

Session 07 (Oral presentation 008)

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Genetics of radiographic signs related to degenerative lumbosacral stenosis and its correlations to canine hip dysplasia in the German shepherd dog



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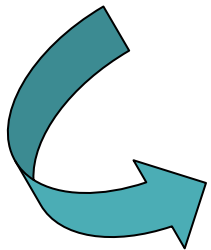
Background

- degenerative lumbosacral stenosis (DLSS) as main cause for cauda equina syndrome (CES)
- clinical importance of CES
 - pain due to compression of nerval structures
 - lameness, paresis or paralysis of hind leg(s)
 - urinary and/or fecal incontinence
- relatively high prevalences of DLSS in large dogs
 - surmised breed disposition:
German shepherd dog



Objectives

- genetic analysis of radiological signs related to DLSS in the German shepherd dog (GSD)
 - heritabilities
 - genetic correlations with canine hip dysplasia (CHD)



implications for future breeding strategies for improved skeletal health in the GSD



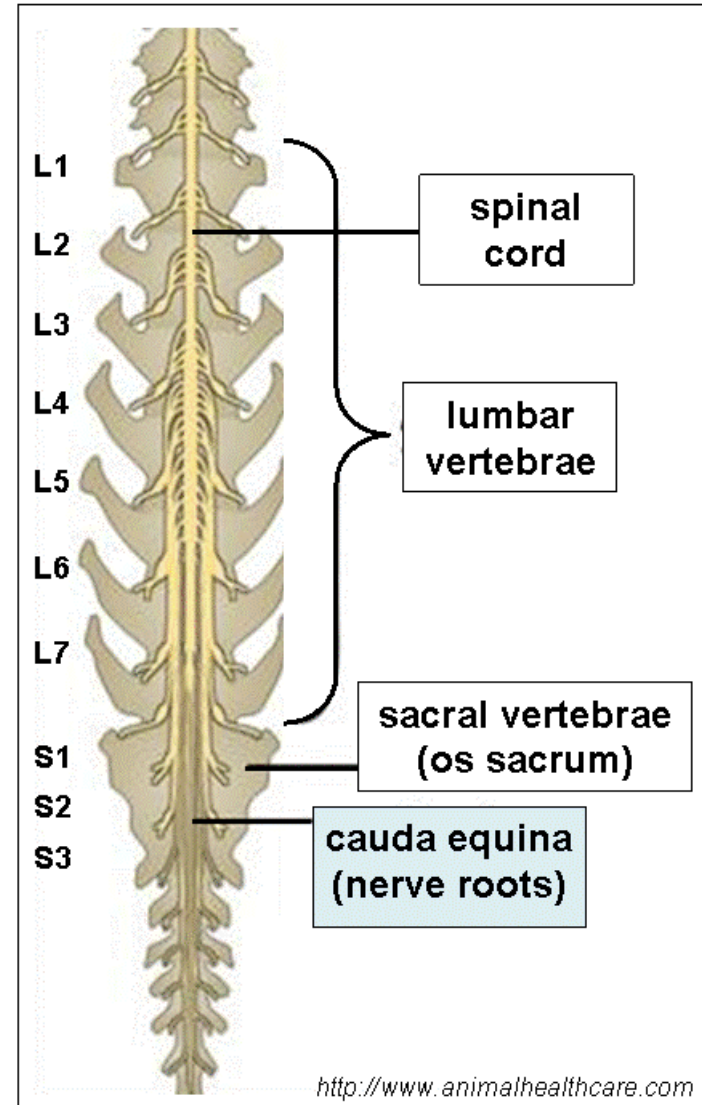
Data sources

- radiographic data
 - (1) DLSS
results of radiographic examinations of the spine
of 572 GSD (95% born in 2000-2007)
 - (2) CHD
database of the German breeding organization for GSD
with CHD information on ~ 180,000 dogs
→ restriction to birth years 2000-2007:
CHD information on 55,672 GSD
- ⇒ **55,758 GSD with DLSS and / or CHD information**
- pedigree data
database of the German breeding organization for GSD

