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Radiographic Screening for Hereditary Skeletal Disorders in Dogs

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ACADEMIC DISSERTATION

To be presented, with the permission of the Faculty of Veterinary Medicine of the University of Helsinki, for public examination in lecture room 5, University main building, on 14 June 2013, at 12 noon.

Helsinki 2013

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Cover: Wirehaired Dachshund Begonia as a self-confident one-year-old in summer 1983.

ISBN 978-952-10-8853-7 (pbk.)
ISBN 978-952-10-8854-4 (PDF)

Unigrafia
Helsinki 2013

Abstract

Screening in dog breeding refers to testing or examining individuals for hereditary diseases or faults. Results can help dog breeders in decision-making when selecting breeding material. Radiographic screening for canine elbow dysplasia (ED) began several decades ago, but genetic improvements have been modest. Several reasons for slow progress exist; perhaps one of the most important is that affected individuals continue to be used for breeding. On the other hand, disorders like lumbosacral transitional vertebrae (LTV) in several dog breeds and intervertebral disc calcifications in Dachshunds are not widely screened even though this would reduce the incidence of debilitating orthopaedic and neurological diseases caused by these disorders. The aim of this study was to initiate radiographic screening protocols for intervertebral disc calcifications and LTV in Finland and to revise the existing Finnish screening protocol for ED. Breeds used were the miniature long-haired and wire-haired Dachshund, Belgian shepherd dog, Labrador retriever and German shepherd dog. The imaging methods applied were radiography and computed tomography (CT).

Occurrence of intervertebral disc calcifications was higher in Finnish miniature Dachshunds than previously reported; 76% of longhaired and 87% of wirehaired variety had at least one calcification. Therefore screening protocol excluding every dog with calcifications from breeding would not be possible. The number of calcifications varied between none and 13, and therefore radiographic screening, together with favouring dogs with fewer calcified discs in breeding, is suggested.

Accuracy of the Finnish screening protocol for mild (grade 1) ED differed between the two breeds studied. In Belgian shepherd dogs, the Finnish protocol based mainly on evaluation of osteophytes was inaccurate, as 47% of the joints free of ED were incorrectly graded as dysplastic and 40% of dysplastic joints were graded as normal. On the other hand, assessment of the radiographic signs indicative of medial coronoid process disease proved to be accurate in this breed; sensitivity and specificity of blurring of the cranial border of the medial coronoid process were 80% and 90%, respectively. In Labrador retrievers, the Finnish protocol proved to be accurate, as sensitivity of grading was 79% and specificity 92%. Osteophytes seen in the supplemental craniocaudal oblique radiographic projection was the most reliable sign of ED in Labrador retrievers with sensitivity of 93% and specificity of 92%. Adding this view might be a valuable addition to the screening protocol. Labrador retrievers with grade 1 ED should not be used for breeding since most of them have ED, as was clearly demonstrated in the study.

LTV was common in Finnish German shepherd dogs studied with occurrence of 40%. A laterolateral (LL) radiograph appeared to be a useful supplement to the currently used ventrodorsal (VD) radiograph in diagnosis of LTV. Sensitivity of the diagnosis based on the VD projection alone was 90% increasing to 100% when LL projection was used together with the VD projection. Additionally, diagnosis of the eighth lumbar vertebra (L8) was only possible based on the LL projection. It is therefore suggested for inclusion in the radiographic screening protocol. The L8 resembled an LTV, and is therefore proposed as a part of the LTV-complex and for consideration when screening for LTV.

Acknowledgements

This thesis work was carried out at the Department of Equine and Small Animal Medicine and at the Veterinary Teaching Hospital, Faculty of Veterinary Medicine, University of Helsinki. I wish to express my gratitude to Professor Satu Sankari and Chief of the Veterinary Teaching Hospital Jussi Anttila for providing the facilities that made this thesis possible. It has been a privilege to study subjects close to my heart.

Financial support provided by the Finnish Kennel Club is gratefully acknowledged.

When the first article of this thesis was published in 2001, I had no idea that it would be the beginning of my life as a scientist and end up as part of my thesis. I was a practitioner, devoted to Dachshunds and their well-being, just visiting the old alma mater. But, as someone has wisely said, you never know.

I am deeply grateful to Professor Herman Hazewinkel and Associate Professor Ingrid Gielen for reviewing the manuscript of this thesis and for their valuable comments, and to Professor Eiliv Svalastoga for accepting the position of opponent at the public examination.

My greatest gratitude is due to my supervisor and mentor Professor Emerita Marjatta Snellman. Our favourite discussion topics, hereditary skeletal diseases and extreme anatomical features of pure-bred dogs, could perhaps be considered somewhat less than riveting, but discussions with Marjatta were and are each time enjoyable since we share the same basic viewpoint. Without Marjatta, I would not be the person I am; she introduced me to the magical world of radiographs and the field of radiographic screening.

I owe an enormous debt of gratitude to my supervisor Professor Outi Vapaavuori for her faith in me and for the generous help and support that she has given me throughout the years. Working with her has always been fun.

My co-author Sari Mölsä, DVM, shared an office with me for several years, which must have been a trying experience. I thank her for her invariably calm and reassuring attitude towards my endless waffling on various issues at work and in life in general.

Co-author Annie Liman, DVM, I thank for being a part of our research team. I am especially grateful to her for teaching me how to evaluate screening radiographs, in addition to the numerous colourful debates on elbow dysplasia screening.

I am grateful to co-authors Mia Norrgård, Karoliina Alm-Packalén and Reea Salomaa. Today, they are all colleagues in veterinary medicine, but at the time of the studies they were enthusiastic students with a deep devotion to dogs.

I am grateful to co-author Jouni Junnila for helping me with statistics. I now understand a bit of it. But just a bit.

My deep gratitude is owed to the radiographers of the Unit of Diagnostic Imaging: Tarja Salonen, Johanna Salomäki, Taina Mäki, Heidi Immonen, Sonja Koiranen and Päivi Viljakainen. They were always willing to help, whether it was taking radiographs, conducting CT studies or searching for missing files. This study would never have been completed without you!

To my colleagues at the Unit of Diagnostic Imaging, I owe a lot. Thank you Hanna Salonen, Vilma Reunanen, Elina Rautala, Merja Laitinen and Mona Wendelin for your support and help.

I thank all of my friends and colleagues at the Faculty of Veterinary Medicine for their contributions.

My gratitude is owed to Arto Ketola and Jari Rantanen for their statistical work.

Carol Ann Pelli is warmly thanked for editing the language of this thesis and three of the original articles.

Anne Luoma is warmly thanked for her kind and reassuring attitude towards me during the final steps of this process.

Many thanks go to the Finnish Kennel Club, the Finnish Dachshund Club, the Finnish German Shepherd Club and the Finnish Border Guard for their cooperation during the studies. Special thanks go to Evi Helin from the Finnish Kennel Club for her invaluable help. She has searched the archives for countless screening radiographs over the years.

I am deeply grateful to all the dog-owners participating in the studies with their dogs. Without them this work would have been impossible.

My trusted friend Lissu Rossi, whom I have known since we both had a Dachshund puppy from the same litter over two decades ago, I thank warmly for seeing me through the thick and thin, always ready to help.

Docent Minna Rinkinen I met for the first time when I was doing my specialization training at the University Teaching Hospital on Hämeentie. Since then, she has been an invaluable friend to me, understanding what it is like to do research and work at the University.

My sister-in-law Helena Juutilainen is specially thanked for being there for me whenever I needed comfort and support.

Finally, I thank my husband Juha Nieminen, without whom this project would never have been accomplished. His love and caring mean everything to me.

I dedicate this thesis to my late father Docent Antti Lappalainen, from whom I inherited the genes for curiosity and who showed me the value and joy of learning.

Contents

List of original publications

This thesis is based on the following publications

I: Lappalainen, A., Norrgård, M., Alm, K., Snellman, M. & Laitinen, O. (2001) Calcification of the intervertebral discs and curvature of the radius and ulna: a radiographic survey of Finnish miniature dachshunds. Acta Veterinaria Scandinavica 42, 229-236.

II: Lappalainen, A.K., Mölsä, S., Liman, A., Laitinen-Vapaavuori, O. & Snellman, M. (2009) Radiographic and computed tomography findings in Belgian shepherd dogs with mild elbow dysplasia. Veterinary Radiology & Ultrasound 50, 364-369.

III: Lappalainen, A.K., Mölsä, S., Liman, A., Snellman, M. & Laitinen-Vapaavuori, O. (2013) Evaluation of accuracy of the Finnish elbow dysplasia screening protocol in Labrador retrievers. Journal of Small Animal Practice 54, 195-200.

IV: Lappalainen, A.K., Salomaa, R., Junnila, J., Snellman, M. & Laitinen-Vapaavuori, O. (2012) Alternative classification and screening protocol for transitional lumbosacral vertebra in German shepherd dogs. Acta Veterinaria Scandinavica 54:27.

The publications are referred to in the text by their roman numerals.

Abbreviations and definiations

0b = borderline
BVA/KC = British Veterinary Association/Kennel Club
BVE = breeding value estimate
CrCd oblique = cranio15°lateral-caudomedial oblique
CT = computed tomography
D35°M-PrLO = dorso35°medial-proximolateral oblique
ED = elbow dysplasia
FCI = Fédération Cynologique Internationale
FCP = fragmented coronoid process
FKC = Finnish Kennel Club
FMCP = fragmented medial coronoid process
HD = hip dysplasia
IDD = intervertebral disc disease
IEWG = International Elbow Working Group
INC = incongruity of the elbow joint
IOHC = incomplete ossification of the humeral condyle
L1-L7 = lumbar vertebrae 1-7
L8 = eighth lumbar vertebra
LL = laterolateral
LTV = lumbosacral transitional vertebra
MCD = medial compartment disease
MCP = medial coronoid process
MCPD = medial coronoid process disease
ML = mediolateral
ML flexed = mediolateral 45° flexed
MRI = magnetic resonance imaging
OA = osteoarthritis
OC = osteochondrosis
OFA = Orthopedic Foundation for Animals
PEVISA = perinnöllisten vikojen ja sairauksien vastustamisohjelma (program against hereditary diseases and defects)
PSM = presomitic mesoderm
S1-S3 = sacral vertebrae 1-3
UAP = ununited anconeal process
UME = ununited medial epicondyle
VD = ventrodorsal
VRT = volume rendering technique

1 Introduction

Radiographic screening for canine hereditary skeletal disorders has been extensively applied for several decades. Hip dysplasia (HD) was the first widely screened disorder (Brass and Paatsama 1983), and screening for elbow dysplasia (ED) followed when it became clear that ED was a frequent cause of lameness in certain dog breeds (Grøndalen 1982a, Grøndalen 1982b). In Finland, dog breeders are highly health-conscious when choosing breeding material; the Finnish Kennel Club (FKC) supports efforts to fight against hereditary diseases by providing a special health programme (PEVISA) (PEVISA... 2009). The PEVISA programmes are voluntary, but when a breed club enters a programme, preconditions for registration of a litter can be set. Screening the sire and dam for HD and ED are the most common obligatory examinations, and several breed clubs have also set limits on accepted dysplasia grades (Rotukohtaiset erityisehdot... 2013).

The ED screening protocol of the FKC (Ohje kyynärnivelen kasvuhäiriöiden... 2011) was established in 1994 and has not since been revised. A single mediolateral (ML) flexed radiograph is required; the main emphasis is on secondary changes (osteophytes), and findings indicative of the primary lesion have received less attention. In many European countries, screening is focused more on diagnosing the primary lesion, and usually at least two radiographic projections are required (Flückiger 2011).

Radiographic screening for other common hereditary skeletal disorders, such as lumbosacral transitional vertebra (LTV), and intervertebral disc calcifications of chondrodystrophic breeds has received less interest worldwide. Because these conditions predispose to severe locomotor diseases, diminishing their prevalence should be an objective. Radiographic screening could be a practical tool since both disorders have a moderately high heritability (Wigger et al. 2009, Jensen and Christensen 2000). Screening might be considered even more important, as two globally very popular breeds suffer commonly from diseases caused by these disorders: cauda equina syndrome in German shepherd dogs and intervertebral disc disease in Dachshunds.

The lion's share of research in veterinary medicine revolves around treating the diseases instead of trying to find ways to reduce their prevalence. The focus of this thesis was on three noteworthy canine hereditary disorders, with the aim of establishing new or improving existing radiographic screening protocols in Finland.

2 Review of the literature

2.1 Radiographic screening for hereditary skeletal disorders in dogs

2.1.1 General principles of screening

In an English dictionary, screening is described as "testing or examining somebody/something for disease, faults, etc." (Hornby 1995). Screening in the context of dog breeding refers to testing dogs for a hereditary disease or defect. It can apply either to potential breeding animals or to a large proportion of the population. Screening is useful only if the disease or fault is hereditary and the trait is measurable. The method used should be objective and measure the trait in question. Selection based on phenotype can be effective if heredity is moderate (Mäki et al. 2000), but genetic progress could be hastened if selection is based on predicted breeding values rather than phenotype (Malm et al. 2008, Mäki et al. 2000, Leppänen et al. 2000c).

One of the main issues in modern dog breeding is health. Only functionally and clinically healthy dogs, with breed-typical conformation, should be used for breeding (Hedhammar and Indrebø 2011). Small founding populations and inbreeding have led to increased homozygosity of several disease alleles, and consequently, to growing numbers of hereditary diseases and diseased individuals in many dog breeds (Lequarre et al. 2011, Ubbink et al. 1998).

Radiographic screening can be considered expensive. Expenses consist of fees for the veterinarian, the scrutinizer and the organization responsible for the scheme. However, costs of screening are less than the value of dogs estimated to have been saved from moderate or severe orthopaedic disease (Swenson et al. 1997a, Swenson et al. 1997b). The attitudes of breeders, dog-owners and veterinarians regarding programmes aimed at controlling canine genetic diseases have seldom been investigated. In one series of questionnaire studies, health-related matters and well-being appeared to be highly valued in Finland, with inherited skeletal diseases considered to be the most important factor affecting canine well-being (Leppänen et al. 2000a, Leppänen et al. 2000b, Leppänen et al. 1999).

Several screening methods are used worldwide, radiography being by far the most common. Others are clinical examination for patellar luxation and heart murmur, ocular examination for eye diseases, auscultation and echocardiography for cardiac diseases (Jalostus ja kasvatus... 2012), magnetic resonance imaging for chiari-like malformation and syringomyelia (Mikä on syringomyelia… 2012) and gene tests for diseases where the disease mutation is known (Canine genetic studies... 2012).

2.1.2 Past and present of radiographic screening

Hip dysplasia (HD), also known as congenital subluxation, was first described in 1935 by Schnelle (Schnelle 1935). The disease was initially considered rare in the dog, but it soon became evident that it is one of the most common and serious developmental hereditary disorders in most large dog breeds (Carlson 1961, Schnelle 1959). Radiographic screening for the disease began in the 1960s, and the screening procedure was internationally set by the Fédération Cynologique Internationale (FCI) two decades later (Brass and Paatsama 1983).

Another debilitating orthopaedic disease that has been radiographically widely screened is elbow dysplasia (ED). The first description of the ununited anconeal process of the ulna (UAP), called the "patella cubiti", is from 1956 (Stiern 1956). Fragmented coronoid process (FCP) and osteochondrosis (OC) were described in 1974 (Olsson 1974). Osteophytes caused by any type of ED were best seen radiographically on the anconeal process in the mediolateral (ML) projection (Grøndalen and Grøndalen 1981).

Radiographic screening for ED began in the 1980s in Scandinavia and in several European countries. The International Elbow Working Group (IEWG) was founded in 1989, and the first international protocol was adopted during the same year (International elbow protocol… 2012). Radiographic screening for hereditary diseases in dogs has become increasingly popular during the past decades. In 2001, a total of 10116 dogs were screened for HD and ED in Finland. In 2011, the number was over twofold, 21846. In many breeds, well over half of the population is screened for either HD or ED, or both.

Several screening protocols for both HD and ED are in use worldwide. Members of the FCI, the British Veterinary Association/Kennel Club (BVA/KV) in Great Britain and the Orthopedic Foundation for Animals (OFA) in North America use extended ventrodorsal radiograph for HD screening, but the scoring differs somewhat between countries (Flückiger 2007). Screening for ED is more heterogeneous. All schemes are basically based on the IEWG protocol, but since there are differences in the ways the screening organizations have adopted the protocol, there is no consensus on which projections should be used or how the radiological findings should be interpreted (IEWG… 2012). Nordic countries (Denmark, Finland, Iceland, Norway and Sweden) have a common scheme and similar scoring principles in HD as well as in ED.

There are also radiographic screening protocols for other skeletal diseases, e.g. spondylosis deformans for the Boxer and intervertebral disc calcification for the Dachshund. These protocols have been established in the 1990s, but they are in use in only a few countries. In Finland, the FKC started screening for spondylosis in Boxers in 2010, and since July 2012 all breeds can have a radiographic grade for this disease. In 2013, the FKC will start screening for intervertebral disc calcifications in chondrodystrophic breeds and for vertebral malformations and lumbosacral transitional vertebrae (LTV) in all breeds.

The dog genome was mapped in 2005 (Lindblad-Toh et al. 2005), and thereafter, the progress in revealing canine disease mutations has been rapid, with mutations behind several defects with monogenic inheritance identified. This has enabled gene tests for certain diseases, such as mucopolysaccharidosis VII in Brazilian terriers (Hytönen et al. 2012) and remitting epilepsy in Lagotto romagnolo dogs (Seppälä et al. 2011), to be devised. With careful planning, the disease carriers can be used for breeding (Lequarre et al. 2011). Gene tests for diseases with monogenic inheritance are already in use as screening tools in many breeds (Genoscoper 2012). Polygenic diseases, such as HD and ED, are a

challenge for research, as there are several genes involved (Clements et al. 2010, Zhu et al. 2009, Janutta et al. 2006).

2.2 Intervertebral disc disease

2.2.1 Anatomy of the intervertebral disc

Intervertebral discs unite adjoining vertebral bodies and exist between all vertebrae, except the atlantis (C1) and axis (C2). Intervertebral discs (Figure 1) are composed of a soft gel-like nucleus pulposus (remnant of the embryogenic notochord) in the centre and a firm, fibrocartilaginous annulus fibrosus surrounding it. The annulus fibrosus consists of parallel fibres running obliquely from one vertebral body to the next. These fibres are important in passing on the stress of upward and sideways movements. The annulus fibrosus is considerably thicker ventrally than dorsally. Near the nucleus pulposus, the fibrous ring has a less distinctive structure and is more cartilaginous (Evans 1993). This region is often referred to as a transitional zone (Braund et al. 1975).

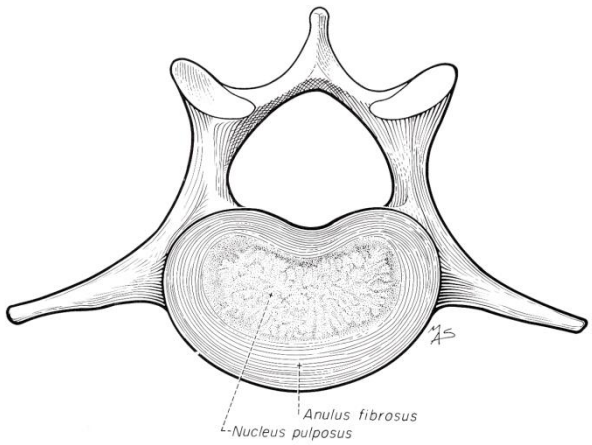

Figure 1 *Intervertebral disc of a young dog (Evans 1993).*

In embryogenesis of the vertebral column, the notochord is the first to develop. The notochordal cells later form sclerotomes, which differentiate into vertebrae and the nucleus pulposus. In a young individual, the gelatinous nucleus pulposus consists of notochordal cells, water and highly hydrated proteoglycans. The outer annulus fibrosus comprises well-defined lamellae of dense white fibrous tissue of collagen fibres. It merges with an inner annulus formed from fibrocartilage (Butler 1988).

For several decades, the intervertebral discs of adult humans and chondrodystrophic dogs have been assumed to not preserve foetal notochordal cells in their nucleus pulposus, unlike most mammals (Hunter et al. 2004, Butler 1988). The two cell types of the adult

nucleus pulposus (the large notochordal cells and the small chondrocytic cells) have been regarded to be of different origins (Cappello et al. 2006, Hunter et al. 2003). However, recent studies have proposed that all cells of the nucleus pulposus are of the same origin, and all mammals retain notochordal cells in their nucleus pulposus (Risbud et al. 2010, Choi et al. 2008).

