

Associations between early radiographic and computed tomographic measures and canine hip joint osteoarthritis at maturity

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OBJECTIVE

To evaluate associations of measures assessed by radiography, 2-D CT, and 3-D CT of the hip joints of immature dogs with osteoarthritis in the same joints at maturity.

ANIMALS

46 hound-type dogs from a colony predisposed to osteoarthritis.

PROCEDURES

Images of hip joints (1/dog) were obtained at 16, 32, and 104 weeks of age. Radiographic measures included Norberg angle, distraction index, and osteoarthritis score. Two-dimensional CT measures included acetabular index, percentage of femoral head coverage, and center edge, horizontal toit externe, acetabular anteversion, and ventral, dorsal, and horizontal acetabular sector angles. Three-dimensional CT measures were femoral head and neck volume, femoral neck angle, and femoral head and neck radius. Differences among measures at 16 and 32 weeks in dogs with different osteoarthritis scores at later time points, relationships among variables at each time point, and relationships of single and combined measures with the presence of osteoarthritis at 104 weeks were evaluated.

RESULTS

The 16- and 32-week distraction index, center edge angle, dorsal acetabular sector angle, horizontal acetabular sector angle, percentage of femoral head coverage, acetabular index, and Norberg angle and the 32-week femoral neck angle varied significantly with osteoarthritis severity at 104 weeks. Presence of osteoarthritis in mature dogs was most strongly associated with 16-week combined measures of distraction index and center edge angle and 32-week combined measures of dorsal acetabular sector angle and Norberg angle.

CONCLUSIONS AND CLINICAL RELEVANCE

Changes in hip joint morphology associated with radiographic signs of osteoarthritis were detectable as early as 16 weeks of age and varied with osteoarthritis severity in adult dogs. The use of combined hip joint measures may improve early identification of dogs predisposed to hip joint osteoarthritis. (*Am J Vet Res* 2015;76:19–27)

Canine hip dysplasia is a complex developmental orthopedic disorder with a prevalence as high as 73% in some breeds.¹ Since the first description of CHD > 50 years ago, radiography has remained the established imaging technology for CHD diagnosis.^{1–7} Early detection of hip joint changes associated with

osteoarthritis characteristic of CHD is vital to the initiation and extent of therapeutic intervention as well as decisions regarding breeding. Advances in imaging modalities such as radiography, CT, and MRI provide critical information about joint structure that may be predictive of the development and ultimate degree of hip joint disease.^{1–3,5–10} Discovery of age- and breed-specific parameters for measures assessed on diagnostic images has increased the accuracy with which these methods can be used to predict joint changes^{1,9,11,12}; however, a continuing need for improved detection is underscored by the current prevalence of hip joint disease in canine companion animals.¹

Efforts to detect and develop treatments for osteoarthritis inherent to CHD contribute to an ever-increasing wealth of knowledge surrounding canine hip joint imaging.^{13–16} The use of CT is routine for diagnosis and assessment of developmental dysplasia of the hip in humans.^{1,3,5,6} Standard measures performed on human 2-D CT images are closely associated with microstructural hip joint degeneration in

ABBREVIATIONS

AAA	Acetabular anteversion angle
AI	Acetabular index
CEA	Center edge angle
CHD	Canine hip dysplasia
CPC	Percentage of femoral head coverage
DASA	Dorsal acetabular sector angle
DI	Distraction index
FHR	Femoral head radius
FHV	Femoral head volume
FNA	Femoral neck angle
FNR	Femoral neck radius
FNV	Femoral neck volume
HASA	Horizontal acetabular sector angle
HTEA	Horizontal toit externe angle
VASA	Ventral acetabular sector angle

dogs with hip joint laxity.¹⁷ Three-dimensional CT models of the hip joint are vital to monitoring joint disease progression and surgical planning in human patients.^{13,16,18–20} These models are also used to identify abnormal hip joint development in children. Similarly, there are predictable volumetric changes in canine hip joint articular components from youth to maturity in dogs predisposed to hip joint osteoarthritis, and specific early changes were shown to correspond to severity of hip joint osteoarthritis that developed at later time points.²¹ The purpose of the study reported here was to evaluate associations of radiographic, 2-D CT, and 3-D CT hip joint measures in immature dogs predisposed to osteoarthritis with development of the disease in the same joint at maturity. Our hypothesis was that measures determined on radiographs, CT images, and CT models of hip joints in dogs at 16 and 32 weeks of age would differ significantly among dogs with different degrees of osteoarthritis severity as determined radiographically at maturity; that combined measures at both 16 and 32 weeks would have stronger associations with presence of osteoarthritis at maturity than single measures; and that the measures best correlated with presence of osteoarthritis at maturity would vary with age.

Materials and Methods

The study was performed in accordance with institutional and National Institutes of Health regulations governing the treatment of vertebrate animals. Procedures were initiated after approval by the University of Wisconsin-Madison and Louisiana State University animal care committees.

DOGS

Forty-six full- or half-sibling, hound-type dogs from 8 litters were used for the study. Dogs were part of a closed research colony and included the progeny of 6 dams and a single sire. Images used for this study had been used in other studies.^{14,21} The dams and sire were unrelated to each other, and all had moderate to severe hip joint osteoarthritis as determined radiographically. The study population included 19 males and 27 females that weighed a mean $\pm$ SD of 5.4 ± 1.0 kg at 16 weeks of age, 21.7 ± 3.6 kg at 32 weeks of age, and 25.8 ± 3.7 kg at 104 weeks of age. One hip joint from each dog was selected for evaluation by means of a randomized block design. Inclusion in the study required a DI^a > 0.3 in both hip joints. Dogs were housed in 1.2 X 2.4-m indoor runs with concrete floors and had 2 hours of unrestricted play time daily. For the first 18 months, dogs were fed puppy food,^b after which they received adult dog food^c; both diets were commercially available and were fed ad libitum. Water was available continuously throughout the study.

