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# EVALUATION DE NOUVELLES PROCEDURES GUIDEES PAR IMAGERIE SUR LA COLONNE LOMBO-SACREE DU CHIEN

# ASSESSMENT OF NEW IMAGING-GUIDED PROCEDURES OF THE LUMBOSACRAL SPINE IN DOGS

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# LIST OF ABBREVATIONS

*Anulus fibrosus* (AF)

Cerebrospinal fluid (CSF)

Computed tomography (CT)

Computed tomographic myelography (CTM)

Degenerative lumbosacral stenosis (DLSS)

Endplates (EPs)

Epidural steroid infiltration (ESI)

Fine needle aspiration (FNA)

Intervertebral disc (IVD)

Intervertebral disc degeneration (IVDD)

Lumbosacral (L-S)

Lumbar vertebra (L)

Magnetic Resonance Imaging (MRI)

*Nucleus pulposus* (NP)

Sacral vertebra (S)

Ultrasound (US)

# **INTRODUCTION**

# I.1. INTERVENTIONAL RADIOLOGY

## ***I. 1. a: Introduction to interventional radiology:***

Interventional radiology is a branch of modern medicine, which provides image guidance to gain access to organs for diagnostic and therapeutic procedures. The first developing branch of interventional radiology concerned the cardiovascular field with angiography being one of the most important applications of interventional radiology in adult and pediatric patients (Kaufman, 2014; Kandasami *et al.,* 2016). Nowadays, in both human and veterinary medicine, imaging-guided procedures are performed in many other fields, essentially with a diagnostic or therapeutic aim (Vignoli et Saunders, 2011; Mahnken *et al*., 2013; Sainani *et al.,* 2013). Theoretically, all the imaging modalities that provide a good anatomic spatial resolution of the target and surrounding anatomical structures can be used to perform interventional imaging. A good visualization of the surrounding anatomical structures is the key of imaging-guidance procedures, with the intrinsic advantage of avoiding critical anatomical structures, compared to the " blind" technique (Mahnken *et al*., 2013). Among the different techniques, fluoroscopy, ultrasound (US), or computed tomography (CT)-guidance are well-established methods, while magnetic resonance (MRI)-guidance has been performed only more recently (Mahnken *et al*., 2013; Kaufman, 2014; Mikhail *et al.,* 2015).

1) Fluoroscopy provides real-time images with high spatial resolution. It is used during musculoskeletal procedures such as percutaneous osteosynthesis or intraarticular drug injections. It can also be used in conjunction with the administration of contrast medium, making this technique particularly suitable for vascular interventions. However, it is a 2D technique, has a low soft tissue contrast resolution and exposes patient and operator to radiation (Mahnken *et al*., 2013).

2) The great advantage of US is the real-time visualization of the needle insertion, low cost and absence of radiation exposure. However, its field of view is limited and bone or air can limit the field of application. It is therefore considered the technique of choice for superficial targets, especially for musculoskeletal procedures (Mahnken *et al*., 2013; Amber *et al.,* 2014; Wilson *et al.,* 205; Orlandi *et al.,* 2016). US-guidance can either be freehand or with needle guidance (Vignoli et Saunders, 2011; Mattoon et Nyland, 2015). The first technique requires more experience, but it is the most versatile. The needle guidance system, on the other hand, uses a biopsy guide attached to the transducer, which makes visualization and insertion of the needle easier. However, the fixed angle of the needle can cause physical limitations making this technique less versatile (Vignoli et Saunders, 2011; Mattoon et

Nyland, 2015). US guidance can also be indirect. This means that the features of the target of interest (size, depth, proximity with other organs) and the needle insertion pathway (depth and angle of insertion) are determined with US, but the insertion of the needle is performed blindly (Vignoli et Saunders, 2011; Mattoon et Nyland, 2015).

3) In contrast, 3-D reconstructions, typical of cross-sectional imaging modalities such as CT or MRI, allow a better visualization of the target and therefore a better planning of the path to the target (Schwarz and Puchalski, 2011; Mahnken *et al*., 2013). However, CT is not a real-time visualization technique. The introduction of CT-fluoroscopy combines the advantages of both fluoroscopy and CT and allows the reduction of the procedure's duration, real-time visualization of critical anatomical structures and faster images reconstruction. In contrast to conventional CT-guidance, radiation exposure of the operator cannot be avoided and it is more expensive (Mahnken *et al*., 2013; Paik, 2014).

4) Besides imaging without ionizing radiation, MR imaging offers advantages such as high soft-tissue contrast, multiplanar imaging without reconstructions, and the ability to measure multiple physical or functional parameters (including flow, perfusion, diffusion, and temperature). However, rapid acquisition sequences and a more open magnet design are required to permit easy access to the patient during the procedure (Westbrook *et al.,* 2011; Campbell-Washburn *et al.,* 2015). Flexible transmit and receive coils have been specially designed to allow access to patients for interventions (Westbrook *et al.,* 2011). Low field permanent magnets are considered the best from the access point of view, but on the other hand their use is limited because of image quality and acquisition time (Westbrook *et al.,* 2011). The restricted availability of MR scanners and special coils, and the need of dedicated non-ferromagnetic biopsy instruments are therefore limiting the use of MRI-guided procedures in both human and veterinary patients (Vignoli et Sanders, 2011; Mahnken *et al*., 2013). Moreover, ferromagnetic materials such as orthopedic protheses or identification chips can be present within the patient and are associated with large imaging artefacts preventing imaging of the area of interest (Gavin, 2009a).

In addition to these classic imaging-guided procedures, the injection of contrast medium is usually suggested to verify the correct position of the needle during different kind of procedures (Johnson *et al*., 1999; Watanabe *et al*., 2002; Bartynski *et al*., 2005).

Imaging-guided procedures can be used as diagnostic or therapeutic means (or as both) or to guide anesthetic procedures, increasing the likelihood of reaching the anesthetic target. The most common imaging-guided diagnostic procedures are fine needle aspiration

(FNA) or biopsy. Ultrasound or CT-guided biopsy or FNA are well-established methods, while MRI-guidance has only been performed more recently. In human medicine, the imaging-guided therapeutic procedures are essentially used in interventional oncology, in the musculoskeletal field, and for pain management (Mahnken *et al.*, 2013; Lee *et al.,* 2016).

a) Thermal ablation is one of the main fields of interventional oncology (Beland et Mayo-Smith, 2014). Its basic aim is to decrease tumor size or to destroy tumor cells by means of heat. Applied imaging-guided techniques of thermal ablation are radiofrequency ablation, laser interstitial thermotherapy, microwave ablation, and high-intensity focused US (Beland et Mayo-Smith, 2014). Another commonly performed therapeutic imaging-guided technique of local tumor ablation is percutaneous ethanol injection. Injection of ethanol leads to tumoral tissue necrosis and local secondary fibrosis (Beland et Mayo-Smith, 2014).

b) In the musculoskeletal field, imaging-guided procedures can vary from local ablation of an osteoid osteoma to percutaneous vertebroplasty or osteoplasty (Irani *et al.,* 2014). Moreover, imaging techniques, more commonly CT or fluoroscopy, are commonly used to guide minimally invasive fracture reductions.

c) In the anesthetic field, imaging-guided procedures, essentially US-guided, are widely used to perform epidural anesthesia (Grau *et al.*, 2001; Karmakar *et al.*, 2009; Bauer *et al.*, 2012) or local plexus blocks (Marhofer *et al.*, 2005; Mejia-Terrazas *et al.*, 2015; Sehmbi *et al.*, 2015; Seidel *et al.*, 2015; Amini, 2016; Neal, 2016). The increased popularity of US-guided epidural anesthesia has been attributed to a more accurate estimation of the depth of the epidural space, and a more optimal determination of the needle path especially in cases of vertebral canal malformations, in cases of obesity, or in obstetric patients where hormonal changes can influence spinal and epidural anatomy (Grau *et al.*, 2001; Karmakar *et al.*, 2009; Bauer *et al.*, 2012). Moreover, US guidance has made nerve blocks a technically feasible, safe, and efficacious option, allowing surgery to be performed without general anesthesia (Mejia-Terrazas *et al.*, 2015; Sehmbi *et al.*, 2015; Seidel *et al.*, 2015).

More specifically, in veterinary medicine interventional radiology has predominantly been used in the diagnostic field, and US or CT-guided FNA or biopsies are commonly performed (Vignoli *et al.*, 2004; Schwarz et Saunders, 2011; Vignoli et Saunders, 2011; Mattoon et Nyland, 2015). Moreover, in recent years, the combined use of several imaging techniques has provided superior diagnostic information. For instance, the US-guided injection of contrast medium is commonly performed to improve the safety and the quality of other diagnostic studies such as pyelography, portography, lymphography, peritoneography (Mattoon et Nyland, 2015) or myelography (Etienne *et al*., 2010).

More recently, imaging-guided therapeutical procedures have been described as in human medicine. The target of these procedures is quite various, involving all the fields of veterinary medicine. For instance, US-guided ethanol injections for the treatment of hyperparathyroidism, hepatic or renal cysts/abscesses, or cervical tumors, as well as US-guided radiofrequency heat ablation have been described (Ahmed *et al.,* 2003; Zatelli *et al.,* 2005; Agut *et al*., 2008; Mattoon et Nyland, 2015). In horses, many studies have been performed focused on the description of US-guided techniques to perform neurological (Audigié, *et al.,* 2004; Pease *et al.,* 2012; Depecker *et al.,* 2014; Mackay, 2014), anesthetic (Morath *et al.,* 2013; O'Neil *et al.,* 2014) or orthopedic procedures (Perrin *et al.,* 2015; Levis *et al.,* 2016; Withcomb et al., 2016). Recently, there also has been an increased interest in therapeutical interventional procedures of the spine in dogs, leading to the description of many imaging-guided techniques (Levy *et al*., 2014; Mackenzie *et al*., 2014; Kneissl *et al*., 2015). These preliminary studies describe and test the feasibility of imaging-guided techniques for the injection of therapeutic molecules perineurally, within the intra-articular facet joints, or within the intervertebral disc (IVD).

As in human medicine, imaging-guidance is used in dogs and cats to perform anesthetic procedures and improve their success rates. The US anatomy of different plexus and nerves (brachial plexus, femoral nerve, sciatic nerve), as well as US-guided anesthetic procedures have been described (Anson *et al.,* 2013; Viscasillas *et al. 2014*; Guilherme et Benigni, 2008; Campoy *et al*., 2010; Echeverry *et al*., 2010; Haro *et al*., 2011; Gregori *et al*., 2014; Anson *et al.,* 2015).

### ***I. 2. b: Interventional spinal pain management in human medicine:***

Low back pain and radiculopathy are common debilitating diseases in human medicine and they are commonly treated by percutaneous injections of corticosteroids within the epidural space (Wilkinson et Cohen, 2013). The mechanism of action of corticosteroids is not completely understood. Suppression of prostaglandin synthesis, decreased formation of inflammatory leukotrienes, decreased edema formation, osmotic dilution and washout of inflammatory cytokines, as well as local enhancement of the blood flow to ischemic nerve roots are among the proposed mechanisms of action (Wilkinson et Cohen, 2013). The target of these injections can be the facet joints or the epidural space (Peh, 2011; Wilkinson et Cohen, 2013). "Blind" techniques can be used, but with a variable success rate depending on the target. For instance, it has been showed that inappropriate needle position can occur in 20-40% of epidural injections (Watanabe *et al.*, 2002; Bartynski *et al.*, 2005). Therefore, many imaging-guided percutaneous techniques have been developed to decrease the failure rate, involving fluoroscopy, CT or US (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002; Hoeltje *et al.*, 2013). Among them, CT-guidance is the preferred modality to perform both facet joint and epidural injections, because the precise and safe needle insertion into the target allows a high accuracy (Hoeltje *et al.*, 2013).

The choice of the technique depends on the target position and different approaches have been used. For facet joint injections, the orientation angle of the needle depends on the conformation of the articular processes (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002; Hoeltje *et al.*, 2013). For epidural injections, a translaminar (synonymous: interlaminar) or a transforaminal access can be used (figure 1). When performing the translaminar access the needle is inserted dorsoventrally in a sagittal plane , passing through the interarcuate ligament to reach the interarcuate space between two adjacents vertebrae. For the transforaminal access, the needle is inserted in an oblique direction (dorsolaterally-ventromedially) to reach the intervertebral foramen. It allows injected molecules to spread more cranially and is the preferred modality in cases of bilateral or multiple spinal compressions, but it is associated with a high likelihood of subarachnoid contamination. On the other hand, the transforaminal access is the most target-specific and is the preferred modality in cases of lateralized or foraminal neural compressions, but it is associated with a high likelihood of inadvertent vascular puncture (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002; Hoeltje *et al.*, 2013).

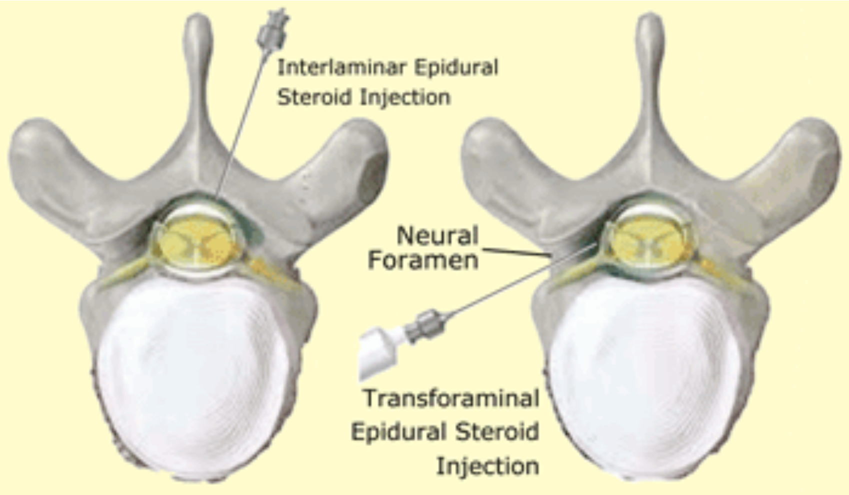


**Figure 1: Figure illustrating the translaminar (synonymous interlaminar) or transforaminal access.** ***Adapted from http: //updates.pain-topics.org/2012/01/harms-of-epidural-steroid-injections.html***

The interpretation of data relative to epidural steroid injections (ESI) is difficult and literature remains controversial about which access should be considered the most effective (Watanabe *et al.*, 2002; De Palma *et al.,* 2005; Carrage *et al.,* 2008; Roberts *et al.,* 2009; Staal *et al.,* 2009; Wilkinson et Cohen, 2013). Commonly, substances injected in the epidural space and facet joints are betamethasone, triamcinolone and methylprednisolone (Watanabe *et al.*, 2002; Peh, 2011; Wilkinson et Cohen, 2013). Local anesthetics such as lidocaine or bupivacaine can also be added, with possible long-term benefits (Watanabe *et al.,* 2002). Different amounts can be injected at the discretion of the physician. For instance, dose of triamcinolone and methylprednisolone can vary respectively between 5 and 80 mg and between 40 and 80 mg. However, no significant differences have been found between patients receiving different doses, concerning pain relief (Owlia *et al.,* 2007; Whynes *et al.*, 2012). Furthermore, no absolute recommendations are established according to the frequency of injections. A spaced procedure interval of 2 weeks is usually recommended and up to 2-3 injections are usually performed (Watanabe *et al.*, 2002; Peh 2011; ). Repetition of the series can be performed with different suggested intervals varying from 2 to 6 months (Watanabe *et al.*, 2002; Peh 2011).

