

Evaluation of the dens-to-axis length ratio and dens angle in toy-breed dogs with and without atlantoaxial instability and in healthy Beagles

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Received September 14, 2016.

Accepted January 25, 2017.

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OBJECTIVE

To evaluate and compare morphological characteristics of the dens in atlantoaxial instability (AAI)-predisposed toy-breed dogs (TBDs) with and without AAI and non-AAI-predisposed healthy Beagles.

ANIMALS

80 AAI-affected and 40 nonaffected TBDs and 40 Beagles.

PROCEDURES

Each dog underwent CT examination of the cervical vertebral column. On median 3-D multiplanar reconstruction images, the dens angle (DA) was measured as were the lengths of the dens and the body of the axis; the dens-to-axis length ratio (ratio of the dens length to the axis body length [DALR]) was calculated. Data were compared among dog groups.

RESULTS

The DALR in nonaffected TBDs and Beagles did not differ significantly. The mean DALR for AAI-affected TBDs was significantly lower than that for nonaffected TBDs. The mean DA of AAI-affected TBDs was significantly greater than that of Beagles and nonaffected TBDs.

CONCLUSIONS AND CLINICAL RELEVANCE

Results indicated that a low DALR might be associated with a high probability of dens abnormalities in TBDs. Additionally, dens length in AAI-affected TBDs appeared to be smaller than that in non-AAI-affected TBDs, given the low DALR in AAI-affected TBDs. Further investigations to determine reference ranges of the DA and DALR and the potential usefulness of those variables as diagnostic markers for AAI in TBDs are warranted. (*Am J Vet Res* 2017;78:1400–1405)

Atlantoaxial instability, commonly affecting small-sized young dogs, results in variable degrees of cervical spinal cord compression.¹⁻⁵ Atlantoaxial instability in TBDs was first reported by Geary et al.⁶ In young TBDs, AAI results from congenital dysplasia of the atlantoaxial joint and may include aplasia or hypoplasia of the dens, nonunion of the dens with the axis, dorsal angulation of the dens, rupture of the tectorial membrane, incomplete ossification of the dorsal neural arch of the atlas, acquired trauma-related instability, subluxation, or dislocation (fracture or ligament rupture). Various pathogenetic factors influence the onset of AAI.^{1-3,6-12} In recent years, AAI has been included among craniocervical junction abnormalities, a general term for congenital malformations in the craniocervical region in small-breed dogs.^{13,14}

In a retrospective study,⁴ dens abnormalities were detected and evaluated in 35 of 46 (76%) small-breed dogs and TBDs. Generally, in the process of di-

agnosis of AAI, only the presence or absence of dens abnormalities is noted. The axis has 7 ossification centers.^{6,15} The dens develops from 2 separate ossification centers: the centrum of the proatlas, which forms the cranialmost quarter portion, and another center, which forms the caudal three-quarter portion.¹⁵ The dens of the axis separates from the body of the atlas during development. The ossification center of the dens forms at birth and joins with the vertebral body of the axis 7 to 9 months after birth.⁶ Vascular-related ischemia may lead to postnatal resorption of at least the middle part of the dens, leading to dens abnormalities.¹⁵ Dysplasia and nonunion of ossification centers in the dens of the axis, when observed on radiographic and CT images, are generally considered examples of dens abnormalities. However, excluding obvious nonunion of the dens and separation of bone, there are no well-defined standards for diagnosis of dens abnormalities in veterinary medicine. Therefore, we chose to focus on the length and angle of the dens of the axis in the study reported here and attempted to evaluate dens abnormalities by measurement of these 2 variables.

The objective of the study reported here was to perform a detailed evaluation and comparison of mor-

ABBREVIATIONS

AAI	Atlantoaxial instability
DA	Dens angle
DALR	Dens-to-axis length ratio
MPR	Multi-planar reconstruction
TBD	Toy-breed dog

phological characteristics of the dens from CT images of the cervical portion of the vertebral column of AAI-predisposed TBDs without AAI, non-AAI-predisposed healthy Beagles, and AAI-predisposed TBDs with AAI that underwent surgery.