The adult canine and human intervertebral discs are avascular, distinct from the sparsely vascularized outer annulus fibrosus (Brunner and Frewein 1989, Taylor and Twomey 1988). The main supply of the intervertebral discs is by diffusion from capillary loops, which pass through the end plates of the vertebrae (Brunner and Frewein 1989). Nutrients and waste products are transported via diffusion mainly through end plates (Rajasekaran et al. 2008, Brunner and Frewein 1989).

2.2.2 Chondrodystrophic breeds

Dog breeds with noticeably short-legged body conformation, such as the Dachshund, Pekingese, Basset hound and Welsh corgi, have been referred to as chondrodystrophic (Stigen and Kolbjørnsen 2007, Stigen, 1991, Hansen 1952), as well as hypochondroplastic (Parker et al. 2009, Jensen and Arnbjerg 2001) and chondrodysplastic (Parker et al. 2009). A recent study demonstrated that expression of a retrogene encoding fibroblast growth factor 4 (fgf4) is strongly associated with chondrodystrophia in 19 dog breeds, including the Dachshund, Welsh corgi and Basset hound. Retrotransposition of processed mRNAs is a common source of novel sequences acquired during the evolution of genomes. Although most retrogenes are rapidly destroyed by debilitating mutations, some become new genes capable of encoding functional proteins. In other words, the chondrodystrophic phenotype developed from a single mutation (Parker et al. 2009).

Chondrodystrophic breeds are genetically predisposed to early intervertebral disc degeneration, as shown in studies of Beagle intervertebral discs (Braund et al. 1975, Ghosh et al. 1975). Interestingly, the Beagle is a breed without mutation in the retrogene fgf4, and genetically, it does not belong to the chondrodystrophic breeds (Parker et al. 2009). In a study by Hansen (1952) comprising 100 cases, 52 of the dogs with disc protrusion were Dachshunds. The two second most commonly affected breeds were the French bulldog and Pekingese. These breeds were shown to differ from the other breeds not only in susceptibility to disc calcification but also in enchondral ossification of bones. The study concluded that this is a type of chondrodystrophy, and the term “chondrodystrophoid breed group” was established (Hansen 1952). The French bulldog has, however, been shown by genetic studies to not belong to this group (Parker et al. 2009).

Associations between acute thoracolumbar disc extrusion and body length as well as between the extrusion and length of the distance between tuber calcanei and patellar tendon were found in a group of dogs in Texas, USA. The shorter the back and hind limbs, the greater the odds of being affected. It was postulated that this could be due to increased chondrodystrophy in smaller individuals (Levine et al. 2006). In a group of Danish Dachshunds, effects of body conformation were not found (Jensen and Ersbøll 2000).

2.2.3 Intervertebral disc degeneration

Nutrient deprivation of the disc leads to disc degeneration (Galbusera et al. 2011, Bibby and Urban 2004, Horner and Urban 2001). Notochordal cells are more susceptible to nutritional stress than adult chondrocytic cells due to their greater energy demand, and since the principal route for the capillaries is through the end plates, end plate changes during growth can lead to replacement of notochordal cells with chondrocytic ones in humans and chondrodystrophic dog breeds (Guehring et al. 2009).

Due to avascularity of the intervertebral disc, motion is essential for nutrient transport. The effect of mechanical loading on the disc has been excessively studied during the past decades, but little is known of the regulation of cellular responses (Chan et al. 2011, Wuertz et al. 2009, Korecki et al. 2008, Huang and Gu 2008, Wang et al. 2007). In a canine study, exercise for 30 minutes daily over three months increased the aerobic metabolism of the disc. The type of the exercise did not have a significant impact (Holm and Nachemson 1983, Urban et al. 1977). Static compression had a catabolic effect on the disc, whereas dynamic load might benefit the synthetic activity and anabolic response of the disc (Wuertz et al. 2009, Korecki et al. 2008, Huang and Gu 2008, Wang et al. 2007). When dynamic compression was applied for excessive durations in a rat tail model, a slow accumulation of changes similar to human disc degeneration occurred (Wuertz et al. 2009). The effect of exercise was studied in a group of 48 Dachshunds, where moderate stair climbing and duration of exercise were correlated with a smaller number of calcified discs. Running next to a bicycle had the opposite effect, being correlated with a greater number of calcified intervertebral discs (Jensen and Ersbøll 2000).

The disc of a chondrodystrophic dog differs from the disc of a non-chondrodystrophic one already at birth. The transitional zone of the disc is markedly thicker and the amount of collagen in the nucleus is clearly higher in the latter (Ghosh et al. 1977, Braund et al. 1975). Degeneration begins early. Hansen (1952) refers to this as “chondroid metamorphosis”, which starts at the transitional (perinuclear) zone already at the age of two months, continuing towards the nucleus pulposus. The nucleus pulposus becomes more chondroid, but remains vital during the early stage. The transitional zone continues to degenerate more or less extensively, sometimes with secondary necrotic calcification. As the degeneration continues, often already under the age of nine months, central and more often peripheral nuclear calcification can be seen macroscopically (Hansen 1952).

Intervertebral disc calcification is regarded as part of the disc degeneration process in both man and dog (Hristova et al. 2011, Karamouzian et al. 2010, Rutges et al. 2010, Benneker et al. 2005, Hansen 1952). In children, it is a rare condition of unknown origin, occurring most often in the cervical spine (Kim et al. 2011a, Spapens et al. 2010, Dai et al. 2004, Dhammi et al. 2002). The calcifications usually disappear (Dai et al. 2004), but they can remain for several years at least (Dhammi et al. 2002). In Dachshunds, disc calcification can disappear after herniation, but resorption of the most degenerated discs is also possible. This has been postulated to be caused by an inflammatory response and phagocytic resorption of the calcified material in the nucleus after tearing of the degenerated annulus fibrosus (Jensen 2001).

2.2.4 Heredity of intervertebral disc disease and intervertebral calcifications

In recent years, growing evidence about the genetic background of intervertebral disc degeneration in men has emerged, and it seems probable that it is a polygenic trait with multifactorial background (Kalb et al. 2012, Weiler et al. 2012, Zhang et al. 2008). There is no reason to anticipate that this would not be true in dogs as well. Several studies have demonstrated familial background for intervertebral disc disease (IDD) and disc calcification in Dachshunds (Jensen and Christensen 2000, Stigen and Christensen 1993, Ball et al. 1982, Havranek-Balzaretti 1980, Funkquist and Henricson 1969). The first indication in the literature that intervertebral disc protrusion of the Dachshund is hereditary was made by Joest, who stated in his book (referred by Hansen 1952) in 1921 that the disease affects only brown Dachshunds (Hansen 1952).

Suggestions to reduce the prevalence of IDD in Dachshunds have been made in the past decades, including breeding dogs with longer legs (Hansen 1964) and excluding high-prevalence lineages from breeding (Ball et al. 1982). Radiographic screening of young Dachshunds for intervertebral disc calcifications was proposed already in the late 1960s (Funkquist and Henricson 1969). A questionnaire study of the offspring of ten Dachshund sires (five short-haired and five wire-haired varieties) revealed that a difference existed between the breed varieties in the occurrence of disc prolapse symptoms. The frequencies were 33.6% for the short-haired and 15.6% for the wire-haired variety, respectively. The authors concluded that the disease was hereditary and suggested either breeding dogs with straighter legs, as suggested earlier by Hansen (1964), or radiographic screening for calcified discs (Funkquist and Henricson 1969).

Havranek-Balzaretti showed in her dissertation that a connection existed between disc calcification and disc prolapse. In that study, 79% of the dogs with, but none of the dogs without, calcified discs had a disc prolapse. The tendency for disc calcification appeared to be hereditary: if both parents were free of calcified discs, 30% of offspring were affected; if one of the parents had calcified discs, 56% of offspring had them; and if both parents had calcified discs, 83% of offspring had them (Havranek-Balzaretti 1980).

In a pedigree study of 536 Dachshunds, IDD showed patterns of a polygenic heritance. In two families, the prevalence of IDD was 62% (52 diseased dogs among 84 dogs from 15 litters), whilst the overall prevalence was 19% (Ball et al. 1982).

In a study based on radiographs of 274 clinically normal 12- to 18-month-old Dachshunds, representing offspring of 75 sires, the conclusion was that heritability estimations for disc calcification were 0.22 (continuous variable) and 0.15 (either/or). A genetic factor was essential for the occurrence of calcified discs in an individual dog, while a common environmental factor was significant in determining the number of calcified discs in affected individuals (Stigen and Christensen 1993).

In a radiographic study of 69 offspring from eight Dachshund sires and 16 dams, a strong correlation was found in the occurrence of intervertebral disc calcification between offspring and parents. The offspring were radiographed at 24-35 months of age, and the occurrence of disc calcification was rated according to four different scales. A strong correlation was found in the occurrence of disc calcification between offspring and mean parent and between offspring and dams on an either/or scale. Significant estimates of heritability of 0.60 and 0.87 were found based on the offspring-sire relationship using the

total score and three-class scale, respectively. Higher correlation estimates were found based on the dam-offspring relationship than based on the sire-offspring relationship, suggesting an effect of maternal environmental factors. The heritability estimates were clearly higher than in the previous study, and it was postulated that this might be due to the more reliable age at which the dogs were radiographed (Jensen and Christensen 2000).

The hereditary basis of disc calcification was shown in a recent genetic study in which a major locus on chromosome 12 was found to harbour genetic variations that affected the development of intervertebral disc calcification in Dachshunds (Mogensen et al. 2011).

2.2.5 Clinical relevance of intervertebral disc disease and intervertebral calcifications

The clinical signs of IDD are wide-ranging, varying from mild temporary to consistent debilitating spinal pain and from slight neurological deficits to para- or tetraplegia. Temporary back or neck pain and ambulatory paraparesis can be treated with cage rest and non-steroidal anti-inflammatory drugs (conservative treatment), but consistent or recurrent pain, non-ambulatory paresis and paralysis require surgical treatment. The prognosis for the disease is generally good, even with conservative treatment. Only dogs with loss of deep pain sensation have a poor prognosis. Recurrence is, however, common (Brisson 2010).

Studies of the occurrence of IDD in the Dachshund are scarce. The occurrence has been estimated to vary between 19% and 36% (Bergknut et al. 2012, Jensen et al. 2008, Ball et al. 1982). IDD is the disease with the highest mortality in Dachshunds in Sweden (Bonnett et al. 2005), and, of all breeds, its occurrence is highest in Dachshunds (Brown et al. 1977, Priester 1976). In a study based on Swedish insurance data, the incidence rate of IDD differed greatly between breeds. Dachshunds had the highest incidence rate, and miniature Dachshunds the highest mortality rate of all breeds. Other breeds at high risk for thoracolumbar IDD were the American and English cocker spaniel, Beagle, Papillon and Miniature Schnauzer (Bergknut et al. 2012).

In a longitudinal study of 61 Dachshunds, the relationship between intervertebral disc calcification and IDD was investigated. The dogs were radiographed at the age of two years, and the number of calcified discs was compared with the clinical status of the dog at the age of eight years. The number of calcified discs at the age of two years was shown to be a good predictor of clinical disease later in life. There was a clear association between number of calcified discs and IDD; dogs with several calcified discs had a greater risk of dying from the disease. By contrast, in dogs with less than three calcifications IDD was rare and the symptoms were less severe (Jensen et al. 2008). Dachshunds with surgically treated IDD were demonstrated to have more calcified discs than Dachshunds of the general population (Rohdin et al. 2010). Multiple calcified discs at the time of first surgery were a radiological finding associated with a higher risk of disease recurrence in all breeds. In Dachshunds, the risk increases in an almost linear manner, as each calcified disc increased the risk of IDD by 1.4 times (Mayhew et al. 2004).

2.2.6 Radiographic screening protocol for disc calcifications in Dachshunds

It was shown on 40 Dachshunds of different varieties that at the age of 24 months all radiographically evident disc calcifications were present, and this lower age limit was established in screening protocols. Since some disc calcifications disappeared, an upper age limit of 30 months was suggested (Jensen and Arnbjerg 2001). A compulsory radiographic screening programme has been adopted in Denmark in 2009 (Dansk Gravhundeklub 2012), and a voluntary programme is available in Finland and Norway (Suomen Mäyräkoiraliitto 2012, Norske Dachshundklubbers forbund 2012). In Finland, over one thousand dogs have been screened for intervertebral calcifications during the past decade (Suomen Mäyräkoiraliitto 2012).

In Denmark, a breeding value estimate (BVE) is being calculated for wire-haired, smooth-haired and long-haired standard Dachshund varieties (Dansk Gravhundeklub 2012). Improvement of the phenotype can already be seen in the wire-haired and long-haired variants, as the mean BVE of the dogs has increased several units in both breeds (Indeks ryg gravhund... 2012). On 1 January 2013, the Danish Dachshund Club introduced a new breeding protocol based on BVE, where the combined index of the sire and dam of the planned mating has to be ≥100 (the average dog has an index of 100; the better the dog, the higher the index) (Dansk Gravhundeklub 2012).

In Denmark, Finland and Norway, a shared screening protocol is in use. The age range of 24-30 months originally proposed (Jensen and Arnbjerg 2001) was considered too narrow for screening protocols, and therefore, the upper age limit has been set higher (36 months in Finland and Norway, 48 months in Denmark). The dog must be sedated and at least four radiographs in laterolateral (LL) recumbence (Figure 2A-D) taken in a way that all intervertebral disc spaces can be seen. The scoring of the calcified discs is as follows: 0 calcifications (free), 1-2 calcifications (mild), 3-4 calcifications (moderate) and ≥5 calcifications (severe). Dogs with ≥5 calcified discs are not recommended for breeding in Finland. These recommendations receive support from a recent study where a clear association between the number of calcified intervertebral discs and clinical disease was observed (Jensen et al. 2008).

Radiography is moderately insensitive in detecting minor calcifications. In a study comparing radiological and histopathologic findings, sensitivity of 60% and specificity of 100% were found for radiography when histopathology was used as the gold standard. Altogether 28.5% calcified discs were identified at the radiographic and 45.7% at the histopathologic examinationof 20 Dachshunds. Small calcifications were seen only in the latter (Stigen and Kolbjørnsen 2007). Computed tomography (CT) has been suggested as a screening tool since it is more sensitive in detecting small calcifications (Rohdin et al. 2010). The most sensitive method for detecting intervertebral disc degeneration is magnetic resonance imaging (MRI), which also allows degeneration of the disc without mineralization to be seen (Amort et al. 2012, Bergknut et al. 2011, Kärkkäinen et al. 1993).

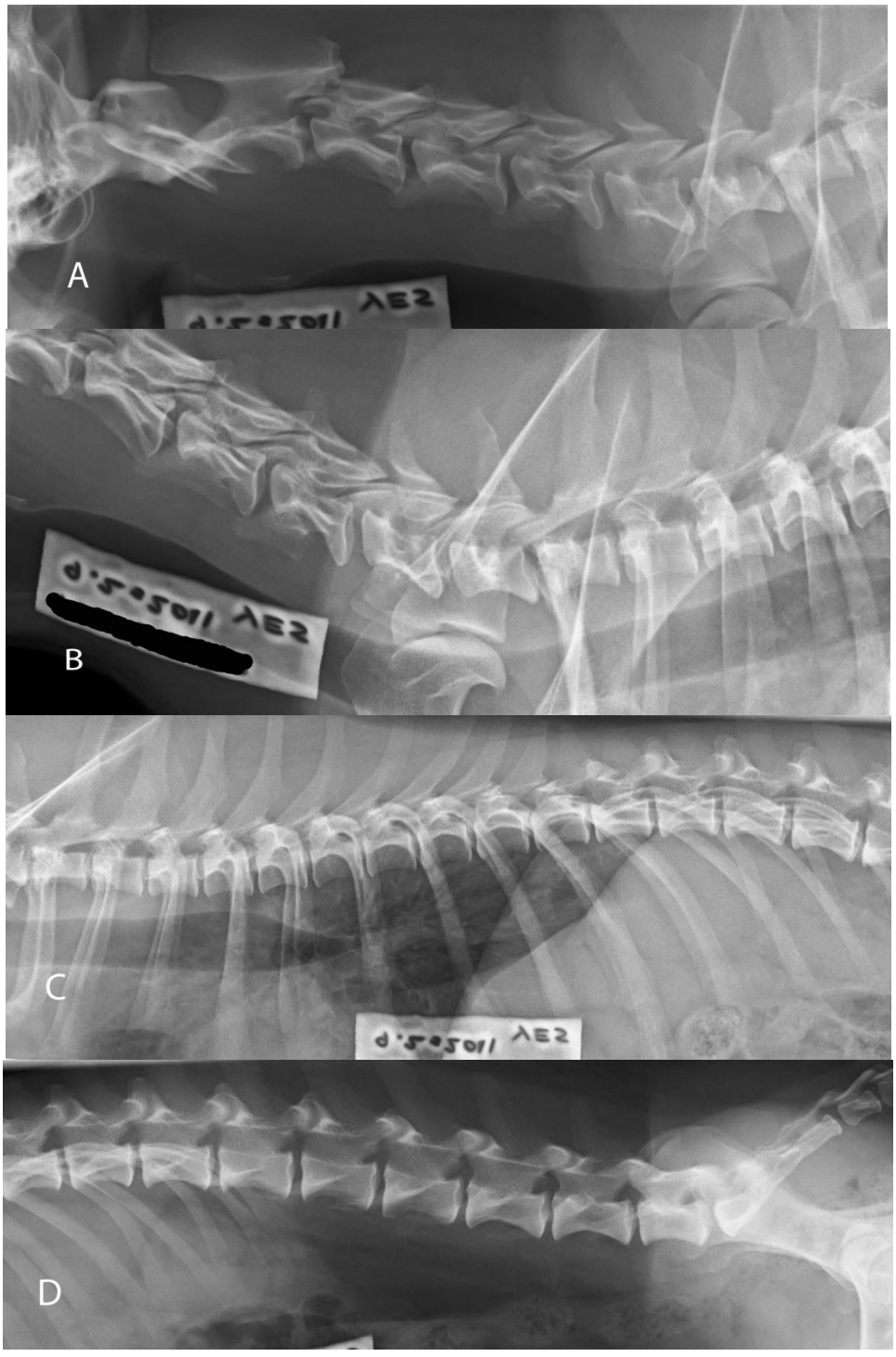

Figure 2 *Laterolateral spinal screening radiographs of a Dachshund. (A) Cervical spine. (B) Cervical-thoracic junction. (C) Thoracic spine. (D) Lumbar spine.*

2.3 Elbow dysplasia

2.3.1 Anatomy of the elbow joint

The elbow joint (articulatio cubiti) of a dog is a composite joint formed by three joints communicating freely with each other. The small lateral humeral condyle (capitulum humeri) (Figure 3) and the head of the radius (caput radii) form the humeroradial joint (articulatio humeroradialis). The humeroulnar joint (articulatio humeroulnaris) is composed of a large pulley-shaped medial part of the humeral condyle (trochlea humeri) and the trochlear notch (incisura trochlearis) of the ulna, also known as the semilunar notch (Figure 3). The third joint is the radioulnar joint (articulatio radioulnaris) located between the proximal radius and ulna.

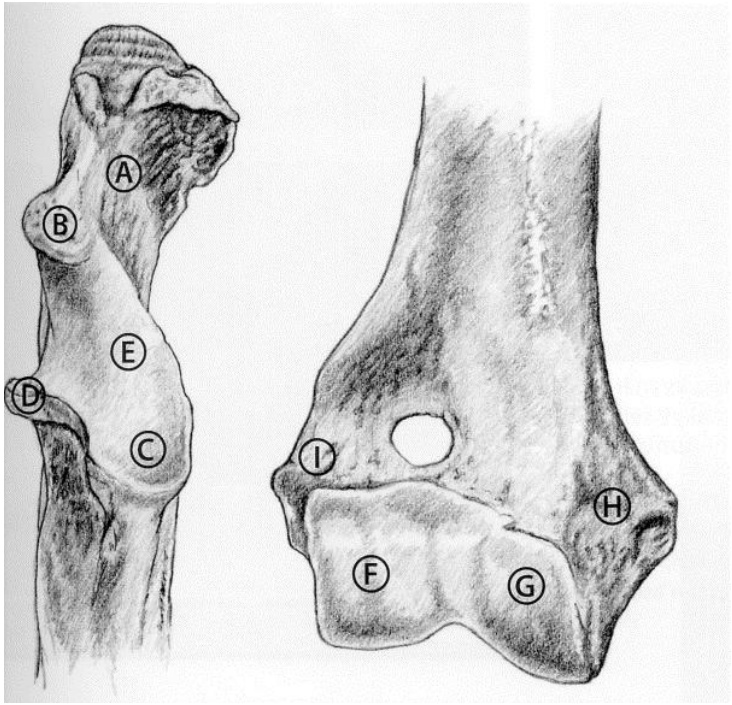

Figure 3 *Cranial view of the right ulna (A=olecranon, B=anconeal process, C=medial coronoid process, D= lateral coronoid process, E=trochlear notch) and humerus (F=capitulum [lateral part of the humeral condyle], G=trochlea [medial part of the humeral condyle], H=medial epicondyle, I=lateral epicondyle) (picture courtesy of Piia Marttinen).*

The coronoid process forms the distal part of the trochlear notch (Figure 3). It is divided into the prominent medial part (medial coronoid process, MCP) and the smaller lateral part (lateral coronoid process). The processes are situated cranioproximally, increasing the surface area of the elbow joint, but they do not take part in the weight-bearing of the limb (Evans 1993). The surface geometry of the MCP differs between breeds (Breit et al. 2010, Breit et al. 2006).