# DEGENERATIVE LUMBOSACRAL STENOSIS IN DOGS

## *I. 2. a: Anatomy of the lumbosacral space:*

**(Adapted from: Fletcher, 1993; Pelagalli et Botte, 1999; De Lahunta et Glass, 2009)**

The lumbosacral (L-S) junction is defined as the bone and connective tissue that surrounds the *cauda equina*. Therefore, the anatomy of this region is complex and many different structures can be identified.

-Bone structures:

The bone structures surrounding the L-S junction are the last lumbar verterbra (L) and the three sacral vertebrae (S), which are fused in the adult and form a unique bone called the sacrum. The nervous and vascular structures pass through the intervertebral foramina that are usually formed by the cranial and caudal vertebral notch of two adjacent vertebrae. Given the fusion of the sacral vertebrae, the sacral intervertebral foramina are not present, but are replaced by the dorsal and ventral sacral foramina. Some anatomic variants exist and occasionally a supernumerary or a transitional vertebra can be present. At the L-S junction a transitional vertebra has mixed morphological features of both a lumbar and a sacral vertebra and it is more commonly present in the German Shepherd dogs and Greater Suisse Mountain dogs (Damur-Djuric *et al*., 2006).

-Neurological structures:

The *conus medullaris* is the last segment of the spinal cord, tapering into an elongate cone approximately at the level of the 6th -7th lumbar vertebra (L). Caudally to the *conus medullaris* the spinal cord is reduced to a terminal filament (*filum terminale)* (Fletcher, 1993; Pelagalli et Botte, 1999). L6, L7, S1-S3 and the first to the fifth caudal spinal nerve roots stream caudally to the *conus medullaris* to reach their respective intervertebral foramen. Collectively, these roots are referred to as the *cauda equina* (figure 2). The peripheral nerves originating from the *cauda equina* are the *n. femoralis, n. ischadicus, n. pelvicus, n.sacralis, n. pudendus,* and *n.caudales*. Their clinical significance is illustrated in Table 1.

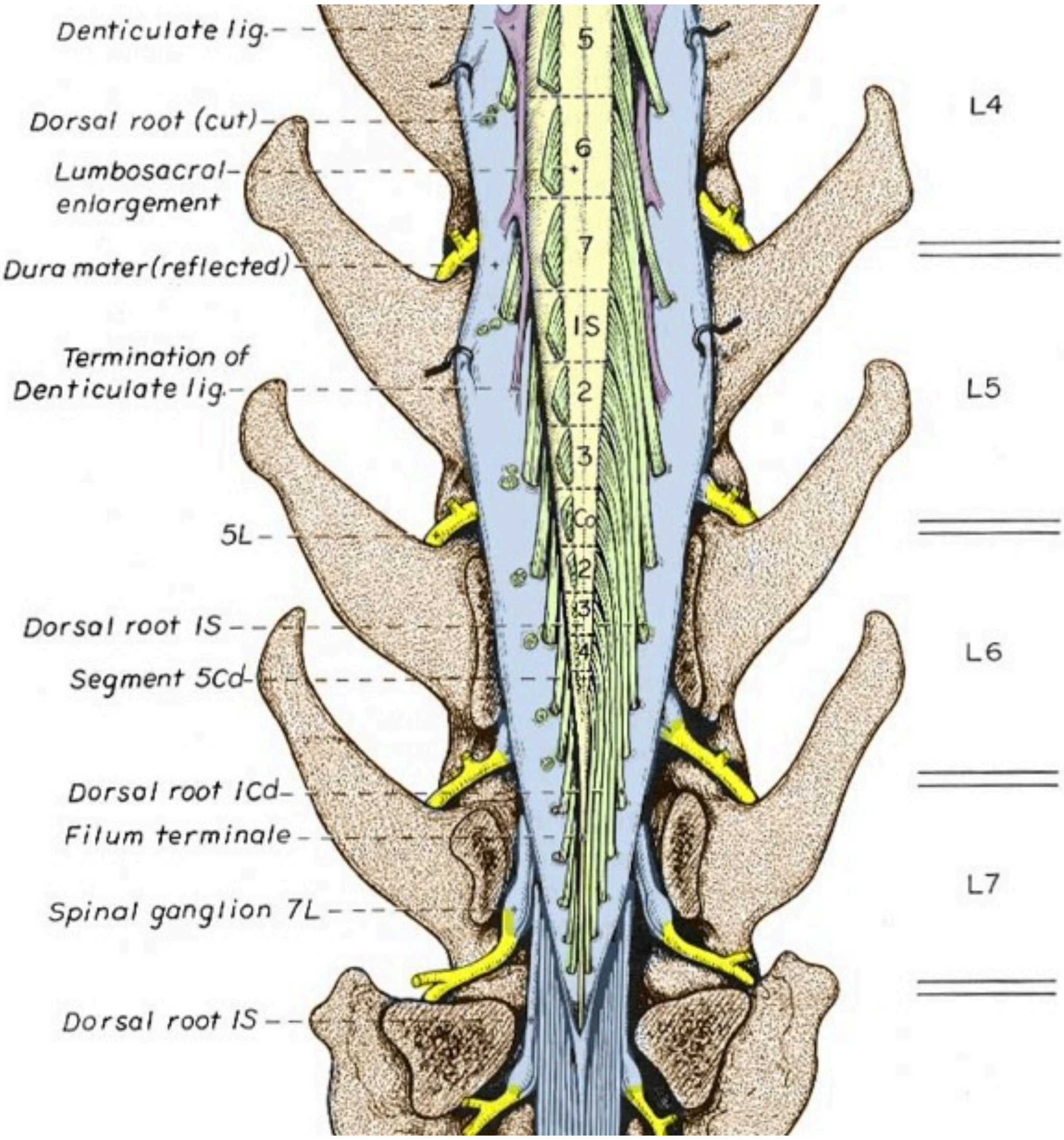


**Figure 2: Enlarged dorsal view of the terminal spinal cord in dogs.**
***Adapted From: http://vanat.cvm.umn.edu/neurLab2/SpCdGross. (17/11/2015).***
**(1Cd= Fisrt sacral nervous root; 1S= First sacral nervous root; 5L= Fifth lumbar nerve; 5Cd= Fifth caudal spinal segment; 7L= Seventh lumbar nerve; Cd= Spinal caudal segment; L4= Fourth lumbar vertebra; L5= Fifth Lumbar vertebra. L6= Sixth lumbar vertebra; L7= Seventh lumbar vertebra ).**

**Table 1.** ***Cauda Equina*****: origin and clinical function of the spinal nerves.**

| Nerve | Segment | Reflex | Function |
|---|---|---|---|
| N. *femoralis* | Ls4-Ls6 | Patellar | Flexion hip<br>Extension stifle |
| N. *ischiadicus* | Ls6-Ss1 | Cranial Tibial<br>Gastrocnemius<br>Withdrawal | Extension hip<br>Flexion stifle<br>Flexion and extension of tarsus<br>Proprioception |
| N. *pelvicus* and *sacrales* | Ss1-Ss3 | | Urinary bladder emptying |
| N. *pudendus* | Ss1-Ss3 | Perineal | Anal and urinary bladder sphincters |
| N. *caudales* | Cds1-Cds5 | | Tail tone |

**(N.= nerve, Ls= Lumbar spinal segment, Ss= Sacral spinal segment, Cds= Caudal spinal segment)**

-Meningeal structures:

Within the vertebral canal, the nervous system is surrounded by the meninges, which differentiate into 3 layers: the *dura mater*, the *arachnoidea,* and the *pia mater*. The *dura mater* is the most superficial layer and caudally envelops the *filum terminale* of the spinal cord. Before the *dura mater* constricts around the *filum terminale*, it forms a sac (dural sac) extending 1-2 cm beyond the end of the spinal cord, the dura mater spinalis. The epidural space separates the *dura mater spinalis* from the periosteum lining the vertebral canal. This space contains fat and the internal vertebral venous plexus. The latter lies on the floor of the vertebral canal. The epidural space is crossed by spinal roots traversing the vertebral canal to reach the intervertebral foramina. The *arachnoidea* is the intermediate layer and is separated from the *pia mater*, which is in direct contact with the spinal cord, by the subarachnoid space in which the cerebrospinal fluid (CSF) flows (figure 3).

The presence of the spinal cord with its surrounding meninges is at the L-S junction is variable. The *conus medullaris* or only the dural sac, which is accompanied by the spinal roots forming the *cauda equina,* can be present. The simultaneously presence of these three structures at the L-S junction is variable according to the breed, with small dogs having a relatively longer spinal cord and a dural end-sac extending well into the sacrum (Lang, 1988).

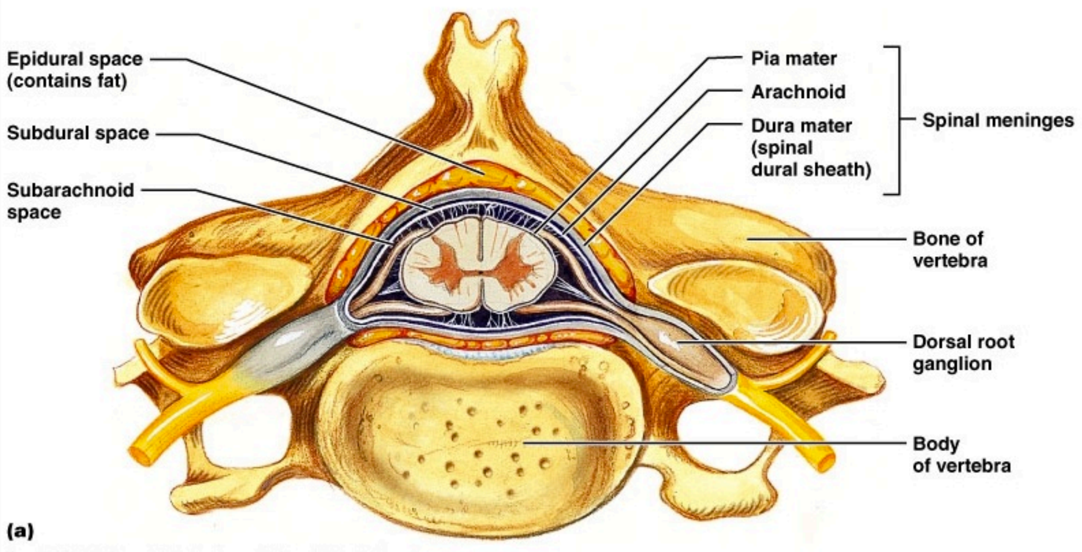
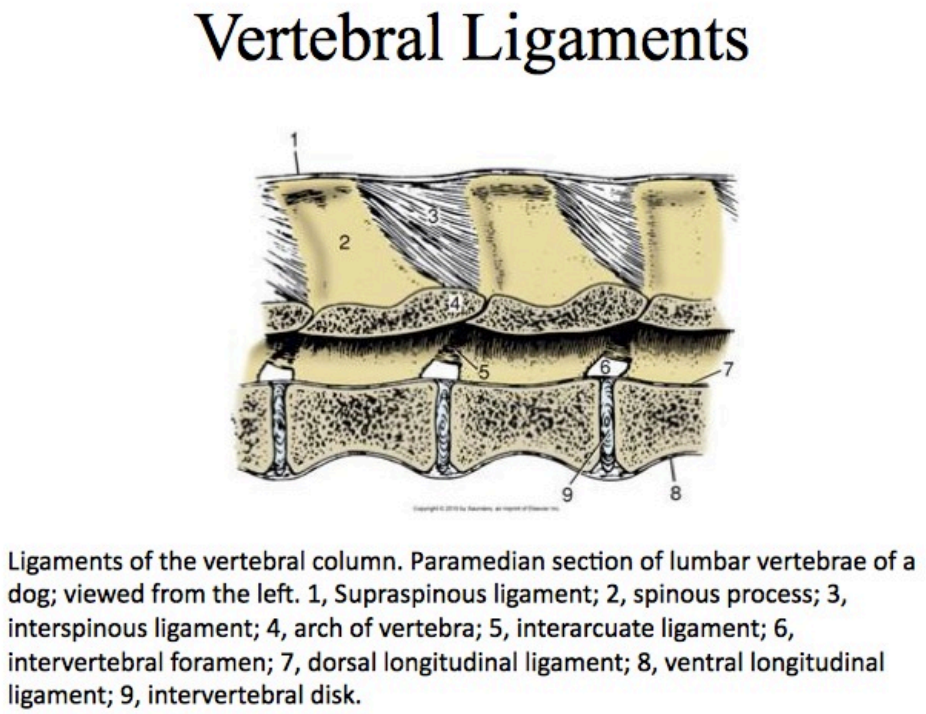


**Figure 3: Transverse image of one vertebra, showing the relationship between the bone, the spinal cord, the spinal meninges and the spinal nerve.** *Adapted from http: //www.apsubiology.org/ anatomy/ 2010/2010_Exam_Reviews/Exam_4_Review / CH _ 12 _ Gross _ Anatomy _ of _ the _ Spinal_Cord. htm (17/11/2015)*

-Connective structures:

The vertebral bodies are interconnected by the IVD. The outer layer of the IVD is the *anulus fibrosus* (AF), a poorly vascularised and barely innervated structure, which consists in a dense network of multiple, organized concentric fibrous lamellae that run obliquely into the adjacent intervertebral bodies. The internal aspect of the IVD is the *nucleus pulposus* (NP), an avascular and not innervated bean-shaped structure, essentially composed of water. Between the AF and the NP a transition zone is identified, which presents intermediate histological features between the adjacent layers passing from a fibrous to a more mucoid/cartilaginous structure (Bergknut *et al.*, 2013). The IVD is bordered cranially and caudally by the cartilaginous endplates (EPs) that are strongly connected with the inner aspect of the AF, whereas its outer aspect forms connections directly with the bony vertebral body epiphyses through the Sharpey's fibres (Bergknut *et al.*, 2013). Adjacent to the cartilaginous EPs there is a densely woven vascular network, which plays an essential role in supplying the IVD with nutrients (Bergknut *et al.*, 2013). The vertebrae are connected at the level of adjacent cranial and caudal articular processes by means of a facet joint consisting of a synovial joint capsule surrounding the articular processes. The L-S vertebral canal is further stabilized by the *ligament longitudinale dorsale* and by the *ligament longitudinale ventrale*, running on the dorsal and ventral aspect of the vertebral bodies respectively, and by the *ligamentum flavum* (synonymous: interarcuate ligament or yellow ligament) between the arches of adjacent vertebrae (figure 4).



