the size or shape of the pituitary gland and may be as small as 1 to 2 mm in diameter. Therefore, pituitary imaging modalities for detection of microadenomas should have a slice thickness of 2 mm or thinner. On images of slices with a thickness ≥ 3 mm, pituitary gland changes and lesions may go unnoticed. With 3-dimensional GE sequences, however, thinner slices can be made and quality may be improved substantially.

The purpose of the study reported here was to determine the best protocol for pituitary gland imaging by use of thin-slice 3-dimensional GE MRI with a 0.2-Tesla open magnet; assess quality of the magnetic resonance images by varying the imaging plane, flip angle, and slice thickness; and determine the effect of administration of contrast medium.

Abbreviations

CT Computed tomography
PDH Pituitary-dependent hyperadrenocorticism
MRI Magnetic resonance imaging
SE Spin echo
GE Gradient echo
MPR Multiplanar reconstruction
P:B Pituitary height to brain area
SNR Signal-to-noise ratio
CNR Contrast-to-noise ratio
ROI Region of interest
SI Signal intensity
Materials and Methods

Dogs—Eleven healthy adult dogs (6 Beagles and 5 crossbred dogs with comparable skull types) were used. The dogs were 2 to 9 years of age (median, 7 years), and body weights ranged from 11 to 24 kg (median, 18 kg). The dogs included 9 sexually intact male dogs and 2 sexually intact female dogs that were not in estrus during the study. Dogs were obtained from the Department of Clinical Sciences of Companion Animals of the Utrecht University. The dogs were used for teaching students in clinical diagnostic exercises and for minor noninvasive studies. During their stay in the department, all dogs received the best standard of care. The experimental protocols of this study were approved by the Ethical Committee of the Utrecht University. Normal pituitary gland function was determined by evaluation of plasma concentrations of adrenocorticotropic, cortisol, growth hormone, luteinizing hormone, and prolactin after IV injection of corticotropin-releasing hormone, growth hormone–releasing hormone, gonadotropin-releasing hormone and thyrotropin-releasing hormone, respectively.

Anesthesia—Food was withheld from all dogs for 18 hours prior to MRI. Following IV administration of medetomidine (50 µg/kg of body weight; Pfizer Animal Health, Swindon, Wiltshire, United Kingdom), 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.

MRI—The MRI was performed with a 0.2-Tesla open magnet with dogs in sternal recumbency and by use of the small multipurpose coil. In all dogs, 2 series of MRI experiments were performed with a 1-month interval between experiments. Contiguous slices of the pituitary gland were obtained with a T1-weighted 3-dimensional GE sequence (flash, 3 dimensional; time of repetition, 34 milliseconds; time of echo, 12 milliseconds; slab thickness, 32 mm; time of acquisition, 22.02 minutes; reconstructed field of view, 140 X 160 mm). For Experiment 1, sequences of transverse (n = 11 dogs), dorsal (11), and sagittal (3) 1-mm-thick slices with a flip angle of 30° were obtained before contrast medium injection. After IV injection of 0.2 mL of contrast medium (377 mg of meglumine gadoterate/mL/kg of body weight, sequences of transverse 1-mm-(n = 10 dogs) and 2-mm-(9) thick slices with a flip angle of 30° were obtained.

For experiment 2, before contrast medium injection, sequences of transverse and dorsal 1-mm-thick slices were obtained. After contrast medium injection, sequences of transverse and dorsal 2-mm-thick slices were obtained. Both before and after contrast medium injection, variations in flip angle were studied. Dogs were randomly assigned to the study protocols, and no divisions were made on the basis of breed, sex, age, or weight. Before contrast medium injection, dogs were studied with a flip angle of 20° (n = 5 dogs), 30° (3; in 1 dog, a flip angle of 30° was unintentionally used instead of a flip angle of 50°, which contributed to the number of measurements in experiment 1), 70° (1), and 90° (1). After IV injection of 0.3 mL of contrast medium/kg, sequences were obtained with the same flip angle as before contrast medium injection, except for the dog that was studied before contrast injection with a flip angle of 90°. In this dog, a flip angle of 70° was used after contrast medium injection.

By use of dedicated computer software, MPRs were made. Dorsal and sagittal reconstructions were made of the transverse series, transverse and sagittal reconstructions were made of the dorsal series, and transverse and dorsal reconstructions were made of the sagittal series.

Anatomy and Dimensions—The anatomy and shape of the pituitary gland, the sella turcica, and the vessels surrounding the pituitary gland were assessed on the series and MPRs. The pituitary bright signal was identified, and size, shape, and localization were assessed on the imaging series.

The height and width of the pituitary gland were measured on the images of the original transverse series before contrast medium injection. Length was measured on the sagittal MPR series from the original transverse series. On the image of the transverse series that contained the largest cross section of the pituitary gland, the edges of the brain were traced and the enclosed area was calculated by the computer. The P:B ratio was calculated by dividing the height of the pituitary gland (mm X 10³) by the area of the brain (mm²) as described for CT measurements of the pituitary gland.

The pterygoid hamular processes and the shape of the sphenoid bone from rostral to caudal were assessed on the transverse series. The thickness of the basisphenoid bone was measured on the image of the transverse series that contained the largest cross section of the pituitary gland. On the sagittal reconstructed series, the location of the pituitary gland was assessed in relation to the tuberculum sellae, the sphenoid bone, and the dorsum sellae.

Quality—Quality was assessed subjectively (visually). Subjective assessment of quality was based on correct identification of the anatomic structures of interest (pituitary gland, pituitary bright signal, arteries, cavernous sinuses, and the sphenoid bone). A subjective comparison was also made between the series. Subjective quality was assessed as good, moderate, or poor for the individual series and as better or worse for comparison between the series.

The SNR and CNR were calculated as an objective reflection of the subjective findings. For each dog, SNRs and CNRs for the pituitary gland and the pituitary bright signal were calculated. The SNRs and CNRs were calculated for the transverse series of experiments 1 and 2 and for the dorsal and sagittal series of experiment 1. The SNRs and CNRs were not calculated for the dorsal series of experiment 2. On the image that contained the largest cross section of the pituitary gland, ROIs were selected representing the pituitary gland, the pituitary bright signal, the brain, and the background (ie, the area around the skull). The size of the ROI of the background and the brain was standardized to 0.2 cm². The sizes of the other ROIs were set to be a reliable representation of the structures to be measured. Magnetic resonance imaging computer software was used to calculate the mean SI and the SD of the pixel intensities in the ROIs.

The SNR of the pituitary gland (SNRpituitary), the pituitary bright signal (SNRpit bright signal), the surrounding pituitary tissue (SNRsur pit tissue), and the brain (SNRbrain) were calculated as the SI divided by the SD of the background intensity as follows:

\[ \text{SNR}_{\text{pituitary}} = \frac{\text{SI}_{\text{pituitary}}}{\text{SD}_{\text{background}}} \]
\[ \text{SNR}_{\text{pit bright signal}} = \frac{\text{SI}_{\text{pit bright signal}}}{\text{SD}_{\text{background}}} \]
\[ \text{SNR}_{\text{sur pit tissue}} = \frac{\text{SI}_{\text{sur pit tissue}}}{\text{SD}_{\text{background}}} \]
\[ \text{SNR}_{\text{brain}} = \frac{\text{SI}_{\text{brain}}}{\text{SD}_{\text{background}}} \]

The CNR of the pituitary in relation to the brain (CNRpituitary-brain) was calculated by subtracting the SNR of the brain from the SNR of the pituitary gland as follows:

\[ \text{CNR}_{\text{pituitary-brain}} = \text{SNR}_{\text{pituitary}} - \text{SNR}_{\text{brain}} \]

The CNR of the pituitary bright signal in relation to the surrounding pituitary tissue (CNRpit bright signal-sur pit tissue) was calculated by subtracting the SNR of the surrounding pituitary tissue from the SNR of the pituitary bright signal as follows:

\[ \text{CNR}_{\text{pit bright signal-sur pit tissue}} = \text{SNR}_{\text{pit bright signal}} - \text{SNR}_{\text{sur pit tissue}} \]

Statistical Analysis—In each specific MRI setting, the number of measurements (and not the number of dogs) was
used to calculate SNR and CNR values. Results are expressed as mean ± SD for SNR and CNR values and as median and ranges for pituitary gland dimensions (height, width, length, and P:B ratio). Results of series with different imaging plane, flip angle, and slice thickness and with or without contrast medium injection were statistically evaluated by use of the Student t test for paired samples because the groups contained the same dogs. For analysis of groups with different dogs, the Student t test for independent samples (2 tailed) was used. A value of P ≤ 0.05 was considered significant.

Results

Anatomy and dimensions—The pituitary gland encompassed the infundibular recess rostrally on the transverse images and became more round to oval towards the caudal aspect (Figure 1). The pituitary gland appeared triangular on dorsal images (Figure 2) and had a protracted bean shape on the sagittal images with the infundibular recess rostrally (Figure 3). The vessels surrounding the pituitary gland were identified on the transverse and dorsal images.