Degenerative lumbosacral stenosis (DLSS)

cauda equina

- caudal end of spinal cord (bundle of nerve roots)
- in the lumbosacral part of the vertebral canal
⇒ compression in case of lumbosacral narrowing of vertebral canal
→ innervation deficits (CES)



Degenerative lumbosacral stenosis (DLSS)

narrowing of vertebral canal at lumbosacral transition

- abnormal tissue growth (ligaments, bone)
- protrusions from intervertebral discs

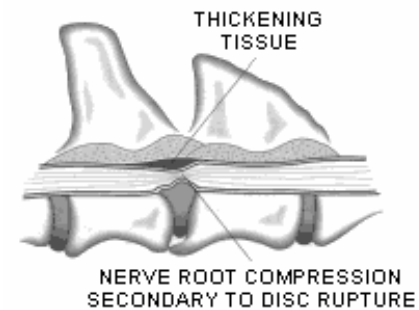
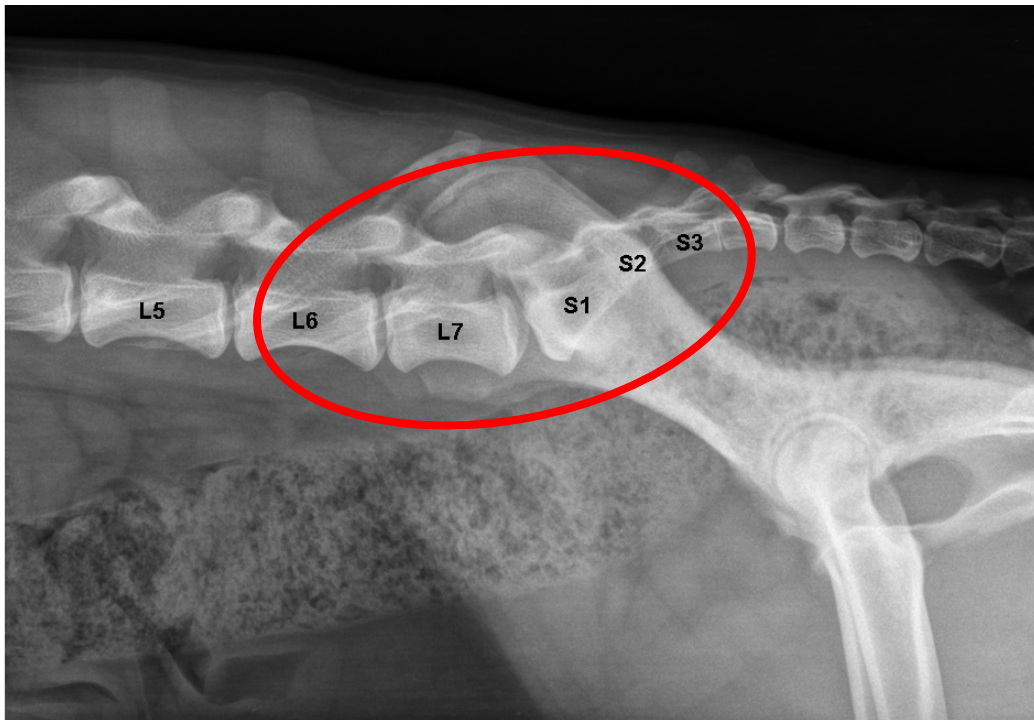
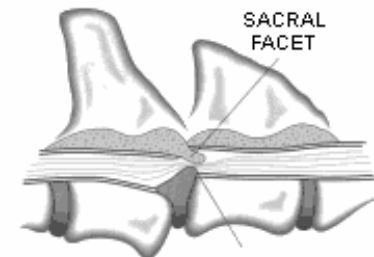


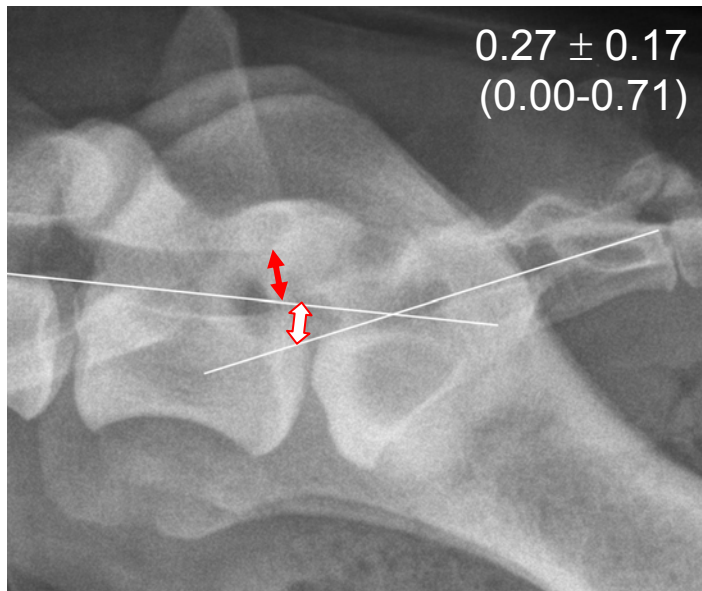
FIGURE 2



Trait definition (DLSS)

- measures at lumbosacral transition, relative to height of vertebral canal in L7 caudal
 - malalignment (L7-S1)
 - intervertebral disc width (L7-S1)

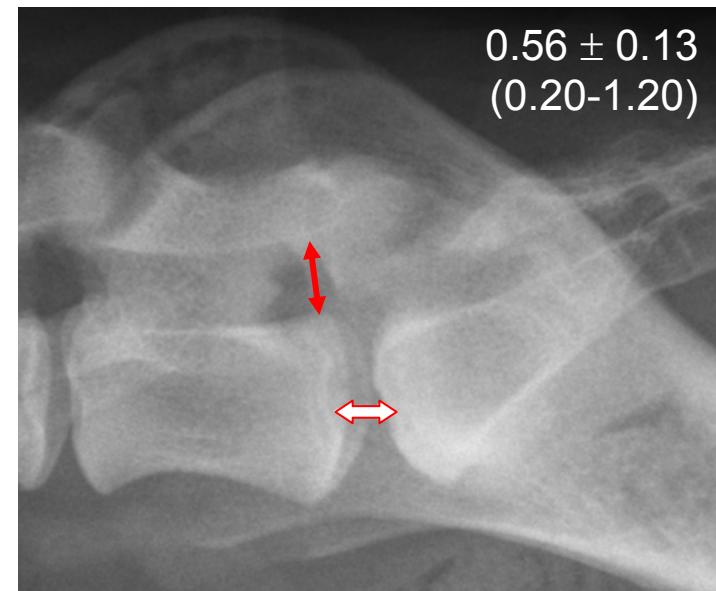
↪ relative measures as continuous DLSS traits (n=2)



↕ height of vertebral canal in L7 caudal (reference)

↕ DLSS measures:

- malalignment (*left*)
- intervertebral disc width (*right*)



Trait definition (DLSS)

- specific findings at lumbosacral transition
 - cranial endplate of os sacrum
 - lumbar and sacral vertebrae (incl. vertebral canal)
 - intervertebral discs

 binary DLSS traits (n=7)

Trait	Prevalence
sacral osteochondrosis dissecans (OCD)	9.3%
lumbosacral transitional vertebra (TRV)	7.5%
sacral sclerosis	41.3%
lumbosacral spondylarthrosis	21.3%
diffuse dorsal contour of sacral vertebral canal	34.8%
lumbosacral intervertebral disc calcification	12.1%
undefined structure in the vertebral canal	25.2%

Genetic analyses

- multivariate estimation of genetic parameters using Gibbs sampling (MTGSAM)
 - relationship matrix including 89,962 animals (5 ancestral generations)
 - genetic correlation analyses (CHD – DLSS)
 - linear animal models (continuous DLSS traits) and linear-threshold animal models (binary DLSS traits)
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Genetic analyses

NOTE:

extreme imbalance between amounts of information on CHD (n=55,672) and DLSS (n=572)



- a) repeated analyses of real data (CHD, DLSS traits) with different starting values for σ_a^2
→ consistency of results?
- b) simulation study on reliability of estimates (h^2 , r_g)
→ bias in case of low (± 0.2) or moderate (± 0.5) genetic correlations? influence of starting values?