Vertebral Ligaments

Ligaments of the vertebral column. Paramedian section of lumbar vertebrae of a dog; viewed from the left. 1, Supraspinous ligament; 2, spinous process; 3, interspinous ligament; 4, arch of vertebra; 5, interarcuate ligament; 6, intervertebral foramen; 7, dorsal longitudinal ligament; 8, ventral longitudinal ligament; 9, intervertebral disk.

**Figure 4: Parasagittal image of the lumbar vertebral column showing the vertebral ligaments**
***Adapted from* http://slideplayer.com/slide/3468966/ *(22/04/2015)***

## ***I. 2. b: Motion pattern of the lumbosacral junction and pathophysiology of degenerative lumbosacral stenosis:***

Terminology regarding *cauda equina* dysfunction is confusing: the term L-S disease refers to all the diseases affecting the L-S region, whilst the term *cauda equina* syndrome refers to neurological dysfunction, originating from compression, destruction, or displacement of the nerve roots of the *cauda equina* (Ramirez et Thrall, 1998; Thomas et Dewey, 2008). Therefore, many diseases can cause the *cauda equina* syndrome: vertebral malformation, idiopathic stenosis, discospondylitis, neoplasia, IVD disease, sacral osteochondrosis, vasculopathy, trauma, fractures, and degenerative lumbosacral stenosis (DLSS) (Meij et Bergknut, 2010).

Degenerative lumbosacral stenosis is a common disorder with a complex multifactorial, not completely understood, ethiopathogenesis, involving particularly the complex motion pattern of this area (Meij et Bergknut, 2010). Biomechanics of the L-S area have been investigated (Benninger *et al.*, 2004). The main types of motion, centered at the L-S IVD, are flexion and extension, whilst lateral and rotational movements seem less important (Benninger *et al.*, 2004). Some studies showed that abnormal motion is influenced by the angle of the articular joint processes, suggesting the articular process tropism as a possible cause of abnormal axial rotation and of increased torsional stress on the IVD (Seiler *et al.*, 2002; Rossi *et al.*, 2004). Moreover, several studies have evaluated how flexion and extension can affect the degree of neural compression, suggesting an intermittent stenosis secondary to gait movement in dogs affected by DLSS (Lang, 1988; Jones *et al.*, 1999; Benninger *et al.*, 2004; Benninger *et al.*, 2006; Gradner *et al.*, 2007; Reynolds *et al.*, 2014). Besides the genetic tropism or angle of articular processes, other causes such as L-S transitional vertebra (Fluckiger *et al.*, 2006) or osteochondrosis of the sacrum (Lang *et al.* 1992) have been shown to predispose to *cauda equina* syndrome. Furthermore, a recent study identified a skeletal and morphological variability of the L-S junction in German Shepherd dogs suggesting a primary L-S stenosis in this breed (Ondreka *et al.*, 2013). The abnormal motion patterns, independently of the underlying causes, and the secondary loss or lack of loadbearing proprieties have been proposed as the initial mechanism leading to IVD degeneration (IVDD). The secondary decrease in IVD width would lead to an ulterior shift of the load bearing from the central to the peripheral part of the spine, such as the ventral aspect of the vertebral bodies and the articular processes. This instability process would finally result in IVD herniation (Hansen Type I), secondary to the chronic IVDD, and in a compensatory proliferation of the surrounding structures (hypertrophy of the interarcuate ligament, epidural fibrosis, thickening of the capsules of the articular processes, osteophytes, and ventral spondylosis) with secondary stenosis of the vertebral canal and intervertebral foramina (De Risio *et al.*, 2000; Meij et Bergknut, 2010).

### ***I. 2. c: Signalement, history and clinical signs of degenerative lumbosacral stenosis:***

Typically middle-aged large-breed dogs and especially German Shepherd dogs and working dogs have a high predisposition to develop DLSS (De Risio *et al.*, 2000; Meij et Bergknut, 2010), increasing the suspicion of a genetic predisposition. Indeed, *cauda equina* syndrome was among the main causes of euthanasia of military German Shepherd and Belgian Shepherd dogs (Moore *et al.*, 2001). At presentation, owners complain about the dog's difficulty to rise, sit or lie down, jump or climb and about urinary or fecal incontinence (De Risio *et al.*, 2000; Sharp et Wheeler, 2005; Thomas et Dewey, 2008; Meij et Bergknut, 2010).

The main neurological finding is pain at the L-S region, evoked by hyperextending the tail or hyperextending the caudal lumbar spine (De Risio *et al.*, 2000; Sharp et Wheeler, 2005; Thomas et Dewey, 2008; Meij et Bergknut, 2010). The origin of the pain is multifactorial. It can be classified as radicular pain (originating from nerve root entrapment), meningeal pain (irritation of the meninges), osteoarthritic pain (degeneration of the periosteum, *ligament longitudinale dorsale* or joint capsules) or, to a lesser extent given the weak innervation of the IVD, discogenic pain (degeneration or tearing of the *AF*) (De Risio *et al.*, 2000). Pain may be manifested or exacerbated during exercise and may result in intermittent unilateral or bilateral lameness. The intermittent status, referred to as neurogenic intermittent claudication, is caused by the dilation of the radicular blood vessel secondary to exercise, causing/worsening the underlying interforaminal stenosis. (De Risio *et al.*, 2000) The neurological examination can also highlight proprioceptive and voluntary motor deficits (De Risio *et al.*, 2000; Sharp et Wheeler, 2005; Thomas et Dewey, 2008; Meij et Bergknut, 2010). The evaluation of spinal reflexes (including patellar, cranial tibial, gastrocnemius, withdrawal and perineal reflexes) is compatible with a lower motor neuron disease: decreased to absent withdrawal and gastrocnemius reflexes, hyperreflexive or normal patellar reflexes, decreased to absent perineal reflex, and proprioceptive deficits (De Risio *et al.*, 2000; Sharp et Wheeler, 2005; Thomas et Dewey, 2008; Meij et Bergknut, 2010).

### ***I. 2. d: Diagnostic imaging of degenerative lumbosacral stenosis:***

Diagnosis of DLSS is based on history, neurological assessment, and correlation of clinical findings and ancillary diagnostic imaging findings. Because of the anatomical features and the complexity of the disease's pathogenesis, several diagnostic-imaging techniques have been described to evaluate the L-S vertebral canal (Ramirez et Thrall, 1998; De Risio *et al.*, 2000; Meij et Bergknut, 2010). Some of these techniques, such as epidurography, discography, and vertebral sinus venography were used in the past, but they are not routinely performed nowadays because of the possible complications and their inability to assess the L-S structures entirely. These techniques have been replaced by CT and MRI, which are now considered the gold standard for diagnosis of DLSS (Meij et Bergknut, 2010). Radiography and myelography, however, can still be considered an important tool for the diagnosis of DLSS, if advanced modalities are not available or declined by the owner for financial reasons.

-Conventional and position-dependent ("dynamic") radiography:

In the past, many studies focused on the possibility of diagnosing DLSS with survey radiography, using different projections with neutral, flexion or extension of the L-S spine. The latter projections are also called stress, positional or "dynamic" projections. The use of the world "dynamic" is debatable. In fact "dynamic" is referred to as something characterized by constant change or movement. When "dynamic" projections are performed, the spine is not moving but it is in a static neutral, flexed or extended position. Therefore the word positional or position-dependent would be more appropriate. However, in literature the world "dynamic" is still widely used. Measurements performed on radiographs in flexed and extended positions aimed to highlight the possible abnormal motion pattern and the eventual instability of the L-S junction and to establish normal values for radiographic pattern (Mattoon et Koblik, 1993; Schmid et Lang 1993). However, results were controversial. For instance one study showed no difference in the degree of sub-luxation of the sacrum between normal and affected German Shepherd dogs (Schimd et Lang, 1993), whilst another study showed that a logistic model based on radiographic parameters (neutral L-S angle>170°, extension angle> 165°, a flexion angle >185°, a total range of motion <20°, a L-S point of intercept cranial to mid-body of L7 or caudal to S1) was able to discriminate normal from affected dogs with an overall accuracy rate of 86% (Mattoon et Koblik, 1993). Recently, it has been shown that the accuracy in detecting the cranial margin of the sacrum on x-rays is only fair (Blume *et al.,* 2015) and this should be taken into account when evaluating the position of the sacrum. However radiography has to be considered the first step in normal work-up for dogs with clinical signs compatible with *cauda equina* compression (Ramirez et Thrall, 1998; De Risio *et al*., 2000; Meij et Bergknut, 2010). Common radiographic findings in dogs affected by DLSS are L-S decreased IVD space, decreased intervertebral L-S foraminal space, spondylosis, degenerative joint disease of the articular processes, and ventral displacement "telescoping" of the sacrum (figure 5). These results are however not specific and a normal radiographic examination does not rule out the presence of L-S disease.

Furthermore, it has been demonstrated that there is no correlation between neurological and radiographic findings (Scharf *et al.,* 2004). Indeed, the main limitation of radiography is the poor ability to assess soft tissue, but on the other hand its great advantage is the possibility to rule out other causes of *cauda equina* syndrome, such as discospondilitis, fracture, luxation or neoplasia of the bone structures (Ramirez et Thrall, 1998; De Risio *et al.*, 2000; Meij et Bergknut, 2010).

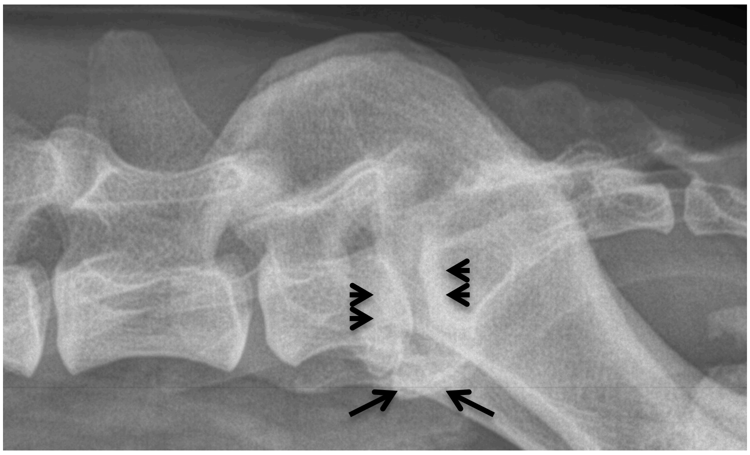


**Figure 5: Radiographic image of the lumbosacral region (latero-lateral projection). This dog presented lumbosacral spondylosis (arrows), sclerosis of the lumbosacral vertebral endplates (arrowsheads) and decreased lumbosacral intervertebral foramen size. These findings are common in dogs affected by degenerative lumbosacral stenosis (cranial of the dog to the reader's left; dorsal of the dog to the top of the image).**

-Myelography:

Myelography consists in the injection of contrast medium to visualize the subarachnoid space and to delineate the spinal cord contours (Roberts et Selcer, 1993). In the past, it was the modality of choice to investigate spinal cord compression (Ramirez et Thrall, 1998), which is usually visualized as an interruption and/or displacement of the contrast medium column. However, the accuracy of myelography for detecting L-S diseases is variable. First of all, it only allows detection of dural sac compressions. It has been demonstrated that the dural sac can extend beyond the sacrum in 80% of dogs, but its exact length cannot be assessed before contrast medium injection (Lang, 1988). Intervertebral foramina stenosis and compression of the spinal roots cannot be assessed with myelography and therefore a normal myelographic study does not rule out *cauda equina* compression (Ramirez et Thrall, 1998). A study focused on flexion-extension myelography ("dynamic" views) of the L-S region showed that size, shape and diameter of the dural sac was constant among the different views in normal dogs but highlighted that a variable degree of compression was visible in flexion/extension compared to the neutral position in affected dogs (Lang, 1988). These "dynamic" views can therefore increase the sensitivity of myelography (Lang, 1988). It has been reported that myelography can increase accuracy of CT for the detection of spinal compression (Shimizu *et al.*, 2009). Thus, in cases of non-diagnostic conventional CT examination, these two techniques can be used in conjunction to perform a CT myelography (CTM), *i.e.* a CT examination after the injection of contrast medium in the subarachnoid space.