The anconeal process (*processus anconeus*) (Figure 3) is the proximal part of the trochlear notch of the ulna. It is a part of the proximal extremity of the ulna called the olecranon. The anconeal process fits in the olecranon fossa (*fossa olecrani*) of the humerus when the elbow is extended.

The ligaments of the elbow joint include the stronger lateral (ulnar) collateral ligament (*ligamentum collaterale laterale*) and the weaker medial (radial) collateral ligament (*ligamentum collaterale mediale*). The thin annular ligament of the radius (*ligamentum annulare radii*) runs transversely around the radius and attaches to the ulna medially and laterally (Evans 1993). The olecranon ligament (*ligamentum olecrani*) (Figure 4) runs on the caudomedial side of the elbow, starting from the humerus at the border between the medial epicondyle and the olecranon fossa. It is tightly bound to the joint capsule during its course and inserts into the anconeal process of the ulna. The olecranon ligament limits the maximal flexion of the elbow joint (Engelke et al. 2005).

The lateral humeroradial part of the joint participates mostly in the weight-bearing function, while the medial humeroulnar part is the stabilizer, restricting movement to the sagittal plane. The radioulnar joint allows some rotation of the antebrachium. The strong collateral ligaments and the anconeal process restrict the lateral movements of the elbow (Evans 1993).

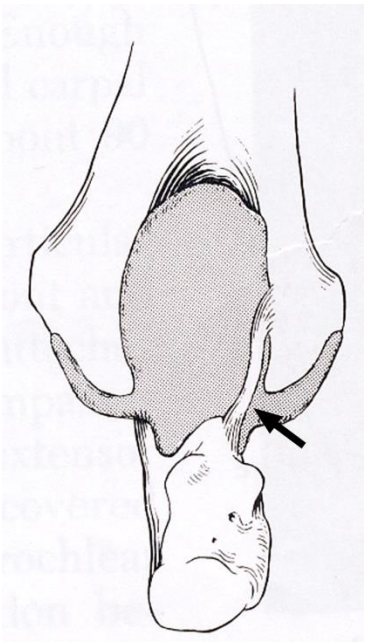

Figure 4 *Proximal view of the flexed left elbow joint to visualize the course of the olecranon ligament (black arrow). The joint capsule is indicated in grey (Evans 1993).*

2.3.2 Four types of elbow dysplasia

2.3.2.1 Terminology

The first congenital elbow disorder described was "patella cubiti" (Stiern 1956). The term elbow dysplasia (ED), introduced in 1961, was defined as a congenital anomaly with definite hereditary transmission. The condition included ununited medial epicondyle (UAP) and osteoarthritis (OA) from no other cause, and it was seen most often in German shepherd dogs (Carlson 1961). In the late 1960s, ED was described to include three congenital fusion defects: UAP, patella cubiti and ununited medial epicondyle (UME) (Ljunggren et al. 1966). Thereafter, osteochondrosis (OC) was suggested as a common aetiology for fragmented medial coronoid process (FMCP), OC and UAP. The sesamoid bone in the tendon of origin of the supinator muscle was in the first reports referred to as an ectopic sesamoid (Wood et al. 1985, Väänänen and Skutnabb 1978).

Today, ED refers to four hereditary developmental disorders of the elbow joint; these are the medial coronoid process disease (MCPD), formerly known as FMCP (or FCP), OC of the medial part of the humeral condyle, UAP, and incongruity of the elbow joint (INC) (Fitzpatrick et al. 2009a, Wisner and Pollard 2007, Wagner et al. 2007, Hazewinkel 2007). Incongruity is currently proposed to be a common aetiology for the other three forms of ED (Morgan et al. 2000a, Wind and Packard 1986, Wind 1986). Each type can present alone or in any combination (Meyer-Lindenberg et al. 2006, Van Ryssen and van Bree 1997, Grøndalen and Grøndalen 1981). Medial compartment disease (MCD) refers to all pathologies (MCPD, OC and the contact or "kissing" lesion caused by friction of the diseased MCP) of the medial side of the elbow joint (Fitzpatrick et al. 2009a).

The terms MCPD and MCD are used throughout this thesis for the sake of clarity. FMCP was a term used in the second article (Study II), and MCPD and MCD in the third (Study III).

2.3.2.2 Medial coronoid process disease (MCPD)

MCPD (Figures 5 and 6), the most common type of ED (Lavrijsen et al. 2012, de Bakker et al. 2012a, Remy et al. 2004), is common in many large dog breeds such as the German shepherd, Golden retriever, Labrador retriever, Rottweiler, Bernese mountain dog, Bullmastiff, Chow Chow and St. Bernard, among others (Fitzpatrick et al. 2009a, Groth et al. 2009, Coopman et al. 2008, Moores et al. 2008, LaFond et al. 2002, Guthrie 1989, Olsson 1983, Grøndalen 1982a). MCPD covers a wide range of medial coronoid pathologies, including superficial fibrillation and fissuring of the cartilage, chondromalacia and single or multiple fragments (FCP) (Fitzpatrick et al. 2009a, Moores et al. 2008, Van Ryssen and van Bree 1997). Deficiency of the growth of the MCP, resulting in smaller humeral contact area and decreased weight-bearing capacity of the MCP, has been proposed to increase risk of MCPD in large breed dogs (Breit et al. 2006).

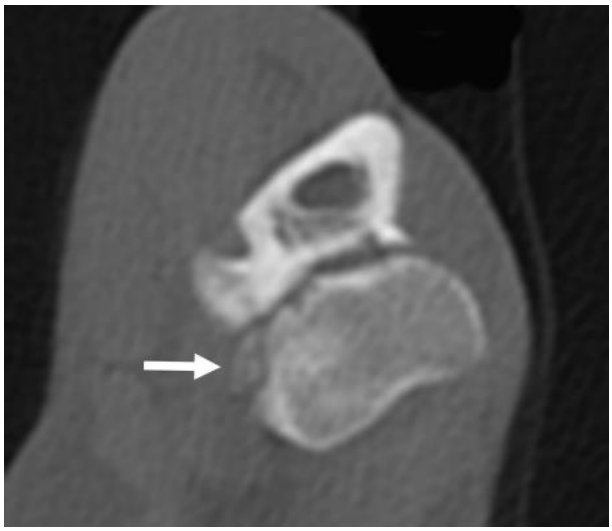

Figure 5 *Transverse computed tomography image of an elbow joint of a Belgian shepherd dog with medial coronoid process disease. A large fragment is evident (arrow).*

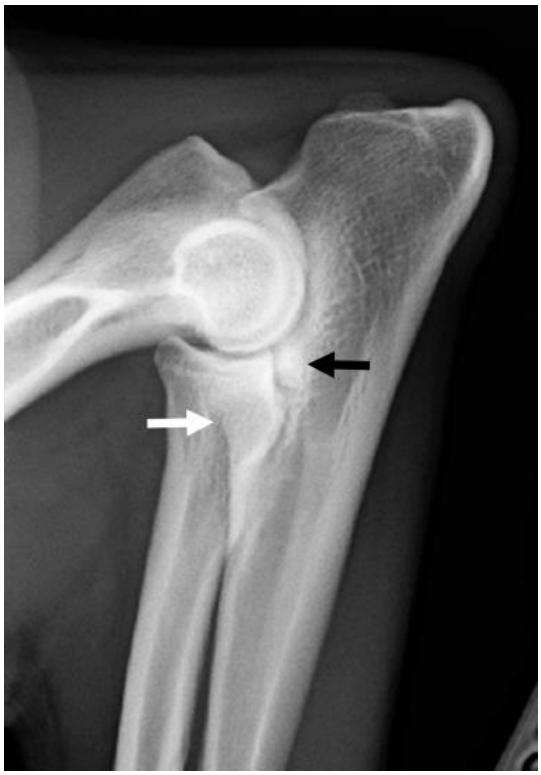

Figure 6 *Mediolateral flexed projection of an elbow joint of a Belgian shepherd dog with medial coronoid process disease. Radiopacity of the medial coronoid process is reduced and the cranial border is blurred (white arrow). Subtrochlear sclerosis is visible distal to the trochlear notch (black arrow).*

2.3.2.3 Osteochondrosis (OC)

OC of the medial humeral condyle (Figure 7) is most common in Labrador and Golden retrievers (Lavrijsen et al. 2012, LaFond et al. 2002, Van Ryssen and van Bree 1997, Bennett et al. 1981). It is defined as an abnormality of enchondral ossification. When an epiphyseal growth plate is affected, the deeper layers of cartilage fail to ossify, resulting in focal abnormal thickening of the articular cartilage. The disease is referred to as osteochondrosis dissecans when separation of the abnormal cartilage and the subchondral bone occurs (Morgan et al. 2000a).

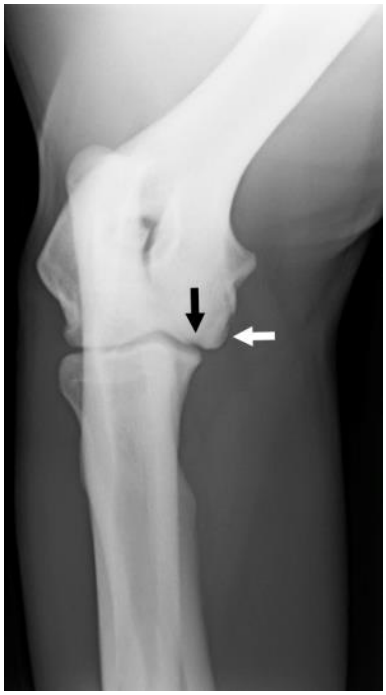

Figure 7 *In the craniocaudal oblique radiograph of a Labrador retriever, a subchondral bone defect on the medial humeral condyle (black arrow) and osteophytes on the medial humeral epicondyle (white arrow) are observed.*

2.3.2.4 Ununited anconeal process (UAP)

UAP (Figure 8) is a condition with a failure of union between the secondary centre of ossification of the anconeal process and the rest of the olecranon. This union should happen before 20 weeks of age (Morgan et al. 2000), although it has postulated that the diagnosis could be made even earlier since the radiographic appearance of UAP and the secondary centre of ossification are distinct from each other (Frazho et al. 2010). The reason for the UAP is suggested to be micro-movement of the cartilage bridge between the separate centre of ossification and the olecranon caused by insufficient curvature of the trochlear notch (Morgan et al. 2000a). The disease has been diagnosed in several large but no small breeds (Frazho et al. 2010); it is most common in Bernese mountain dogs and German shepherd dogs (LaFond et al. 2002).

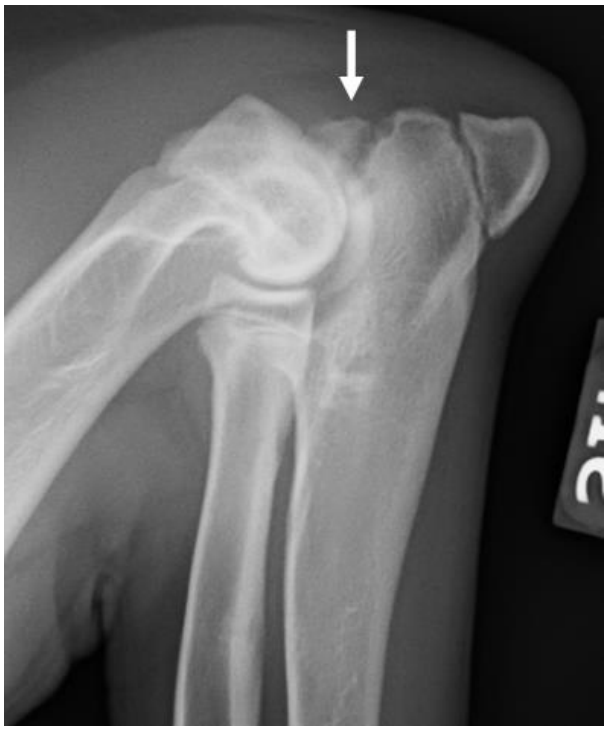

Figure 8 *Mediolateral flexed radiograph of a young American Staffordshire terrier with an ununited anconeal process (arrow).*

2.3.2.5 Incongruity (INC)

INC has been described as a malalignment of the joint surfaces of the elbow (Samoy et al. 2006). Some degree of incongruity (synonym incongruence) is considered normal (Preston et al. 2000, Wind 1986), but a more severe form has been proposed as a cause of ED and OA (Wind 1986). The degree of incongruity and the breed involved determine whether the result is mild OA without clinical importance, MCD or UAP (Proks et al. 2011, Gemmill et al. 2005, Morgan et al. 2000a). New bone formation on the anconeal process is often the first radiographic sign of OA (Grøndalen 1982a) and has been shown to be caused by INC (Seelig 2010). INC has been diagnosed in several dog breeds, but it appears to be most common in Bernese mountain dogs (Lavrijsen et al. 2012). Two different types of INC have been postulated: asynchronous growth of the radius and ulna, leading to a step between the proximal radial articular surface and the medial coronoid process of ulna (Figure 9), and underdevelopment of the ulnar trochlear notch, resulting in a notch with an inadequate curvature to encompass the humeral trochlea. The latter can be a consequence of an overly rapid growth rate of the humeral head relative to the growth rate of the trochlear notch (Wind and Packard 1986). Variation in the shape of the trochlear notch between breeds exists, but an association between the shape and MCPD is not established (Janach et al. 2006, Collins et al. 2001).

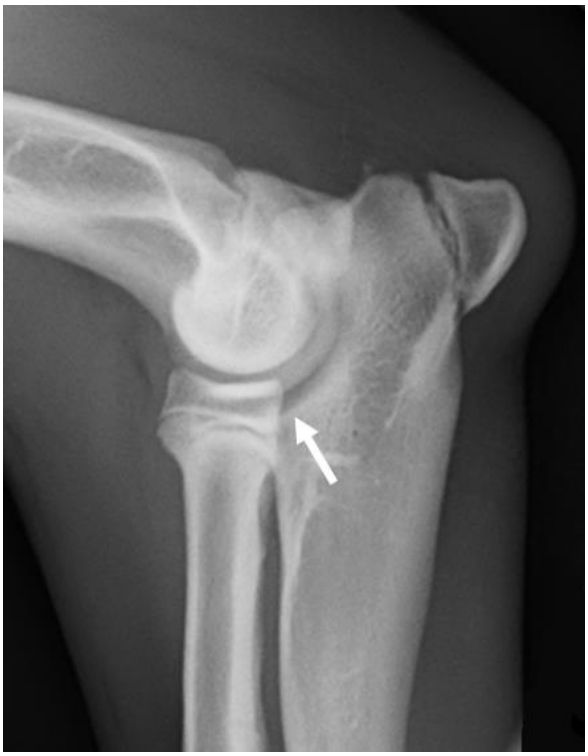

Figure 9 *Severe radioulnar incongruity in a young American Staffordshire terrier. A step between the radial head and the medial coronoid process is evident (arrow) in the mediolateral radiograph.*

2.3.2.6 Other developmental elbow diseases

Some elbow conditions are not considered to be included in ED (Hazewinkel 2007), e.g. calcified bodies seen near or at the medial epicondyle of the humerus (Figure 10). Calcified bodies have been referred to as ununited medial epicondyle (UME) (Paster 2009, Piermattei et al. 2006, Zontine et al. 1989), medial epicondylar spur (Kirberger 2006), ossified disc of the joint capsule (Price and King 1977) or calcified body in the joint capsule (Gøndalen and Braut 1976). In recent literature, these conditions are grouped together, as they are all new bone formation of tendons, either at the insertion or further away of the joint (Van Ryssen et al. 2012, de Bakker et al. 2012a, de Bakker et al. 2012b, de Bakker et al. 2011). The term flexor enthesopathy, used in human medicine, was suggested, and the condition was divided into two entities: secondary when it is part of the degenerative process seen together with another elbow disease, and primary when it is the only abnormality of the elbow joint (Van Ryssen et al. 2012, de Bakker et al. 2012a, de Bakker et al. 2011). Primary flexor tendinopathy can be a cause of lameness (Van Ryssen et al. 2012, de Bakker et al. 2012a, Piermattei et al. 2006, Meyer-Lindenberg et al. 2004), and it has been seen in several dog breeds (Van Ryssen et al. 2012). In Labrador retrievers, a hereditary background has been suggested (Paster et al. 2009).

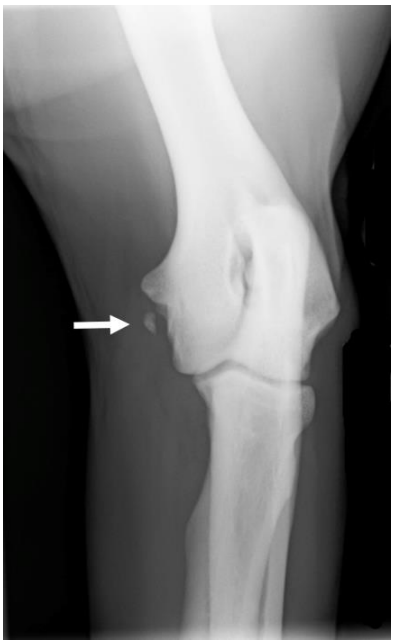

Figure 10 *Craniocaudal oblique radiograph of an adult Labrador retriever with a calcified body adjacent to the medial humeral epicondyle (arrow) consistent with flexor enthesopathy.*

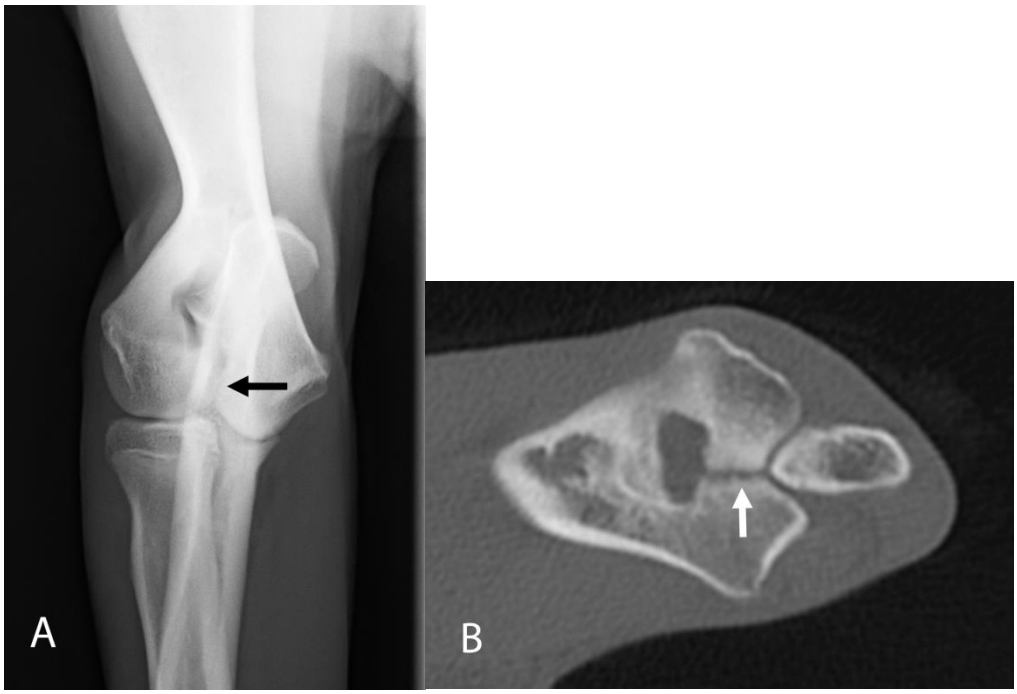

Figure 11 *Incomplete ossification of the humeral condyle in a Wachtelhund. (A) A craniocaudal oblique radiograph where an abnormal radiolucent line (arrow) is hazily seen between medial and lateral part of the humeral condyle. (B) A dorsal computed tomography image of the same elbow joint. Incomplete ossification is clearly visible (arrow).*

Incomplete ossification of the humeral condyle (IOHC) (Figure 11A,B) is most frequently seen in spaniel breeds (Piola et al. 2012, Martin et al. 2010, Langley-Hobbs et al. 2008, Miller 1995), although other breeds can also be affected (Martin et al. 2010). It can cause lameness as such (Fitzpatrick et al. 2009b) or progress to condylar fractures (Martin et al. 2010, Witte et al. 2010).