Materials and Methods

Dogs

Medical records of AAI-affected dogs that underwent surgery between February 2005 and November 2014 at the Veterinary Medical Teaching Hospital, Nippon Veterinary and Life Science University, or at the YPC Tokyo Animal Orthopedic Surgery Hospital were retrieved. Among the 153 dogs that had AAI and underwent surgery, the top 4 breeds (Chihuahua, Toy Poodle, Yorkshire Terrier, and Miniature Dachshund) that underwent preoperative CT examination were identified. The study population included 80 dogs of AAI-predisposed toy breeds that developed AAI and underwent surgery (AAI-affected TBDs [28 Chihuahuas, 20 Toy Poodles, 20 Yorkshire Terriers, and 12 Miniature Dachshunds]) and 40 dogs of AAI-predisposed breeds (nonaffected TBDs [10 Chihuahuas, 10 Toy Poodles, 10 Yorkshire Terriers, and 10 Miniature Dachshunds]), which had undergone MRI and CT examinations and were confirmed as lacking spinal cord compression by the dens of the axis on the ventral side, dorsal compression, atlantooccipital overlapping, or Chiari-like malformation.^{13,16,17} The study population also included 40 healthy Beagles (a breed that is not predisposed to AAI). After the CT examination, the Beagles were euthanized by IV administration of barbiturates for reasons unrelated to the study. Euthanasia was performed in accordance with the Guideline for Care and Use of

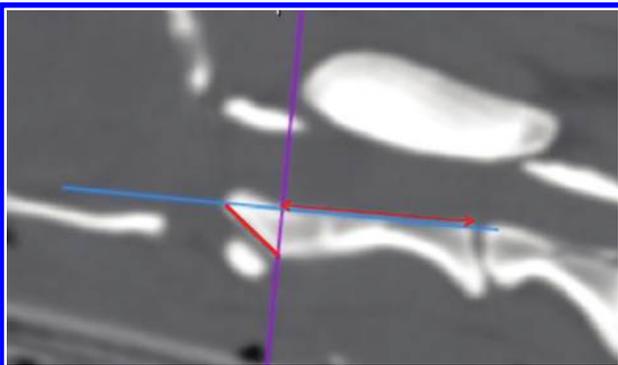


Figure 1—Median image of the axis of a Beagle reconstructed from CT images by 3-D MPR. To determine the DALR, a line (purple line) is first drawn passing through the tip of the dens and the dorsocaudal aspect of the body of the axis. Another line (blue line) is then drawn perpendicular to the first, passing through the base of the ventral aspect of the dens. In this image, length of the dens (red line [no arrowheads]) is defined along the perpendicular line as the distance from the tip of the dens to the ventral base of the dens. Length of the body of the axis (red line with arrowheads) is measured as the distance from the point of intersection of the 2 lines to the dorsocaudal aspect of the axis. Thus, DALR is defined as the ratio of the length of the dens to that of the axis body.

Laboratory Animals of the Nippon Veterinary and Life Science University (approval No. 46J-27).

CT examination and morphological evaluation

Image acquisition was performed with 80- and 160-slice CT scanners^a at a scan speed of 0.5 seconds, slice thickness of 0.5 mm, and slice interval of 0.5 mm. For CT evaluation, the dogs were anesthetized and positioned in dorsal recumbency, with the neck extended and stabilized with a wedge-shaped stabilizer. Adhesive tape was used to ensure that the head, cervical portion of the vertebral column, and thoracic portion of the vertebral column would not rotate. For each dog, morphological evaluation of the axis was performed with image-processing software^b for reconstruction of CT DICOM data into 3-D MPR images. In accordance with procedures reported by Parry et al,¹⁸ CT images were visualized at a window width and level of 2,500 and 500 Hounsfield units, respectively.

Calculation of the DALR

Except in cases of clear nonunion of the dens and separation of bone, we focused on the length of the dens of the axis to identify dens abnormalities. A few of the AAI-affected TBDs had complications such as dysplasia of the spinous process of the axis. Because there is no report of dysplasia in the body of the axis, to our knowledge, we used the length of the body of the axis as the reference standard in this study.