-Computed Tomography:

Computed tomography is considered with MRI one of the gold standard procedures for the diagnosis of DLSS (Ramirez et Thrall, 1998; Meij et Bergknut, 2010). When performing a CT examination, different image reconstruction algorithms can be chosen. A medium spatial frequency algorithm associated with the use of a soft tissue window is considered the best to assess the soft tissue structures. Instead, high spatial frequency algorithms and a bone window are used to assess body parts with inherently wide contrast object such as bone (Schwarz et O'Brien, 2011). A specific CT protocol for the examination of the spine with dogs in dorsal recumbency has been recommended (100-120 kilovolts, 200 milliampere/ second, slice width of 1-2 millimeters) (Seiler *et al.,* 2011). In dogs affected by DLSS common findings using are disc herniation, hypertrophy of the interarcuate ligament and of the joint capsules, vertebral spondylosis, EPs sclerosis, sacral osteochondrosis, or ventral displacement of the sacrum (figure 6) (Ramirez et Thrall, 1998; Meij et Bergknut, 2010).

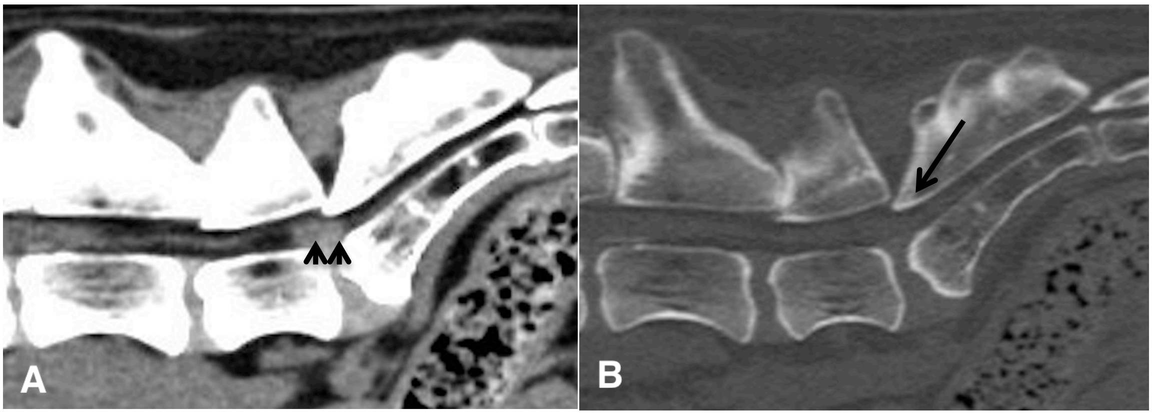


**Figure 6: Computed Tomography images (sagittal multiplanar reconstruction) of the lumbosacral region of dog affected by degenerative lumbosacral stenosis. In the soft tissue window image (A), a severe disc protrusion with loss of epidural fat is visible (arrowsheads). In the bone window image (B) the ventral displacement of the roof of the sacrum (arrows), called as "telescoping" is evident (cranial of the dog to the reader's left; dorsal of the dog to the top of the image).**

Moreover, it has been shown that intravenous injection of iodinated non-ionic contrast medium can help in the visualization of soft tissue, increasing the assessment of neural compression by soft tissue structures (Jones *et al.*, 1999). CT is faster and less expensive than MRI but its main disadvantages, beside the use of ionizing radiation, is its poor ability to assess soft tissue structures, such for example spinal cord and other nervous structures (Ramirez et Thrall, 1998; Meij et Bergknut, 2010). To increase the accuracy in detecting spinal cord compression, CTM can be performed combining the advantages of myelography and CT (figure 7). However, as for myelography the results of CTM depend on the length of the dural sac (figure 8).

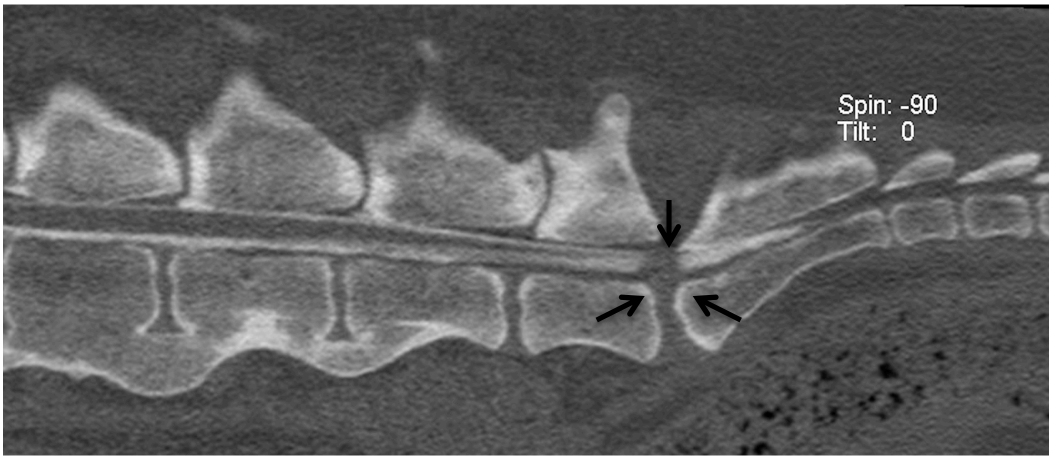


**Figure 7: Computed tomographic-myelography image of the lumbosacral region (sagittal multiplanar reconstruction, bone window, neutral position) in a dog affected by degenerative lumbosacral stenosis. The contrast medium fills the subarachnoid space of the lumbar spine and dural sac (myelography), but there is a focal loss of contrast medium visualization at the lumbosacral junction (arrows). This finding is indicative of spinal cord compression. Also notice the severe vertebral spondylosis affecting the cranial lumbar spine and the degenerative joint disease of the articular process (cranial of the dog to the reader's left; dorsal of the dog to the top of the image).**

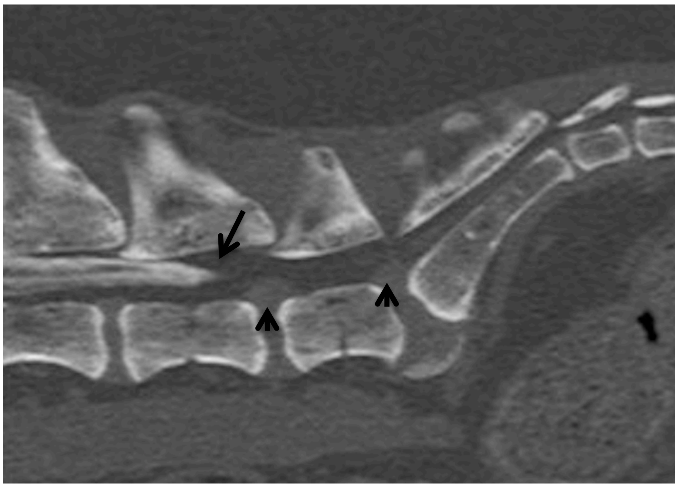


**Figure 8: Computed tomographic-myelography image of the L-S region (sagittal multiplanar reconstruction, bone window, neutral position). Discal protrusions (arrowsheads) are visible at L6-L7 and L7-S1, associated with L7-S1 spondylosis. In this dog, the dural sac filled by contrast medium ends at the level of the mid-body of L6, limiting the usefulness of the injection of contrast medium in the subarachnoid space to assess spinal cord compression.**

Similarly to CT and myelography, CTM examination of the L-S region can be performed with the spine in flexion and extension. The comparison between these views and the neutral position can point out a different degree of compression, usually more important during the extension of the LS spine, highlighting the intermittent nature of the compression (figure 9).

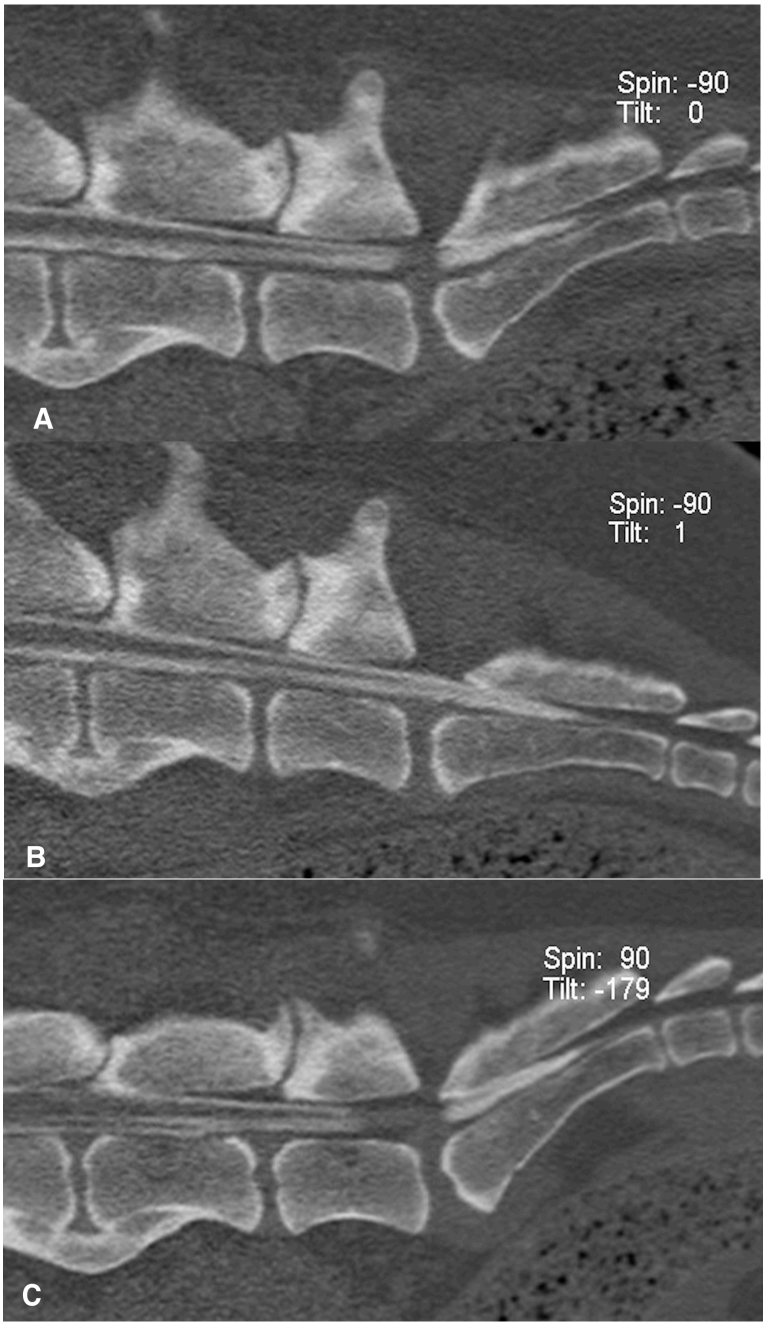


**Figure 9: Computed tomographic-myelography images of the lumbosacral region (sagittal multiplanar reconstruction, bone window) in a dog affected by degenerative lumbosacral stenosis. Images'acquisition has been performed with the lumbosacral spine in neutral position (A), in flexed position (B) and in extended position (C). The intermittent nature of the spinal cord compression, visible as a focal loss of contrast medium column, is noticed: the most severe compression is visible in the extended position, whilst no compression is visible in the flexed position (cranial of the dog to the reader's left; dorsal of the dog to the top of the image).**

-Magnetic Resonance Imaging:

In human medicine, MRI is considered the modality of choice for the detection of *cauda equina* compression. Flexion-extension studies have been used to highlight intermittent foraminal stenosis, in cases where no stenosis was visible in the neutral position despite the presence of significant clinical signs (Weishaupt *et al.*, 2000).

To perform an MRI examination of the spine different sequences can be chosen to highlight different anatomic and pathologic aspects (Gavin, 2009b). In T2-weighted images both fluid and fat are hyperintense. Bright fluid in images is desirable as most pathologic abnormalities have an increased fluid signal (Gavin, 2009b). In STIR sequences there is a uniform loss of fat signal, whilst fluid-filled structures are displayed as bright on a generalized dark background, making the identification of pathologic lesions easier (Gavin, 2009b). In T1-weighted sequences fat is hyperintense and fluid is hypointense. Abnormal tissue has often an increased vascular supply, therefore the administration of intravenous contrast medium leads to an increased signal intensity (Gavin, 2009b). More specifically on T2-weighted images, normal IVDs have a high NP signal surrounded by a medium AF signal. Epidural fat has very high signal intensity and appears bright white. The signal intensity is related to the concentrations of matrix hyaluronic acid and glycosaminoglycans, which in turn attract and hold water. Substances with highest glycosaminoglycans concentration, such as the IVD, will have a prominent T2 signal. On T1-weighted sequences, the normal IVD is of uniform medium signal intensity, slightly greater than that of the spinal cord, nerve roots and bone marrow. Common findings in dogs affected by DLSS are IVD degeneration and protrusion, loss of epidural fat or subarachnoid space visualization, and dural sac or nerve root compression (figures 10 and 11) (Ramirez *et* Thrall, 1998; De Risio *et al.*, 2000; Meij *et* Bergknut, 2010). However, studies focused on the comparison between MRI and clinical or surgical observations reported that the degree of compression determined by MRI at the time of presentation was not proportional to disease severity (Jones *et al.*, 2000; Mayhew *et al.*, 2002; Suwankong *et al.*, 2006).