RADIOGRAPHY

At 16, 32, and 104 weeks of age, each dog was anesthetized, and hip-extended and distraction radiographs were obtained as previously described^{11,22} and submitted to an analysis center^d for determination of the DI (femoral head displacement during maximum joint distraction, normalized to the FHR) and osteoarthritis score.^{1,6} Descriptive osteoarthritis scores were assigned numeric values (none = 0, mild = 1, moderate = 2, and severe = 3) for statistical analysis. Digital hip-extended radiographic images (400 dpi, 8-bit grayscale, tagged image file format) were used to measure the Norberg angle with graphics software.^d The

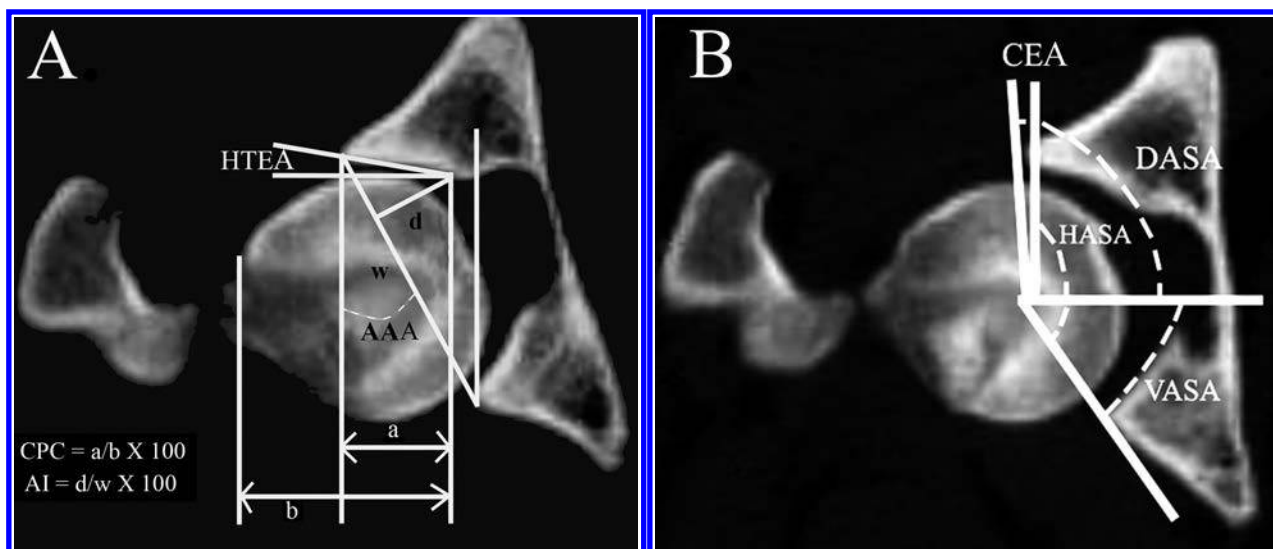


Figure 1—Schematic representations of 2-D CT measures applied in a study to evaluate use of measures assessed by means of radiographs, 2-D CT images, and 3-D CT models of 46 hip joints in 46 immature hound-type dogs to predict osteoarthritis in the same joints at maturity. A—Measurements for determining orientation of the acetabular roof in a coronal plane (HTEA), percentage of the femoral head covered by the acetabulum (CPC), depth of the acetabulum (AI), and slope of the acetabulum in a longitudinal plane (AAA) are shown. B—Measurements for determining dorsolateral coverage of the femoral head by the bony acetabulum (CEA), dorsal coverage of the femoral head by the bony acetabulum (DASA), ventral coverage of the femoral head by the bony acetabulum (VASA), and global acetabular coverage of the femoral head (HASA) are shown.

Norberg angle was measured between a line connecting the center of both femoral heads and a line extending from the center of the femoral head to the cranial aspect of the ipsilateral acetabular rim.¹¹

CT EVALUATION

Following radiography, CT scans of the pelvis were performed. Dogs were placed in dorsal recumbency with hip joints extended, adducted, and rotated slightly internally, as previously described.^{1,2,17} Transverse pelvic imaging was performed at 1.5-mm slice widths.^c

All 2-D measurements were performed on digital CT images^f (**Figure 1**). These measurements^d were performed on images that included an acetabular fossa, a well-defined sourcil, a round femoral head, and a fovea capitis. For purposes of CT measurements, the femoral head was considered a semicircle with the midpoint of the semicircle baseline corresponding to the center of the femoral head. The CEA, HTEA, VASA, DASA, HASA, AAA, AI, and CPC were measured as previously described.^{1,6,17} Each measure was used to quantify variables as follows: CEA, bony acetabulum dorsolateral coverage of the femoral head; DASA, bony acetabulum dorsal coverage of the femoral head; VASA, bony acetabulum ventral coverage of the femoral head; HASA, global acetabular coverage; HTEA, orientation of the roof of the acetabulum in the dorsal plane; AI, depth of the acetabulum; CPC, percentage of the femoral head covered by the acetabulum; and AAA, slope of the acetabulum in the sagittal plane.

For 3-D measurements, software^g was used to construct 3-D volume-rendered surface models of the pelvis from 2-D CT images with thresholds set at 537 and

3,056 Hounsfield units.⁷ Models were disarticulated to isolate the femoral head and neck. The FHV was defined as the volume of the capital epiphysis above the physal scar. The FNV calculation was based on the same models between the physal scar and a line between the most ventral aspect of the trochanteric fossa and the most dorsal aspect of the lesser trochanter (**Figure 2**). The FHR and FNR were determined on spheres^h approximating (with a software best-fit algorithm) the femoral head and femoral neck, respectively, on 3-D models (**Figure 3**). The FNA was the cranial angle formed by a line between the femoral head and neck sphere centers and a line corresponding to the central axis of the femoral metaphysis. The FHV:FNV and FHR:FNR ratios were calculated from the software-determined volume and radius.