2.3.3 Heredity

ED is regarded as a quantitative genetic trait with an environmental influence (Mäki et al. 2004, Mäki et al. 2002, Mäki et al. 2000, Beuing et al. 2000). Moderate to high heritability has been found in several breeds (Lavrijsen et al. 2012, Stock et al. 2011, Hartmann et al. 2010, Janutta et al. 2006, Beuing et al. 2005, Beuing et al. 2000, Mäki et al. 2000, Swenson et al. 1997a, Studdert et al. 1991). On the other hand, in the Finnish Belgian shepherd population, the heritability estimate was only 0.11, which can be regarded as low (Mäki 2012). A major gene has been suggested to affect ED in the Rottweiler breed (Mäki et al. 2004), and different genes have been speculated to be responsible for different types of ED (Stock et al. 2011, Ubbink et al. 2000, Ubbink et al. 1999, Padgett et al. 1995, Grøndalen 1982b).

2.3.4 Clinical relevance

ED is a common orthopaedic disease of mainly large breed dogs, the prevalence being 20-60% in affected breeds (Coopman et al. 2008, Remy et al. 2004, Kirberger and Stander 2007, Mäki et al. 2000, Audell 2000, Morgan et al. 1999). ED is more common in males than females (Kirberger and Stander 2007, Janutta et al. 2006, Beuing et al. 2000, Morgan et al. 1999, Grøndalen 1982a). The first signs of all types of ED usually present when the dog is 4-6 months old (Schulz 2007), but onset of MCPD can be much later (Vermote et al. 2010, Fitzpatrick et al. 2009a, Meyer-Lindenberg et al. 2002). ED can be unilateral or bilateral, and lameness and pain elicited by palpation and flexion/extension of the elbow joint are hallmarks of the disease. Lameness can be intermittent, exacerbated by exercise or most obvious after rest (Schulz 2007).

OA is secondary to all types of ED. Age at onset and severity of OA vary (Meyer-Lindenberg et al. 2002, Lang et al. 1998, Grøndalen 1982b, Grøndalen 1979) and are affected by breed (Smith et al. 2001), gender (Lang et al. 1998), activity (Sallander et al. 2006) and body condition (Huck et al. 2009, Comhaire and Snaps 2008, Sallander et al. 2006). Clinical findings include muscle atrophy, elbow joint swelling and decreased range of motion, pain and crepitus of the elbow joint (Schulz 2007). UAP can manifest with no or mild clinical signs and is often an incidental finding on radiographs (Morgan et al. 2000a).

2.3.5 Radiography and computed tomography as diagnostic tools

2.3.5.1 Radiography

Radiography is the most common and widely available modality for elbow joint imaging (Cook and Cook 2009, Cogar et al. 2008). The projections usually used are ML 45° flexed (ML flexed) (Figure 12A) and cranio15°lateral-caudomedial oblique (CrCd oblique) (Figure 12B) (Robins 1980). Osteophytes on the anconeal process are easy to see from the ML flexed view (Figure 13), which makes it suitable for screening schemes based on OA (Keller et al. 1997, Olsson 1983, Grøndalen 1979).

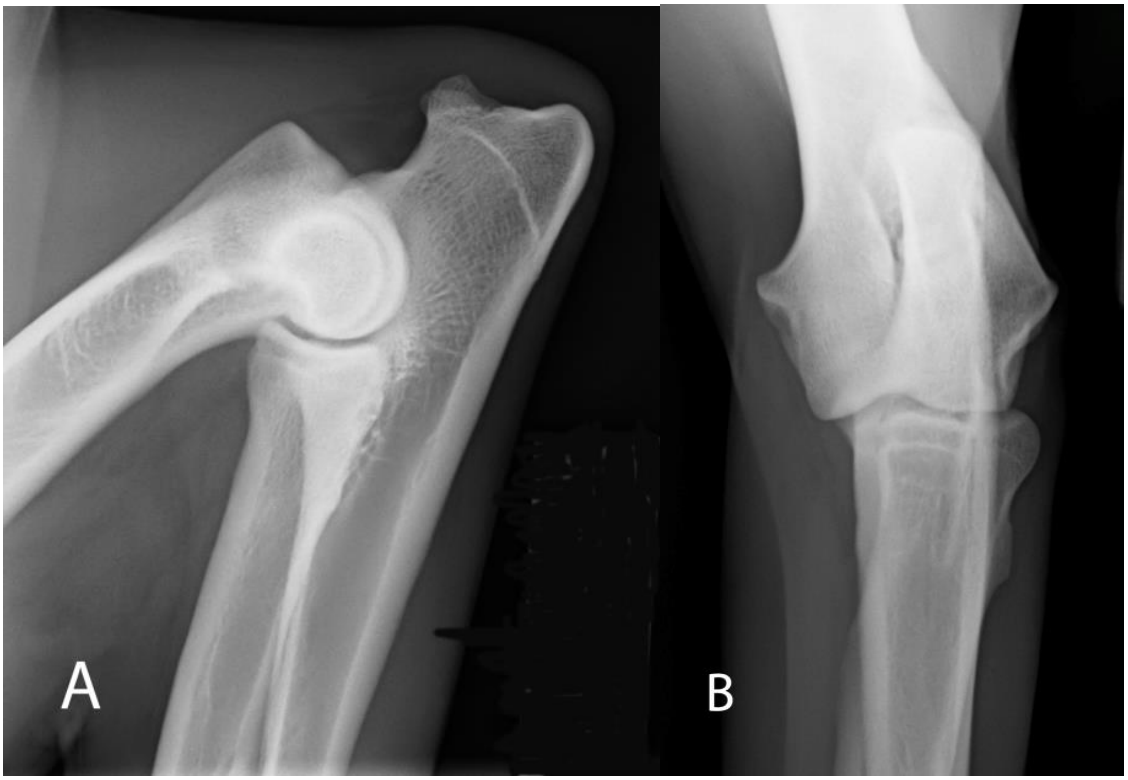

Figure 12 *Radiographs of a canine elbow joint. (A) A mediolateral flexed projection. (B) A craniocaudal oblique projection.*

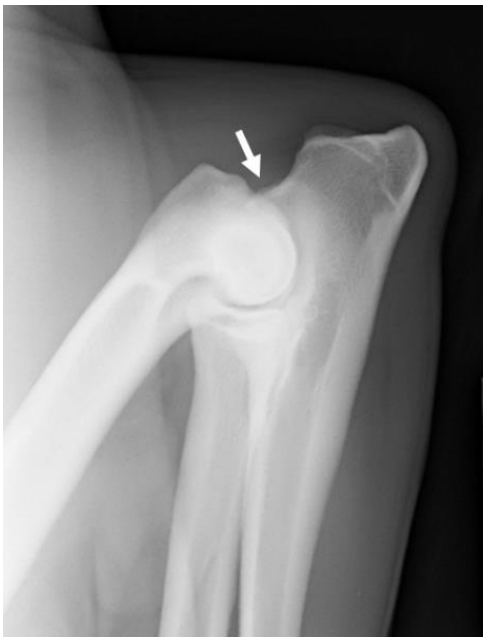

Figure 13 *Mediolateral flexed projection of an elbow joint of a Labrador retriever with elbow dysplasia grade 1. Ostophytes are visible on the dorsal border of the anconeal process (arrow).*

MCPD can be a diagnostic challenge radiographically since the radiological findings are often sparse or non-existent (Goldhammer et al. 2010, Punke et al. 2009, Olsson 1983). Therefore, an approach using secondary osteophytes as an indicator of ED has been advocated in screening protocols (Keller et al. 1997, Grøndalen 1979). Abnormal contour and indistinctive cranial border of the MCP are radiological signs frequently seen in MCPD (Figure 6) (Fitzpatrick et al. 2009a, Hornof et al. 2000, Lang et al. 1998, Keller et al. 1997). Subtrochlear sclerosis, manifesting as increased radiopacity at the base of the coronoid process (Figure 6), has proved to be a reliable indicator of MCPD (Fitzpatrick et al. 2009a, Smith et al. 2009, Burton et al. 2008, Burton et al. 2007, Lang et al. 1998, Keller et al. 1997), and methods for its measurement from radiographs have been developed (Proks et al. 2010, Smith et al. 2009, Draffan et al. 2009, Burton et al. 2007).

The most sensitive projections for detection of the cranial border of MCP and MCP pathology are extended mediocaudal-laterocranial oblique (M15°Cd-LCrO) (Miyabayashi et al. 1995) and distomedial-proximolateral oblique (Di35°M-PrLO) (Haudiquet et al. 2002) projections.

OC is radiographically best diagnosed from CrCd oblique radiographs as a radiolucent defect at the articular surface of the medial humeral condyle (Figure 7) (Morgan et al. 2000a, Grøndalen 1982a). If the lesion is in a more caudal location, the conventionally angled CrCd view will not reveal it. A differential diagnosis for OC on radiographs is an abrasive contact ("kissing") lesion caused by MCPD (Kirberger 2006, Morgan et al. 2000a).

UAP is readily diagnosed from a ML flexed radiograph (Figure 8), which allows evaluation of the anconeal process without superimposition of other bony structures (Keller et al. 1997, Grøndalen 1982a, Grøndalen 1979).

INC can be difficult to diagnose when mild, but in severe cases the diagnosis is more straightforward (Figure 9) (Samoy et al. 2012, Samoy et al. 2011). In vitro methods evaluating accuracy of radiographs and CT in diagnosis of INC are based on shortening of the radius; they measure radioulnar incongruity, but do not take into account humeroradial incongruity (Samoy et al. 2011, Wagner et al. 2007, Blond et al. 2005, Mason et al. 2002). A radiographic index has been proposed to measure the humeroulnar incongruity (Proks et al. 2011). Controversial results have emerged regarding the association between INC and MCPD, as INC is not always present at the time of diagnosis (Kramer et al. 2006, Gemmill et al. 2005).

2.3.5.2 Computed tomography

Radiographs are two-dimensional images of an object. CT produces an image of a thin slice of the object, and thus, superimposition of other structures, a drawback of radiographs, is avoided. Another significant advantage of CT is superb contrast resolution, enabling subtle differences in contrast to be reliably discerned. Contrast resolution of screen-film radiography is approximately 5%, whereas in CT it is 0.5%. This means that with CT minimal differences in tissue density can be observed (Bushberg et al. 2002).

CT is considered an accurate method for imaging the canine elbow joint (de Rycke et al. 2002, Rovesti et al. 2002), although some lesions might not be visible (Groth et al. 2009, Moores et al. 2008). CT can in most cases clearly show MCPD (Figure 5), which may otherwise be difficult to diagnose (Samoy et al. 2012, Groth et al. 2009, Klumpp et al. 2010, Vermote et al. 2010, Moores et al. 2008, Gemmill et al. 2005, Rovesti et al. 2002, Reichle et al. 2000, Keller et al. 1997, Carpenter et al. 1993). CT has also been used in diagnosis of INC (Samoy et al. 2012, House et al. 2009, Wagner et al. 2007, Kramer et al. 2006, Holsworth et al. 2005, Gemmill et al. 2005), and three-dimensional image rendering can be a reliable tool in estimation of mild radioulnar incongruity (Böttcher et al. 2009).

2.3.6 Radiographic screening protocols

Several different screening schemes for ED exist. The three best-known and largest organizations are IEWG, British Veterinary Association/Kennel Club (BVA/KC) and Orthopedic Foundation for Animals (OFA).

2.3.6.1 International Elbow Working Group (IEWG)

The IEWG protocol (Fückiger 2011) suggests that at least one 45-60° flexed ML projection of each joint is required (Figure 12A). The medial coronoid process is best identified with the limb extended and 15° supinated, and an additional CrCd oblique view is strongly recommended to identify OC lesions (Figure 12B). Radiological evaluation is based on OA

and/or the presence of one or more primary lesions (MCPD, OC, UAP and INC) (Table 1). The radiographic screening evaluation should be done at a minimum age of 12 months (Flückiger 2011). Anatomic locations used for grading of elbow OA in the IEWG protocol are presented in Figure 14.

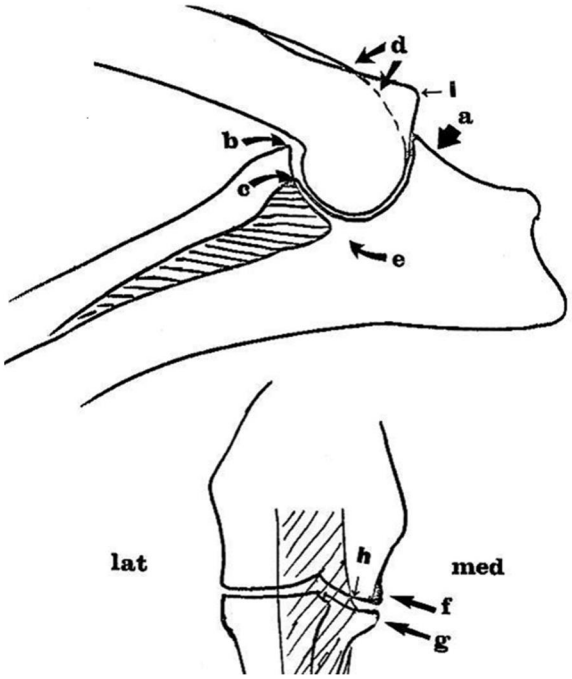

Figure 14 *Anatomical locations used for grading of elbow osteoparthritis in the International Elbow Working Group protocol. a=the proximal surface of the anconeal process, b= the cranial aspect of the radial head, c=the cranial border of the medial coronoid process, d=the caudal surface of the lateral condylar ridge, e=sclerosis of the trochlear notch at the base of the coronoid processes, f= the medial surface of the medial epicondyle, g=the medial border of the medial coronoid process, h=indentation of the subchondral bone (osteochondrosis-like lesion) (Hazewinkel 2007).*

The IEWG protocol is in use in most European countries, including the Nordic countries, but notable differences exist in the number of projections required and in the evaluation of findings. Common denominators of all schemes are the ML 45° flexed projection (however, in Switzerland, the opening angle is 90-110°) and grading of OA based on the height of osteophytes. Otherwise, the protocols differ. In Nordic countries, only one ML flexed projection is used, while in many countries at least two (Swiss Association for Small Animal Medicine 2012) and in some countries four (Lavrijsen et al. 2012) projections of each elbow are required. Evaluation of the ML radiographs also has some fundamental differences between countries. In Finland, OA is graded similarly to the protocol of the IEWG, but the findings indicative of primary lesion are less weighted (Table 2). Sclerosis as such is not scored as ED. A borderline (0b) grade is recorded in the database as grade 0 (Ohje kyynärnivelen kasvuhäiriöiden... 2011).

Table 1 *Elbow dysplasia scoring and radiographic findings used by the three biggest organizations (IEWG, BVA/KV and OFA).*

ED scoring	0	1	2	3
Radiographic findings of IEWG	Normal elbow joint No evidence of incongruency, sclerosis or OA	Presence of osteophyte < 2 mm high (mild OA) Minor sclerosis of the base of the coronoid processes	Presence of osteophytes of 2 - 5 mm high (moderate OA) Obvious sclerosis of the base of the coronoid processes Step of 3-5 mm between radius and ulna (suspect INC) Indirect signs for a primary lesion (UAP, FCP, OC)	Presence of osteophytes > 5 mm high (severe OA) Step > 5 mm between radius and ulna (obvious INC) Obvious presence of a primary lesion (UAP, FCP, OC)
Radiographic findings of BVA/KC	Normal	Osteophytes at any site Ò2mm	Osteophytes 2-5mm or a primary lesion (UAP, FCP, OC) with no osteophytes	Osteophytes >5mm or a primary lesion (UAP, FCP, OC) with osteophytes
Radiographic findings of OFA		Minimal bone change along anconeal process of ulna (< 3mm)	Additional bone proliferation along anconeal process (3-5 mm) and subchondral bone changes (trochlear notch sclerosis)	Well-developed degenerative joint disease with bone proliferation along anconeal process >5 mm

ED = elbow dysplasia, IEWG = International Elbow Working Group, BVA/KC = British Veterinary Association/Kennel Club, OFA = Orthopedic Foundation for Animals, OA = osteoarthritis, INC = incongruence, FCP = fragmented coronoid process, OC = osteochondrosis, UAP = ununited anconeal process

IEWG: In some countries a borderline score between ED 0 and ED 1 is given to dogs with minimal anconeal process modelling of undetermined aetiology.
BVA/KC: Joint incongruity and sclerosis are not graded as lesions and there is no borderline grade.

Table 2 *Elbow dysplasia grades and their definitions used in the Finnish screening protocol*

Grade 0 (free)	No signs of OA
Grade 1 (mild)	Mild OA with osteophyte formation of < 2 mm detected usually on the dorsal surface of the anconeal process
Grade 2 (moderate)	Osteophytes on the dorsal surface of the anconeal process 2-5 mm high, changes in the MCP or the joint is mildly deformed
Grade 3 (severe)	Marked degenerative changes visible, or osteophyte formation on the anconeal process is over 5 mm high, UAP

OA = osteoarthritis, MCP = medial coronoid process, UAP = ununited anconeal process

2.3.6.2 British Veterinary Association/Kennel Club (BVA/KC)

The ED scheme of the BVA/KC differs from the IEWG protocol since two projections (ML 45° flexed and ML 110° flexed) are required and grades 2 and 3 are differently evaluated (Table 1) (Dennis 2012)

2.3.6.3 Orthopedic Foundation for Animals (OFA)

The OFA screening protocol is based on maximally flexed ML radiographs, and the minimum age of the dog is two years (Elbow dysplasia grades... 2010). The grading of the lesions is presented in Table 1.

2.3.6.4 Other screening protocols

Other radiographic screening schemes have been proposed. Grading systems based on combined numerical values from seven different radiological findings, such as osteophytes and findings indicative of primary pathology, have a higher sensitivity for predicting ED than the grading based on OA alone (Lang et al. 1998). Measurements of the size, proportions and alignments of the elbow joint (elbow angles) as predictors of ED appeared to be unsuitable for screening in German shepherd dogs (Janutta et al. 2005). Computerized measurements of radiographic anatomical parameters of the elbow are proposed as a method for evaluation of ED in the Bernese mountain dog (Stein et al. 2012).

In a genetic analysis comparing the IEWG protocol, a protocol based on elbow angles and a protocol based on evaluating seven different radiographic criteria in German shepherd dog elbows, the heritability estimate was slightly higher for the IEWG protocol than for the others. The screening protocols were shown to cover two genetically different traits (MCPD and OC/UAP), and progress in genetic improvement could be faster if these diseases were treated as separate traits (Janutta et al. 2006).

2.4 Sacrum and lumbosacral transitional vertebra

2.4.1 Anatomy of the sacrum

The sacrum (*os sacrum*) (Figure 15) consists of three fused vertebrae (*vertebrae sacrales*). In the adult dog, it is wedge-shaped and four-sided. It lies between iliac bones and articulates with them via the auricular surface (*facies auricularis*) of the wing (*ala ossis sacri*), which represents the transverse process of the first sacral vertebra (S1) (Evans 1993).

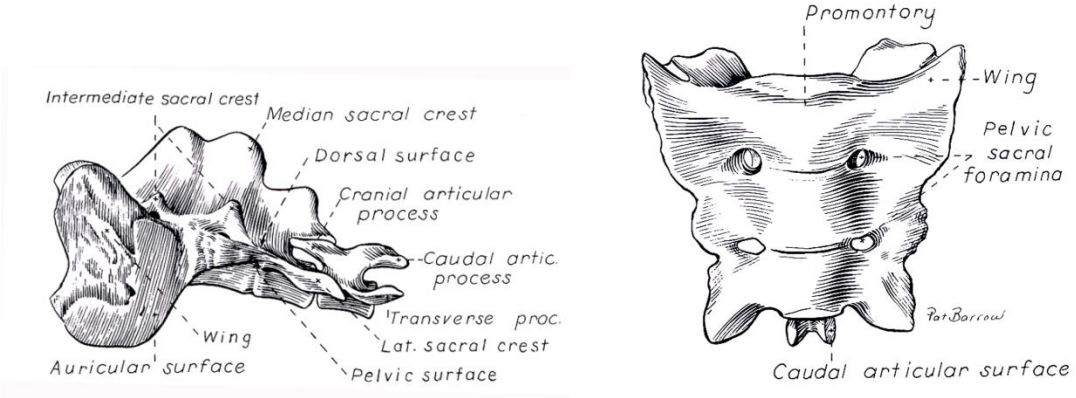

Figure 15 *Lateral (left) and ventral (right) views of the canine sacrum (Evans 1993).*

The ventral pelvic surface (*facies pelvina*) of the sacrum is concave and forms the bony dorsal border of the pelvic canal. There are two pairs of pelvic sacral foramina (*foramina sacralia pelvina*), just lateral to the fused sacral bodies, through which the blood vessels and the ventral branches of the first two sacral nerves run. Two transverse lines (*lineae transversae*) on the pelvic surface represent the fused intervertebral spaces. The transverse processes of the second and third vertebrae form the thin and narrow lateral sacral crest (*crista sacralis lateralis*). The caudal angle of the lateral sacral crest frequently articulates with the adjacent transverse process of the first caudal vertebra (Evans 1993).