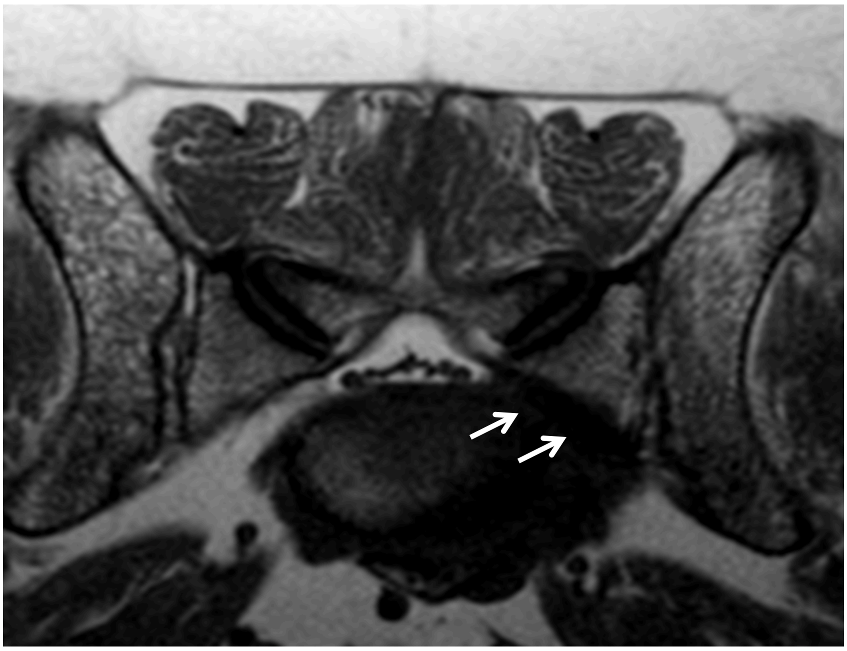


**Figure 10: Transverse T2-w magnetic resonance image of the lumbosacral region. Notice the complete obliteration of the left intervertebral foramen by severe lateral spondylosis (arrows) and the secondary absence of visualization of the foraminal epidural fat. Ventral spondylosis is also visible (right of the dog to the reader's left; dorsal of the dog to the top of the image).** ***Courtesy of Dr. V. De Busscher and Dr. Finck, ChesterGates.***

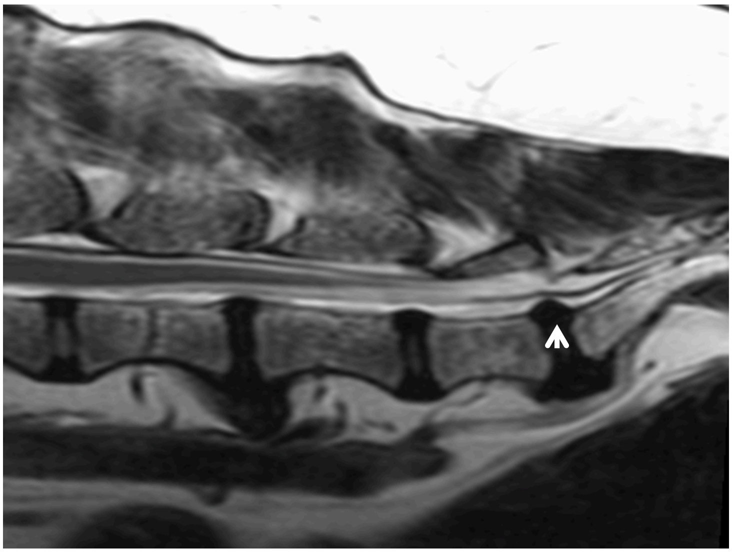


**Figure 11: Sagittal T2-w magnetic resonance image of the lumbosacral canal. There is a generalized loss of T2-w hyperintensity of the last lumbar intervertebral discs associated with protrusion dorsally within the vertebral canal. At the lumbosacral junction the intervertebral disc protrusion(arrowsheads) is more important and there is a secondary loss of epidural fat visualization and dorsal displacement of the *cauda equina* roots (cranial of the dog to the reader's left; dorsal of the dog to the top of the image).** ***Courtesy of Dr.V. De Busscher and Dr. Finck, ChesterGates***

-Computed Tomography *versus* Magnetic Resonance Imaging:

In general CT is the gold standard to evaluate bone structures, given the superior spatial resolution and the possibility to acquire thinner slices. Also, it is faster and cheaper than MRI (Da Costa et Samii, 2010). To increase visualization of spinal cord compression, myelography in conjunction with CT (*i.e* CTM) can be performed. However, this technique increases the duration of the procedure and the risk of complications associated with myelography (Da Costa et Samii, 2010). On the other hand, MRI has a better soft tissue resolution with a better assessment of all neural structures, as well as ligaments, joint capsule, and IVD and myelography is not unnecessary (Da Costa et Samii, 2010). Studies comparing agreement between different imaging modalities have been performed, focusing on different regions of the spinal cord and different diseases. For instance, a study comparing CT *versus* MRI in the diagnosis of DLSS showed a high agreement between these two modalities (Suwankong *et al.*, 2006). Another study evaluated the association between diagnostic findings with MRI and CT and outcome after surgical treatment. Both MRI and CT were effective to identify neural compression, but no significant association between results of imaging studies and postoperative outcome was identified (Jones *et al.*, 2000). In summary, considering its better soft tissue resolution, MRI can be considered the modality of choice for the detection of *cauda equina* compression. However, from a practical point of view, in veterinary medicine MRI systems are less available than CT scanners and more expensive. Therefore, CT examination of the L-S spine, especially if associated with myelography, can be considered a good alternative for the diagnosis of DLSS.

## ***I. 2. e: Treatments:***

Both conservative and surgical treatments have been proposed in cases of DLSS ( De Riso *et al.,* 2000; Sharp et Wheeler, 2005; Dewey, 2008; Meij et Bergknut, 2010).

-Conservative treatment:

The aim of conservative treatment is to reduce pain. It is based on body weight reduction, change in exercise pattern, predominantly by introducing a regular walking activity of short duration to maintain muscle tone, and the use of nonsteroidal anti-inflammatory drugs per os (De Riso *et al.,* 2000; Meij et Bergknut, 2010). However, toxicity of non steroidal anti-inflammatory drugs is reported, especially affecting the gastro-intestinal and renal system. Indeed, gastric ulcers and nephropathy are the most common reported complications (Khan *et* Mclean, 2012). A controversial opinion exists concerning the use of systemic corticosteroids because of their collateral effects (Meij et Bergknut, 2010). In a recent study, medical treatment in dogs affected by DLSS resulted in an overall success rate of 55% (De Decker *et al*., 2014). Lumbosacral ESI have also been proposed with an improvement in the 79% of the patients. However, in this retrospective study dogs' improvement was assessed by the owners following a prescheduled table and a systematic neurological evaluation was not performed (Janssens *et al*., 2009).

-Surgical treatment:

The aim of surgical treatment is to decompress the *cauda equina* and to free entrapped nerve roots. Candidates for surgical treatment are dogs with moderate to severe clinical signs (pain and neurologic deficits), unresponsive to conservative treatment (Meij et Bergknut, 2010). Among the suggested surgical techniques, the preferred modality is usually the dorsal laminectomy, which is sometimes followed by additional procedures when further decompression is required, such as partial discectomy consisting of dorsal fenestration (or dorsal annulectomy), nuclear pulpectomy (or nucleotomy), foraminotomy, and rarely, facetectomy (Sharp et Wheeler, 2005; Dewey, 2008; Meij et Bergknut, 2010; Saulnier-troff *et al.,* 2014). When ventral subluxation of S1 is present, stabilization by fixation and fusion can be suggested (Sharp et Wheeler, 2005; Dewey, 2008; Meij et Bergknut, 2010). Outcome after decompressive surgery ranges from good to excellent (Meij et Bergknut, 2010), but urinary and fecal incontinence are poor prognostic predictors with usually no improvement despite surgery (De Risio *et al*., 2001; Meij et Bergknut, 2010). Moreover, working dogs have less favorable results, probably related to their activity (Meij et Bergknut, 2010). Different intra, early or late postoperative complications have been described with surgical treatment. For instance, formations of adhesions between the nerves and the surrounding soft tissue or intra-articular fractures have been described with laminectomy and fixation-fusion technique (Sharp et Wheeler, 2005; Jeffery *et al.,* 2014).

-Conservative vs surgical treatment:

(Adapted from De Risio, 2000; Dewey, 2008; Meij et Bergknut, 2010)

Current treatments in dogs affected by DLSS are based primarly on severity of clinical signs. In a dog with pain, but in absence of neurological deficits, medical treatment is considered the first option. Besides the administration of NSAIDs, gabapentin can also be used as pain neuromodulator. Conservative treatment does not resolve the underlying problem and it tends to be eitheer transiently effective or ineffective.

In presence of moderate to severe lumbosacral pain, unsuccessful medical treatment or in presence of neurological deficits the surgical treatment could be the best option. The choice of the surgical method (dorsal laminectomy vs fuxion-fixation or foraminotomy) should be done after the imaging assessment of the spinal cord compression. The outcome of surgical treatment is good to ecellent (73% to 93%), even if complications such adhesions, implant failure, fracture of the articular process have been described. Urinary incontinence is considered a poor prognostic factor.

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# AIMS OF THIS PROJECT

# GENERAL AND SPECIFIC AIMS

## *II. 1. a: General aim of the project:*

Recently in veterinary medicine it has been an increased interest in developing new-imaging guided techniques with the final aim to reduce the failure rate of techniques, commonly performed blindly, or to guide the injection of molecules within the interest's target for therapeutic intent. Therefore, it was essential to investigate the feasibility of new imaging-guided techniques and to assess their accuracy and clinical safety. The final aim of this project was to develop new interventional radiological procedures of the L-S spine in dogs. Indeed, a variety of "blind" procedures with a variable failure's rate are commonly performed in this region and currently there are no highly successful therapies in the treatment of DLSS. For instance, among the "blind" procedures epidural anesthesia is commonly performed blindly, by palpation of the seventh lumbar spinous process and iliac wings. However, failure of the blind technique has been reported, predominantly related to obesity or congenital malformations of the vertebral column. In old dogs, especially large breed dogs, the L-S region is as well often affected by degenerative changes leading to the compression of the *cauda equina*. This disease is often multifactorial and IVD degeneration as well as degenerative joint disease of the facet joints are among the main causes of compression.

## *II. 1. b Specific aims of the project:*

The specific aims of this thesis were:

- to develop an US-guided epidural access of the L-S space, which could be potentially used to improve the epidural injections success rate;
- to develop CT-guided facet joints injections and CT-guided epidural injections at the L-S space and to assess their difficulty and accuracy;
- to assess the clinical safety of CT-guided steroid facet joints and epidural injections at the L-S space;

The hypothesis were that:

- It is possible and safe to perform US-guided epidural access at the L-S space;
- It is possible to perform CT-guided facet joints injections and different accesses of CT-guided epidural injections; the difficulty to perform these techniques and their accuracy is variable according to the access;
- CT-guided corticosteroid facet joints injections and CT-guided corticosteroid epidural injections can be considered clinically safe.

# **ARTICLES**

# FEASIBILITY OF ULTRASOUND-GUIDED EPIDURAL ACCESS AT THE LUMBOSACRAL SPACE IN DOGS

*From*: LIOTTA A., BUSONI V., CARROZZO M.V., SANDERSEN C., GABRIEL A., BOLEN G. Feasibility of Ultrasound-guided Epidural Access at the Lumbo-sacral space in Dogs. *Vet Radiol Ultrasound,* 2015, 56, 220-228.

This study was presented:
-as oral presentation at the EAVDI Congress 2013 in Lisbon (Portugal) where it was awarded the "EAVDI award";
- as poster presentation at the FARAH day, October 2013, where it was awarded the best poster presentation price.

## ***Summary***

**Epidural injections are commonly performed blindly in veterinary medicine. The aims of this study were to describe the lumbosacral (L-S) ultrasonographic anatomy and to assess the feasibility of an ultrasound (US)-guided epidural injection technique in dogs. A cross sectional anatomic atlas of the L-S region and *ex-vivo* US images were obtained in 2 cadavers to describe the US anatomy and to identify the landmarks. Sixteen normal weight cadavers were used to establish two variations of the technique for direct US-guided injection, using spinal needles or epidural catheters. The technique was finally performed in 2 normal weight cadavers, in 2 overweight cadavers and in 5 live dogs with radiographic abnormalities of the L-S spine. Contrast medium was injected and computed tomography (CT) was used to assess the success of the injection. The anatomic landmarks to carry out the procedure were the 7th lumbar vertebra, the iliac wings and the 1st sacral vertebra. The target for directing the needle was the trapezoid-shaped echogenic image between the contiguous articular facets of the L-S vertebral canal visualized in a parasagittal plane. The spinal needle or epidural catheter was inserted in a 45° craniodorsal-caudoventral direction through the subcutaneous tissue and the interarcuate ligament until reaching the epidural space. Computed tomographic examination confirmed the presence of contrast medium in the epidural space in 25/25 dogs, although a variable contamination of the subarachnoid space was also noted. The US-guided epidural injection technique is feasible in normal weight and overweight dogs, with and without radiographic abnormalities of the spine.**

## ***Introduction***

Epidural injections are commonly performed in both human and veterinary medicine to administer anaesthetic and analgesic drugs (Torske et Dyson, 2000; Jones, 2001; Valverde, 2008; Bauer *et al.*, 2012),corticosteroids (Wilkinson et Cohen, 2013) or to inject contrast medium during epidurography. In human medicine it has been estimated that blind epidural injections of steroids for pain control fail in 25-30% of cases (White, 1983) and the reported success rate for blind epidural catheter placement at first attempt is approximately 60% (Bauer *et al.*, 2012). Factors contributing to success or failure of catheter placement can be surgery related, operator dependent or patient dependent (Bauer *et al.*, 2012). In particularly, obesity, spinal anatomy, soft tissue edema or pregnancy (where hormonal changes cause general loosening of soft tissue) are reported to influence success rate (Grau *et al.*, 2001; Bauer *et al.*, 2012). In small animals failure rate of the "blind" technique has been estimated to range from 7 to 12% (Troncy *et al.*, 2002). Several factors may influence the success of the blind technique, including patient obesity, vertebral anatomic variations and operator's experience (Jones, 2001; Valverde, 2008). Tests such as the "hanging drop" and the "loss of resistance" tests are realized to assess the correct needle placement (Jones, 2001; Valverde, 2008). However several factors including tissue plugs obstructing the needle, increased central venous pressure, or negative pressure associated to supraspinous fat are reported to influence sensitivity and specificity of these tests (Bartynski *et al.*, 2005; Valverde, 2008) and the "loss of resistance" test has a reported failure rate of 30% (Bartynski *et al.*, 2005).