Repeatability and reproducibility (the intraclass and interclass correlation coefficients, respectively) were determined for the 3-D CT measurements with results generated by 3 individuals (AAA, LK, and MJL) 3 times on 8 images.¹ Intraclass and interclass correlation coefficient were rated as follows: ≥ 0.75 was excellent, 0.50 to 0.74 was good, 0.25 to 0.49 was fair, and ≤ 0.24 was poor.^{17,23} Repeatability of 2-D CT measures and the Norberg angle have been previously established.^{1,6,14}

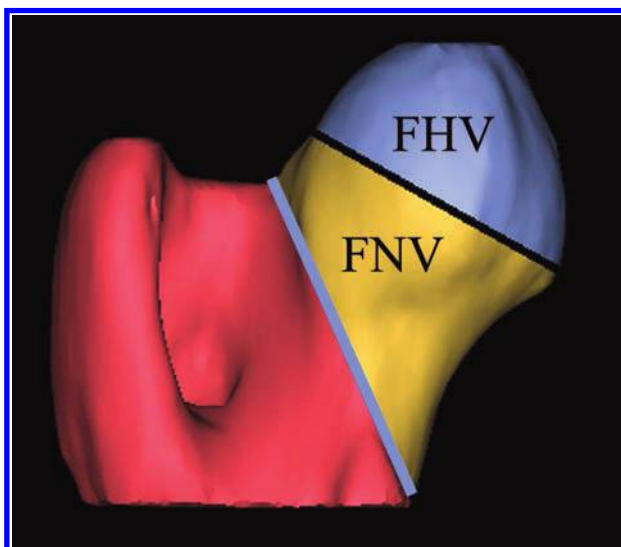


Figure 2—Three-dimensional CT model (caudocranial view) of the proximal aspect of a canine femur demonstrating the regions used to measure the FHV (blue) and FNV (yellow). The FHV was determined from measurement of the capital epiphysis, defined by the dorsal and ventral limits of the physal scar (represented by a black line). Similarly, the FNV was measured on the same models between the physal scar and a line between the most ventral aspect of the trochanteric fossa and the most dorsal aspect of the lesser trochanter (blue line).

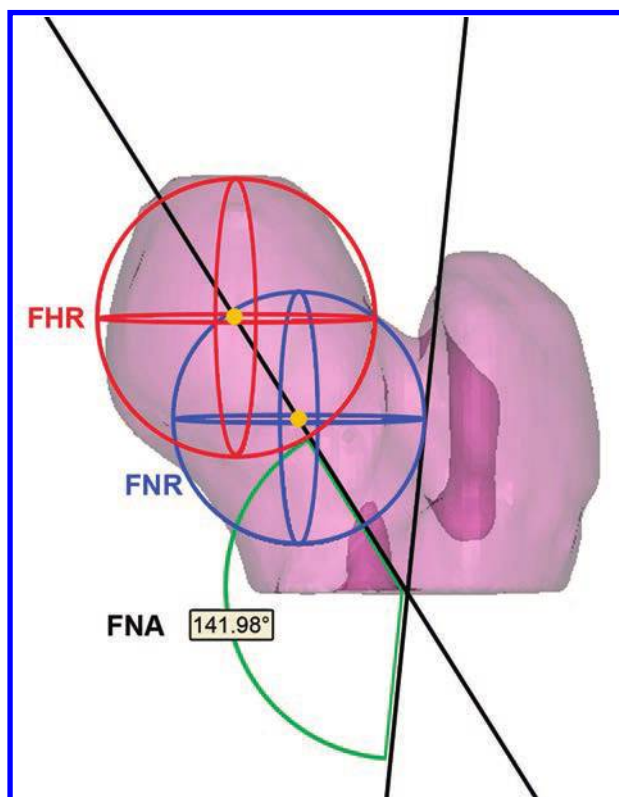


Figure 3—Three-dimensional CT reconstruction (caudocranial view) illustrating regions of measurement for the FHR (red sphere), FNR (blue sphere), and FNA of a canine femur. Spheres approximating the femoral head and femoral neck were used to determine the FHR and FNR, respectively. The FNA was the cranial angle formed by a line through the centers of the femoral head and neck spheres and a line corresponding to the central axis of the femoral metaphysis.

STATISTICAL ANALYSIS

Values are reported as mean $\pm$ SD. Results of the Shapiro-Wilk test showed the data were normally distributed. Correlation analysis was performed to examine relationships between variables at each age with Pearson product moment correlations. Repeated-measures ANOVA models were used to quantify differences within each measure for dogs at different ages. Additionally, differences among combined values of each measure sorted by age or osteoarthritis scores, 16-week measure values sorted by 32- and 104-week osteoarthritis scores, and 32-week measure values sorted by 104-week osteoarthritis scores were evaluated with ANOVA models. Significant differences were evaluated with Tukey Studentized range tests. The strength of single and combined measure relationships with presence of osteoarthritis at maturity was determined with stepwise regression modeling. All analyses were performed with commercially available software.¹ Values of $P \leq 0.05$ were considered significant.

Results

Forty-six hip joints (1 hip joint/dog) were included in the study. There was no radiographic evidence of osteoarthritis in any dog at 16 weeks of age. At 32 weeks of age, 32 joints had an osteoarthritis score of 0, 5 had a score of 1, 2 had a score of 2, and 7 had a score of 3 on the 3-point scale. At 104 weeks of age, 26 hip joints had an osteoarthritis score of 0, 7 had a score of 1, 3 had a score of 2, and 10 had a score of 3.

When all osteoarthritis scores were combined to evaluate the independent effect of age on each measure, most measure values were significantly ($P < 0.05$) different among ages (**Table 1**). When data from all ages were combined to assess the independent effect of osteoarthritis score on each measure, most measure values also differed significantly among osteoarthritis scores (**Table 2**).