The median sacral crest (*crista sacralis medialis*) is situated on the dorsal surface (*facies dorsales*) of the sacrum, and it consists of the three fused spinous processes. Two indentations of the crest are at the site of the fusions. There are two pairs of dorsal sacral foramina (*foramina sacralia dorsalia*). The intermediate sacral crest (*crista sacralia intermedia*) is formed from three low processes representing the mamilloarticular processes of adjacent segments and their connecting ridges (Evans 1993).

The base of the sacrum (*basis ossis sacri*) points cranially. The cranioventral ridge-like part of the base is called the promontory (*promontorium*). It forms the dorsal boundary of the pelvic inlet. Dorsal to the base is the opening for the sacral canal (*canalis sacralis*). At this level, there is a concave caudal recession in the medial plane of the dorsal wall of the sacrum. The sacral canal passes through the bone and is formed by the coalescence of the three vertebral foramina. The base articulates with the last lumbar vertebra via the cranial articular process (*processus articularis cranialis*). The caudal wide apex (*apex ossis sacri*)

articulates with the first caudal vertebra via the caudal articular process (*processus articularis caudalis*) (Evans 1993).

2.4.2 Embryogenesis of the sacrum

The sacrum develops, as do the other vertebrae, from three primary ossification centres. In the dog, the centrum of the first segment appears at day 40 of gestation, and all three segments are present at day 43. First and second segments have additional ossification centres laterally, which represent ancestral forms of "ribs" and develop to the ventral parts of the sacral wings. The fusion of sacral vertebral bodies is complete at the age of 6 months. Before this, intervertebral fibrocartilages mark the separation (Evans 1993).

In the early embryo, the notochord, the first manifestation of the spinal column, is present as a rod of cells surrounded by a sheath of paraxial presomitic mesoderm (PSM). It forms somites along the two sides of the notochord, receiving cells from the tailbud (the caudal end) of the embryo. Periodically, a group of cells separates from the cranial PSM to form a new somite. Caudal cell addition and cranial cell deduction mostly occur at similar rates, so the PSM remains constant in length, and somites appear to form in the cranial to caudal direction as the body axis elongates (Pourquie 2003).

The regulation of vertebrate segmentation and somite formation is complex. Synchronous oscillation in the PSM is referred to as the segmentation clock. The "clock and wavefront" mechanism is a general scheme for somitogenesis, which allows mathematical description of the length of each somitic segment (S) from the formula $S = vT$ (v = velocity of the wavefront, T = period of the clock), and total number of somites (n) from the formula $n = d/T$ (d = total duration of segmentation, T = period of the clock) (Cooke and Zeeman 1976). Periodicity of somite formation is controlled by the synchronous oscillation of gene expression in the PSM (Pourquie 2003). Several cyclic segmentation clock genes have been found, but different individual genes are cyclic in different species (Oates et al. 2012). The exact number of somites in a vertebrate species is dependent on the segmentation clock rate; a fast clock rate results in a large number of small somites (Gomez and Pourquie 2009), and an extended somite segmentation clock period results in fewer somites (Kim et al. 2011b, Schroter and Oates 2010).

Sclerotomes develop from somites and surround the notochord, partly enclosing it. Eventually, sclerotomes become cartilage, and the notochord stays within the centrum. The lateral parts of the sclerotome grow dorsally to form the neural arches and ventrolaterally to form the transverse and costal processes and part of the body. The spinous processes develop after the neural arches meet and fuse (Evans 1993).

Hox genes are essential regulators of the craniocaudal arrangement of the axial skeleton, and a mistake in the regulation causes a cranial reformation of the vertebra. Mammals have 39 *Hox* genes arranged in four clusters, each composed of two to four members of 13 paralogous groups. The function of *Hox* genes has been studied in murine models using knock-out mice. Loss of *Hoxd11* function causes sacral patterning changes in mice, leading to extra lumbar or sacral vertebrae (Davis and Capecchi 1994). In mice with a disrupted *Hox10* paralogous group, all lumbar and sacral vertebrae have ribs, and in mice with a disrupted *Hox11* paralogous group all sacral vertebrae have a lumbar form (Wellik and Capecchi 2003). *Hox* genes do not regulate the number of somites formed, but rather their morphology (Wellik 2009).

The mechanisms that stop the segmentation of somites and regulate the number of somites are poorly understood (Oates et al. 2012). *Hox* and the *Caudal*-type homeobox genes (*Cdx*) are needed in the termination of somitogenesis and body elongation (Young et al. 2009, Aulehla and Pourquie 2009, van den Akker et al. 2002).

2.4.3 Lumbosacral transitional vertebra

2.4.3.1 Morphology

Lumbosacral transitional vertebra (LTV), a congenital malformation of S1 and/or the last presacral vertebra, is caused by a mistake in embryogenesis. The definition of LTV varies in the veterinary literature (Wigger et al. 2009, Damur-Djuric et al. 2006, Morgan 1999). It has been described as a vertebra having features of both lumbar and sacral vertebrae, in which a disc space exists between the first (S1) and second (S2) sacral segments (Morgan 1999) (Figure 16). The terms "sacralization" when the last presacral vertebra has characteristics of a sacral vertebra and "lumbarization" when the S1 resembles a lumbar vertebra are commonly used in both human (Mahato 2011, Konin and Walz 2010) and veterinary literature (Newitt et al. 2009, Breit and Kunzel 2002, Morgan et al. 2000b, Larsen 1977). If the true number of lumbar vertebrae is unknown, as can be the case in diagnostic imaging studies, differentiating between sacralization and lumbarization may be challenging (Breit et al. 2003, Morgan et al. 2000b).

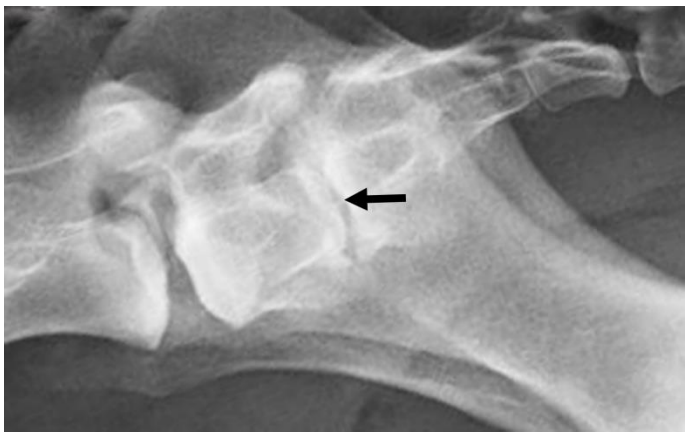

Figure 16 *Laterolateral radiograph of a German shepherd dog with a lumbosacral transitional vertebra. The radiolucent space between first and second sacral vertebrae is visible (arrow).*

Morphology of the LTV is highly variable (Figure 17A,B,C). The shape of the transverse process and its contact with the ilium vary, and these changes can be asymmetrical or symmetrical (Wigger et al. 2009, Damur-Djuric et al. 2006, Morgan. 1999, Breit et al. 2003, Castellvi et al. 1984, Larsen 1977). The term costal process has been used synonymously with the term transverse process (Breit et al. 2003).

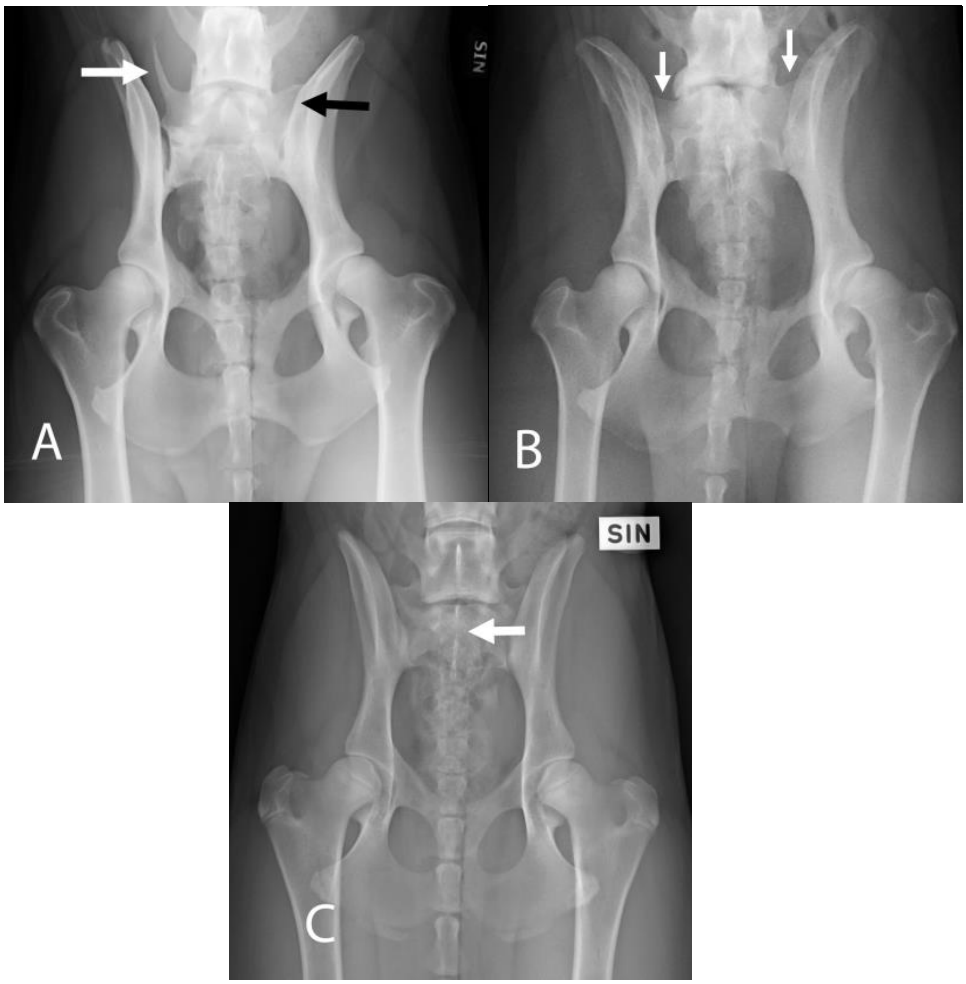

Figure 17 *Different types of lumbosacral transitional vertebrae in German shepherd dogs as seen on ventrodorsal radiographs.(A) A lumbosacral transitional vertebra with a transverse process resembling lumbar type on the right (white arrow) and sacral type on the left (black arrow),(B) A lumbosacral transitional vertebra with the transverse processes (arrows) superimposing with the iliac bones (arrows). (C)A lumbosacral transitional vertebra where the only abnormality is the separation between S1 and S2 (arrow).*

2.4.3.2 Heredity

The LTV is proposed to be hereditary (Wigger et al. 2009, Damur-Djuric et al. 2006, Morgan 2000, Morgan et al. 1999), but studies on the model of heritance are lacking in dogs and other animals. The high incidence of LTV in certain dog breeds, especially German shepherd dogs, suggests a familial basis (Morgan 2000).

2.4.3.3 Clinical relevance

LTV is a congenital anomaly reported in several species, including man, dog, horse, cat, wolf and horned antelope (Apazidis et al. 2011, Newitt et al. 2009, Räikkönen et al. 2009, Bron et al. 2007, Damur-Djuric et al. 2006, Haussler et al. 1997, Wegner 1959). It is common at least in man and dog. The mean prevalence in people based on published studies is 12.3%, but the range between studies is wide (4-35.9%) (Bron et al. 2007). A recent study reported a prevalence of 35.6% in the general population (Apazidis et al. 2011). In dogs, the prevalence has ranged between 2.3% and 29.0%, differing according to breed. Especially in German shepherd dogs, the incidence is high (4.3- 29.0%) (Wigger et al. 2009, Damur-Djuric et al. 2006, Morgan 1999, Larsen 1977).

LTV was first thought to be clinically insignificant in dogs (Morgan 1968). Later, it has become evident that LTV predisposes to premature degeneration of the lumbosacral junction (Figure 18) and is a frequent cause of cauda equina syndrome, particularly in German shepherd dogs (Flückiger et al. 2006, Moore et al. 2001, Morgan et al. 1993). In man, the clinical picture of LTV, also known as Bertolotti's syndrome (Quinlan et al. 2006), is controversial. It predisposes to early disc degeneration (Quinlan et al. 2006, Luoma et al. 2004) and has been associated with lumbar back pain, disc protrusions and nerve root pain (Quinlan et al. 2006, Taskaynatan et al. 2005, Otani et al. 2001). However, the connection between increased risk of spinal pathology and LTV has been questioned (Elster 1989).

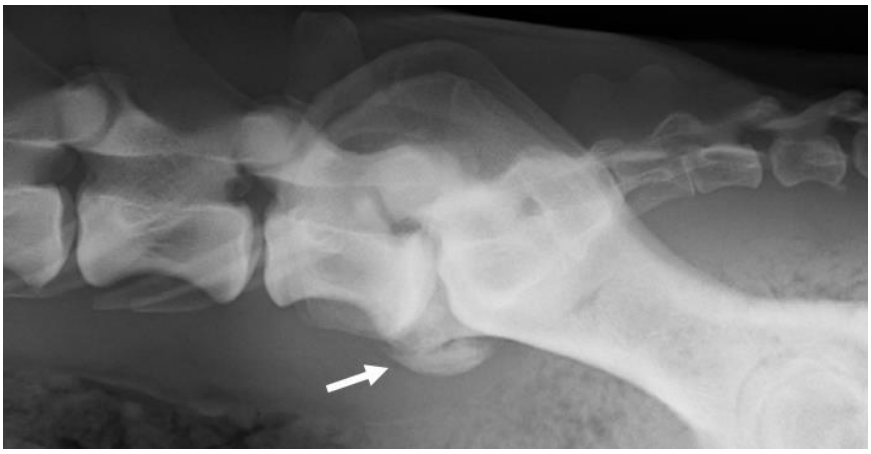

Figure 18 *Laterolateral radiograph of a German shepherd dog with a lumbosacral transitional vertebra. Spondylosis of the lumbosacral space (arrow) is indicative of a degenerative process.*

In dogs, degenerative changes of the lumbosacral area and clinical findings do not always match (Steffen et al. 2007, Scharf et al. 2004, Jones and Inzana 2000), and therefore, more advanced imaging methods, like MRI and CT, are needed to confirm nerve root compression in clinical cases (Suwankong et al. 2006, Steffen et al. 2004, Mayhew et al. 2002, Jones et al. 2002, Jones et al. 1999, de Haan et al. 1993).

An association between LTV and unilateral HD has been suggested. The coverage of the acetabulum over the femoral head is smaller on the side of the lesser sacroiliac contact, and development of unilateral dysplasia on that side is possible (Julier-Franz 2006, Morgan 1999).

Numerical variations in lumbar vertebrae occur at least in humans, dogs, cats and horses (Apazidis et al. 2011, Newitt et al. 2009, Newitt et al. 2008, Breit and Kunzel 2002, Haussler et al. 1997). These have not been considered part of the LTV complex (Damur-Djuric et al. 2006). However, the presence of the eighth lumbar vertebra (L8) (Figure 19A,B) may be part of the complex since the widest diameter of the vertebral canal is at the same level in dogs with seven and eight lumbar vertebra if L8 is assumed to be S1 in the dogs with eight lumbar vertebrae (Breit and Kunzel 2002).

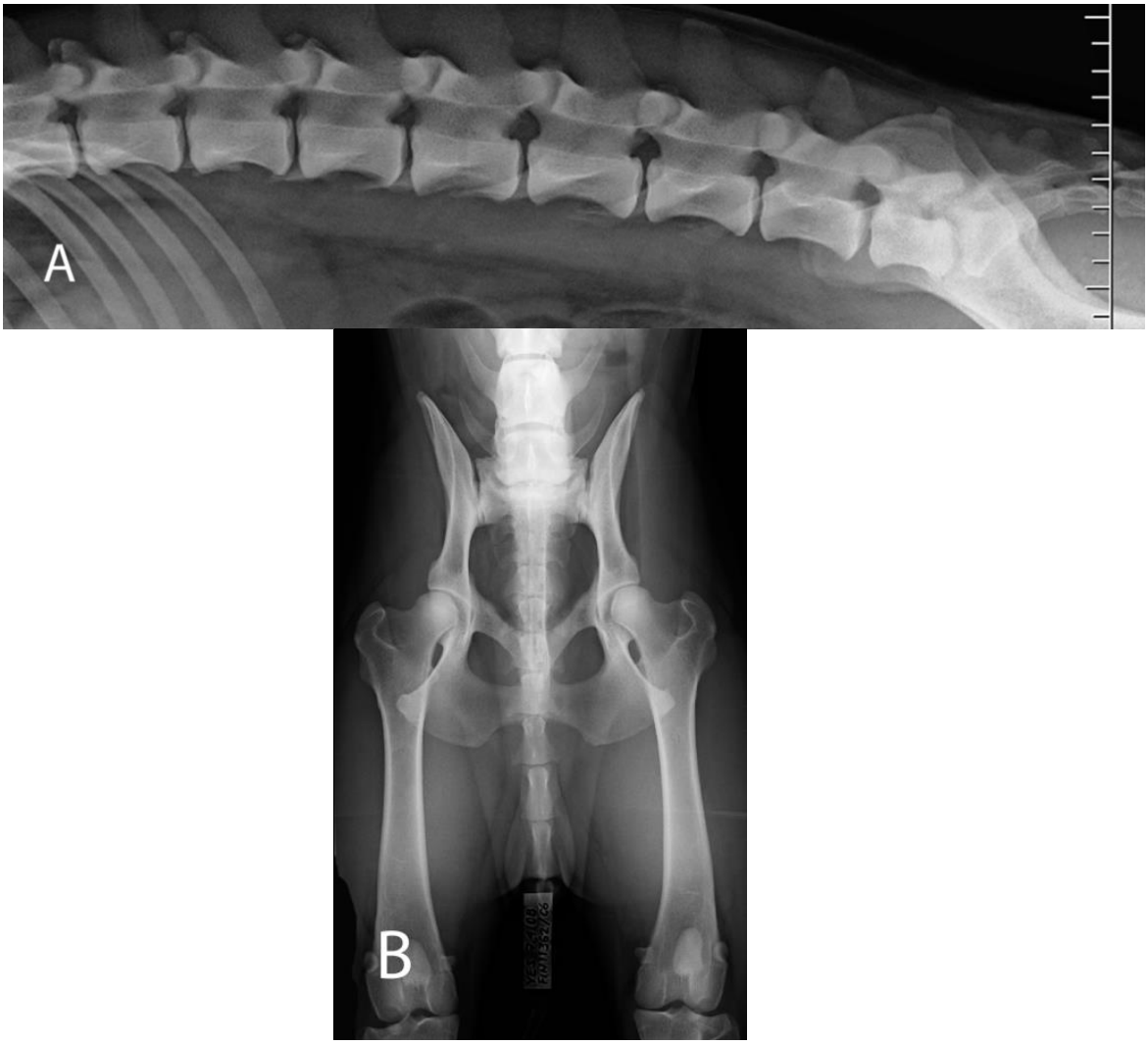

Figure 19 *A laterolateral lumbar spine radiograph (A) and aventrodorsal extended hip radiograph (B) of a German shepherd dogwith eight lumbar vertebrae.*

2.4.3.4 Radiographic screening protocols

In dogs, LTV is usually diagnosed radiographically using ventrodorsal (VD) radiographs (Figure 17C) (Wigger et al. 2009, Damur-Djuric et al. 2006, Breit et al. 2003). VD projection with hind limbs abducted can improve the visibility of the lumbosacral disc space, facilitating diagnosis of LTV (Damur-Djuric et al. 2006). LL projection (Figures 16 and 18) can also help in differentiating normal anatomy from an LTV (Morgan 1999).