In human medicine many image-guided epidural injections technique have been described and the use of US-guidance is well established (Johnson *et al.*, 1999; Watanabe *et al.*, 2002; Karmakar *et al.*, 2009; Brinkmann *et al.*, 2012). In particular, administration of steroid drugs has now become a widely performed procedure by neuroradiologists as nonoperative treatment for disc protusions associated with low back pain and radiculopathy as well as for other spinal conditions and it has become increasingly recognized that image guidance and epidurography increase the accuracy of needle placement improving the chances of beneficial results from the injection (Johnson *et al.*, 1999; Watanabe *et al.*, 2002; Karmakar *et al.*, 2009; Brinkmann *et al.*, 2012).In veterinary medicine a large number of different US-guided regional techniques have now been described and there is a widespread interest in using these techniques in clinical practice. In particularly, an US-guided technique for lumbar subarachnoid puncture has been described (Etienne *et al.*, 2010) and the US-guided placement of an epidural catheter has been recently described in a dog (Viscasillas *et* *al. 2014*). Nevertheless, a study describing the US anatomy of the L-S region and evaluating the feasibility of the US-guided epidural injection technique on a larger number of dogs is lacking.

The aims of this study were to describe the US anatomy of the L-S region, and to assess the feasibility of direct US-guidance for epidural injection in radiographically normal dogs and in dogs with radiographic abnormalities of the L-S spine.

## ***Materials and Methods***

### *Dogs*

Twenty-two dog cadavers, euthanized for reasons unrelated to the study, were used to describe the US anatomy, to establish the US-guided injection technique and to assess its feasibility. Most cadavers were studied within 24 hours, though in few cases the procedure was delayed up to 4 days, during which the body was kept refrigerated at 4 degrees. Five live skeletally mature dogs were used with the approval of the Belgian Animal Care and Use Committee (nr 1432) to confirm *in-vivo* feasibility of the technique. The dogs were classified as normal weight or overweight if their body condition score was inferior or superior than 6/9, respectively. A radiographic examination of the region (latero-lateral and ventro-dorsal views) was realized to class each dog as normal or with L-S radiographic abnormalities. Live dogs were anesthetized using methadone (Comfortan®, 10 mg/ml, Eurovet Animal Health BV, AE Bladel, The Netherlands), propofol (Diprivan®, Cordon Pharma S.p.A, Caponago, Italy) and isoflurane (Iso-vet, Piramal Health Care, Morphet, UK). During the procedure on live dogs cardiac and respiratory rates were carefully evaluated. Moreover, other complications secondary to the epidural injection, such as hyperthermia, abscess formation in proximity of the site of injection or onset of neurologic signs, were ruled out performing daily clinical examinations for one week after the procedure.

### *Material and general US procedure*

Ultrasound images were obtained with the dogs in sternal recumbency and the hindlimbs pulled forward alongside the body of the animal. The hair was clipped and alcohol was used to improve skin coupling. Two US machines (Aloka 3500 Prosound, and Aloka Prosound SSD-Alpha10, Aloka Co. Ltd., Tokyo, Japan) equipped with a linear and a microconvex 5-10 MHz probes were used. Each US procedure was performed with the marker of the probe directed cranially (sagittal and parasagittal scan) or towards the operator (transverse scan).

*Procedure of the study on US anatomy*

First US images of isolated caudal lumbar vertebrae and sacrum placed in a water bath were obtained. Then US images of the L-S region were obtained in 2 cadavers, which were then frozen and used to obtain transverse and parasagittal 5 mm-thick sections to compare with US-images.

*Procedure of the study on US-guided epidural injection*

The technique for US-guided injection was established in 16 cadavers with normal body condition score and with radiographically normal L-S region, in 2 cadavers with normal body condition score and radiographic abnormalities of the L-S region (decrease in size of the L-S intervertebral space compared to adjacent intervertebral spaces, vertebral spondylosis, L-S epiphyseal sclerosis, degenerative joint disease of the articular facets) and in 2 cadavers with a body condition score superior to 6 and radiographic abnormalities of the L-S region (Table 1). The technique was then applied in 5 live dogs, all of them with radiographic abnormalities of the L-S spine (Table 1). A 22 gauge spinal needle (Terumo Co. Ltd., Japan) with a bevel of Quicke, whose length varied (70mm-90mm) depending on the dog's size and an epidural catheter introduced via a 18 gauge Tuohy (B-Braun ®, Melsungen, Germany) were used (figure 1). In 10/16 cadavers where spinal needle was used, two variations of the technique were performed: the needle was stopped immediately after piercing the interarcuate ligament (5/10) or it was advanced to the floor of the vertebral canal and then withdrew 1-2 mm (5/10). The epidural catheter was used in 6/16 dogs and it was advanced approximately 1 cm, after piercing the interarcuate ligament. In 2/2 cadavers with alteration of L-S bone profile and 2/2 cadavers with both a body condition score superior to 6 and alteration of L-S bone profile the US-guided technique was performed using a spinal needle, which was advanced until the floor of the vertebral canal and then withdrew 1-2 mm (Table 1). In 5/5 live dogs the spinal needle was instead stopped immediately after piercing the interarcuate ligament.

The "loss of resistance test" was performed before the injection in live dogs. When the needle tip or the epidural catheter were in the vertebral canal 0,1 ml/kg of iohexol (300 mgI/ml Omnipaque TM, GE Healthcare, Belgium) was used as contrast medium and injected in the epidural space. The procedure was always performed by the same operator (AL), with US experience, but without any previous experience in performing epidural access.

**Table 1: Number of Cadavers/Dogs, Results of Radiographic Examination of the Lumbosacral Spine, Material and Technique Used to Establish and Evaluate the Ultrasonographic-Guided Epidural Injection.**

| | 16 cadavers (1-24kg) | 2 cadavers (18-20kg) | 2 cadavers (40-60kg) | 5 live dogs (10-16kg) |
|---|---|---|---|---|
| X-ray lumbosacral spine examination: | Normal | Abnormal* | Abnormal* | Abnormal* |
| Spinal needle: | 10/16 | 2/2 | 2/2 | 5/5 |
| - After piercing the interarcuate ligament | 5/10 | / | / | 5/5 |
| - Until the floor | 5/10 | 2/2 | 2/2 | / |
| Epidural catheter: | 6/16 | / | / | / |

***Decrease in size of the lumbosacral intervertebral space compared to adjacent intervertebral spaces, vertebral spondylosis, lumbosacral epiphyseal sclerosis, and degenerative joint disease of the articular facets.**

**Figure 1 illustrating the epidural catheter and the spinal needle**

*Evaluation of injection accuracy and contrast medium distribution*

Contrast medium has been injected in all animals and to confirm its presence in the epidural space and therefore the success of the technique, a CT examination (Siemens Somatom 16-Slices, Germany) of the L-S spine was performed after the injection with the dog in dorsal recumbency. Scans were made in helical acquisition mode with a slice thickness of 1 mm and a pitch of 0,8. Technical settings were 120–140 kV, 200–300 mA, window width 2500 Hounsfield Units (HU) and window level of 500 HU for bone tissue, a window width of 350 HU and window level of 40 HU for spine.

The possible presence of subarachnoid contamination was scored. Scores were recorded a single time by a single operator (AL). In transverse section the subarachnoid contamination circumference was compared to the spinal cord circumference and a half point was attributed per each half circumference of the spinal cord involved by the subarachnoid contamination. In a similar way in sagittal section the subarachnoid contamination lenght was compared to the body length of the 7th lumbar vertebra and a half point was attributed each time that the length of the subarachnoid contamination was less or equal to half of the vertebral body lenght. If both the ventral and dorsal contrast column was visualized on sagittal section only the longest one was scored. Based on the sum of this score, five groups were identified: absence of subarachnoid contamination (0 points), minimal subarachnoid contamination (from 1 to 1,5 points), mild (from 2 to 2,5 points), moderate (from 3 to 3,5 points), and severe (more than 3,5 points).

## ***Results***

### US anatomy

A female Cocker Spaniel cadaver (15 kg) and a female cross-breed cadaver (13 kg) were used to obtain the anatomical sections. Anatomical sections correspond well with US images (figure 2 and 3).

On US images all bony structures appeared as hyperechoic surfaces associated to distal acoustic shadowing. In transverse US images the spinous processes appeared as a hyperechoic spot (figure 4), in longitudinal images their surface was seen as a curved hyperechoic line or, for the sacrum, as a continuing hyperechoic surface with three notches, while in parasagittal image they were not visualized. On transverse images, the vertebral arch was partially hidden by distal acoustic shadowing of the spinous process and appeared as a thin hyperechoic surface deep and lateral to it (figure 4), while it was not visualized on longitudinal image on strict sagittal image. Instead, on parasagittal images the vertebral arch of L7 appeared as a mildly convex hyperechoic line, while the sacral vertebral arch was visualized as a three-notched hyperechoic surface asociated with distal acoustic shadowing. The body was visualized as a thin hyperechoic horizontal surface, when performing the US parasagittal scan at the level of the interarcuate space. The articular facets of L5-L6-L7 appeared as convex hyperechoic surfaces, lateral to the spinous process (transverse section) (figure 4) or cranio-lateral to the interarcuate space (parasagittal section). The cranial articular facets of S1, together with the cranial part of the sacrum's wing, appeared as oblique, slight sigmoid-shaped, hyperechoic line (transverse section) (figure 2) or a convex hyperechoic surface, caudomedial to the L-S interarcuate space. The transverse process of L5, L6, L7 and the *crista sacralis lateralis* of the sacrum appeared as a hyperechoic horizontal line, lateral to the base of the vertebral arch (figure 4). The ilium's wings were visualized when performing the transverse section of the L-S junction and they appeared as oblique hyperechoic surfaces, located close to the transducer's surface, lateral to the sacroiliac joint (figure 1). The external soft tissues surrounding the L-S vertebral canal were hypoechoic muscles and the echoic lumbar fascia. The vertebral canal was seen as a round or trapezoid-shaped space (respectively in transverse and parasagittal section) bordered dorsally by the hyperechoic interarcuate ligament and ventrally by the hyperechoic longitudinal ligament. In the transverse section, the epidural space was occupied by the hypoechoic epidural fat. The US appearance of the nervous structures was different according to the section: in transverse images nervous structures appeared as multiple, small, rounded-shaped hyperechoic spots, sometimes containing a hypoechoic center, while in parasagittal sections they appeared as thin tapering hyperechoic images, sometimes containing hypoechoic center line. However, it was not possible to differentiate *conus medullaris*, dural sac or nerve roots forming the *cauda equina*. In parasagittal sections no nervous structures were visualized.

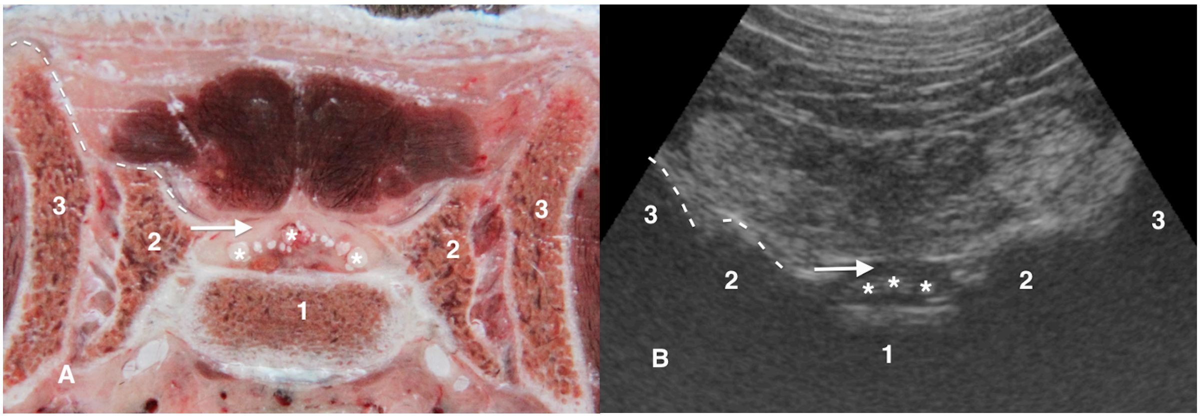

**Figure 2: Comparison between the anatomic transverse slice (A) and transverse ultrasonographic image (B) of the lumbosacral region.**
**The sigmoid-shaped hyperechoic interface (dotted line) associated with distal acoustic shadow corresponds to the right wing of the sacrum (2) and to the right wing of the ilium (3). Within the vertebral canal the epidural space appears hypoechoic (arrow) and surrounds the echoic internal nervous structures (*). The vertebral canal is ventrally bordered by the cranial epiphysis of the first sacral vertebra (1).**

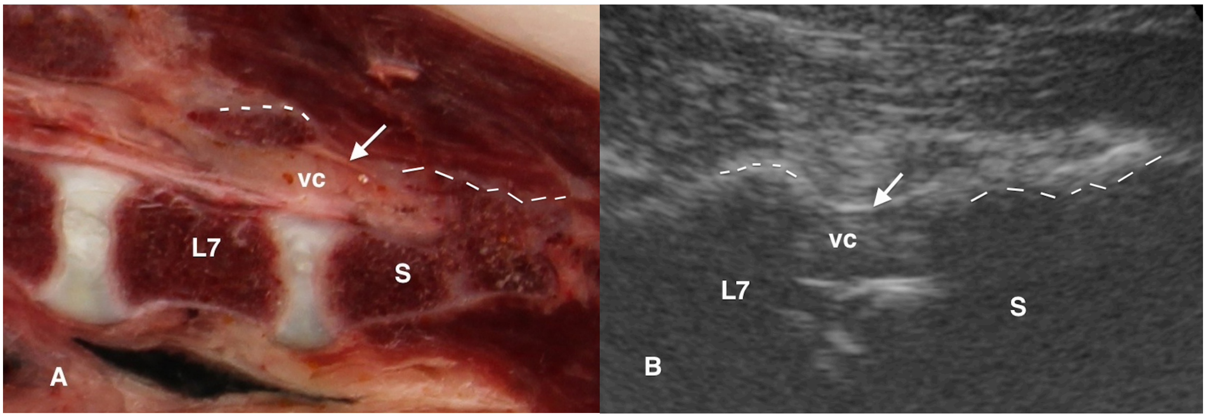

**Figure 3: Comparison between the anatomic parasagittal slice (A) and the parasagittal ultrasonographic image (B) of the lumbosacral region. The caudal aspect of the lamina of the seventh lumbar vertebra (L7) appears as a curved hyperechoic line associated with distal acoustic shadow (curved dotted line). The lamina of the sacrum (S) appears as a notched hyperechoic line (notched dotted line) associated with distal acoustic shadow. The vertebral canal (vc) is bordered dorsally by a thin hyperechoic line (arrow) which corresponds to the interarcuate ligament.**