To measure the lengths of the dens and the body of the axis on median 3-D MPR images reconstructed from CT images, a line was drawn passing through the tip of the dens and the dorsocaudal aspect of the axis. Another line was drawn perpendicular to the first, passing through the base of the ventral aspect of the dens. The distance between the tip of the dens and the base of the ventral aspect of the dens was defined as the length of the dens. In the same image, the distance between the point of intersection of the 2 lines and the dorsocaudal aspect of the axis was defined as the length of the body of the axis. The DALR was then calculated as the ratio of length of the dens to that of the axis body (**Figure 1**). The DALRs of the 160 study dogs (80 AAI-affected TBDs, 40 Beagles, and 40 nonaffected TBDs) were compared groupwise as follows: nonaffected TBD group vs the Beagle group, each of the 4 breeds in the nonaffected TBD group vs the Beagle group, and interbreed comparisons among nonaffected TBDs. Furthermore, we compared the overall DALRs of nonaffected and AAI-affected TBDs as well as the DALRs of each breed in those 2 groups. The length of the body of the axis was used as the reference standard; however, a limitation of this variable is that its measurement on sagittal CT images is challenging in dogs with separation or dislocation of the dens. In such cases, we measured the lengths of the separated bone and the base of the dens remaining on the cranial aspect of the axis; the

sum of these 2 measurements was considered as the length of the dens for calculating the DALR. In addition, AAI-affected TBDs with aplasia of the dens were excluded from the analyses.

Assessment of the DA

Because dorsal angulation of the dens has also been implicated as a cause of AAI,^{2,3} the angle of the dens of the axis was used to evaluate dens abnormalities. For measurement of the DA on median 3-D MPR images reconstructed from CT images, a line was drawn parallel to the vertebral canal floor of the axis, passing through the base of the ventral aspect of the dens. In the same image, another line was drawn from the base of the ventral aspect of the dens to the tip of the dens. The angle between these 2 lines was defined as the DA (**Figure 2**). The DAs among the study dogs were compared groupwise as follows: nonaffected TBD group vs the Beagle group, each of the 4 breeds in the nonaffected TBD group vs the Beagle group, and interbreed comparisons among nonaffected TBDs. Furthermore, we compared the overall DAs of nonaffected and AAI-affected TBDs as

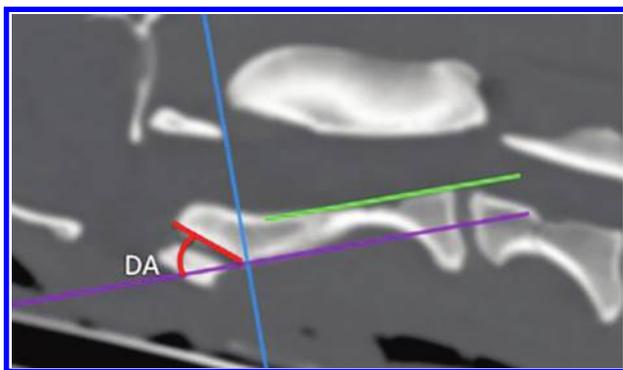


Figure 2—Median image of the axis of a Beagle reconstructed from CT images by 3-D MPR. To calculate the DA, a line (purple line) is drawn parallel to the vertebral canal floor of the axis (green line), passing through the ventral base of the dens. Another line (red line) is drawn from the base of the ventral aspect of the dens (blue line) to the tip of the dens. The angle between these 2 lines is defined as the DA (curved red line).

well as the DAs of each breed in those 2 groups. In addition, AAI-affected TBDs with aplasia or separation of the dens were excluded from the analyses.

Statistical analysis

Statistical analysis was performed with statistical processing software.^c A paired Student *t* test was performed for comparison of DALR or DA between nonaffected TBDs and Beagles, between each of the 4 breeds of nonaffected TBDs and Beagles, between nonaffected and AAI-affected TBDs, and among individual breeds in the nonaffected and AAI-affected TBD groups. In addition, interbreed comparisons of DALR or DA in the nonaffected TBD group were performed by use of the Bonferroni method. Significance was determined at a value of $P < 0.05$.

Results

Detailed information regarding sex, age, and body weight of the 160 dogs included in the study were summarized (**Table 1**). There was no significant difference ($P = 0.771$) in mean \pm SE overall DALR between the nonaffected TBDs (0.40 ± 0.007) and Beagles (0.40 ± 0.005). Comparison of mean DALR for each of the 4 breeds of nonaffected TBDs and Beagles revealed that the mean DALR of Yorkshire Terriers (0.37 ± 0.011) was significantly ($P = 0.008$) lower than that of Beagles, whereas the mean DALR of Miniature Dachshunds (0.43 ± 0.010) was significantly ($P = 0.010$) higher than that of Beagles. The mean DALRs of nonaffected Chihuahuas (0.40 ± 0.017) and Toy Poodles (0.39 ± 0.011) were not significantly (Chihuahuas, $P = 0.891$; Toy Poodles, $P = 0.309$) different from that of Beagles. Comparison of DALR among the 4 breeds of nonaffected TBDs revealed that the mean DALR of Miniature Dachshunds was significantly ($P = 0.012$) higher, compared with that of Yorkshire Terriers; however, comparisons among the other dog breeds revealed no significant differences in mean DALR.