Screening for LTV in healthy dogs is rare, and no such studies exist. A screening scheme using VD extended hip radiographs is in use in Switzerland, where the Swiss Dysplasia Committee recently introduced a four-scale grading, in which type 0 is a normal lumbosacral area, type 1 is a sacrum with S1 separated from the median crest of the sacrum, type 2 is a symmetrical LTV and type 3 is an asymmetrical LTV (Flückiger et al. 2009). In Finland, LTV is reported to the owner as additional information when screening for HD (Ohje lonkkanivelen kasvuhäiriön... 2011). The Finnish Kennel Club has established a screening protocol based on the results of **Study IV** in 2013.

3 Aims of the study

The main goal of this study was to initiate and improve Finnish radiographic screening protocols for certain hereditary musculoskeletal disorders.

The following questions were addressed:

1. How common is intervertebral disc calcification in the Finnish miniature Dachshund population?

2. Are curvature of front limbs and number of intervertebral disc calcifications in individual miniature Dachshunds related?

3. Is the Finnish elbow dysplasia (ED) screening protocol based on signs of osteoarthritis (OA) accurate when addressing the radiographically mild form (ED grade 1) in Belgian shepherd dogs and Labrador retrievers?

4. Is the laterolateral radiographic projection needed in screening for lumbosacral transitional vertebra (LTV) in German shepherd dogs?

5. Is the eighth lumbar vertebra part of the LTV complex in German shepherd dogs?

4 Materials and methods

4.1 Ethical approval of study protocols

The study protocols were approved by the Ethics Committee of the Faculty of Veterinary Medicine, University of Helsinki (**Studies I, II** and **III**). **Study IV** was based on existing radiographs and CT studies.

4.2 Dogs

Study I: Long-haired and wire-haired miniature Dachshunds (chest circumference less than 35 cm) were selected from the FKC register based on their regional as well as familial backgrounds by sorting them according to their sires and owners' postal codes. Every tenth dog (altogether 221 dogs) was selected from the list and a questionnaire was sent to the owner. These dogs accounted for 8.1% of the total miniature Dachshund population registered during 1988-1996. The owners were requested to enrol their dog in the study. The dogs were excluded if they had a disease preventing sedation or were pregnant.

In all, 174 owners (79%) returned the questionnaire. A radiographic study was conducted on 124 miniature Dachshunds (79 long-haired and 45 wire-haired), representing 4.5% of the miniature Dachshund population registered by the FKC during 1988-1996. The long-haired dogs were from 64 sires and 73 dams, and the wire-haired dogs were from 32 sires and 38 dams. The mean age for both variations was 4 (range 1-9) years. The mean weight for the long-haired Dachshund was 5.8 (range 2.7-11.0) kg and for the wire-haired Dachshund 6.0 (range 3.5-8.9) kg.

Studies II and III: Belgian shepherd dogs and Labrador retrievers were selected from the FKC database in chronological order, starting from the latest entry (November 2007). The aim was to include dogs with a time interval as short as possible between the initial grading and this study. An inclusion criterion was ED grade 1 (or grade 0b in Belgian shepherd dogs) in one elbow and grade 0 in the other to obtain a matched number of grade 1 (grade 0b) and grade 0 elbow joints. The elbow joints graded as 0 served as radiologically normal controls in the evaluation of radiographs. Forty dogs of both breeds were identified and the owners were contacted and requested to enrol their dog in the study. Exclusion criteria were pregnancy and any illness preventing sedation.

Eighteen Belgian shepherd dogs (11 males and 7 females) and 13 Labrador retrievers (7 males and 6 females) participated, thus 36 and 26 elbow joints, respectively, were investigated. Presenting data for the dogs are summarized in Table 3. Three of the 18 Belgian shepherd dogs were recruited during the study; two of them were older, a female aged 6.5 years and a male aged 4 years, and they were originally radiographed as 1 for one elbow joint and 0 for the other, five and two years earlier, respectively. The third dog was originally graded as 1 for both elbow joints. Of the Belgian shepherd dogs, 12 had one elbow joint graded as 1 and the other as 0, one dog had both elbow joints graded as 1, four dogs had one elbow joint graded as 0b and the other as 0 and one dog had both elbow joints graded as 0b. All Labrador retrievers had one elbow joint graded as 1 and the other as 0.

An orthopaedic examination was conducted on 16 Belgian shepherd dogs and on all Labrador retrievers; the temperament of two Belgian shepherd dogs prevented the examination to be carried out while the dogs were awake. In the examination, none of the dogs had evidence of an elbow-related problem.

Table 3 *Weight and age at the time of the study and at the time of the initial radiographic screening of 18 Belgian shepherd dogs and 13 Labrador retrievers.*

	Mean weight (range) in kg	Mean age (range) in months	Mean age at the time of the initial grading (range) in months	Mean time between studies (range) in months
Belgian shepherd dogs				
Males (n=11)	28 (17-32)			
Females (n=7)	24 (20-28)			
Total (n= 18)		34 (15-78)	22 (12-49)	12 (1-60)
Labrador retrievers				
Males (n=7)	36(30-46)			
Females (n=6)	29(25-32)			
Total (n=13)		22 (16-28)	15 (12-19)	8 (2-11)

n = number of dogs

4.3 Questionnaire

In **Study I**, a questionnaire was sent to the owners selected from the FKC database as described in Section 4.1. Each owner was asked whether their dog had had any symptoms of IDD (unwillingness to jump or walk, unexplained pain or ataxia) and whether it had been treated for this.

4.4 Diagnostic imaging

4.4.1 Radiographs and radiographic projections

Studies I, II and III: All radiographic studies were performed at the Veterinary Teaching Hospital of the University of Helsinki. In **Study I,** a screen-film technique was used, and in **Studies II and III** a digital image plate (computed radiography) system with a dedicated workstation was used. The dogs were sedated to allow correct positioning according to the anaesthesia protocol used in the hospital. The radiographic projections used are presented in Figures 2 and 12A,B.

Study IV: The VD pelvic (Figure 19A) and LL lumbar spine **(**Figure 19B**)** radiographs were collected from three sources: 1) FKC hip dysplasia screening radiographs in 2007, when an additional LL projection of the lumbar spine, as requested by the national breed club, was included in the screening radiographs, 2) radiographs from the Finnish Border Guard of dogs (born 1995-2006) withdrawn from active service and 3) radiographs collected from the database of the Veterinary Teaching Hospital of the University of Helsinki between May 2005 and March 2011 of dogs radiographed for various reasons. Digital radiographs from the hospital data base were evaluated on the workstation; all others were either film radiographs or digital radiograph prints. In all, 228 German shepherd dogs were included in the study (79 males and 149 females). The mean age of the dogs was 42 (range 5-134) months.

4.4.2 Evaluation of radiographs

Study I: Evaluation of the radiographs was done together by the author and Mia Norrgård, and the results recorded were based on consensus. The number of calcified discs was calculated, and their location in the vertebral column was recorded. Every visible calcification was included (Figure 20A), also very small or less opaque ones (Figure 20B). The measurements used in evaluating the curvature of the radius and ulna are shown in Figure 21. The ratio between "a" and "b" was used as a value for the curvature.

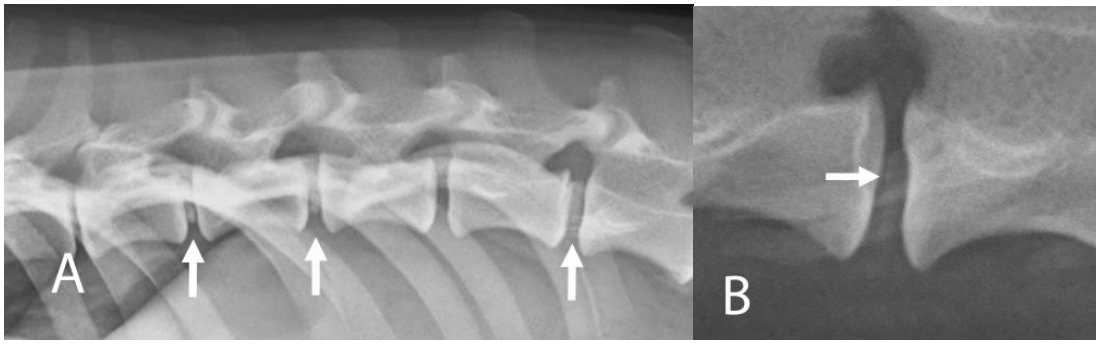

Figure 20 *Laterolateral radiographs of a Dachshund. (A) Several calcified intervertebral discs (arrows) at the thoraco-lumbar junction. (B) A small calcification (arrow) of a lumbar intervertebral disc superimposed on the transverse process. The projection is slightly oblique.*

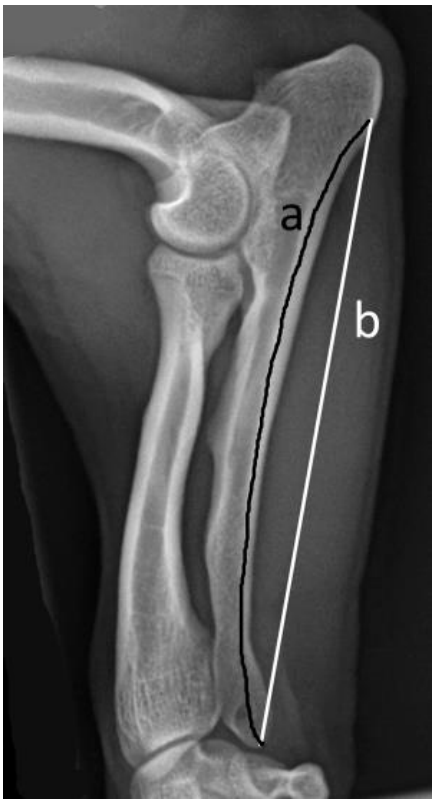

Figure 21 *Curvature ratio defined as the length of a (the curved line along the ulna between the distal epiphyseal line of olecranon and the distal end of the styloid process) divided by the length of b (the straight line between the end points of a).*

Study II: First, the ML flexed radiographs obtained for this study and the initial screening radiographs received from the FKC archives were evaluated. Second, the ML flexed and CrCd oblique radiographs obtained for this study were assessed together. All radiographs were assessed by the author according to IEWG guidelines, with an emphasis on radiographic signs indicative of a primary lesion (Table 1). The images were randomized and evaluated without knowledge of the findings of the contralateral joint or of the other study. Details of the assessment are presented in Figure 22. The height of new bone formation on the proximal border of the anconeal process was measured with a ruler, and blurring of the cranial edge of the MCP and subtrochlear sclerosis was subjectively graded as mild (+) or moderate to marked (++). Uncertain changes were graded as negative (-). Sclerosis was defined as a loss of trabecular bone pattern. Annie Liman, who had done the initial grading, graded the ML flexed radiographs according to FKC guidelines without knowledge of the findings of the contralateral joint or of the initial screening study (Table 4). Finally, findings from all sets of radiographs were compared with each other.

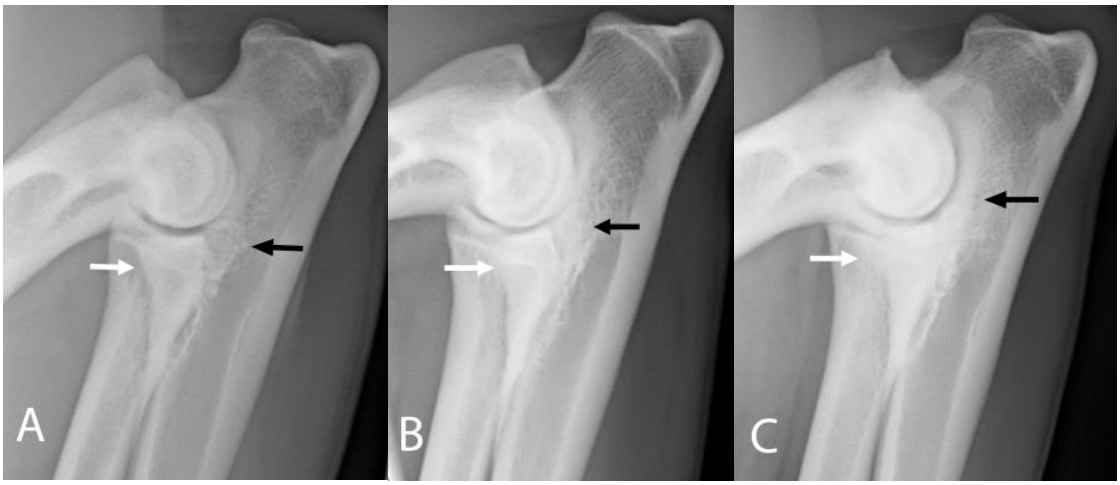

Figure 22 *Grading of the cranial edge of the medial coronoid process and of the subtrochlear sclerosis on mediolateral flexed radiographic projection used in the study. (A) A normal elbow joint. No abnormal sclerosis is visible (black arrow). The cranial contour of the medial coronoid process is clearly delineated (white arrow). (B) Mild subtrochlear sclerosis and blurring of the cranial edge of the medial coronoid process. The sclerotic area is seen distal to the trochlear notch only (black arrow), and the cranial contour of the medial coronoid process is not clearly seen (white arrow). (C) Moderate to marked subtrochlear sclerosis and blurring of the cranial edge of the medial coronoid process. The sclerotic area extends proximally around the trochlear notch (black arrow) and the shape of the medial coronoid process is abnormal (white arrow).*

Table 4 *Grading of the cranial border of the medial coronoid process and subtrochlear sclerosis of elbow joints.*

Cranial border of the MCP	
Negative (-)	Normal
Mild (+)	Unclear cranial contour of the MCP but the MCP is evenly opaque and normal in shape
Moderate to marked (++)	Abnormal shape and/or opacity of the MCP
Sclerosis	
Negative (-)	Normal
Mild (+)	Sclerotic area at the base of the coronoid process only
Moderate to marked (++)	Sclerotic area extends proximally around the trochlear notch

MCP = medial coronoid process

Study III: Evaluation of the radiographs was done as in **Study II,** with the exception that only one set of radiographs (ML flexed and CrCd oblique projections) was assessed. The initial screening radiographs were not used in this study.

Study IV: The author and Reea Salomaa independently evaluated the VD and LL radiographs for the existence and type of LTV without knowledge of the findings of the

other projection. They then evaluated both projections together, and diagnosis of an LTV was based on consensus. An LTV seen in the VD projection was diagnosed and classified into three types based on the morphology of the transverse processes, according to a previously published scheme (Damur-Djuric et al. 2006) (Table 5). Each type was further divided into symmetrical and asymmetrical subcategories. The radiolucent space between the S1 and S2 spinous processes (separation of S1 spinous process from the median crest of the sacrum) was recorded in the VD projection (Figure 17C) and was termed type 4. In the LL radiographs, diagnosis of an LTV was based on the visibility of a radiolucent line between S1 and S2 (Figure 16). Dogs with L8 (Figure 19A,B) were included in the LTV group.

Table 5 *Classification of the lumbosacral transitional process based on the morphology of the transverse process (Damur-Djuric et al. 2006).*

Type	Transverse process
1 (lumbar)	Resembles lumbar vertebra
2 (intermediate)	Partly superimposed on the ilium (the tip is free)
3 (sacral)	Totally superimposed on the ilium or resembles sacral vertebra

The number of lumbar vertebrae was counted using the last thoracic vertebra as a reference point. The first lumbar vertebra (L1) was the vertebra caudal to this vertebra. To assess the appearance of the last presacral vertebra, the LL radiographs were evaluated for the position of the seventh and the length of the sixth and seventh (L6-L7) vertebrae (and L8 when present). The position of L7 relative to the ilium was recorded (Figure 23). Additionally, the midcorpus length (mm) of L6 and L7 (Figure 24) was measured with a ruler, and the relative length was calculated from a formula (length of L6/length of L7) to remove the effect of size of the dog. In dogs with eight lumbar vertebrae, the length of L8 was measured with a ruler, its relative length was calculated from a formula (length of L7/length of L8) and its position relative to the ilium was recorded.

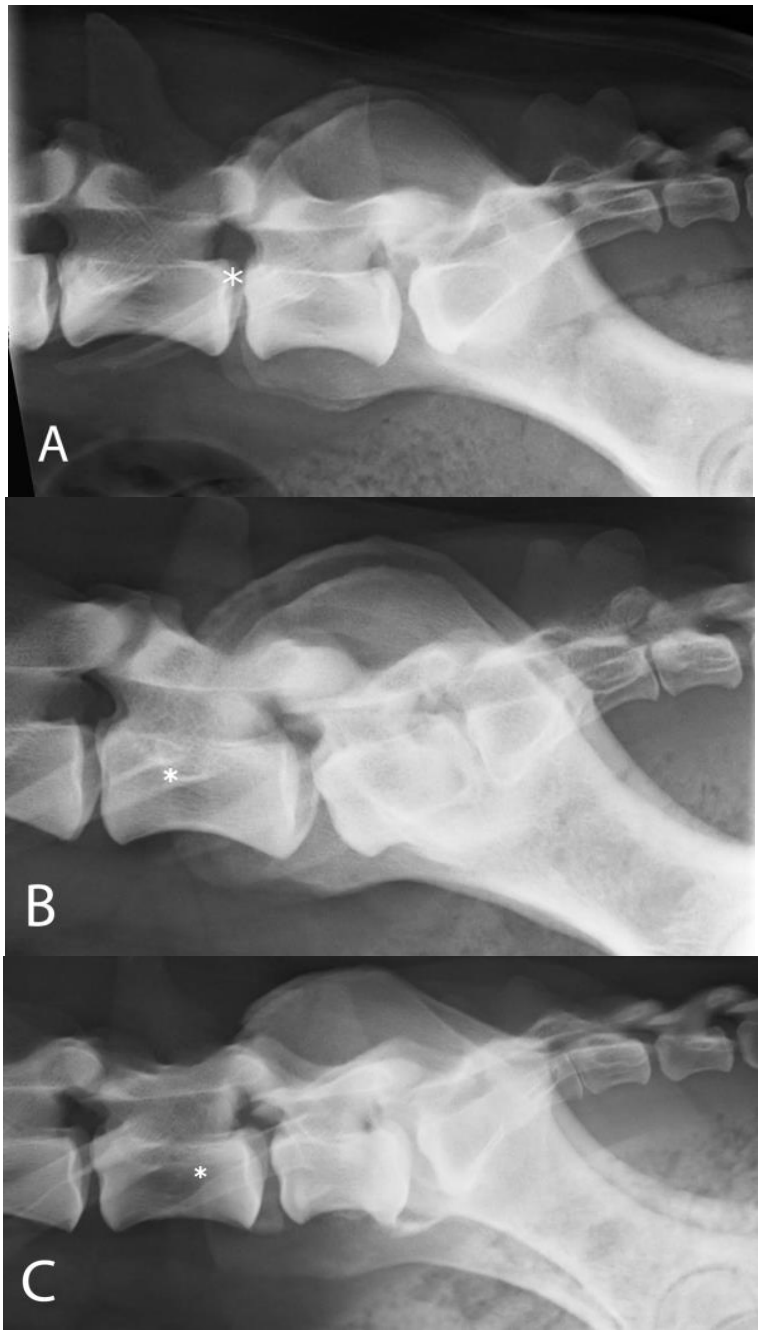

Figure 23 *Laterolateral radiographs of the lumbosacral area of three different dogs illustrating grading of the position of the seventh lumbar vertebra. (A) A German shepherd dog with radiographically normal lumbosacral junction. The position was graded as caudal. The cranial borders of the iliac bones are superimposed on the disc space between the sixth and seventh lumbar vertebrae (asterisk). (B) A German shepherd dog with a lumbosacral transitional vertebra. The position was graded as intermediate. The cranial borders of the iliac bones are superimposed on the cranial half of the seventh lumbar vertebra (asterisk). (C) A German shepherd dog with eight lumbar vertebrae. The position was graded as cranial. The cranial borders of the iliac bones are superimposed on the caudal half of the seventh lumbar vertebra (asterisk).*

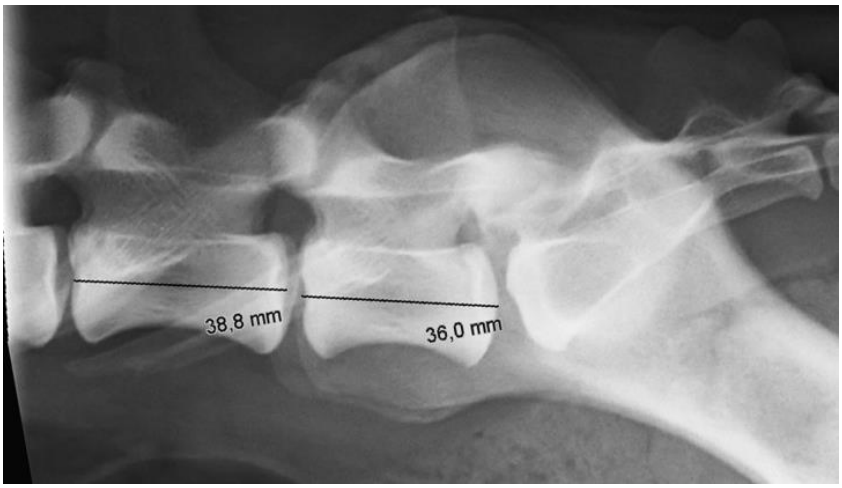

Figure 24 *Laterolateral radiograph of the caudal lumbar spine of a German shepherd dog with radiographically normal lumbosacral junction illustrating measurements of the mid-body lengths of the sixth and seventh lumbar vertebrae.*

4.4.3 Computed tomography

Studies II and III: CT imaging of the elbow joints was performed immediately after radiography, with the dog in left recumbence and the elbows flexed 90° (Figure 25). Plastic foam was placed between the front legs to position the elbows symmetrically**.** Data were obtained with a helical dual slice scanner (Somatom Emotion Duo, Siemens AG, Forchheim, Germany) with a bone algorithm. Slice thickness was 1.0 mm, feed/rotation 2 mm and reconstruction increment 0.5 mm.