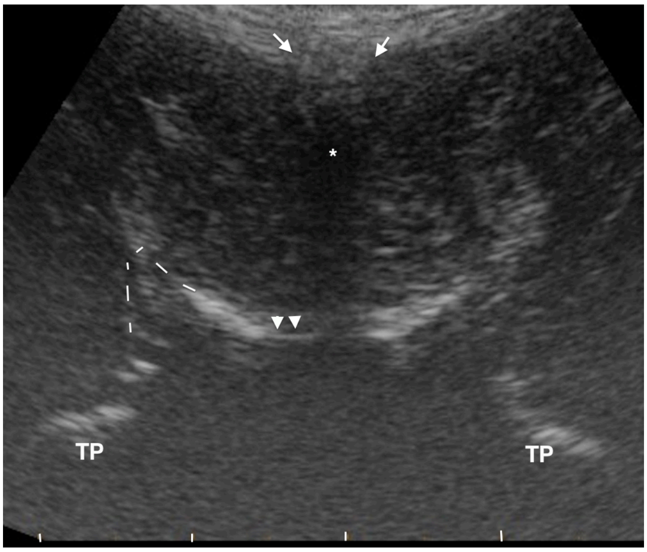

**Figure 4: Ultrasound transverse image of the seventh lumbar vertebra.**
**The spinous process (arrows) appears as a hyperechoic spot associated with distal acoustic shadow (*). The vertebral arch (arrows head) is partially hidden by the distal acoustic shadow and is visualised as a thin horizontal hyperechoic line lateral to it. The lateral convex hyperchoic line (dotted line) is the articular process. The beginning of the transverse process (TP) is also visualised.**

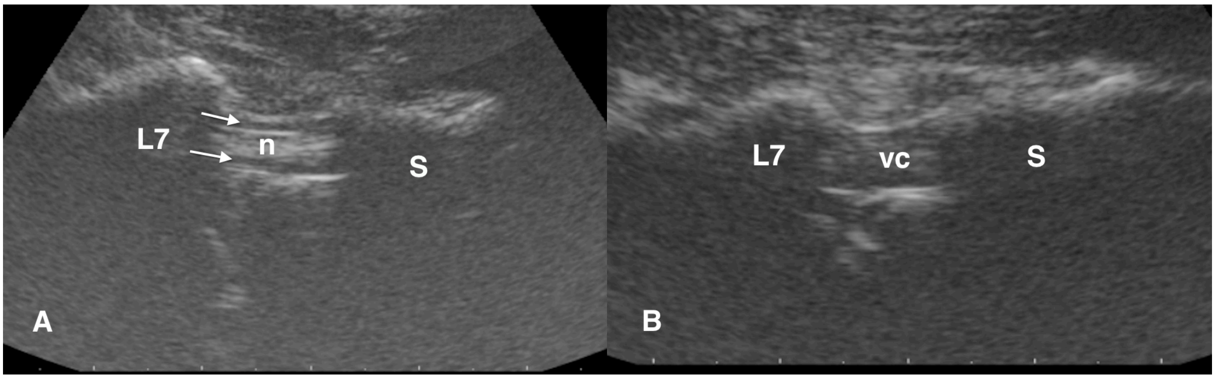

**Figure 5: Comparison between ultrasound parasagittal images of the lumbosacral region of two different cadavers showing the variable visualisation of the internal nervous structures of the vertebral canal. On the A image the internal nervous structures (n) are well visualised within the vertebral canal. On the B image no structures are clearly visualised. L7: 7th lumbar vertebra; S: Sacrum; Arrows: epidural space; VC: vertebral canal.**

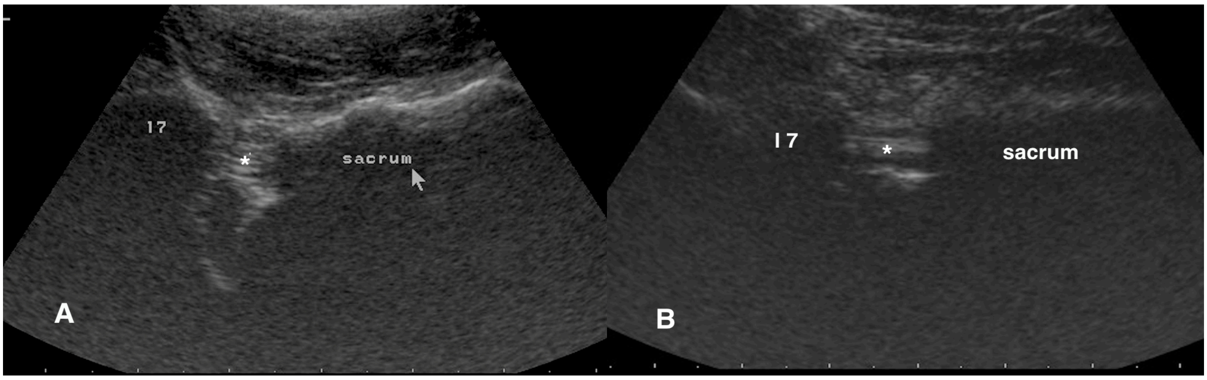

**Figure 6: Comparison between ultrasound parasagittal images of the lumbosacral region of two different cadavers with (A) and without radiographic abnormalities of the lumbosacral spine (B). On image A the interarcuate space (*) is reduced in size compared to B, secondary to a decreased intervertebral disc space of the lumbosacral space.**

<u>*US-guided epidural injection*</u>

Sixteen normal weight cadavers with a normal L-S spine (one Shar-Pei dog and 15 cross-breed dogs; 10 male, 6 female; body weight ranging from 1 kg to 24 kg with a mean of 15 kg), two normal weight cadavers with an abnormal L-S spine (a male Boxer weighting 20 kg and a female cross-breed dog weighting 18 kg), two overweight dogs with an abnormal spine (a female Rottweiler weighting 40 kg and a male Dog de Bordeaux weighting 60 kg) and 5 live Beagle dogs (3 female, 2 male, ranging from 12 to 16 kg) were used. The vertebral canal at the L-S junction was easily visualized. The US-guided technique was performed using as anatomic landmarks L7, the iliac wings and S1. A parasagittal approach was chosen. The spinous process of L7 was first identified on transverse images and then the probe was moved caudally to identify the iliac wings, the sacro-iliac junction, the spinous process of S1 and the L-S vertebral space. After rotation of the transducer of 90° and lateral displacement of the probe, a parasagittal US image of the region was obtained, to obtain the best visibility of the L-S canal.

Visualization of the deep structures varied depending on size of the dog, amount of subcutaneous fat and skin's hydration of the cadaver (figure 5). The target for needle direction was the trapezoid-shaped vertebral canal in the L-S space, visualized in a parasagittal plane between the contiguous articular facets. Depending on dog's size, sometimes the probe had to be slightly tilted (dorsolaterally-ventromedially) to obtain the largest access. A window without nervous structures was choosen to perform the procedure. The spinal needle or epidural catheter was inserted slowly in a craniodorsal-caudoventral direction at an angle of approximately 45° under US-guidance (figure 7). The needle tip progression was followed in real-time until it reached the vertebral canal and the epidural space (figure 7).

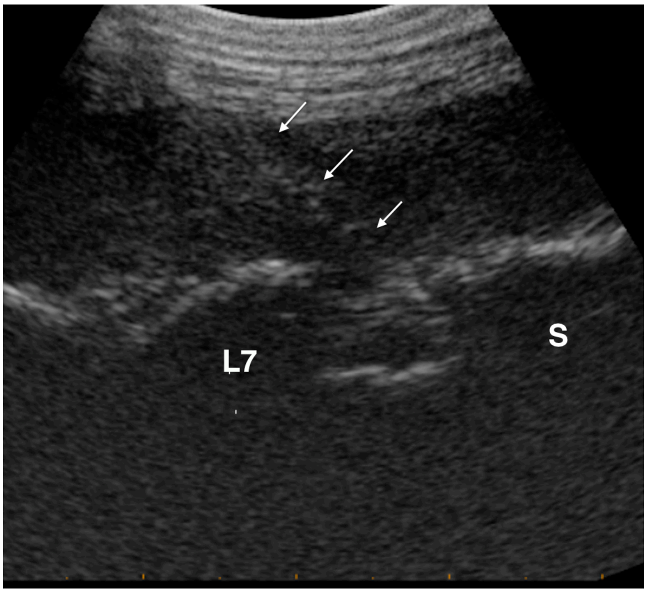

**Figure 7: Ultrasound parasagittal image of the lumbosacral region of a cadaver during the insertion of the needle (arrows) into the vertebral canal. L7: 7th lumbar vertebra, S: sacrum.**

Both the variations of the procedure performed with spinal needles and the procedure performed with epidural catheter were easily performed in all normal weight cadavers with normal L-S spine, without differences regarding the dog's size. Application of the technique was instead subjectively more difficult in one of the 2 cadavers with L-S radiographic abnormalities and in one of the 2 overweight cadavers. In fact recognition of anatomical landmarks in these cadavers was more difficult because of modified shape of the bony surfaces and reduced image quality because of subcutaneous fat. Once anatomic landmarks were recognized, needle placement was easily performed. In the live dogs, although radiographic examination showed mildly decreased intervertebral L-S space and moderate to severe spondylosis in 5/5 dogs, the US-guided epidural injection was easily realized without complications neither during the procedure nor at and after waking up. There was no subjective difference in performing the technique between cadavers and live dogs.

*Evaluation of accuracy and contrast medium distribution*

CT examination confirmed the presence of contrast medium in the epidural space of all cadavers and live dogs (figure 8). The spread of contrast medium was heterogeneous with a larger amount localized in proximity of the L-S junction. A various amount of contrast medium was noted in the subarachnoid space (figures 9 and 10) in 17/20 cadavers (85%) and in all live dogs (100%) (Table 2). Subarachnoid contamination was minimal in 7/20 (35%), mild in 4/20 (20%), moderate in 3/20 (15%) cadavers and minimal in 5/5 live dogs (100%). Severe subarachnoid contamination was not present. There was no difference in occurrence of subarachnoid contamination among cadavers injected with the spinal needle and cadaver injected with the epidural catheter, although contamination severity was higher when using the spinal needle compared to the epidural catheter. No difference was observed when the spinal needle was advanced until the floor or stopped immediately after piercing the interarcuate ligament.

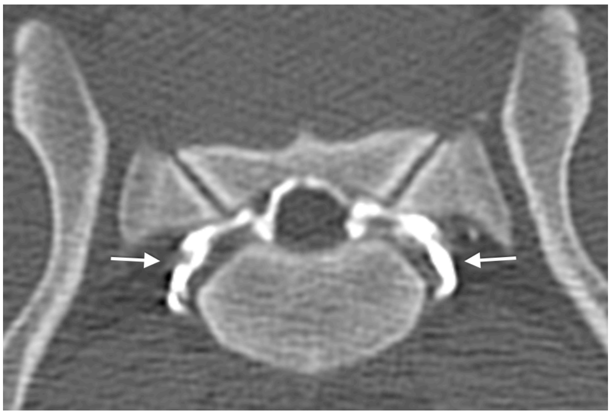

**Figure 8: Transverse computed tomography image of the lumbosacral region showing the presence of contrast medium in the epidural space and at the exit of the intervertebral foramina (arrows). (Image reconstruction: bone window, window level =2500 HU, window level= 500 HU).**

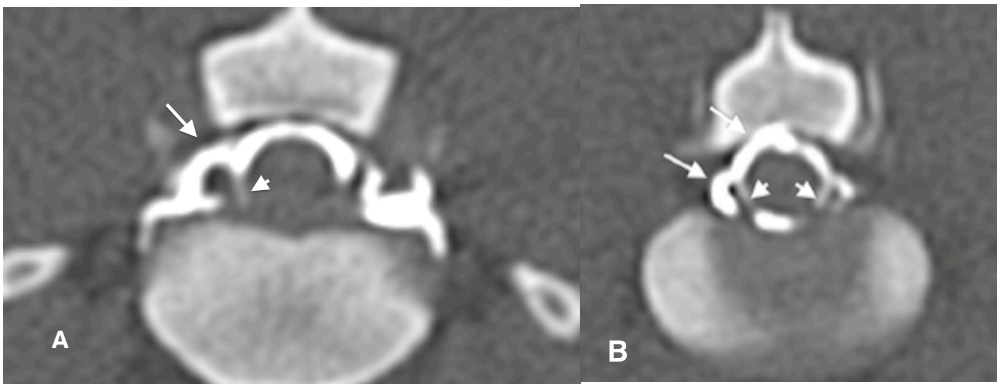

**Figure 9: Transverse computer tomography images (bone window) of the fifth (A) and sixth (B) lumbar vertebra showing the contrast medium in the epidural space (arrows) and different degree of subarachnoid contamination (short arrows).**
**(Image reconstruction: bone window, window level =2500 HU, window level= 500 HU).**

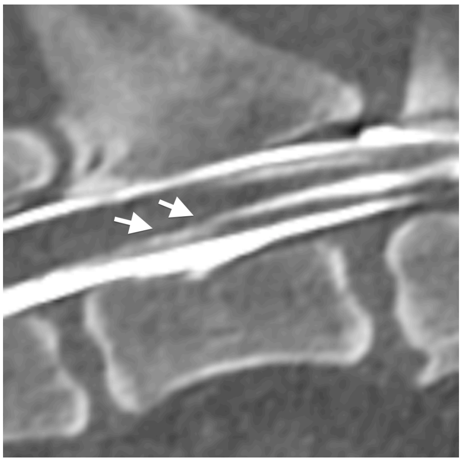

**Figure 10: Reconstructed sagittal computed tomography image (bone window) centered on the seventh lumbar vertebra showing the contrast medium in the epidural space and the subarachnoid contamination (arrows). In this case the ventral contrast column was used to score the subarachnoid contamination and its length was compared to the vertebral body length of the seventh lumbar vertebra. It was approximately three times the value of the mid-vertebra length and 1,5 score was attributed to this cadaver.**