The mean \pm SE overall DA of the nonaffected TBDs ($37.6 \pm 0.7^\circ$) was significantly ($P = 0.003$)

Table 1—Signalment of 80 AAI-predisposed TBDs with AAI, 40 AAI-predisposed TBDs without AAI (nonaffected TBDs), and 40 non-AAI-predisposed healthy Beagles.

Variable	Group		
	AAI-affected TBD	Nonaffected TBD	Beagle
Sex (No. of dogs)			
Sexually intact male	27	15	28
Castrated male	12	13	0
Sexually intact female	29	7	12
Spayed female	12	5	0
Age (mo)			
Mean \pm SD	40.6 \pm 40.2	96.4 \pm 44.5	10.5 \pm 4.6
Median (range)	16.0 (5.0–149.0)	96.5 (6.0–180.0)	14.0 (11.0–24.0)
Weight (kg)			
Mean \pm SD	2.5 \pm 1.1	4.0 \pm 1.9	10.5 \pm 1.5
Median (range)	2.1 (1.0–7.0)	3.9 (1.5–8.9)	10.6 (7.6–14.0)

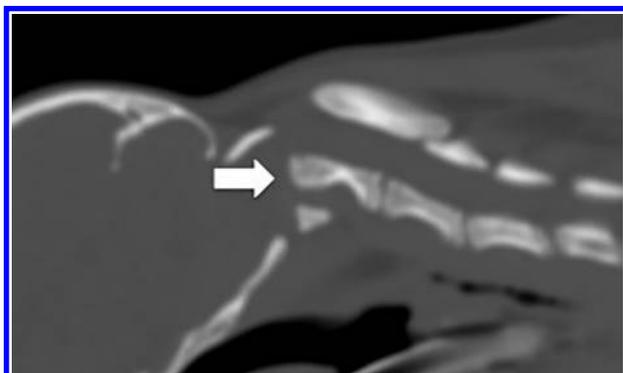


Figure 3—Median CT image of a Toy Poodle with AAI and aplasia of the dens. The dens structure is not visible on the cranial side of the axis (arrow).

greater than that of Beagles ($34.8 \pm 0.5^\circ$). Comparison of mean DA for each of the 4 breeds of nonaffected TBDs and Beagles revealed that the mean DAs of Chihuahuas ($37.8 \pm 1.3^\circ$) and Yorkshire Terriers ($40.8 \pm 1.3^\circ$) were significantly ($P = 0.020$ and $P < 0.001$, respectively) greater than that of Beagles. The mean DAs of nonaffected Toy Poodles ($35.8 \pm 0.8^\circ$) and Miniature Dachshunds ($36.1 \pm 1.9^\circ$) were not significantly (Toy Poodles; $P = 0.411$; Miniature Dachshunds, $P = 0.524$) different from that of Beagles. There were no significant differences in DA among the 4 breeds of nonaffected TBDs.

In the 80 AAI-affected TBDs, aplasia of the dens (**Figure 3**) was confirmed in 6 of the 28 Chihuahuas, 3 of the 20 Toy Poodles, and 1 of the 12 Miniature Dachshunds; none of the 20 Yorkshire Terriers had aplasia of the dens. In addition, separation of the dens was confirmed in 7 Chihuahuas, 8 Toy Poodles, 8 Yorkshire Terriers, and 4 Miniature Dachshunds. Thus, 10 AAI-affected TBDs were excluded from analysis of the DALR because of aplasia of the dens, and 37 AAI-affected TBDs were excluded from analysis of the DA because of aplasia or separation of the dens.