The 16-week DIs of hip joints with a 32-week osteoarthritis score of 0 were significantly smaller

Table 1—Mean $\pm$ SD hip joint measures determined by use of radiography, 2-D CT images, and 3-D CT models of 46 hip joints in 46 dogs at 16, 32, and 104 weeks of age, with all osteoarthritis scores combined at each age.

Measure	16 weeks	32 weeks	104 weeks
DI	0.65 $\pm$ 0.15 ^a	0.74 $\pm$ 0.19 ^b	0.70 $\pm$ 0.22 ^b
CEA (°)	-2.46 $\pm$ 7.99 ^a	-2.46 $\pm$ 12.22 ^a	-12.41 $\pm$ 14.17 ^b
VASA (°)	48.30 $\pm$ 5.37 ^a	46.61 $\pm$ 4.07 ^b	47.78 $\pm$ 3.65 ^{a,b}
DASA (°)	87.02 $\pm$ 7.83 ^a	82.01 $\pm$ 12.06 ^b	77.20 $\pm$ 13.38 ^c
HASA (°)	135.32 $\pm$ 9.98 ^a	128.58 $\pm$ 13.29 ^b	124.99 $\pm$ 13.24 ^c
CPC (%)	52.80 $\pm$ 7.75 ^a	47.73 $\pm$ 8.86 ^b	42.60 $\pm$ 11.62 ^c
AI	30.63 $\pm$ 4.59 ^b	32.16 $\pm$ 3.46 ^a	28.02 $\pm$ 7.62 ^c
AAA (°)	21.59 $\pm$ 4.96 ^a	19.51 $\pm$ 5.45 ^b	16.67 $\pm$ 6.73 ^c
Norberg angle (°)	102.90 $\pm$ 6.99 ^a	93.42 $\pm$ 16.16 ^b	94.99 $\pm$ 12.07 ^b
FHV (mm ³)	14,698.48 $\pm$ 4,000.32 ^a	10,731.84 $\pm$ 2,401.95 ^b	12,058.09 $\pm$ 2,814.99 ^b
FNA (°)	135.86 $\pm$ 15.61 ^a	150.33 $\pm$ 5.97 ^b	146.51 $\pm$ 10.32 ^b
FHR (mm)	18.69 $\pm$ 2.36 ^a	16.90 $\pm$ 0.93 ^c	17.68 $\pm$ 1.38 ^b
FNR (mm)	18.39 $\pm$ 2.12 ^a	17.29 $\pm$ 1.06 ^b	18.06 $\pm$ 1.47 ^a
FHV:FNV ratio	1.08 $\pm$ 0.24 ^a	0.91 $\pm$ 0.33 ^b	0.94 $\pm$ 0.31 ^b
FHR:FNR ratio	1.01 $\pm$ 0.03 ^a	0.98 $\pm$ 0.04 ^b	0.98 $\pm$ 0.05 ^b

Descriptive osteoarthritis scores were determined radiographically and assigned numeric values (none = 0, mild = 1, moderate = 2, and severe = 3). Only measures with significant differences among ages are shown.

^{a,b,c}Within a row, values with different superscript letters are significantly ($P < 0.05$) different.

Table 2—Mean $\pm$ SD hip joint measures of the same sample as in Table 1 with data for all time points (16, 32, and 104 weeks of age) combined, sorted according to osteoarthritis score.

Measure	Osteoarthritis score			
	0 (n = 104)	1 (n = 12)	2 (n = 5)	3 (n = 17)
DI	0.63 $\pm$ 0.17 ^a	0.76 $\pm$ 0.10 ^a	0.82 $\pm$ 0.09 ^{a,b}	1.00 $\pm$ 0.00 ^b
CEA (°)	-2.30 $\pm$ 7.87 ^a	-12.38 $\pm$ 10.56 ^{a,b}	-11.86 $\pm$ 19.35 ^{a,b}	-20.60 $\pm$ 20.71 ^b
DASA (°)	86.85 $\pm$ 7.68 ^a	75.64 $\pm$ 8.69 ^b	69.78 $\pm$ 6.87 ^{b,c}	61.06 $\pm$ 9.25 ^c
HASA (°)	134.41 $\pm$ 9.64 ^a	122.61 $\pm$ 9.20 ^{a,b}	117.68 $\pm$ 11.79 ^{b,c}	108.89 $\pm$ 7.11 ^c
HTEA (°)	18.50 $\pm$ 6.35 ^a	23.72 $\pm$ 6.92 ^{a,b}	30.66 $\pm$ 9.18 ^b	21.75 $\pm$ 5.72 ^a
CPC (%)	50.84 $\pm$ 6.35 ^a	47.87 $\pm$ 12.92 ^a	42.30 $\pm$ 6.33 ^a	30.00 $\pm$ 9.67 ^b
AI	31.22 $\pm$ 4.23 ^a	31.91 $\pm$ 3.42 ^a	34.16 $\pm$ 1.61 ^a	22.134 $\pm$ 8.66 ^b
AAA (°)	21.54 $\pm$ 4.26 ^a	16.13 $\pm$ 5.11 ^{a,b}	10.74 $\pm$ 1.76 ^{b,c}	10.05 $\pm$ 5.08 ^c
Norberg angle (°)	101.77 $\pm$ 7.37 ^a	94.03 $\pm$ 9.34 ^{a,b}	88.75 $\pm$ 14.69 ^b	73.61 $\pm$ 13.29 ^c
FNA (°)	144.82 $\pm$ 13.46 ^{a,b}	149.56 $\pm$ 1.49 ^a	148.83 $\pm$ 4.10 ^a	135.60 $\pm$ 11.10 ^b

Only measures with significant ($P < 0.05$) differences among osteoarthritis scores are shown.

See Table 1 for remainder of key.

Table 3—Mean $\pm$ SD 16-week hip joint measures for the same sample as in Table 1, sorted according to osteoarthritis score at 32 weeks of age.

Measure	Osteoarthritis score			
	0 (n = 32)	1 (n = 5)	2 (n = 2)	3 (n = 7)
DI	0.59 $\pm$ 0.11 ^a	0.65 $\pm$ 0.07 ^{a,b}	0.84 $\pm$ 0.15 ^b	0.82 $\pm$ 0.16 ^b
CEA (°)	0.47 $\pm$ 5.71 ^a	−3.54 $\pm$ 7.81 ^{a,b}	−7.30 $\pm$ 12.02 ^{a,b}	−13.66 $\pm$ 6.70 ^b
DASA (°)	89.79 $\pm$ 5.81 ^a	86.02 $\pm$ 7.29 ^{a,b}	82.75 $\pm$ 12.37 ^{a,b}	76.33 $\pm$ 6.58 ^b
HASA (°)	138.35 $\pm$ 7.47 ^a	129.92 $\pm$ 7.30 ^{a,b}	133.30 $\pm$ 27.72 ^{a,b}	125.93 $\pm$ 10.86 ^b
CPC (%)	54.54 $\pm$ 7.40 ^a	51.94 $\pm$ 6.56 ^{a,b}	52.10 $\pm$ 3.25 ^{a,b}	45.61 $\pm$ 7.75 ^b
AI	31.40 $\pm$ 4.03 ^a	32.42 $\pm$ 4.28 ^{a,b}	28.40 $\pm$ 7.07 ^{a,b}	26.46 $\pm$ 5.09 ^b
Norberg angle (°)	105.59 $\pm$ 5.11 ^a	99.82 $\pm$ 2.10 ^{a,b}	103.30 $\pm$ 2.69 ^a	92.73 $\pm$ 7.73 ^b

Only measures with significant ($P < 0.05$) differences among 32-week osteoarthritis scores are shown.
See Table 1 for remainder of key.

Table 4—Mean $\pm$ SD 16-week hip joint measures for the same sample as in Table 1, sorted according to osteoarthritis score at 104 weeks of age.

Measure	Osteoarthritis score			
	0 (n = 26)	1 (n = 7)	2 (n = 3)	3 (n = 10)
DI	0.57 $\pm$ 0.11 ^a	0.65 $\pm$ 0.11 ^{a,b}	0.71 $\pm$ 0.08 ^{a,b}	0.81 $\pm$ 0.15 ^b
CEA (°)	1.03 $\pm$ 5.13 ^a	0.77 $\pm$ 6.79 ^a	−8.13 $\pm$ 4.69 ^b	−12.09 $\pm$ 7.29 ^b
DASA (°)	90.24 $\pm$ 5.33 ^a	90.18 $\pm$ 6.88 ^a	81.93 $\pm$ 4.91 ^{a,b}	77.97 $\pm$ 7.31 ^b
HASA (°)	138.59 $\pm$ 7.25 ^a	137.96 $\pm$ 8.22 ^{a,b}	128.97 $\pm$ 3.81 ^{a,b}	126.97 $\pm$ 13.30 ^b
CPC (%)	54.98 $\pm$ 8.01 ^a	54.29 $\pm$ 4.57 ^{a,b}	49.00 $\pm$ 4.62 ^{a,b}	47.22 $\pm$ 6.98 ^b
AI	30.93 $\pm$ 3.98 ^{a,b}	32.40 $\pm$ 4.14 ^{a,b}	35.30 $\pm$ 3.36 ^a	27.22 $\pm$ 4.96 ^b
Norberg angle (°)	105.95 $\pm$ 4.62 ^a	103.47 $\pm$ 6.71 ^{a,b}	99.47 $\pm$ 3.02 ^{a,b}	95.62 $\pm$ 7.93 ^b

Only measures with significant ($P < 0.05$) differences among 104-week osteoarthritis scores are shown.
See Table 1 for remainder of key.

Table 5—Mean $\pm$ SD 32-week hip joint measures for the same sample as in Table 1, sorted according to osteoarthritis score at 104 weeks of age.

Measure	Osteoarthritis score			
	0 (n = 26)	1 (n = 7)	2 (n = 3)	3 (n = 10)
DI	0.63 $\pm$ 0.16 ^a	0.81 $\pm$ 0.14 ^{a,b}	0.81 $\pm$ 0.07 ^{a,b}	0.96 $\pm$ 0.07 ^b
CEA (°)	0.91 $\pm$ 7.04 ^a	−8.84 $\pm$ 4.67 ^{a,b}	−9.37 $\pm$ 16.78 ^{a,b}	−17.26 $\pm$ 24.75 ^b
DASA (°)	89.51 $\pm$ 7.30 ^a	80.40 $\pm$ 6.18 ^{a,b}	73.00 $\pm$ 5.03 ^{b,c}	61.87 $\pm$ 9.61 ^c
HASA (°)	136.40 $\pm$ 9.58 ^a	127.53 $\pm$ 7.29 ^{a,b}	120.20 $\pm$ 2.91 ^{b,c}	107.76 $\pm$ 7.36 ^c
HTEA (°)	15.27 $\pm$ 5.49 ^a	20.03 $\pm$ 3.45 ^{a,b}	23.40 $\pm$ 6.07 ^{a,b}	24.25 $\pm$ 8.16 ^b
CPC (%)	49.88 $\pm$ 5.13 ^a	53.48 $\pm$ 14.44 ^a	43.17 $\pm$ 9.47 ^{a,b}	33.04 $\pm$ 9.70 ^b
AI	31.53 $\pm$ 3.22 ^{a,b}	32.94 $\pm$ 4.52 ^{a,b}	35.13 $\pm$ 4.42 ^a	26.22 $\pm$ 9.05 ^b
AAA (°)	22.38 $\pm$ 3.12 ^a	19.88 $\pm$ 3.42 ^{a,b}	16.10 $\pm$ 6.28 ^{b,c}	10.62 $\pm$ 5.64 ^c
Norberg angle (°)	100.42 $\pm$ 7.64 ^a	99.31 $\pm$ 8.14 ^a	89.43 $\pm$ 6.47 ^a	72.28 $\pm$ 20.11 ^b
FNA (°)	152.17 $\pm$ 5.23 ^a	150.57 $\pm$ 3.79 ^{a,b}	150.46 $\pm$ 2.88 ^{a,b}	145.51 $\pm$ 7.39 ^b

Only measures with significant ($P < 0.05$) differences among 104-week osteoarthritis scores are shown.
See Table 1 for remainder of key.

than those of joints that had 32-week scores of 2 or 3 (Table 3). The 16-week CEA, DASA, HASA, CPC, and AI of joints with a 32-week score of 0 were significantly larger than those of joints with a 32-week score of 3, and the 16-week Norberg angles of joints with 32-week scores of 0 or 2 were significantly larger than those with a score of 3.