**Table 2: Degree of subarachnoid contamination.**

| **Degree of subarachnoid contamination** | **Group 1**<br>*16 cadavers* | | **Group 2***<br>*2 cadavers* | **Group 3****<br>*2 cadavers* | **Group 4*****<br>*5 live dogs* |
|---|---|---|---|---|---|
| | Spinal needle | Epidural catheter | | | |
| **Absent** | 2/10 | 1/6 | | | |
| **Minimal** | 4/10 | 5/6 | 1/2 | | 5/5 |
| **Mild** | 3/10 | | | | |
| **Moderate** | 1/10 | | | 2/2 | |
| **Severe** | | | | | |

***normal weight cadaver with radiographic abnormalities of the lumbosacral spine. **overweight cadavers with radiographic abnormalities of the lumbosacral spine. *** normal weight dog with radiographic abnormalities of the lumbosacral spine.**

## ***Discussion***

Feasibility of the US-guided epidural access was demonstrated by presence of contrast medium in the epidural space in normal weight and overweight dogs, with and without radiographic abnormalities of the L-S spine. Although time needed to successfully achieve the puncture and number of needle redirections were not recorded, and correlation between procedure length, obesity or L-S disease were not studied, all US-guided punctures of the present study were accurate. To accurately verify the feasibility of the US-guided technique, our study was divided into a cadaver and *in vivo* study. The cadaveric study aimed to establish the procedure and to verify its feasibility even in conditions, such as obesity or vertebral malformations, which usually influence negatively the success rate of the "blind technique". The *in vivo* study aimed to determine safety of the procedure for a future application in clinical setting and to rule out the altered permeability of the meninges secondary to post-mortem alterations as unique responsible for the subarachnoid contamination. Two variations of the epidural technique have been described (Jones, 2001; Valverde 2008; Torske et Dyson 2000) and in our study we assessed the feasibility of both. The first variation consists in advancing the needle until the floor of the vertebral canal and then withdrawing it 1-2 mm; the second variation consists in stopping the needle immediately after piercing the *flavum ligament*. With the first technique, there is a decreased possibility of subarachnoid injection, but if the needle is too parasagittal it could be within the vascular plexus. With the second technique the vascular plexus is likely avoided, but there is an increased risk to be within the subarachnoid space

The US-guided technique described in this study for epidural injections is realized at the L-S space, which is the most common site used in small animals and provides the largest access to the epidural space (Valverde, 2008). Other sites, such as intervertebral spaces between 3rd sacral and 1st caudal vertebra or between 1st and 2nd caudal vertebrae, have not been tested in the present study although they have been described as potential sites for epidural puncture (Roberts et Selcer, 1993; Ramirez et Thrall, 1998; Johnson *et al.*, 1999; Valverde, 2008). The hind limbs were pulled forward with the purpose to increase the L-S space (Roberts et Selcer, 1993; Ramirez et Thrall, 1998; Johnson *et al.*, 1999; Valverde, 2008; Di Concetto *et al.*, 2012). A parasagittal approach was chosen as it allowed the best visibility of the target area. A comparison of feasibility and contrast spread to a sagittal approach has not been performed in the present study. The bony anatomic landmarks used in this study were L7, S1 and the iliac wings. US features of the explored area were similar to previous US description of caudal lumbar region (Hudson et Kramer 2008; Etienne *et al.*, 2010), sacro-iliac joint (Jones *et al.*, 2012) or epidural space (Karmakar *et al.*, 2009). In agreement with a previous study (Etienne *et al.*, 2010), clear visualization of nervous structures within the vertebral canal was variable and depended on dog's size, fat or skin quality. In human medicine, US of the spine is routinely used in neonates until 6 months of age to assess spinal disease, such as spinal dysraphism given the degree of ossification of their caudal spine. Through the non-ossified vertebrae, the terminal part of the spinal cord is easily visualized using high frequency probes and the *cauda equina* is described as a set of echoic linear structures surrounding the hyperechoic *filum terminale (Dick et al., 2002)*. In adult humans, the *cauda equina* has been described as multiple horizontal hyperechoic shadows, sometimes associated with pulsations (Karmakar *et al.*, 2009). In dogs, the nervous anatomy at the L-S junction is variable. In medium-size and large dogs the *conus medullaris* ends approximately at L6-L7, but in small dogs it may end more caudally (Fletcher, 1993). Moreover, approximately 80% of dogs have a dural sac extending well into the sacrum (Lang, 1988). US technique used in the present study did not allow clear differentiation of *conus medullaris*, dural sac, *filum terminale,* or nerve roots forming the *cauda equina,* possibly given their size and their close localization one to the others in relation to resolution of the probe used. However US features of the nervous structures appeared very similar to US description in humans (hyperechoic structures sometimes containing a hypoechoic center, round or elongated and tapering, depending on section plan), although no pulsation of the *cauda equina* was noticed in live dogs.

The time to perform the technique was not recorded. However, the injection was considered subjectively more difficult and less fast in the obese dogs or in dogs with anatomic malformations. Indeed, in these dogs the anatomic landmarks were more difficult to identify. Approximately the time to perform the injection varied between 5 and 10 minutes.

A various amount of subarachnoid contamination after epidural injection was observed in this study. The low number of dogs does not allow us to extrapolate statistically significant conclusions in relation to needle or technique, however the amount of contamination was lower in live dog than in cadavers. Because of *post-mortem* loss of resistance and increased permeability of tissues, it may be postulated that subarachnoid contamination would be more important in cadavers compared to live dogs. However dural puncture may also have occurred in both cadavers and live dogs as this is a reported complication in epidural analgesia in humans resulting in post-dural puncture headache

(Lang, 1988; Norris *et al*., 1989; Macarthur *et al*., 1993; Reynolds, 1993; Bezov *et al*., 2010; Waise et Gannon, 2013). In parturients receiving epidural anaesthesia, the incidence of dural puncture is reported to be between 0 and 2.6% (Reynolds, 1993) and incidence is reported to be inversely related to the anaesthetist's experience (Macarthur *et al*., 1993) and to be correlated to size and shape and kind of the used needle (Bezov *et al*., 2010; Waise et Gannon, 2013). In a study on flexion-extension myelography it has been shown that more than 80% of the dogs had a dural sac extending well into the sacrum (Lang, 1988). In these dogs the average diameter of the dural sac at the level of the L-S junction was large enough to allow successful application of myelographic techniques. In the present study the needle may have therefore prickled the dural sac when entering the epidural space or during the injection, even if a parasagittal approach with the craniodorsal-caudoventral directed needle was used and no CSF was noted during the procedure in live dogs. In the current study the more important subarachnoid contamination when using the spinal needle compared to the epidural catheter supports this hypothesis. In fact, the use of epidural catheter does not eliminate the possibility of technique's failure, but the bevel of the Tuohy needle of the epidural catheter is considered less traumatic than spinal needle because of its curved shape, which facilitates its insertion directly in the epidural space (Valverde, 2008). When US-guidance was applied in live dogs of this study, only the spinal needle's technique was tested because in clinical daily activity the use of an epidural catheter is limited by its cost. Further studies would be interesting to evaluate occurrence and severity of subarachnoid contamination depending on needle used and potential interest of US-guidance to reduce dural puncture and contrast leakage in epidural injection in dogs. In this study the procedure has been performed always by the same operator and this represents a limitation as transferability to operators with lower or no US experience was not assessed. Moreover, live dogs used for the study were relatively few and clinically normal.

US-guided parasagittal epidural access is a feasible technique in normal dogs, in dogs with L-S radiographic abnormalities and in overweight dogs. The information contained in this paper should serve as a base for further investigations of the application of this technique in clinical settings. Moreover, further studies need to be performed to evaluate the advantages of the US guidance compared to the blind epidural technique.

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# TECHNIQUE, DIFFICULTY AND ACCURACY OF COMPUTED TOMOGRAPHY-GUIDED EPIDURAL AND INTRA-ARTICULAR FACET JOINT INJECTIONS IN DOGS

*Adapted from*: LIOTTA A., SANDERSEN C., COUVREUR T., BOLEN G. Technique, Difficulty, and Accuracy of Computed Tomography-Guided Translaminar and Transforaminal Lumbosacral Epidural and Intraarticular Lumbar Facet Joint Injections in Dogs. *Vet Radiol Ultrasound,* 2015, **57:**191-198

This study was presented as oral presentation at the 17th IVRA meeting 2015 in Perth, Australia.

## *Summary*

**In human medicine, spinal pain and radiculopathy are commonly managed by computed tomography (CT)-guided facet joint injections and by transforaminal or translaminar epidural injections. In dogs CT-guided lumbosacral (L-S) epidural or lumbar facet joint injections have not been described.**

**The aim of this study was to develop techniques and to assess their difficulty and accuracy. Two cadavers were used to establish the techniques and 8 cadavers to assess difficulty and accuracy. Contrast medium was injected and a CT scan was performed after each injection. Accuracy was assessed according to epidural or joint space contrast opacification. Difficulty was classified as easy, moderately difficult or difficult, according to the number of short-ranging CT scans needed to follow the insertion of the needle.**

**A total of 6 translaminar and 5 transforaminal epidural and 53 joint injections were performed. Translaminar injections had a high success rate (100%), were highly accurate (75%), and easy to perform (100%). Transforaminal injections had an inferior success rate (75%), were accurate (75%), and moderately difficult to perform (100%). Success rate of facet joint injections was 63% and was higher for larger facet joints, such as L7-S1. Accuracy of facet joint injections ranged from accurate to highly accurate depending on the volume injected. In 58% of cases, injections were moderately difficult to perform. Possible complications of epidural and facet joint injections were subarachnoid and vertebral venous plexus puncture and periarticular spread respectively. Further studies are suggested to evaluate *in-vivo* feasibility and safety of these techniques.**

## ***Introduction***

*Cauda equina* syndrome is characterized by lower back pain and neurological dysfunction due to displacement or compression of the *cauda equina* spinal nerve roots. It is a multifactorial disorder including traumatic, vascular, inflammatory, neoplastic, as well as degenerative etiologies (Thomas et Dewey, 2008). In dogs, DLSS is considered the most common cause *of cauda equina* syndrome. It is characterized by abnormal motion pattern and loss or lack of load-bearing properties leading to IVDD and herniation, as well as compensatory new bone production and thickening of surrounding soft tissue structures, such as hypertrophy of the interarcuate ligament, epidural fibrosis, and degenerative facet joint disease (Sharp et Wheeler, 2005; Thomas et Dewey, 2008; Meij et Bergknut, 2010). Conservative and surgical treatments have both been described (Sharp et Wheeler, 2005; Meij et Bergknut, 2010). Conservative treatment is based on pain management through oral administration of nonsteroidal anti-inflammatory drugs, body weight reduction and change in exercise pattern. Surgical treatment, on the other hand, aims at decompressing the *cauda equina* and freeing entrapped nerve roots by dorsal laminectomy, distraction and fusion, or a combination of both (Sharp et Wheeler, 2005; Meij et Bergknut, 2010; Saulnier-Troff *et al.,* 2014). Medical treatment tends to be ineffective long-term, whilst many intra, early or late postoperative complications have been described with surgical treatment (Sharp et Wheeler, 2005; Thomas et Dewey, 2008; Meij et Bergknut, 2010). More recently, a retrospective study suggested ESI as an alternative to surgical treatment (Janssens *et al.*, 2009).

In human medicine, local lumbar spinal pain and radiculopathy are commonly managed by ESI or by intraarticular facet joint steroid injection (Watanabe *et al.*, 2002; Wilkinson et Cohen, 2013). Although different methods have been described to verify the correct placement of the needle in the epidural space, inappropriate needle position may occur in 25-40% of “blind” epidural injections (Watanabe *et al.*, 2002; Bartynski *et al.*, 2005). Therefore, many imaging-guided percutaneous techniques have been described (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002), involving both, transforaminal (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002; Valverde, 2008; Buenaventura *et al.*, 2009) or translaminar access (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002; Buenaventura *et al.*, 2009; Parr *et al.*, 2009) and intraarticular facet joint access (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002; Boswell *et al.*, 2007). Among the different techniques, human literature considers CT-guidance as the preferred technique (Silbergleit *et al.*, 2001) to perform both ESI and facet joint injections, because it allows safe needle progression and a precise positioning at the target (Hoeltje *et al.,* 2013) allowing a high accuracy with a described 94% procedural technical success rate (Weininger *et al.*, 2013).

In dogs, there is an increasing interest concerning imaging-guided percutaneous techniques of the vertebral spine (Etienne *et al.*, 2010; Gregori *et al.*, 2014; Levy *et al.*, 2014; Liotta *et al.*, 2014; Mackenzie *et al.*, 2014) and both US-guided epidural access and US - guided cervical articular process access have been described (Gregori *et al.*, 2014; Levy *et al.*, 2014; Liotta *et al.*, 2014). Nevertheless, feasibility and safety of CT-guided caudal lumbar epidural and facet joint injections have never been described in dogs. The investigation of spinal diseases in dogs is routinely performed by CT or MRI examination (Mai *et al.*, 2014). Theoretically, ESI could be a valid alternative every time a spinal compression by herniated disc or hypertrophic flavum ligament is identified and when surgery is not recommended or declined by the owner, or where daily medical treatment with non steroidal anti-inflammatory drugs can be contraindicated because of chronic nephropathy or gastric ulcers (Khan et Mclean, 2012). Therefore, the use of CT may be concurrently warranted for both diagnostic and therapeutic purposes, such as steroid injections.

The aim of this study was to describe techniques, difficulty and accuracy of CT-guided transforaminal and translaminar L-S epidural and lumbar facet joint injections in dogs.

## *Materials and Methods:*

### *General procedures:*

Computed tomography scans (Siemens Somatom 16-Slices, Germany) were made in helical acquisition mode with a slice thickness of 1 mm and a pitch of 0.8. Technical settings were 120–140 kV, 200–300 mA, window width 2500 Hounsfield Units (HU) and window level of 500 HU for bone tissue, a window width of 350 HU and window level of 40 HU for spinal cord.

Routine biopsy software (biopsy mode software, delivered on the Sensation Acquisition Workplace), consisting of 10 short-ranging CT scans (Kv 120, mAs 50) with a slice thickness of 0.75 mm, was applied to perform the CT-guided injection. The contrast medium, Iohexol (300mg/mL Omnipaque TM, GE Healthcare, Belgium,) was injected with a 22 gauge spinal needle (Terumo Co. Ltd., