Comparison of three-view thoracic radiography and computed tomography for detection of pulmonary nodules in dogs with neoplasia

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Objective—To compare the detection of pulmonary nodules by use of 3-view thoracic radiography and CT in dogs with confirmed neoplasia.

Design—Prospective case series.

Animals—33 dogs of various breeds.

Procedures—3 interpreters independently evaluated 3-view thoracic radiography images. The location and size of pulmonary nodules were recorded. Computed tomographic scans of the thorax were obtained and evaluated by a single interpreter. The location, size, margin, internal architecture, and density of pulmonary nodules were recorded. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for thoracic radiography (with CT as the gold standard).

Results—21 of 33 (64%) dogs had pulmonary nodules or masses detected on CT. Of the dogs that had positive CT findings, 17 of 21 (81%) had pulmonary nodules or masses detected on radiographs by at least 1 interpreter. Sensitivity of radiography ranged from 71% to 95%, and specificity ranged from 67% to 92%. Radiography had a positive predictive value of 83% to 94% and a negative predictive value of 65% to 89%. The 4 dogs that were negative for nodules on thoracic radiography but positive on CT were all large-breed to giant-breed dogs with osteosarcoma.

Conclusions and Clinical Relevance—CT was more sensitive than radiography for detection of pulmonary nodules. This was particularly evident in large-breed to giant-breed dogs. Thoracic CT is recommended in large-breed to giant-breed dogs with osteosarcoma if the detection of pulmonary nodules will change treatment. (J Am Vet Med Assoc 2012;240:1088–1094)

Pulmonary metastatic disease is common with many neoplastic diseases in dogs.1–3 The detection of pulmonary metastases is important because it can considerably impact staging, prognosis, and treatment options. In small animals, 3-view thoracic radiography, consisting of the right and left lateral and ventrodorsal or dorsoventral views, is considered the standard for detecting pulmonary metastases.1–3 Computed tomography has become more widely available and has an increasing role in the diagnosis of thoracic disease in small animals.4–9 In people, CT is considered the gold standard for detection of pulmonary nodules because CT is able to detect smaller nodules with greater frequency than is survey radiography.10 Computed tomography is recommended as a routine screening test for people with malignancies that have a high propensity to metastasize to the lungs and in those patients in which the finding of metastases would have a major impact on management.10–12

The literature mentions CT for detection of pulmonary metastatic disease in small animals6,7,13,14; however, reports6,13,14 quantitatively addressing the benefit of CT, compared with thoracic radiography in dogs, for pulmonary metastases detection are few. The 2 main advantages of CT, compared with thoracic radiography, are elimination of superimposition by thoracic structures and superior contrast resolution. These allow for detection of small nodules that would otherwise go unnoticed. One of the main differences between thoracic CT performed in people and animals is the necessity of general anesthesia for animals. The requirement of anesthesia can be confounding because of the resulting poor aeration of the lung (atelectasis), which can decrease nodule conspicuity14,15.

The purpose of the study reported here was to compare 3-view thoracic radiography with thoracic CT for the detection of pulmonary metastatic disease in dogs with confirmed neoplastic diseases. The hypothesis was that CT would detect a larger number of pulmonary nodules than found on radiographs but that there may be variability in nodule detection on the basis of nodule size and density, patient size, and type of neoplasia.

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Materials and Methods

Case selection—The Kansas State University Institutional Animal Care and Use Committee approved the study. Approval via client consent forms was obtained from the owners before enrollment in the study. For inclusion in the study, the dogs were required to have confirmed cancer of a type that had the potential to metastasize to the lungs in the nodular form (eg, osteosarcoma, carcinoma, high-grade sarcoma, and melanoma).

Imaging procedures—Each patient had 3-view radiography performed consisting of right and left lateral and ventrodorsal views. Radiographs were obtained with a medium-speed film system or were digital radiographs, with either a direct or indirect system. A grid was used in all patients > 10 cm in thickness. All radiographs were assessed as being of adequate diagnostic quality. Three interpreters that were blinded to the patient information evaluated radiographs. The interpreters consisted of 2 board-certified radiologists and a minimally trained student interpreter. All 3 films from a study were interpreted together. The location (lung lobe affected) and size of the pulmonary nodules were recorded.

Computed tomographic scans were obtained with a third-generation scanner within 7 days after radiography was performed for inclusion in the study (most were performed within 24 to 48 hours). General anesthesia was used for all patients, and protocols differed dependent on the anesthesia service. In most dogs, anesthesia was induced with propofol to effect, then maintained with isoflurane in 100% oxygen. The CT scans consisted of helical scans with a slice thickness of 3 to 7 mm dependent on patient body size, a pitch of 1, and reconstruction interval of 1. For the toy and small breeds, slice thickness was 3 mm. Slice thickness was 5 mm for medium breeds and 7 mm for large to giant breeds. The field of view was also variable dependent on patient size. Prior to the CT acquisition, the dogs were hyperventilated with 4 to 5 breaths followed by breath holding for the length of the scan at 20 cm H2O. Total scan time was < 60 seconds. All CT scans were considered of adequate diagnostic quality without substantial evidence of atelectasis. The CT scans were evaluated by a radiologist on a picture archive and communication system with the interpreter blinded to patient information. In general, the CT images were evaluated at a lung window (window width, 2,000 HU; window length, –350 HU); however, the interpreter could change the brightness, contrast, and magnification as desired. The location, size, margin (irregular or indistinctly marginated vs smooth or distinctively marginated), internal architecture, and density of the pulmonary nodules were recorded. Location included lung lobe and whether the nodule was in contact with a pleural surface (subpleural) or did not contact the pleural surface (parenchymal).

Statistical analysis—Analysis was performed with a commercially available statistical package. Values of P < 0.05 were considered significant. Sensitivity (percentage of true-positive results), specificity (percentage of true-negative results), positive predictive value (percentage of dogs with positive radiograph findings that were positive for pulmonary nodules on CT), and negative predictive value (percentage of dogs with negative radiographic findings that were negative for pulmonary nodules on CT) were calculated for thoracic radiographs (with CT as the gold standard) as follows:

Sensitivity = TP/(TP + FN) × 100
Specificity = TN/(TN + FP) × 100
Positive predictive value = TP/(TP + FP) × 100
Negative predictive value = TN/(TN + FN) × 100

where FN is number of false negatives, FP is number of false positives, TN is number of true negatives, and TP is number of true positives.

Overall accuracy calculated as the number of dogs correctly identified as either positive or negative for pulmonary nodules on radiographs with a similar CT finding was determined for each interpreter. The likelihood of a positive radiographic finding being identified as a positive finding on CT and, conversely, the likelihood of a negative radiographic finding being confirmed as negative on CT were determined for each of the 3 interpreters.

Results

Patient population—There were 33 dogs included from 2002 to 2007. The dogs ranged in age from 5 to 15 years (mean ± SD, 9.3 ± 2.8 years). There were 3 sexually intact males, 14 neutered males, and 16 neutered females. Dogs included 25 large- and giant-breed dogs: 6 large mixed-breed dogs, 5 Labrador Retrievers, 3 Rottweilers, 2 Golden Retrievers, 2 Doberman Pinchers, and 1 each of Saint Bernard, Great Dane, Vizsla, Gordon Setter, Chesapeake Bay Retriever, Irish Setter, and Irish Water Spaniel. The remaining 8 dogs were of toy, small, and medium breeds: 2 small mixed-breed dogs and 1 each of Pomeranian, Australian Shepherd Dog, Toy Poodle, Beagle, Jack Russell Terrier, and Australian Kelpie. All dogs had confirmed neoplasia that included 13 osteosarcomas, 4 oral melanomas, 4 pulmonary adenocarcinomas, 3 soft tissue sarcomas (elbow area, shoulder area, and ventral body wall), 3 squamous cell carcinomas (laryngeal, digit, and supraspinatus muscle), 2 hemangiosarcomas (renal and subcutaneous hind limb), and 1 each of mammary gland carcinoma, ventral neck carcinoma, salivary gland adenocarcinoma, and hepatocellular carcinoma.

Imaging findings—Twenty-one of the 33 (64%) dogs had pulmonary nodules or masses detected on CT. Of these 21 dogs, 17 (81%) had pulmonary nodules or masses detected on radiographs by at least 1 radiologist (15 [71%] by both radiologists). A pulmonary nodule was diagnosed in 2 of 33 (6%) dogs by at least 1 board-certified radiologist (1 [3%] by both radiologists) on radiographs that was not confirmed on CT. In the 17 dogs that had nodules visible on radiographs that were confirmed on CT, radiographs underestimated the number of nodules in 6 dogs, compared with CT.

The 4 dogs that were negative for nodules on radiography by both radiologists but positive on CT were all large- to giant-breed dogs with osteosarcoma. These dogs were a Saint Bernard with 3 nodules (diameter, one 2 mm
and one 1 cm and one 2 x 1.4 cm; Figure 1), Rottweiler with 7 nodules (diameter, one 2 mm, two 3 mm, two 4 mm, one 5 mm, and one 6 x 9 mm; Figures 2 and 3), Labrador Retriever with a solitary 4 mm-diameter nodule, and Rottweiler with 2 nodules (diameter, both 3 mm).

When all nodules were evaluated, 37 nodules ranging in size from 3 mm to 10 cm in diameter were detected on radiography and 89 nodules ranging in size from 2 mm to 8 cm in diameter were detected on CT. The difference in the upper limit of the size is expected as a result of magnification on radiographs. On CT, the location of the nodules consisted of 13 in the right cranial lung lobe, 12 in the right middle lung lobe, 23 in the right caudal lung lobe, 6 in the accessory lung lobe, 19 in the left cranial lung lobe, and 16 in the left caudal lung lobe. Those adjacent to the thoracic wall were considered subpleural (n = 28), whereas the remaining nodules were surrounded completely by aerated lung (parenchymal [61]). Seventy-six of the nodules were round, with smooth margins and solid internal architecture. The remaining 13 nodules had a range of shapes (ovoid, polygonal, irregular, or multilobulated). There were 5 nodules that had a ground-glass appearance, 2 that were cavitary (thick walled), and 4 that contained air bronchograms.

The density of the nodules ranged from –667 to 48 HU. The nodules with low density measured in HUs, closer to that of normal lung, were those that were small on thicker slices (2- to 3-mm-diameter nodules on a slice thickness of 5 to 7 mm). The greatest number of nodules detected on diagnostic imaging was 15 on radiography and also 15 on CT, although in different patients. Two of the 33 (6%) dogs had at least 7 nodules detected by at least 1 observer on radiographs. Six of the 33 (18%) dogs had at least 7 nodules detected with CT.

Statistical results—For interpretation of the radiographs, there was near perfect agreement between the 2 radiologists and fair to moderate agreement between the less experienced interpreter and the radiologists (Table 1).

For statistical analysis by use of CT as the gold standard for pulmonary nodule detection, sensitivity (true-positive results) of thoracic radiography for the identification of a nodule for the 3 interpreters ranged from 71% to 95%. Specificity (true-negative results) for thoracic radiography for the identification of a nodule ranged from 67% to 92%. For thoracic radiography, this resulted in a positive predictive value of 83% to 94% and a negative predictive value of 65% to 89%. Radiographic detection accuracy ranged from 79% to 85%. The likelihood ratio that a positive thoracic radiographic finding came from a dog that was positive for a nodule on CT ranged from 2.9 to 8.6. The likelihood ratio that a negative thoracic radiographic finding came from a dog that was positive for a nodule on CT was 0.1 to 0.3 (Table 2).
Interestingly, in a previous study, the present study was specifically designed to include in 11 of 28 (39%) dogs with general thoracic disease and lung masses or nodules were either confirmed or found visible on radiographs. This may be a result of 2-view chest radiography images (ie, nodule positive or nodule negative) obtained from 33 dogs with confirmed neoplasia. In a previous study that was not reported but smaller radiographic nodules detected, then this could account for some of the disparity in detection rate.

When analyzing the size (>5 mm) and number of nodules detected on CT and the likelihood that nodules would be detected on radiographs, the radiologists were 25 to 47 times as likely to identify nodules on radiographs if the CT nodules were >5 mm (P = 0.02); however, the CI for this OR was wide (1.7 to 393.2), reflecting the low number of dogs with nodules of <5 mm identified on radiographs. For all interpreters, the number of nodules visualized with CT did not significantly affect the likelihood of identifying a positive radiographic finding.

## Discussion

In dogs, 3-view thoracic radiography will likely remain the standard for evaluation of pulmonary metastatic disease because of the lower cost and increased availability, compared with CT. In previous studies that determined the value of CT in supplement to thoracic radiographs for evaluation of thoracic disease, additional lung masses or nodules were either confirmed or found in 11 of 28 (39%) dogs with general thoracic disease and in 2 of 21 (9.5%) dogs with mammary gland carcinoma. The present study was specifically designed to include dogs that would have a high incidence of pulmonary metastases. Interestingly, in a previous study of dogs with pulmonary metastatic disease, only 9% of the nodules visible with CT were detected on radiographs. In the present study, 37 of 89 (41%) nodules seen with CT were visible on radiographs. This may be a result of 2-view studies used in the previous study or a difference in type of imaging system (conventional film vs digital, which was not specified). Additionally, the lower limit of nodule size that was reliably detected on radiographs in the previous study was 7 to 9 mm in diameter and with CT was 1 mm in diameter. Our nodule size lower limit on radiographs was lower (3 mm diameter), and our CT lower limit of detection was higher (2 mm diameter) than those in the previous study. If there were 1-mm-diameter nodules on CT scans in the present study that were not reported but smaller radiographic nodules detected, then this could account for some of the disparity in detection rate.

Adequate aeration of the lung requires some form of pulmonary ventilation. Although all CT scans in the present study were considered diagnostic, there were a few dogs that had irregular, ill-defined, and heterogeneous opacity in the ventral aspects of the cranial and middle lung lobes consistent with atelectasis. Because of the need for anesthesia, a small amount of atelectasis is often unavoidable. Dogs were placed in sternal recumbency during the CT scans in an attempt to minimize underaeration and hypostatic congestion.

Spatial resolution plays a role in the detection of pulmonary nodules in both radiography and CT. Decreasing collimation (slice thickness) reduces partial volume averaging, which can increase sensitivity and accuracy of pulmonary nodule detection. Studies have shown that decreasing collimation (decreased slice thickness) increases the number of nodules detected. In a study in people that compared thin- versus thick-section CT, it was found that nodules measured significantly larger on 1-mm CT images, compared with 5-mm CT images. The recommendation was to use thick sections for nodule detection (to decrease interpretation times), then use thinner sections for nodule characterization. This can be done if 2 image sets are reconstructed concurrently from the same raw data. In a study comparing CT protocols in a small (4-kg [8.8-lb]) and large (38-kg [83.6-lb]) dog, it was concluded that 3-mm thick CT images (vs 5 mm thick) increased sensitivity and accuracy for the small dog and that 5- and 7-mm-thick images were similar for the large dog. Increasing pitch can result in a decrease in spatial and contrast resolution. Pitch (1, 1.5, and 2) and reconstruction interval (0.5 and 1) did not affect nodule detection in that study. It was concluded that a slice thickness of 3 mm for small dogs and 5 mm for large dogs, with a pitch of 2 and a reconstruction interval of 1, should be used. Thus, the imaging protocol used in the present study was in line with current recommendations for the smaller dogs, but more accurate detection may have been possible if thinner slices were used in the larger dogs.

In people, it has been reported that pulmonary metastases are generally bilateral and peripheral (subpleural) and predominate in the middle and lower zones rather than the apices. This distribution is important in that it affects the potential for needle aspiration or biopsy and surgical resection (metastasectomy). In the dogs of the present study, approximately one-third of the nodules were subpleural and all lung lobes were affected, with the right caudal lung lobe having the most nodules. In dogs, it is reported that the right caudal lung lobe is the most common anatomic location of primary pulmonary neoplasia. This anatomic preference is believed to be a result of greater lung tissue mass.

The shape and internal structure of the nodule is considered in people when trying to discriminate ma-

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Table 2—Sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios of 3-view thoracic radiography findings, compared with CT as the gold standard for nodule detection.
Lymphoid versus benign disease. Polygonal and tubular to flat-shaped structures are most likely benign. Clustered nodules tend to be infectious, whereas round nodules are more likely malignant. In the dogs of the present study, most nodules were round. Nodules that are spiculated, have nonsolid (ground-glass) internal architecture, or contain air (cavitation, pseudocavitation, or air bronchograms) are more likely to be malignant in people. Most dogs had solid nodules, although the other patterns were recognized in 13 of the 89 (15%) nodules. The density of nodules in the present study had a very large range. The lower densities are thought to be a result of mean volume calculation from normal lung around the nodule (eg, a 2-mm-diameter nodule on a 7-mm-thick slice would be closer to normal lung than soft tissue density). The upper limit of density (48 HU) is consistent with soft tissue. None of the nodules in the present study had calcification, either subjectively or on objective measurements. Theoretically, it is possible that small nodules on a thick slice could be calcified and still retain a low density. The finding of calcification within a nodule in people is associated predominantly with benign disease. If a person has a tumor that is known to have frequent calcification of metastases, then the likelihood increases greatly that a nodule represents true metastases. Tumor types in people with calcified metastases include osteogenic sarcoma, chondrosarcoma, synovial sarcoma, and carcinomas of the ovary, breast, colon, or thyroid gland. Laminated or central, or popcorn, calcification is considered more likely benign in people, whereas punctuate calcification can be either benign or malignant, and eccentric calcification is considered most likely malignant. Nodules with a density > 164 HU on noncontrast studies are considered calcified.

In addition to density of a nodule, size also plays an important role in detection. In the study comparing CT protocols for detection of pulmonary nodules in dogs, nodule size < 3 mm diameter versus > 3 mm diameter did not affect nodule detection. In the present study, we considered 5 mm diameter as a size cutoff for likelihood of detection on radiographs if the nodule was seen on CT. This size cutoff was chosen because it is often referred to as a size that can be detected on radiographs. This size was only significant (2.3 times) for one of the observers. In people, a lesion > 3 cm diameter (mass rather than nodule) is considered malignant, and in general, the larger the nodule, the higher the risk of malignancy.

The number of nodules may also play a role in detection of benign versus malignant disease. A study in people with osteosarcoma determined that all patients with > 7 nodules on thoracic CT had metastatic disease. Because histologic analysis was not performed and because of the small number of patients with > 7 nodules, statistical analysis could not be performed in the present study. Differentiation between benign and metastatic lesions on the basis of morphological features, distribution, size, number, and attenuation characteristics have been attempted in people with conflicting results and much overlap. Without histologic evaluation of the individual nodules in the present study, conclusions could not be drawn on the etiology; however, the study shows the variety of expected appearances of nodules in dogs as visualized with CT. As noted in people, the variation in nodule appearance in the present study would suggest that a portion of the nodules may not be metastatic.

The sensitivity of radiography for pulmonary metastatic detection is estimated at 65% to 97%, compared directly with histologic evaluation. Our results were similar, with the sensitivity of radiography ranging from 71% to 93%, depending on the observer. Computed tomography can result in both false-positive and false-negative findings. False positives can result from end-on vessels. The most reliable method of distinguishing a nodule from a vessel is to look for branching or continuity of the structure with a vessel on contiguous slices. Nodules can also be overlooked or confused with other disease. This is particularly true if there is concurrent parenchymal infiltration, atelectasis, fibrosis, or pleural effusion.

In the study comparing CT protocols in a small and large dog, the interobserver and intraobserver repeatability was variable, suggesting nodule detection may be more dependent on the observer rather than on the choice of CT protocol. Although intraobserver repeatability was not assessed in the present study, the interobserver agreement for detection of pulmonary nodules on thoracic radiographs was excellent between radiologists (interpreters 1 and 2). The higher specificity of the radiologists would be expected; however, the higher specificity of the less trained observer (interpreter 3) and the similar accuracy between observers was unexpected. Nodule detection or reporting may be influenced if the interpreter considers the potential impact of the detection of finding a nodule may have on the patient outcome. Some observers may underread equivocal nodules, whereas others may overinterpret equivocal nodules. Although patient outcome was not an influence in the present study, the less experienced observer was concerned about missing nodules; therefore, the individual was more likely to count an equivocal area as a nodule, which may have led to the high sensitivity but lower specificity. Interpreter 1 was more inclined to disregard an area that was equivocal, which likely resulted in the lower sensitivity and higher specificity.

A major limitation of the present study is that the number of pulmonary nodules was not confirmed via histologic evaluation, nor were the nodules confirmed to be metastatic. In people, studies that evaluate lung nodules are acceptable if CT is used as the gold standard because small nodules can be missed on histologic evaluation. In direct conflict with this information, another study found that pulmonary metastasis detection with CT in 4 dogs with osteosarcoma was only 56%, compared with histologic evaluation. Results of the present study must be interpreted with these inherent limitations. Ideally, a study could be designed to include histologic evaluation, but this was not feasible because of the clinical nature of the present study. Because most of the tumor types in the present study have a high propensity of metastasizing to lung, it is presumed that a number of the nodules were metastases. In people with extrathoracic neoplasia, studies have
shown that 77% to 93% of nodules were metastases. In people, false-positive results are seen with nonneoplastic conditions such as hamartoma, sarcoidosis, silicosis, histoplasmosis, tuberculosis, inflammatory pseudotumor, intrapulmonary lymph nodes, small pulmonary infarcts, focal areas of fibrosis, or intraluminal pleural plaques. 10,19

Another limitation is the lack of IV contrast media for CT evaluation. Contrast enhancement patterns are one of the features that are evaluated in people. 22 Further, during the study, the radiology department switched from analog to digital radiographic imaging. This may have impacted the ability to detect pulmonary metastases on radiographs and would have ideally been standardized for the present study. Three of the 4 large-breed dogs that had pulmonary nodules on CT not detected on radiographs had analog films. A larger number of patients would have been beneficial for statistical evaluation by dog size and tumor type. Neither interobserver variability nor growth rate over time were assessed. Growth rate would have been interesting to assess because it is one of the most important signs in determining etiology of a pulmonary nodule. 19,22,23

As would be expected on the basis of past and current literature, CT is more sensitive than radiographs for detection of pulmonary nodules. In large- to giant-breed dogs, it is more difficult to detect small to moderately sized nodules. The cost-benefit ratio of any diagnostic test should be considered for each patient to determine whether the test should be performed. In the case of thoracic CT, the financial expense, radiation exposure, and potential impact of anesthesia are all considerations. It may be beneficial to recommend CT in large-breed dogs with osteosarcoma if the detection of nodules will change treatment (eg, surgical amputation vs no amputation). From the present study, the second indication for thoracic CT (specifically looking for pulmonary metastases) would be in dogs with primary pulmonary neoplasia. If metastases are present, the treatment is often altered (surgical lung lobectomy vs medical treatment). 21 This was the case in 1 of the 4 dogs in the present study with primary pulmonary neoplasia. The CT finding of a nodule in another lung lobe resulted in cancellation of surgery. In addition, CT can be used to identify abnormal tracheobronchial lymphadenopathy, 21,28,29 which was not addressed specifically in the present study.

It is unknown whether there is a true benefit of earlier recognition of pulmonary nodules via CT in terms of treatment and prognosis. The importance (metastatic vs nonmetastatic) of a nodule cannot be determined with CT alone. In children with extremity osteosarcoma, both the number of nodules and the number of lung lobes involved affected overall survival time. 30 For individual malignancies, such as osteosarcoma, future studies with larger numbers of patients having additional follow-up and histologic evaluation would be helpful to assess the impact of early detection of pulmonary nodules with CT on long-term survival time.

References


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**From this month’s AJVR**

**Effects of isoflurane anesthesia with and without dexmedetomidine or remifentanil on quantitative electroencephalographic variables before and after nociceptive stimulation in dogs**

Anne M. Kulka et al

**Objective**—To evaluate the influence of various anesthetic protocols and 3 multiples of isoflurane minimum alveolar concentration (MAC) before and after supramaximal stimulation on electroencephalographic (EEG) variables in dogs.

**Animals**—6 adult healthy Beagles (mean ± SD body weight, 16.3 ± 1.0 kg).

**Procedures**—All dogs underwent 3 anesthesia sessions with a minimum of 1 week separating sessions: isoflurane alone, isoflurane and a constant rate infusion of dexmedetomidine (3 µg/kg/h, IV; isoflurane and dexmedetomidine [ID]), and isoflurane and a constant rate infusion of remifentanil (18 µg/kg/h, IV; isoflurane and remifentanil [IR]). The MAC of isoflurane was determined via supramaximal electrical stimulation. Quantitative variables (frequency bands and their ratios, median frequency, 95% spectral edge frequency [SEF], and an EEG index) were determined directly before and after supramaximal stimulation at 0.75, 1.0, and 1.5 times the MAC for each session of 20-second epochs.

**Results**—Isoflurane MACs for isoflurane alone, ID, and IR were 1.7 ± 0.3%, 1.0 ± 0.1%, and 1.0 ± 0.1%, respectively. Prestimulation 95% SEF decreased significantly with increasing MAC during the isoflurane alone and ID sessions. Significant decreases in 0 frequency band (0.5 to 3.5 Hz) presence and significant increases in β frequency band (> 12.5 Hz) presence, median frequency, and 95% SEF after stimulation were dependent on the MAC and anesthetic protocol. The EEG index had the strongest correlation with increasing MAC during the isoflurane alone session (ρ = −0.89) and the least in the IR session (ρ = −0.15).

**Conclusions and Clinical Relevance**—Anesthesia with isoflurane alone resulted in the greatest overall EEG depression of all protocols. Use of remifentanil depressed the EEG response to nociceptive stimulation more strongly than did dexmedetomidine. The EEG variables evaluated did not appear useful when used alone as indicators of anesthetic depth in dogs. (Am J Vet Res 2012;73:602–609)