The pituitary gland was prominent with slightly irregular borders on the transverse images in 3 dogs. A prominent invaginating infundibular recess was seen in 2 dogs with a caudally located pituitary bright signal. In 1 dog, this infundibular recess divided the pituitary gland in 2 parts on the sagittal view, and in another dog, the infundibular recess formed the center in a ring-shaped pituitary gland on the transverse images (Figure 4).

The rostral and ventral borders of the sella turcica were identified on transverse and sagittal images (Figures 1, 3, and 4). The caudal border formed by the dorsum sellae was more difficult to identify on the transverse series, and in 1 dog, it had an asymmetrical appearance.

In all dogs, a pituitary bright signal was detected (Figure 1). The pituitary bright signal was dorsocaudal in 3 dogs, centrodorsal in 4 dogs, central in 2 dogs, and completely caudal in 2 dogs. In 1 dog that had a caudally located bright spot, a small supplemental hyperintense area was seen in the region of the infundibular stalk (Figure 5). The bright signal was prominent and round on the transverse images and triangular on the dorsal images in 7 dogs. In 2 dogs, the bright signal had an asymmetrical appearance. In one of those dogs, the signal resembled a small irregular nodule, and in the other dog, the bright signal was U-shaped around the infundibular recess.

Pituitary gland height ranged from 4 to 6 mm (median, 5 mm), width ranged from 5 to 9 mm (median, 6

Figure 1—Representative transverse magnetic resonance image of the pituitary gland before (A) and after (B) IV injection of contrast medium in a healthy 2-year-old Beagle. p = Pituitary gland. bs = Bright spot. v = Third ventricle. cca = Caudal communicating artery. bc = Basal cistern. mp = Mucoperiosteal layer of the sphenoid bone. ocb = Outer cortical bone. cb = Cancellous bone. icb = Inner cortical bone. R = Right.

Figure 2—Representative dorsal magnetic resonance image after MPR from transverse MRI through the pituitary gland in a healthy 2-year-old Beagle. i = Infundibulum. ca = Carotid artery in cavernous sinus. Ro = Rostral. See Figure 1 for remainder of key.
mm), and length ranged from 7 to 9 mm (median, 8 mm). The P:B ratio ranged from 0.21 to 0.31 (median, 0.26).

The hamular processes were identified on the original transverse images. The hamular processes and the basisphenoid bone were best seen on the images of the 1-mm-thick series with a flip angle of 20° and 30°. Visibility of these structures was highly dependent on the contrast density of the surrounding tissues. The thickness of the basisphenoid bone on the transverse image that contained the largest cross section of the pituitary gland ranged from 2 to 6 mm (median, 4 mm). The following layers could be identified in the structure of the sphenoid bone (from nasopharynx to neurocranium): mucoperiosteal layer, outer cortex, cancellous bone, and inner cortex (Figures 1 and 3). The inner cortex was bordered by the pituitary gland (Figure 1). The position of the pituitary gland in relation to the tuberculum sellae and the dorsum sellae was best seen on sagittal reconstructed images (Figures 3 and 4).

Quality—The image quality in the 1-mm-thick transverse and dorsal images with a 30° flip angle was good as assessed subjectively. From these series, high-quality MPRs were produced. The pituitary gland and the sellar floor were more difficult to distinguish on the dorsal images than on transverse images. The 1-mm-thick sagittal images with a 30° flip angle were of poor quality as assessed subjectively. There were no significant differences in SNR of the pituitary gland between the dorsal, transverse, and sagittal images (Table 1). The CNR between the pituitary bright signal and the surrounding pituitary tissue was not different between dorsal and transverse images (Table 2).

There was no difference in image quality, as assessed subjectively, between the series made with a flip angle of 20° or 30°. The images of the series made with a flip angle of 50° were considerably darker, and the images of the series made with a flip angle of 70° or 90° were of very poor quality. The SNR of the pituitary gland on the transverse images was significantly higher when the flip angle was 20° than when the flip angle was 50° (Table 1). The pituitary bright signal was better delineated from the remaining pituitary tissue on the images of the series made with a flip angle of 50° than on the series made with a flip angle of 30°, and there was less ability to subjectively detect the signal on the series with a flip angle of 20°. The CNR between the pituitary bright signal and the surrounding pituitary tissue on the images of the series made with a flip angle of 30° was higher than that on the images of the series made with a flip angle with 20° or 50°; however, this difference was not significant (Table 2).

On the basis of subjective assessment, 2-mm-thick transverse images were of moderate quality but had less spatial resolution than 1-mm-thick images. Dorsal
images obtained after MPR from 2-mm-thick transverse series revealed considerably less spatial resolution than the dorsal images obtained after MPR of the 1-mm-thick transverse series. The SNR of the pituitary gland was significantly ($P = 0.005$) higher on 2-mm-thick transverse images than on the 1-mm-thick transverse images, both with a 30° flip angle (Table 1).

As subjectively assessed, the image of the pituitary gland was strongly enhanced after injection of contrast medium. The dorsal border of the pituitary gland was more demarcated after contrast medium administration, but delineation between the lateral borders of the pituitary gland and the cavernous sinuses was not improved, compared with images obtained before contrast medium administration. The SNR of the pituitary gland was not significantly different between images obtained before versus after contrast medium administration; however, the CNR was significantly ($P < 0.001$) higher on images obtained after administration (Table 1). The delineation between the bright signal and surrounding pituitary tissue became less pronounced after injection of contrast medium.

Table 1—Mean ± SD SNR$_{pit}$ and CNR$_{pit-brain}$ of measurements obtained from T1-weighted GE 3-dimensional (flash 3 dimensional) MR images in healthy dogs.

<table>
<thead>
<tr>
<th>No. of measurements</th>
<th>Imaging plane</th>
<th>Flip angle (degrees)</th>
<th>Slice thickness (mm)</th>
<th>Contrast medium used</th>
<th>SNR$_{pit}$</th>
<th>CNR$_{pit-brain}$</th>
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<tr>
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<td>Tra</td>
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<tr>
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<td>Yes</td>
<td>17.65 ± 3.36</td>
<td>3.75 ± 1.39</td>
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<tr>
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<td>2</td>
<td>Yes</td>
<td>24.50 ± 3.17</td>
<td>3.45 ± 1.52</td>
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*In 1 dog, it was not possible to determine an ROI containing only the pituitary gland.

Tra = Transverse. Dor = Dorsal. Sag = Sagittal. pit = Pituitary.

Table 2—Mean ± SD CNR$_{bright pit}$, between the pituitary bright signal and the surrounding pituitary gland tissue of the same dogs as in Figure 2.

<table>
<thead>
<tr>
<th>No. of measurements</th>
<th>Imaging plane</th>
<th>Flip angle (degrees)</th>
<th>Slice thickness (mm)</th>
<th>Contrast medium used</th>
<th>CNR</th>
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<tr>
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*See Table 1 for key.
Discussion

In the present study, a 0.2-Tesla open MRI scanner was used for pituitary gland imaging in healthy dogs. As subjectively assessed, the optimal quality of the MRI was achieved with a T1-weighted gradient echo (flash 3-dimensional) sequence with a slice thickness of 1 mm and a flip angle of 30° before and after IV injection of contrast medium. The SNR and CNR values strengthened these subjective findings but should be interpreted with care because of the variations in number of dogs studied with the different sequences. The superior differentiation of the soft tissues with MRI resulted in detailed images of the pituitary gland, the surrounding structures and vessels. Pituitary gland vascularization on magnetic resonance images may give valuable information but should be interpreted with care because vessel resolution is influenced by vessel position, size, and flow direction. The infundibular recess invaginates more deeply into the pituitary gland in dogs than in humans. Also, considerable anatomic variation in size and shape of the pituitary gland has been described. The deeply invaginating infundibular recess that was seen in 2 dogs in the present study was probably a normal anatomic variation.

In humans, T1-weighted SE sequences are considered the most useful sequences for MRI of the pituitary gland. Three-dimensional GE imaging of the pituitary gland, allowing for thinner slices, has been mentioned as an option for detection of small lesions of the pituitary gland. In transverse CT of the canine pituitary gland, a slice thickness of 2 mm is used which with the use of SE sequences, the minimum slice thickness is 3 mm. Preliminary examinations with the SE sequences on canine skulls revealed insufficient spatial resolution. Therefore, the 3-dimensional GE sequence was chosen, instead of the SE technique, to obtain the desired spatial resolution. However, GE images are prone to magnetic susceptibility and motion artifacts. In our study, there were no obvious artifacts affecting the magnetic resonance images, which can be explained by the use of a low magnetic field strength, the small size of the canine sphenoid bone containing only little air and the use of anesthesia during MRI. However, the acquisition time of SE sequences is considerably longer than that of SE sequences in low- and high-field systems.