Figure 25 *A Belgian shepherd dog positioned for the computed tomography study of elbow joints.*

Study IV: CT studies of the dogs were retrieved from the hospital database between May 2005 and March 2011. Sixteen studies were found. According to the protocol used in the hospital, the dogs had been in dorsal recumbence with the hind limbs extended during the examination, and the imaging parameters had been similar to those used in **Studies II** and **III**.

The images were reconstructed with Syngo Multi Modality Workplace (Siemens AG, Erlangen, Germany). Transverse, sagittal and dorsal plane images were used in all studies, and a three-dimensional volume rendering technique (VRT) was used in **Study IV**. The author evaluated all of the images in Studies II and III together with Marjatta Snellman, and the diagnosis was based on consensus.

4.5 Statistical analyses

Study I: Standard errors were calculated by estimators designed to be used with simple random sampling. The χ^2 test was applied to evaluate differences between dogs with calcifications and dogs with IDD in relation to sex, age group and offspring group. A Kruskal-Wallis analysis of variance was used to test for differences in the median number of calcifications between age groups and for differences in the median of the curvature ratio between groups formed according to the health and calcification status of the dogs. The Mann-Whitney test was used when testing for differences in median numbers of calcifications between sexes and groups of offspring. The results were expressed as percentages (± standard error) and as means (standard deviation) or medians.

Studies II and III: Fischer's exact test in table analysis was applied to test the significance of the association between radiographic and CT signs of ED. In **study III** Kappa statistics was used to assess agreement between grading and ED status based on CT. Agreement with kappa value was interpreted as follows: < 0 = less than chance, 0.01 - 0.20 = slight, 0.21 - 0.40 = fair, 0.41 - 0.50 = moderate, 0.61 - 0.80 = substantial, 0.81 - 0.99 = almost perfect. (Viera and Garrett 2005). The sets would differ only if their kappa coefficients differ (=combined kappa is statistically significant).

Study IV: Sensitivity was calculated for the ventrodorsal radiographic projection in diagnosis of LTV with non-parametric χ^2 test. A one-sided p-value was used to determine the statistical significance of the difference. The relationship between type of lumbosacral junction and relative length of L6 /L7 was investigated with generalized logit model for multinomial data. Descriptive statistics of the relationship between type of lumbosacral junction and location of L7 were provided. The difference between types of lumbosacral junction was analysed with one-way analysis of variance.

Statistical significance was set at the 5% level in all studies. SAS System version 9.1 was used in **Study II** and version 9.2 (SAS Institute Inc., Cary, NC, USA) in **Studies III** and **IV** for all statistical calculations.

5 Results

5.1 Incidence of intervertebral disc calcifications and intervertebral disc disease in Finnish miniature Dachshunds

Calcified discs were found in 60 (76%) of the 79 long-haired miniature Dachshunds and in 39 (87%) of the 45 wire-haired ones. In the long-haired miniature Dachshunds, the mean number of calcifications was 2.5 (median 2.0, range 0-13) and in the wire-haired Dachshunds 3.4 (median 2.0, range 0-11). The number and percentage of calcifications per dog are presented in Figure 26A,B. No significant difference emerged between long-haired and wire-haired miniature Dachshunds in the percentage of dogs with calcifications or clinical signs of IDD, or in the number of calcifications within a single dog. The presence of calcification was not related to sex or age in either breed, nor was age related to number of calcified discs.

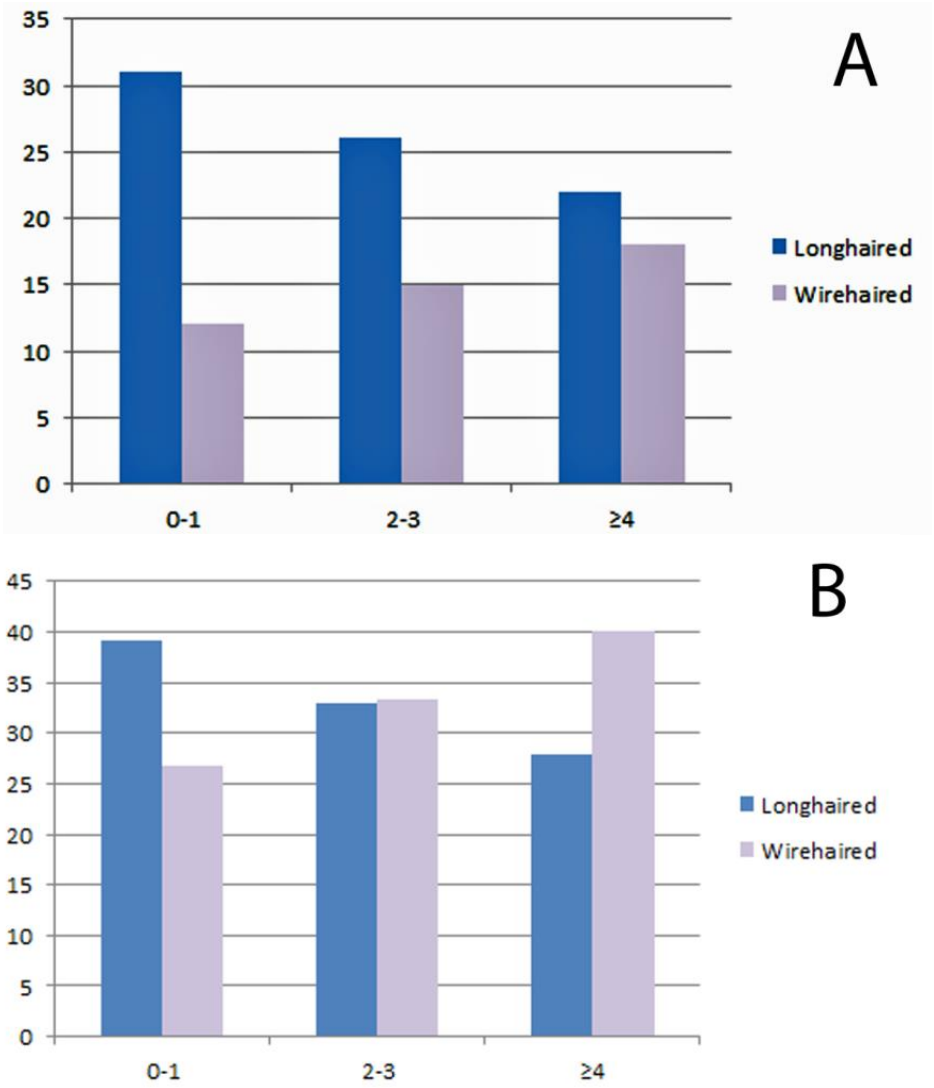

Figure 26 *Number (A) and percentage (B) of calcifications in the 79 long-haired and 45 wire-haired miniature Dachshunds. 0-1, 2-3, ≥4 = number of calcifications.*

According to the questionnaire, 20 (17.5%) of the 114 long-haired Dachshunds and 12 (20.0%) of the 60 wire-haired Dachshunds showed clinical signs of IDD (diagnosed by a veterinarian in 28 [88%] of 32 dogs). Two dogs had been euthanized because of IDD before the radiographic study. Of the dogs in the radiographic study, 13 (16.5%) of 79 long-haired dogs and 7 (15.6%) of 45 wire-haired dogs revealed signs indicative of IDD. Altogether 19 (19%) of 99 dogs with calcified intervertebral discs in the radiographic study had signs indicative of IDD. One (4%) of 25 dogs without calcifications had clinical signs of IDD.

5.2 Curvature of the radius and ulna in Finnish miniature Dachshunds as an indicator of disc calcifications

In healthy dogs without calcifications, the median number of the ratio "a/b" (Figure 21) was 1.14, in healthy dogs with calcifications it was 1.15 and in diseased dogs with calcifications it was 1.16. No statistical difference existed between the three groups. Only one dog without calcified discs had clinical signs of IDD and was excluded from this part of the study.

Studies II and III

5.3 Elbow dysplasia based on computed tomography in Belgian shepherd dogs and Labrador retrievers

According to the CT study (Figure 5), MCPD was evident in five joints (14%) in three Belgian shepherd dogs (19%). Two dogs were affected bilaterally and the third unilaterally. UAP, OC or INC was not seen in any dog. Thirty-one elbow joints (86%) were free of ED based on the CT images.

MCD was found in 14 joints (54%) in ten Labrador retrievers (77%); four dogs were bilaterally affected and six had a unilateral disease. In one joint, a smooth bone fragment adjacent to the medial epicondyle was present. No other abnormalities were detected, and the lesion was interpreted as flexor enthesopathy and graded as free of ED. In five joints, a subchondral bone defect in the medial condyle was seen. Three dogs (23%) were free of ED based on CT.

5.4 Comparison of radiological findings and computed tomography of elbow dysplasia in Belgian shepherd dogs and Labrador retrievers

The radiological findings of the ML flexed radiographs for Belgian Shepherd dogs and Labrador retrievers are presented in Tables 6 and 7, respectively. When comparing the grading results and disease status based on CT in Belgian shepherd dogs, 17 joints free of ED were graded as dysplastic, and two of the elbows with MCPD were graded as free of ED (grade 0b) (Figure 27A). In the initial screening, 12 joints free of ED were graded as dysplastic and three joints with MCPD were graded as free of ED (grade 0 or 0b) (Figure 27B). In Labrador retrievers, one joint free of ED was graded as dysplastic and three joints with MCD were graded as free of ED (Figure 28). Sensitivity and specificity of the

different radiographic signs as indicators of ED and grading for both breeds are presented in Table 8. A significant association existed between ED and blurring of the cranial edge of the MCP and between ED and subtrochlear sclerosis in both breeds. When grading results of the individual joints in our study were combined, there were no false-negative Belgian shepherd dogs based on the new grading, but 12 (67%) were incorrectly graded as positive for ED. Grading was reliable in Labrador retrievers, with high specificity (92%) and relatively high sensitivity (79%). Agreement between grading and ED status was substantial (kappa 0.69). Two dogs were incorrectly graded; one dog with bilateral MCD based on CT was graded as free of ED and one dog without MCD was graded as ED1.

Table 6 *Radiographic signs of 36 joints with and without medial coronoid process disease based on computed tomography images in 36 joints in Belgian shepherd dogs in the present and initial radiographs*

Present radiographs	Blurring of MCP			Sclerosis			Bony opacity on AP (mm)		
	-	+	++	-	+	++	0	0-2	Ó2
MCPD (n=5)	0	1	4	1	3	1	2	1	2
Without MCD (n=31)	28	3	0	28	3	0	9	16	6
Initial radiographs									
MCPD (n=5)	0	1	4	1	3	1	2	1	2
Without MCD (n=31)	28	3	0	28	3	0	9	16	6

Figures refer to the number of joints. MCPD = fragmented medial coronoid process, MCP = medial coronoid process, AP = anconeal process, , - = free + = mild, ++ = moderate to marked

Table 7 *Radiographic signs indicative of a primary lesion with and without medial compartment disease based on computed tomography images of the 26 joints in 13 Labrador retrievers*

	Blurring of MCP			Sclerosis		
	-	+	++	-	+	++
MCD (n=14)	2	9	3	3	7	4
Without MCD (n=12)	10	2	0	9	3	0

Figures refer to number of joints. MCP = medial coronoid process, MCD = medial compartment disease, - = free + = mild, ++ = moderate to marked

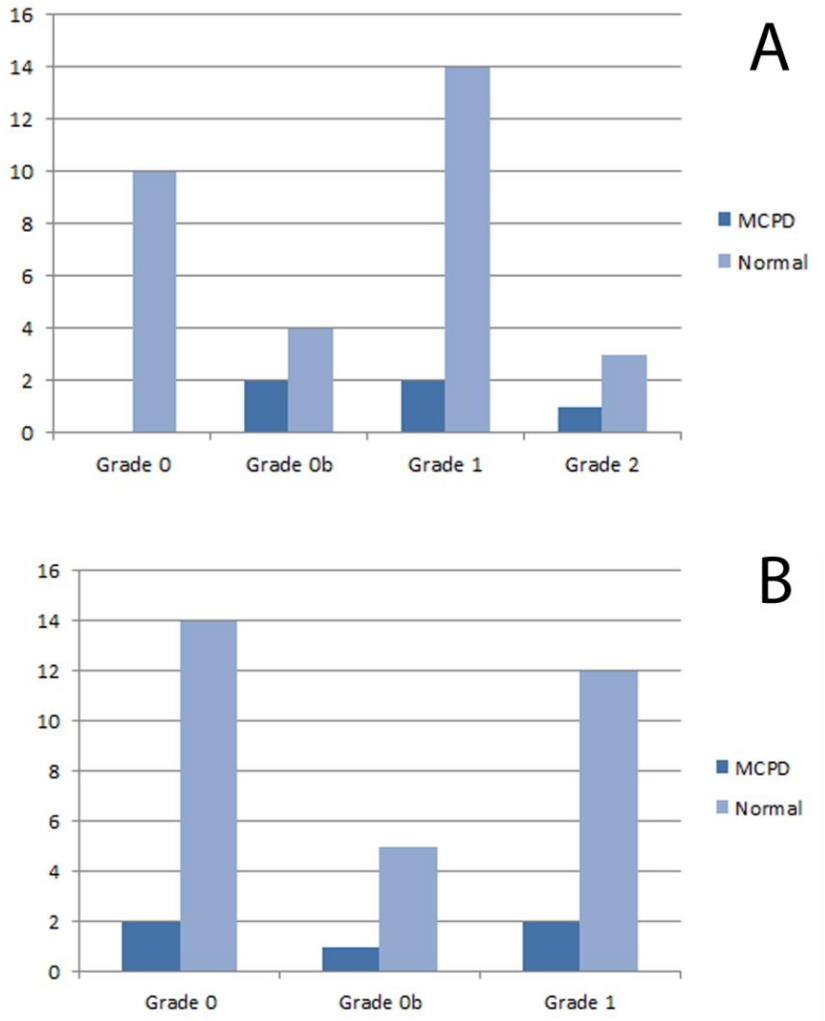

Figure 27 *Radiographic grading of the 36 joints with and without medial coronoid process disease based on computed tomography in 18 Belgian shepherd dogs. (A) Radiographs of this study. (B) Radiographs of the initial screening. MCPD=medial coronoid process disease, 0b=borderline dysplasia.*

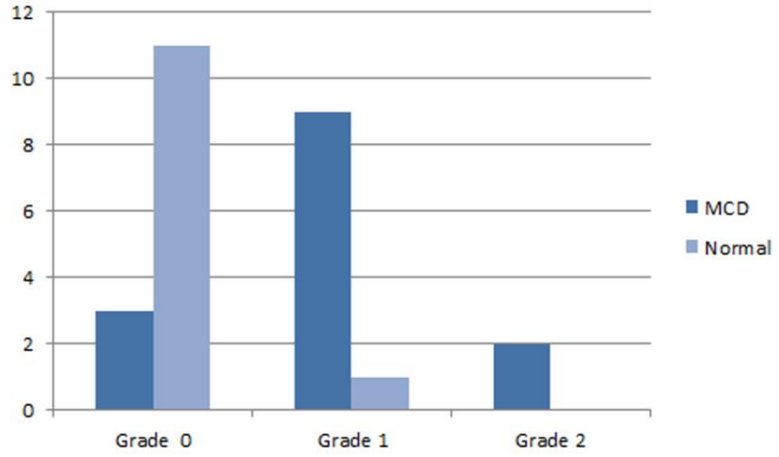

Figure 28 *Radiographic grading of the 26 joints with and without medial compartment disease based on computed tomography in 13 Labrador retrievers. MCD=medial compartment disease.*

5.5 Supplemental craniocaudal oblique radiographic projection

In the CrCd oblique view, a radiolucent subchondral bone defect on the medial humeral condyle was observed in five joints (Figure 7) and flexor enthesopathy in one joint (Figure 10). Medial osteophyte formation was seen in 13 dysplastic joints and in the joint with flexor enthesopathy. In one dysplastic joint, no osteophytes were seen in the CrCd oblique projection, nor were osteophytes seen in the ML flexed projection of this joint. The CrCd oblique view would have assisted in correct diagnosis of MCD in three cases; in two dysplastic joints given grade 0, and in one normal joint given grade 1, taking the total number of correct diagnoses to 25 out of 26. Sensitivity and specificity of osteophytes seen on the CrCd oblique radiograph were 93% and 92%, respectively (Table 8).

Study IV

5.6 Diagnosis of the lumbosacral transitional vertebra

An LTV was diagnosed in 92 dogs (40%), based on VD and/or LL radiographs. Ten dogs with eight vertebrae were included in the LTV group. In six of these dogs, the only abnormal radiological finding was a short and caudally positioned L8. Of the 228 dogs, 217 (95%) had seven, ten (4%) had eight and one with an LTV (0.4%) had six lumbar vertebrae.

An LTV was diagnosed from both projections in 15 (16%) of 92 cases, from only the VD radiograph in 62 cases (67%) and from only the LL radiograph in ten cases (9%). All of the cases diagnosed based only on the VD projection had normally fused sacral bodies. All dogs with eight lumbar vertebrae were diagnosed by the LL projection only. A significant improvement ($p = 0.003$) was detected in the sensitivity of the diagnosis when the LL projection was used together with the VD projection compared with the VD projection alone.

A CT study had been performed on 16 dogs; nine had an LTV and seven were normal. In CT images, a deep indentation between the first and second spinous process of the median crest (Figure 29) was seen in five dogs. In VD radiographs, this was seen as separation of the S1 spinous process from the median crest of the sacrum (Figure 17C). One dog classified as type 4 based on radiographs was diagnosed as having a small unilateral transverse process (Figure 30). In two dogs, the classification based on ventrodorsal radiographs would have changed from lumbar to intermediate type (Figure 31).