Results

I. Heritability estimates

Trait	high $SV_{\sigma a^2}$	low $SV_{\sigma a^2}$
Canine hip dysplasia (CHD)	0.21	0.21
<u>Relative DLSS measures</u>		
malalignment	0.77	0.37
intervertebral disc width	0.90	0.40
<u>Specific alterations at lumbosacral transition</u>		
sacral osteochondrosis dissecans (OCD)	0.24	0.04
lumbosacral transitional vertebra (TRV)	0.31	0.07
sacral sclerosis	0.60	0.02
lumbosacral spondylarthrosis	0.35	0.05
diffuse dorsal contour of sacral vertebral canal	0.32	0.04
lumbosacral intervertebral disc calcification	0.18	0.02
undefined structure in the vertebral canal	0.16	0.05

standard errors (h^2): ≤ 0.1

Results

I. Heritability estimates

- CHD:
 - stable (not influenced by starting values)
 - moderate ($h^2 = 0.21$)
- DLSS traits:
 - instable (influenced by starting values)
 - moderate to high for continuous traits ($h^2 = 0.37$ - 0.90),
low to moderate for binary traits ($h^2 = 0.02$ - 0.60)

Results

II. Additive genetic correlation estimates

Trait	high $SV_{\sigma a^2}$	low $SV_{\sigma a^2}$
<u>Relative DLSS measures</u>		
malalignment	-0.12	-0.21
intervertebral disc width	-0.07	-0.19
<u>Specific alterations at lumbosacral transition</u>		
sacral osteochondrosis dissecans (OCD)	0.10	0.25
lumbosacral transitional vertebra (TRV)	-0.27	-0.14
sacral sclerosis	-0.42	-0.23
lumbosacral spondylarthrosis	-0.37	-0.49
diffuse dorsal contour of sacral vertebral canal	0.27	0.35
lumbosacral intervertebral disc calcification	-0.39	-0.30
undefined structure in the vertebral canal	-0.27	-0.24

 positive  negative

standard errors (r_g): 0.1-0.2

Results

II. Additive genetic correlation estimates

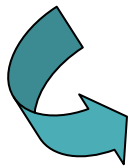
- acceptably stable (some, but mostly minor influence of starting values)
 - closer genetic correlations between CHD and binary traits than between CHD and continuous traits
 - directions of genetic correlations:
 - positive sacral OCD,
diffuse dorsal contour of sacral vertebral canal
 - negative malialignment, intervertebral disc width,
sacral sclerosis, lumbosacral spondylarthrosis,
undefined structure in the vertebral canal,
TRV, lumbosacral IVD calcification
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Conclusions

- indications of relevant genetic determination of radiographic signs related to DLSS
 - implications of genetic correlations with regard to CHD-oriented breeding strategies:
 - feasibility of concurrent selection against OCD-related DLSS
 - possible interference of selection against TRV-related DLSS
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Conclusions

- indications of relevant genetic determination of radiographic signs related to DLSS
- implications of genetic correlations with regard to CHD-oriented breeding strategies:
 - feasibility of concurrent selection against OCD-related DLSS
 - possible interference of selection against TRV-related DLSS



issues of further studies (*in progress*):

- verification of radiographic data analyses
(more radiographic data; longer Gibbs chains)
 - closer investigation of intervertebral discs and soft tissues
(combination of radiographic and MRT data)
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Thank you!