For comparison of the DALR of nonaffected and AAI-affected TBDs, data were available for 40 nonaffected dogs (10 dogs of each breed) and for 70 AAI-affected dogs (22 Chihuahuas, 17 Toy Poodles, 20 Yorkshire Terriers, and 11 Miniature Dachshunds). Comparison of data from nonaffected and AAI-affected TBDs revealed that the mean \pm SE overall DALR of AAI-affected TBDs (0.36 ± 0.009) was significantly lower ($P = 0.001$) than that of the nonaffected TBDs (0.40 ± 0.007). Among individual dog breeds in the nonaffected and AAI-affected TBD groups, the mean DALR of AAI-affected Chihuahuas (0.35 ± 0.014) was significantly ($P = 0.049$) lower than that of nonaffected Chihuahuas (0.40 ± 0.017). The mean DALR of AAI-affected Toy Poodles (0.34 ± 0.017) was significantly ($P = 0.020$) lower than that of nonaffected Toy Poodles (0.39 ± 0.011). Although the mean DALR of AAI-affected Yorkshire Terriers (0.33 ± 0.013) was lower than that of nonaffected Yorkshire Terriers (0.37 ± 0.011), this difference was not significant ($P = 0.081$). The mean DALR of AAI-affected Miniature Dachshunds (0.44 ± 0.044) did not differ significantly ($P = 0.737$)

from that of nonaffected Miniature Dachshunds (0.43 ± 0.010).

For comparison of the DA of nonaffected and AAI-affected TBDs, data were available for 40 nonaffected dogs (10 dogs of each breed) and for 43 AAI-affected dogs (15 Chihuahuas, 9 Toy Poodles, 12 Yorkshire Terriers, and 7 Miniature Dachshunds). Comparison of data from nonaffected and AAI-affected TBDs revealed that the mean \pm SE overall DA of AAI-affected TBDs ($41.0 \pm 1.0^\circ$) was significantly ($P = 0.007$) greater than that of nonaffected TBDs ($37.6 \pm 0.7^\circ$). The mean DA of each breed of AAI-affected TBDs was as follows: Chihuahua, $41.2 \pm 1.3^\circ$; Toy Poodle, $37.5 \pm 2.5^\circ$; Yorkshire Terrier, $42.8 \pm 1.6^\circ$; and Miniature Dachshund, $42.0 \pm 3.1^\circ$. The mean DA of each breed of nonaffected TBDs was as follows: Chihuahua, $37.8 \pm 1.3^\circ$; Toy Poodle, $35.8 \pm 0.8^\circ$; Yorkshire Terrier, $40.8 \pm 1.3^\circ$; and Miniature Dachshund, $36.1 \pm 1.9^\circ$. There were no significant breed-specific differences in mean DA between AAI-affected TBDs and the corresponding nonaffected TBDs; however, for all breeds, the mean DAs of AAI-affected TBDs were greater than those of the corresponding nonaffected TBDs.

Discussion

In the present study, there was no significant difference in mean DALR of non-AAI-affected TBDs and that of medium-sized healthy Beagles. This finding has suggested that the DALR could be used as a common indicator of dens abnormalities in several dog breeds. However, because there were significant differences in mean DALR among the nonaffected TBDs, DALR might vary depending on breed. Furthermore, the fact that the mean overall DALR of AAI-affected TBDs was significantly lower than that of nonaffected TBDs has suggested that AAI-affected dogs might have smaller dentes than non-AAI-affected dogs; this proposed association was supported by data obtained from AAI-affected and nonaffected Chihuahuas and Toy Poodles. However, surprisingly, Miniature Dachshunds had the highest DALR among the dog breeds included in the present study regardless of whether they did or did not have AAI, indicating that AAI in Miniature Dachshunds might have an etiopathogenesis that does not involve a hypoplastic dens. However, data regarding the cause of AAI in Miniature Dachshunds, which is a chondrodystrophoid breed, are lacking. In addition, among the 4 breeds of nonaffected and AAI-affected TBDs in the present study, nonaffected and AAI-affected Yorkshire Terriers had the greatest DAs (although the difference was not significant), whereas the mean overall DA of AAI-affected TBDs was significantly greater, compared with that of Beagles and nonaffected TBDs. The findings of the present study (eg, the mean overall DA of AAI-affected TBDs being significantly greater than that of nonaffected TBDs) have suggested that dorsal deviation of the dens, as indicated by a large DA, renders dogs susceptible to development of AAI. Compared with findings for Beagles, the mean DAs of Chihua-

huas and Yorkshire Terriers were greater, whereas the mean DAs of Toy Poodles and Miniature Dachshunds were not significantly different. This may be an indication that the DA might vary depending on breed and that it might be related to development of AAI. However, young dogs in their period of growth were included in the present study, and it must be considered that the measurements of DALR and DA might potentially have been influenced by growth in young dogs.