The 16-week DIs of hip joints with a 104-week osteoarthritis score of 0 were significantly smaller than those of joints with a 104-week score of 3 (Table 4). The 16-week CEAs of joints with 104-week scores of 0 or 1 were significantly larger than those of joints with 104-week scores of 2 or 3, and the 16-week DASAs of

joints with 104-week scores of 0 or 1 were significantly larger than those of joints with a 104-week score of 3. The 16-week AIs of joints with a 104-week score of 2 were significantly greater than those of joints with a 104-week score of 3, and the 16-week Norberg angles, HASAs, and CPCs of joints with a 104-week score of 0 were significantly larger than those of joints with a 104-week score of 3.

The 32-week DIs and HTEAs of hip joints with a 104-week osteoarthritis score of 0 were significantly smaller than those of joints with a 104-week score of 3 (Table 5). The 32-week CEAs of joints with a 104-week score of 0 were significantly larger than those of joints

Table 6—Pearson product moment correlation coefficients among hip joint measures for the same sample as in Table I at 16, 32, and 104 weeks of age.

Variable	DI	CEA	VASA	DASA	HASA	HTEA	CPC	AI	AAA	Norberg angle	FHV	FNV	FNA	FHR	FNR	FHV:FNV ratio
16 weeks																
CEA	-0.60	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
VASA	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
DASA	-0.60	0.97	—	—	—	—	—	—	—	—	—	—	—	—	—	—
HASA	-0.55	0.80	0.63	0.84	—	—	—	—	—	—	—	—	—	—	—	—
HTEA	—	-0.39	—	-0.38	—	—	—	—	—	—	—	—	—	—	—	—
CPC	-0.35	0.58	—	0.56	0.36	-0.37	—	—	—	—	—	—	—	—	—	—
AI	—	0.40	—	0.37	—	—	0.52	—	—	—	—	—	—	—	—	—
AAA	—	0.49	-0.67	0.46	—	-0.43	0.53	—	—	—	—	—	—	—	—	—
Norberg angle	-0.54	0.64	—	0.62	0.52	—	0.44	—	0.37	—	—	—	—	—	—	—
FHV	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
FNV	—	—	—	—	—	—	—	—	—	—	0.66	—	—	—	—	—
FNA	—	—	—	—	—	—	-0.36	—	—	—	-0.65	-0.59	—	—	—	—
FHR	—	—	—	—	—	—	—	—	—	—	0.87	0.86	-0.82	—	—	—
FNR	—	—	—	—	—	—	—	—	—	—	0.82	0.93	-0.77	0.98	—	—
FHV:FNV ratio	—	—	—	—	—	—	—	—	—	—	—	-0.51	—	—	—	—
FHR:FNR ratio	—	—	—	—	—	—	—	—	—	—	0.59	—	-0.56	0.54	0.36	0.54
32 weeks																
CEA	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
VASA	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
DASA	-0.65	0.46	—	—	—	—	—	—	—	—	—	—	—	—	—	—
HASA	-0.63	0.44	0.45	0.95	—	—	—	—	—	—	—	—	—	—	—	—
HTEA	0.66	-0.47	—	-0.81	-0.71	—	—	—	—	—	—	—	—	—	—	—
CPC	—	0.32	—	0.63	5.58	-0.45	—	—	—	—	—	—	—	—	—	—
AI	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
AAA	-0.54	0.36	—	0.86	0.72	-0.77	0.61	—	—	—	—	—	—	—	—	—
Norberg angle	-0.55	—	—	0.45	0.47	-0.48	—	—	0.41	—	—	—	—	—	—	—
FHV	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
FNV	-0.37	—	—	—	—	—	—	-0.47	—	—	—	—	—	—	—	—
FNA	-0.34	—	—	0.31	—	—	—	—	0.34	0.52	—	—	—	—	—	—
FHR	—	—	—	—	—	—	—	-0.41	—	—	0.54	0.60	—	—	—	—
FNR	—	—	—	—	—	—	—	-0.48	—	—	—	0.93	—	0.77	—	—
FHV:FNV ratio	—	—	—	—	—	—	—	0.33	—	—	0.71	-0.69	—	—	-0.55	—
FHR:FNR ratio	—	—	—	—	—	—	—	—	—	—	0.60	-0.59	—	—	-0.47	0.86
104 weeks																
CEA	-0.85	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
VASA	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
DASA	-0.84	0.99	—	—	—	—	—	—	—	—	—	—	—	—	—	—
HASA	-0.81	0.94	—	0.96	—	—	—	—	—	—	—	—	—	—	—	—
HTEA	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
CPC	-0.78	0.91	—	0.90	0.89	—	—	—	—	—	—	—	—	—	—	—
AI	-0.61	0.73	—	0.73	0.72	—	0.91	—	—	—	—	—	—	—	—	—
AAA	-0.76	0.88	-0.57	0.85	0.71	-0.32	0.77	0.61	—	—	—	—	—	—	—	—
Norberg angle	-0.73	0.88	—	0.88	0.83	—	0.81	0.64	0.78	—	—	—	—	—	—	—
FHV	0.36	-0.47	—	-0.46	-0.52	—	-0.56	-0.54	-0.30	-0.48	—	—	—	—	—	—
FNV	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
FNA	-0.53	0.74	—	0.73	0.67	—	0.81	0.78	0.68	0.64	-0.58	—	—	—	—	—
FHR	0.44	-0.62	—	-0.61	-0.62	—	-0.71	-0.70	-0.49	-0.60	0.75	0.35	-0.68	—	—	—
FNR	—	-0.45	—	-0.44	-0.42	—	-0.50	-0.46	-0.40	-0.46	0.55	0.38	-0.59	0.74	—	—
FHV:FNV ratio	0.46	-0.53	—	-0.53	-0.55	—	-0.56	-0.55	-0.40	-0.46	0.70	-0.60	-0.59	0.37	—	—
FHR:FNR ratio	—	—	—	—	-0.31	—	-0.32	-0.36	—	—	0.34	—	-0.56	0.36	-0.35	0.32

Only significant ($P < 0.05$) coefficients are shown.

— = Not applicable.

that had a 104-week score of 3. The 32-week DASAs, HASAs, and AAAs of joints with a 104-week score of 0 were significantly larger than those of joints that had a 104-week score of 2 or 3, and those of joints with a 104-week score of 1 were also significantly larger than those with a score of 3 at 104 weeks. The 32-week CPCs of joints with a 104-week score of 0 or 1 were significantly larger than those of joints with a 104-week score

of 3, whereas the 32-week AIs of joints with a 104-week score of 2 were significantly greater than those of joints with a 104-week score of 3. The 32-week Norberg angles of joints that had scores of 0, 1, or 2 at 104 weeks were significantly larger than those of joints with a 104-week score of 3. For 3-D measures, the FNAs of joints with a 104-week score of 0 were significantly greater than those of joints with a 104-week score of 3.

Results of regression analysis revealed that the combined 16-week hip joint measures that had the greatest association with presence of osteoarthritis at 104 weeks were DI and CEA ($r^2 = 0.55$; $P = 0.004$). Combined 32-week measures that had the strongest association with presence of osteoarthritis were DASA and Norberg angle ($r^2 = 0.79$; $P = 0.002$); FNA alone at 32 weeks was also significantly associated ($r^2 = 0.19$; $P = 0.003$) with presence of osteoarthritis. Addition of more values to the regression models reduced the strength of the correlations.

Many 2-D hip joint measures were significantly correlated within ages (**Table 6**), as were 3-D hip joint measures. Ventral acetabular sector angle had the fewest correlations with other 2-D or 3-D measures. Relationships between 2-D and 3-D measures were most common at 104 weeks of age. Intraclass correlations coefficients (repeatability) of FNV, FNA, and FNR were 0.98, 0.90, and 0.99, respectively, and interclass correlation coefficients (reproducibility) were all ≥ 0.99 .

Discussion

The study reported here included a comprehensive evaluation of canine hip joint development from youth to maturity in a population of dogs with joint laxity thought to contribute to joint changes characteristic of CHD. Standard and novel measures were used to quantify changes in 1 hip joint in each of 46 dogs on the basis of radiographic and CT images obtained at 16, 32, and 104 weeks of age. The study results confirmed that some measures on images from 16 and 32 weeks of age vary among hip joints that develop osteoarthritis with different degrees of severity at maturity. Further, age and osteoarthritis scores affected measure values independently. Combined 2-D measures were significantly associated with presence of osteoarthritis at maturity, and the combinations that had the strongest association varied by age. When joints were grouped by osteoarthritis severity, the number of 2-D measures that differed significantly among groups was greater at 32 weeks of age than at 16 weeks. The hip joint in dogs undergoes rapid development between 3 and 8 months of age, so predictive diagnostic tests are typically most accurate during that time.^{1,5,6,9,24,25}

There are no distinctions among different types of CHD; this is in contrast to developmental dysplasia of the hip in humans, where distinctions are made between primary acetabular dysplasia and abnormal femoral development.^{15,16,18-20,26-29} In a previous study²¹ with images used in the present investigation, the femoral head and acetabular volumes of hip joints in dogs changed consistently relative to each other despite osteoarthritic changes. In the same study,²¹ ratios of the volume of the femoral head within the acetabulum to the femoral head and acetabular volume at 16 and 32 weeks of age differed significantly between dogs with severe versus no hip joint osteoarthritis at maturity. Given that CHD is characterized by acetabular and femoral head flattening in conjunction with bony proliferation at the base of the femoral head,^{1,30} we sought

to evaluate novel measures focused on the femoral head and neck and their relationship as a means of determining predictable femoral changes associated with development and with hip joint osteoarthritis at maturity.

Of the 3-D measures assessed, only the FNA at 32 weeks of age differed significantly between hip joints that had no osteoarthritis and those that had severe osteoarthritis at maturity; smaller angles were associated with severe osteoarthritis. The prognostic value of this measure was not improved by combining it with others, possibly because other measures describe the relationship between acetabulum and femur from various perspectives, and the FNA only includes the femur. Therefore, FNA measurement may provide a mechanism to predict development of osteoarthritis on the basis of femoral structure. Results of the present study support that femoral changes associated with development of hip joint osteoarthritis in dogs occur early in joint development.

The HASA, DASA, AI, and AAA in the hip joints of dogs decreased significantly with increasing age. These results may reflect decreased values associated with increased osteoarthritis incidence in the study population over time, considering that all osteoarthritis grades were combined for analysis. Based on this assumption, decreases in these measures may be reflective of joint changes associated with osteoarthritis. Assessment of the novel measures in this study also revealed decreases in FHV:FNV and FHR:FNR ratios with age from 16 to 32 weeks; however, differences between values corresponding to osteoarthritis severities were not significant, potentially limiting the value of the individual measures to predict osteoarthritis. When hip joint measures obtained at all ages were evaluated together, DI and CEA incrementally increased, whereas DASA, HASA, CPC, AAA, and Norberg angle decreased with increasing osteoarthritis severity. This supports that values change predictably with osteoarthritis severity regardless of age, an important consideration when identifying measures to evaluate in different breeds at various ages. These measures may have the widest applicability for quantification of conformational changes associated with CHD, although their utility in dogs of various breeds and ages must be investigated to confirm this. Another consideration is that changes in cartilage thickness associated with age and osteoarthritis may contribute to differences in measures among ages and osteoarthritis severities. Further analysis of these measures on hip joint images that show articular cartilage will provide additional information about their relationships with each other and joint changes attributable to age and disease.