T1-weighting in GE sequences is typically manipulated by changing the flip angle. Contrast is mainly proton-density weighted at low flip angles (10°) and becomes more T1-weighted for higher flip angles. However, this effect is accompanied by a loss of signal because of the magnetic field inhomogeneity effects caused by the missing 180° echo pulse used in SE techniques (T2 effects), which greatly affects the GE sequence. As subjectively assessed, there was no difference in image quality between the images made with a flip angle of 20° and those made with a flip angle of 30°, except for detection of the pituitary bright signal, which was more distinct on the images of the series made with a flip angle of 30°. The images of the series made with a flip angle of 50° already had much signal loss, and the images of the series made with a flip angle of 70° or 90° were of very poor quality.

Injection of contrast medium is usually not necessary for detection of lesions of the pituitary gland in humans, but for microadenomas, it may give additional information and is therefore recommended. In the present study, injection of contrast medium provided images with improved definition of the dorsal border of the pituitary gland, but obscured the pituitary bright signal and the borders between the pituitary gland and the cavernous sinuses. Therefore, a pituitary gland MRI protocol should contain image sequences obtained before and after administration of contrast medium.

In humans, the pituitary bright signal was first thought to be caused by fat within the sella turcica. However, the origin of the pituitary bright signal was later determined to be the neurohypophysis. There is considerable variation in the rate of detection of the pituitary bright signal in healthy humans (63% to 100%), which is explained by individual variation, differences in age, and different MRI settings. There remains some controversy about the exact origin of the high SI, but the intensity appears to depend on the vasopressin concentration in the posterior lobe, and the signal is absent in humans with central diabetes insipidus. Furthermore, the pituitary bright signal is thought to correspond to only a part of the neurohypophysis. In the present study, the pituitary bright signal was detected in all dogs, but delineation depended on the imaging protocol. The differences in size, shape, and location of the pituitary bright signal are probably more attributable to physiologic variation than to variation in anatomic features of the neurohypophysis. However, in 2 dogs with a deep infundibular recess, the pituitary bright signal was displaced caudally. There was no explanation for the small hyperintense nodule in the region of the infundibular stalk in 1 dog, although in a human patient without sellar or parasellar disease, it was reported that the pituitary bright signal was located in the area of the median eminence.

In the dogs of the present study, the pituitary height, length, and width and the P:B ratio were comparable to values for healthy dogs in other studies. With the single-slice CT scanner, the distance was measured in tenths of a millimeter. With the software of the MRI machine used in this study, the distance was measured to a resolution of 1 millimeter and accuracy was decreased, compared with the single-slice scanner. Therefore, measurements had to be done with the greatest care. Furthermore, subjective assessment of the size and shape of the pituitary gland in relation to the cavernous sinuses, as described for CT of the pituitary gland in dogs, remains important.

Microsurgical transsphenoidal hypophysectomy is an effective method of treatment for dogs with PDH.
The position of the pituitary gland in relation to the surgical landmarks, such as the hamular processes, may vary among dogs of different breeds and even among dogs of the same breed.\(^1\) It seems that CT is superior to MRI for accurate preoperative localization of the pituitary gland in relation to the hamular processes and the shape of the outer cortical lamina of the sphenoid bone.\(^1\) Although the sphenoid bone itself was visible with MRI, the shape of the outer cortical lamina was difficult to discern on transverse MR images because of insufficient resolution. The hamular processes were visible on the transverse images of MRI series, but their detection depended on the imaging protocol and the intensity of the surrounding tissues. The hamular processes could not be identified on the transverse MPRs of the dorsal series of scans because the ventral lining of the slab was positioned dorsally to the nasopharynx and the hamular processes protrude into the nasopharynx. In comparison with CT in dogs,\(^2\) the sagittal MPRs give valuable information on the intracranial relation between the pituitary gland and the bordering bone structures (ie, the tuberculum sellae and the dorsum sellae).

\(^{a}\) Domitor, SmithKline Beecham Animal Health BV, Zoetermeer, The Netherlands.
\(^{b}\) Dippvan-10, Zeneca BV, Ridderdorik, The Netherlands.
\(^{c}\) Forene, Abbott Laboratories BV, Maarssen, The Netherlands.
\(^{d}\) Magnetom Open Viva, Siemens AG, Erlangen, Germany.
\(^{e}\) Dotarem, Guerbet Nederland BV, Gorinchem, The Netherlands.
\(^{f}\) Siemens AG, Erlangen, Germany.

References