Table 8 *Sensitivity and specificity for radiographic findings and grading of the 36 elbow joints in 18 Belgian shepherd dogs and of the 26 joints in 13 Labrador retrieverst*

	The present study					The initial screening			
	Blurring of MCP*	Subtrochlear sclerosis	Bony opacity on AP	Osteophytes CrCd	Grading	Blurring of MCP*	Subtrochlear sclerosis	Bony opacity on AP	Grading
Belgian shepherd dogs									
Sensitivity (%)	80	80*	40	N/A	60	80*	40*	60	40
Specificity (%)	90	90*	29	N/A	45	100*	97*	39	62
Labrador retrievers									
Sensitivity (%)	86	79*	N/A	93*	79*	N/A	N/A	N/A	N/A
Specificity (%)	83	75*	N/A	92*	92*	N/A	N/A	N/A	N/A

MCP= medial coronoid process, AP=anconeal process, CrCd=craniocaudal projection, N/A= not available, * = p Ò0.05

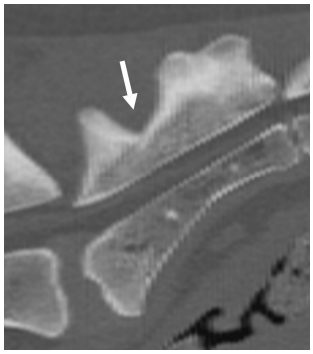

Figure 29 *Computed tomography midplane sagittal reconstruction image of the dog in Figure 17C, with separation of the first spinous process from the median crest of the sacrum (arrow).*

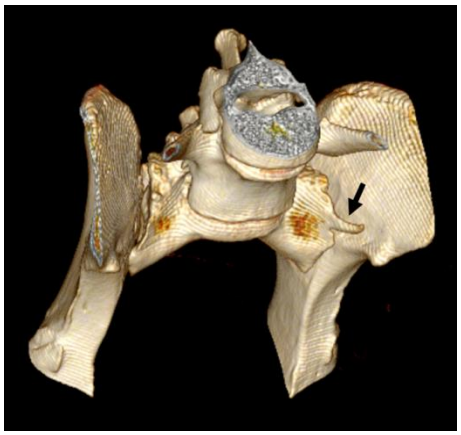

Figure 30 *Computed tomography volume-rendering technique image of the sacrum of a German shepherd dog radiographically diagnosed as type 4. A small transverse process on the left side, not visible on the radiographs, is seen (arrow).*

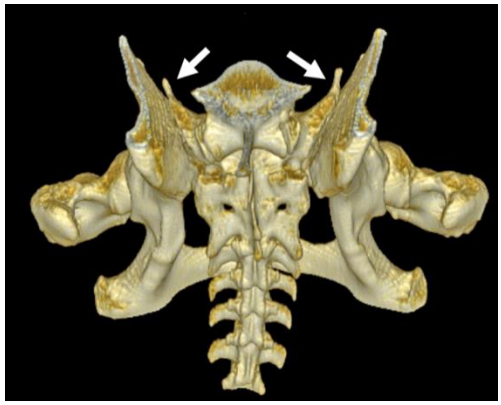

Figure 31 *Computed tomography volume-rendering technique image of the sacrum of a German shepherd dog diagnosed radiographically as a symmetrical lumbar type. The tips of the transverse processes (arrows) were superimposed on the iliac wings on the ventrodorsal radiograph.*

5.7 Eighth lumbar vertebra as part of the lumbosacral transitional vertebra complex

All dogs with L8, but none with normal lumbosacral junctions, had cranial position of the L7 in relation to the ilium (Figure 23C). Clear differences were detected in the relative length of L6/L7 when comparing dogs with any type of LTV and those with normal lumbosacral junctions (Figure 32). The proportion of dogs belonging to the group with L8 compared with the group with normal lumbosacral junction was 14.2-fold higher (95% CI 3.41 - 59.4) when the relative length of L6/L7 decreased by 0.1 units. The difference between LTV and type 4 against normal junctions was also significant, but a bit smaller; the odds ratios were 3.14 (95% CI 1.23 - 8.01) and 2.18 (95% CI 1.17 - 4.05), respectively. In other words, the longer the L7 in relation to the L6, the greater the probability of an LTV. Type 4 did not differ from the other types of LTV in the relative length of L6/L7.

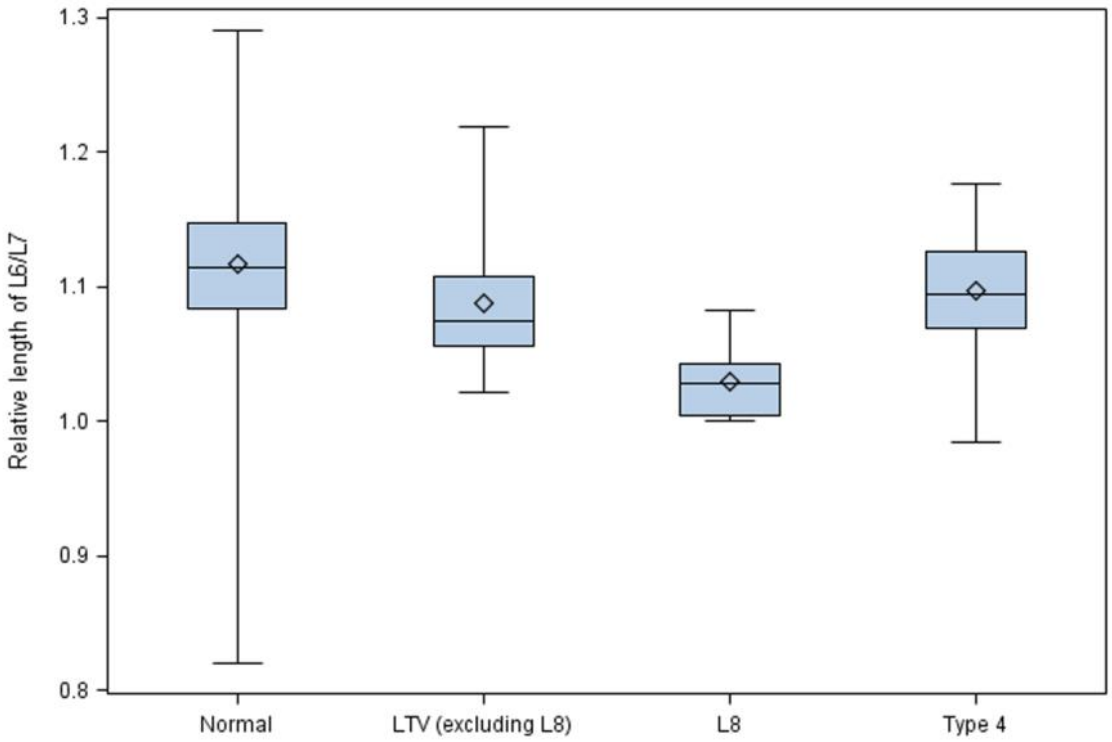

Figure 32 *Box plot of the mean relative length of the sixth and seventh lumbar vertebrae in the 228 German shepherd dogs, with median (horizontal line), mean (square), upper and lower quartiles (box), sample maximum (upper whisker) and sample minimum (lower whisker) indicated. Normal = normal lumbosacral junction, LTV = lumbosacral transitional vertebra of types 1–3, L8 = eighth lumbar vertebra, Type 4 = separation of S1 spinous process from the median crest of the sacrum.*

6 Discussion

6.1 Radiographic screening for intervertebral disc disease in miniature Dachshunds

The study was planned and conducted to look into the incidence of intervertebral disc calcifications in the Finnish miniature Dachshund population. The purpose was to determine how common calcifications were in the miniature Dachshund population in Finland. The miniature varieties were chosen because their populations in Finland were smaller than the populations of standard Dachshunds; the smaller the population, the fewer dogs needed for a meaningful analysis of the population. The proportion of dogs with calcifications was 76% in the long-haired miniature Dachshunds and 87% in the wire-haired variety, respectively. The incidence was clearly higher than in previous studies, where 40-60% of the Dachshunds had calcifications (Stigen 1996, Stigen 1991, Havranek-Balzaretti 1980). Several reasons for this can be proposed, but the genetic aspect is probably the most important (Mogensen et al. 2011, Jensen and Christensen 2000, Stigen and Christensen 1993, Ball et al. 1982, Funkquist and Henricson 1969). In many studies, the dogs were geographically from limited areas, potentially influencing the results. We sorted the dogs from the FKC register according to sire and postal code, thus ensuring that offspring of a certain sire or dogs from a certain area were not over-represented.

The proportion of dogs with ≥ 4 calcifications was high and even higher in the wire-haired (40%) than in the long-haired (28%) variant. The difference between breeds was, however, not significant. The age of the dog was unrelated to the number of calcifications, unlike in the study of Stigen (1996), where older dogs had more calcifications than younger ones. The finding of Stigen (1996) contradicts the studies of Jensen (2001) and Jensen and Arnbjerg (2001), where the number of calcified discs was highest at the age of two years.

The occurrence of IDD in Dachshunds with calcified discs varies between studies. It is difficult to make comparisons since the mean age of the dogs differs. According to a study of 100 dogs with a mean age of 7.4 years by Havranek-Balzaretti (1980), 79% of the dogs with calcified intervertebral discs had signs of IDD. Stigen (1996) found that 24% of dogs less than six years of age with calcifications had signs of spinal disease. In our study, 19% of dogs with calcified intervertebral discs had signs indicative of IDD. The mean age of radiographed dogs in our study was only four years and probably some of them developed clinical signs of IDD later in life, as the peak incidence of IDD is between four and six years (Priester 1976, Gage 1975). Our study was conducted several years ago, and since then new evidence of the relationship between number of calcified intervertebral discs and IDD has emerged (Rohdin et al. 2010, Jensen et al. 2008, Mayhew et al. 2004). Dogs without calcifications seldom appear to suffer from IDD (Jensen et al. 2008, Stigen 1996, Havranek-Balzaretti 1980). In our study, only one dog without calcifications had shown signs of IDD.

Since our study was published, over one thousand Dachshunds have been screened for intervertebral disc calcifications in Finland (Suomen Mäyräkoiraliitto 2012). However, only a small proportion of the Finnish Dachshunds are radiographed for intervertebral calcifications, and screening has not gained general acceptance amongst breeders. This

might improve in the future since the screening protocol has been accepted by the FKC, and from 1 June 2013 onwards the grading results will be saved in the FKC breeding database and be visible in open access pedigrees (KoiraNet… 2012) on the FKC web site. In Denmark, breeding instructions based on radiographic screening (dogs with ≥5 calcifications were not allowed to be used in breeding) has had a positive effect on BVEs (Indeks ryg gravhund… 2012). On 1 January 2013, the Danish Dachshund Club introduced a new protocol based on BVE, where the combined index for the intervertebral disc calcifications of the sire and dam of the planned mating must be ≥100 (the average dog has an index of 100; the better the dog, the higher the index). Studies on the effect of screening in reducing IDD in Dachshunds have yet to be published.

Chondrodystrophy is an anomaly in skeletal development that causes disproportionally short and curved extremities due to retarded and prematurely arrested closure of the growth plates. Early intervertebral disc degeneration accompanies this type of dwarfism (Hansen 1952). Hansen (1964) has postulated that curvature of the legs is proportional to the degree of chondrodystrophy and by breeding straight-legged Dachshunds the occurrence of IDD could be reduced. However, the differences in the curvature of the radius and ulna between individuals were very small in our study, and the curvature was not related to the IDD status of the dog.

6.2 Radiographic screening for elbow dysplasia in Belgian shepherd dogs and Labrador retrievers

We studied Belgian shepherd dogs and Labrador retrievers radiographically and with CT to evaluate the accuracy of the Finnish ED screening protocol in two different breeds. These breeds were chosen to the stydy since they have fairly similar screening statistics according to the Finnish Kennel Club's database (12% and 17%, respectively), but Belgian shephedrd dogs seldom have clinical elbow disease compared to Labrador retrievers (Fitzpatrick et al. 2009a, Groth et al. 2009, Coopman et al. 2008, Moores et al. 2008, LaFond et al. 2002, Guthrie 1989, Olsson 1983, Grøndalen 1982a).

The accuracy of the FKC grading of mild ED differed clearly between the breeds in our study. In Belgian shepherd dogs, grading based on the FKC protocol was unreliable, yielding high percentages of both false-positives and false-negatives. However, in Labrador retrievers the protocol proved to be accurate in grading dogs as dysplastic or non-dysplastic. In Belgian shepherd dogs, blurring of the cranial edge of the MCP and subtrochlear sclerosis were reliable signs of MCPD. In Labrador retrievers, the accuracy of radiographic signs indicative of MCPD was good and equivalent to the accuracy of grading. This suggests that the evaluation method used in Finland is adequate for Labrador retrievers, but less so for Belgian shepherd dogs. In Finland, evaluation of screening radiographs has recently changed to some extent, with grading focusing more on radiographic signs indicative of MCPD.

Radiographic screening for ED from one ML flexed radiograph is common in many countries, including Finland. Screening in all Nordic countries has mostly been based on secondary lesions, the main reason for this being difficulty in detecting primary lesions from radiographs, which are often of suboptimal technical quality (Audell 2005). It has been

proposed that secondary lesions, particularly osteophytes on the proximal aspect of the anconeal process, can be measured more reliably and used as indicators for ED (Olsson 1983, Grøndalen 1982a ,Grøndalen and Grøndalen 1981). However, the early studies did not focus on the indirect signs of MCPD, such as lack of visualization of the MCP and subtrochlear sclerosis, when evaluating the radiographs for MCPD.

The use of secondary lesions in a screening protocol where the minimum age is commonly 12 months is based on the assumption that osteophytes develop in juvenile animals. The first reports on ED mostly reported findings in Rottweilers, which usually develop elbow OA during adolescence (Grøndalen 1982a). In most instances, new bone formation is clearly seen on the anconeal process by the age of one year (Grøndalen 1982a). In our study, there were only minimal or no degenerative changes visible on radiographs of four of the five dysplastic joints in three Belgian shepherd dogs of different ages. This is in accordance with a prior report of arthroscopically confirmed MCPD in adult dogs with no or only mild OA (Meyer-Lindenberg et al. 2002). On the other hand, the secondary changes were visible on the radiographs of Labrador retrievers, and these changes were a good indicator of MCD in this breed.

Osteophytes arise usually first on the proximal surface of the anconeal process (Keller et al. 1997), where enthesophytes can also develop (Tellhelm 2007). A recent study showed that the insertion area of the olecranon ligament on the proximal aspect of the anconeal process is separate from the area where new bone develops, and the olecranon ligament is not involved in the process (Seelig 2010). It was impossible with certainty to differentiate osteophytes from normal anatomic variation of the anconeal process in Belgian shepherd dogs in our study using CT. However, differentiating between osteophytes and normal anatomy of the anconeal process might have less weight in evaluation of the screening radiographs in Belgian shepherd dogs if the radiological findings of MCPD weigh more in grading.

Osteophytes seen on the CrCd oblique view were the most sensitive sign of ED in Labrador retrievers. The dogs were several months older (mean age 22 months) than the minimum screening age of 12 months. It is not clear whether a supplemental CrCd oblique projection to the current protocol would increase the reliability of the grading if the dogs were screened at the age of 12 months. However, a CrCd view alone would have given a definite diagnosis of MCD in 19% of the joints, as a subchondral bone defect in the medial humeral condyle was observed. Additionally, the CrCd oblique view might increase reliability of assessing OA, and it would also give increased confidence in grading the joint as dysplastic with ED grade 3 instead of ED grade 1 due to a confirmed primary lesion.

One Labrador retriever had unilateral flexor enthesopathy. The bone fragment clearly visible in the CrCd oblique view was not seen in the ML flexed view. This condition is not considered a part of ED (Kirberger 2006), but since it can be a cause of lameness (de Bakker et al. 2012a) and is thought to be hereditary in Labrador retrievers (Paster et al. 2009), collecting data as part of the screening protocol would be beneficial. Without a CrCd view, a substantial proportion of these lesions could be missed (de Bakker et al. 2012a). On the other hand, CrCd oblique projection was not helpful in screening for ED in Belgian shepherd dogs, again emphasizing differences between breeds.

6.3 Radiographic screening for lumbosacral transitional vertebra in German shepherd dogs

Incidence of LTV in German shepherd dogs was 40% in our study, which is markedly higher than in previous studies (Damur-Djuric et al. 2006, Larsen 1977). At least two explanations exist for this discrepancy. In our study, separation of the S1 spinous process from the median crest of the sacrum was classified as an LTV, which partly explains the high incidence since the aforementioned radiographic sign was found in 62 (27%) dogs. In a recent study (Wigger et al. 2009) in which separation of the S1 spinous process was classified as LTV, the incidence of LTV was 29%. The other reason for the high incidence in our study was that dogs with L8 as the only abnormal finding were classified as having an LTV, in contrast to earlier studies.

The last presacral vertebra (L8) resembled LTV in LL radiographs; it was short and caudally positioned in all ten dogs with L8. The angle and disc space of the lumbosacral junction in these dogs resembled the normal condition, but the position of the L8 relative to the ilium was near the normal S1 vertebra. Additionally, L7 was positioned more cranially in relation to the ilium and the relative length of L6/L7 was smaller. These findings support those of a study of the vertebral canal in dogs with numerical vertebral variation, where the widest diameter of the vertebral canal was at the same level in dogs with seven and eight lumbar vertebra, if L8 was assumed to be S1 in the dogs with eight lumbar vertebrae (Breit and Kunzel 2002). Additionally, the relative length of L6/L7 in our study was comparable in dogs with separation of the S1 spinous process from the median crest as the only abnormality and dogs with LTV, suggesting similar morphology.

The LL lumbar spine projection used in our study made the diagnosis of L8 possible. A significant increase occurred in the diagnostic accuracy of LTV when the LL radiograph was included in the protocol in addition to the VD projection. Every missed case on the VD projection had L8. On the other hand, some of the radiographic signs, such as separation of the S1 spinous process from the median crest of the sacrum, were visible only on VD projection.

With CT, we showed that variation of morphology in the LTV was wide, even with the rather small number of cases. The dogs were classified into intermediate (type 2) or sacral (type 3) types based on visibility of the transverse process in the VD radiographs. This classification proved to be suboptimal since the visibility of the transverse processes of the LTV on radiographs was dependent on the projection and superimposition of the ilium, which influenced the classification.

In Switzerland, the Swiss Dysplasia Committee recently introduced a four-scale grading, in which type 0 is a normal lumbosacral area, type 1 is a sacrum with S1 separated from the median crest of the sacrum, type 2 is a symmetrical LTV and type 3 is an asymmetrical LTV (Flückiger et al. 2009). This grading was not published when we planned our study, but it seems reasonable since it does not attempt to classify the LTV based on the appearance of the transverse processes, which can lead to erroneous classification, as observed here.

Separation of the S1 spinous process from the median crest as the only abnormality might be a genetically mild form of the LTV, and selection against the trait could decrease the incidence of more serious forms of the LTV in German shepherd dogs. The L8 appeared

to be part of the LTV complex, and therefore, it seems sensible to establish L8 and the LL projection as parts of the screening protocols. In the FKC, screening for LTV will begin on 1 June 2013, and the projections used in this study are required in the protocol. The grading will be similar to the one used in Switzerland, but in Finland there will also be a type 4 for an abnormal number of lumbar vertebrae (L8 and L6).

6.4 Limitations of the study

The main limitation of **Study I** was the wide age range of participating dogs. For more accurate assessment of the number of calcified intervertebral discs per dog, the dogs should have been two to three years old. At the time of the study, the appearance of calcifications before two years of age and the disappearance thereafter had not yet been reported (Jensen and Arnbjerg 2001, Jensen 2001). The dogs radiographed at a suboptimal age might have influenced the number of affected dogs, and hence, the incidence of intervertebral calcifications. Still, the incidence of several calcifications was high in both breeds (28% in long-haired and 40% in wire-haired variations), and this was an important observation for future screening recommendations.

The main limitations of **Studies II and III** were the small number of dogs and the lack of arthroscopic confirmation of the status of joints assessed as free of ED. Participating dogs were clinically sound, and hence, arthroscopy was not performed. Instead, CT was used as the gold standard, although some lesions might not be visible with this modality (Groth et al. 2009, Moores et al. 2008). The best predictor for an abnormal arthroscopic examination has been shown to be the presence of osteophytes on CT images (Moores et al. 2008). This gives support that our results are reliable since the osteophytes seen on CrCd oblique radiographs were also visible on CT images.

None of the dogs with ED were found to be lame on orthopaedic examination, but it is possible that lameness could have been revealed using force plate analysis (Voss et al. 2007).

A limitation of **Study IV** was the lack of radiographs of the total spine since it can be argued that a transitional vertebra in the thoracolumbar junction can cause the extra vertebra. However, the markedly caudal position of L8 speaks in favour of an LTV.

7 Conclusions

The four studies were conducted to establish new screening protocols in Finland (**Studies I** and **IV**) and to identify ways of improving the current ED protocol (**Studies II** and **III**).

1. The occurrence of intervertebral disc calcifications in Finnish miniature Dachshunds was high, 76% in the longhaired and 87% in the wirehaired variety. Therefore screening protocol excluding every dog with calcifications from breeding would not be possible. Screening for intervertebral disc calcifications in Dachshunds commenced in Finland based on our study as well as on other studies published at that time.

2. Radiographs of the radius and ulna are of no benefit in breeding programmes for IDD in Dachshunds, as there was no difference in the curvature of the ulna between dogs with and without symptoms of IDD.

3. In Belgian shepherd dogs, osteophytes should not be used as the sole criterion when screening for ED, as both sensitivity and specificity were ≤ 62%. In Labrador retrievers the Finnish screening protocol based mostly on osteophytes can be considered adequate, as agreement between grading and ED status was substantial (kappa 0.69). Including the CrCd oblique projection in the protocol would assist in grading subtle cases and also reveal MCD in Labrador retrievers. To decrease the prevalence of MCD in this breed, it is crucial that dogs with "mild" (grade 1) ED are not used for breeding. Most of these dogs have MCD, as shown here.

4. LL radiographs of the lumbar spine would be a valuable supplement in the screening protocol for LTV in German shepherd dogs, as it increased sensitivity of the diagnosis with 10% and made diagnosis of L8 possible.

5. L8 appeared to be part of the LTV complex, as it resembled S1 in position and length. Including it in the screening programs of LTV is proposed.

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