Consistent with established knowledge, DI values in this study were greater in hip joints that developed severe osteoarthritis than in those with no osteoarthritis. Although there were significant differences in the 16- and 32-week DI of hip joints without osteoarthritis at maturity, compared with those that developed severe osteoarthritis, no differences in DI were found

for those that developed mild or moderate osteoarthritis versus severe or none. This was true for most measures in the present study. In an effort to increase the prognostic value of measures, various combinations were assessed to identify those that had the strongest association with development of hip joint osteoarthritis in mature dogs. At 16 weeks, the combination of DI and CEA had the strongest association with hip joint osteoarthritis at 104 weeks, and at 32 weeks, the DASA and Norberg angle combination had the strongest association with this outcome.

The fact that DI and CEA both represent 2-D dorsolateral coverage of the femoral head by the acetabulum supports that the relationship between the 2 articular surfaces substantially affects joint formation at approximately 16 weeks of age. The relative fit of the femoral head in the acetabulum is critical to normal hip joint development in dogs and humans, but past a certain stage of development, it may be less important.^{15,29,31,32} The DI and CEA may complement each other, given that the CEA is a static angle measure and the DI provides a more dynamic perspective of the relationship between the femoral head and acetabulum.^{1,7}

The DASA and Norberg angle are measures of the dorsal coverage of the femoral head by the acetabulum. They differ in that the DASA is measured on a central section or slice of the femoral head and the Norberg angle is measured on a 3-D structure compressed to a 2-D image. The DASA has been shown previously to have a strong association with the radiographic osteoarthritis score, Orthopedic Foundation for Animals confirmation scores, and DI; both DASA and Norberg angle reportedly have a strong relationship with hip joint articular cartilage microdamage.¹⁷ In the present study, the mean Norberg angle at 16 weeks of age was greater than the threshold value of 105° in dogs that did not develop hip joint osteoarthritis. However, by 32 weeks of age, this value was < 105° in all study dogs, including those that did not develop osteoarthritis at maturity. This is consistent with earlier reports¹¹ that Norberg angle has variable relationships with osteoarthritis that differs among dog breeds. The DASA was significantly associated with osteoarthritis when all osteoarthritis grades and all ages were considered together in the present study; Norberg angle was significantly associated with osteoarthritis when all ages were considered together. It is reasonable to consider that the combination of these 2 measures was better than either alone for early prediction of adult hip joint osteoarthritis.

Notably, the measure combinations (DI and CEA; DASA and Norberg angle) that had the strongest associations with hip joint osteoarthritis at maturity did not necessarily have the strongest correlations with each other at the 3 time points (ages) evaluated in the study. The alignment of the linear changes in measures reflected by the Pearson product moment correlations are not necessarily related to their independent or combined degree of association with de-

velopment of hip joint osteoarthritis. The measures that had the strongest associations with this outcome when combined provided information on specific hip joint characteristics (static and dynamic dorso-lateral and dorsal femoral head coverage by the acetabulum). However, within combinations, the measures provided information about a similar characteristic from different perspectives. Our results support the potential that morphological changes associated with abnormal hip joint development vary throughout development. Information such as this may be valuable to target diagnostic imaging measures based on patient age.

Some limitations to the study included the evaluation of a homogeneous group of dogs and conclusion of the study when dogs were 104 weeks old. Additional relationships between early hip joint measures and the development or severity of osteoarthritis in adult dogs may have been identified with longer study duration. Further, the use of these measures should be evaluated in other dog breeds. Although it is established that there are strong correlations between articular microstructural changes and 2-D CT measurements,¹⁷ radiographically detectable changes often lag behind joint degeneration.^{1,6} Future studies that include more direct joint surface examination through methods such as arthroscopy may provide additional information about the relationship between radiographic and CT hip joint measures and joint degeneration.

The advantages of 3-D hip joint models for diagnostic, prognostic, and therapeutic purposes are well recognized, and these are used for such purposes in human patients, but they have yet to be fully realized in dogs.^{13,18-20,25,26,28,33} Investigations such as the present study contribute to continued progress in this field. The results of this study, taken together, support the utility of combined radiographic and CT measures at early ages to predict hip joint osteoarthritis in dogs at maturity and provide a basis for formulation of future interventional treatments and guidance regarding reproductive decisions. Further, the results of this study contribute to understanding of joint alterations within the complex CHD syndrome that have strong associations with joint degeneration. Continued investigations with larger numbers and different breeds of dogs are necessary to further refine and expand measures to be applied clinically and incorporated into computer model databases.

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Footnotes

- a. PennHIP Analysis Center, Malvern, Pa.
- b. PMI Nutrition Prime Formula, PMI Nutrition, Henderson, Colo.
- c. PMI Nutrition Adult Formula, PMI Nutrition, Henderson, Colo.
- d. Adobe Photoshop, version 8.0, Adobe Systems Inc, Seattle, Wash.

- e. GE Highlight Advantage, General Electric Medical Systems, Milwaukee, Wis.
- f. eFilm, Merge eFilm, Milwaukee, Wis.
- g. Mimics, version 14.12, Materialise, Ann Arbor, Mich.
- h. 3-matic, version 6.0, Materialise, Ann Arbor, Mich.
- i. SAS, version 9.0, SAS Institute Inc, Cary, NC.

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