In previous reports,^{1,2,4,6} the prevalence of abnormal conformation of the dens was found to be high among dogs with AAI. However, these rates were based on subjective evaluation of radiographs by individual researchers, without application of any objective criteria. Geary et al⁶ reported that of 10 AAI-affected dogs, 9 had aplasia or separation of the odontoid process. Denny et al¹ reported that of 30 AAI-affected dogs, 29 had hypoplastic deformity of the odontoid process. Thomas et al² reported that of 23 AAI-affected dogs, 17 had aplasia or separation of the odontoid process; additionally, 2 of these dogs had a dorsally angulated dens. Beaver et al⁴ reported that of 46 AAI-affected dogs, 35 had aplasia or separation of the odontoid process. In the present study, 37 of 80 (46.3%) AAI-affected TBDs had aplasia or separation of the dens, as revealed by detailed morphological evaluation of CT images. In particular, we evaluated hypoplasia of the dens by determination of the DALR (calculated as the ratio of length of the dens to that of the axis body), which might be an objective indicator of dens abnormalities. Compared with reports of previous studies,^{1,2,4,6} the present study had a larger sample size. Because 43 of the 80 (53.7%) AAI-affected TBDs did not have aplasia or separation of the dens in our study, it might be feasible to diagnose subtle dens abnormalities by evaluating the dens on the basis of the measurements we used. Dorsal angulation of the dens has also been implicated as a cause of AAI,^{2,3} some reports have proposed odontoidectomy in dogs with AAI with dorsal angulation of the dens.¹⁹ During development, the dens of the axis separates from the body of the atlas and joins with the body of the axis 7 to 9 months after birth.⁶ To date, there is no description of diseases that develop as a direct result of dorsal angulation of the dens. On the basis of the authors' experience, deformities of the dens, including angulation, might cause compression of the spinal cord.

The present study revealed significant differences in DALR and DA between AAI-affected and nonaffected TBDs. Thus, we believe that the DALR and DA might be important factors for predicting the development of AAI in dogs. In addition, because there were significant differences in DALR and DA among the dog breeds, it was necessary to analyze the DALR and the DA of each dog breed; the same variable should be evaluated in a larger population of AAI-predisposed TBDs to confirm our findings. On the basis of the results of the present study alone, it

appears that perhaps neither DALR nor DA are useful for predicting development of AAI, which then suggests that various factors other than dens abnormalities—such as rupture of the transverse ligament and incomplete ossification of the atlas—also influence the onset of AAI.

Atlantoaxial instability might pose a serious threat for health in TBDs. It would be very useful if the breed-specific or individual-dog risk of onset of AAI could be determined. The findings of the present study have suggested that in AAI-predisposed TBDs with low DALR and large DA, there is a possibility that AAI might readily develop. It is our practice to caution the owners of dogs with low DALRs and large DAs not to tug strongly at the craniocervical portion of their vertebral column. We also consider that these dogs might not be suitable for breeding.

In the present study, we attempted to perform a detailed evaluation of the morphological characteristics of the dens in AAI-affected and nonaffected TBDs and healthy Beagles. The study results indicated that, although low DALR might be predictive of a high probability of dens abnormality, the DALR and DA are not likely to be adequate objective indicators of the development of AAI in TBDs. Various factors influence the onset of AAI in TBDs; therefore, detailed evaluation of morphological characteristics of the dens of the axis, including assessment of the DALR and DA, in a larger population of dogs might help establish definitive standards for determining a dog's future risk of AAI.

Acknowledgments

No third-party funding or support was received in connection with this study or the writing or publication of the manuscript. The authors declare that there were no conflicts of interest.

The authors thank Editage for English language editing.

Footnotes

- a. Aquilion PRIME (TSX-303a) 80 and 160-slice CT scanner, Toshiba Medical Systems Corp, Tochigi, Japan.
- b. OsiriX DICOM Viewer, Pixmeo SARL, Geneva, Switzerland.
- c. SPSS, version 23, IBM Corp, Armonk, NY.

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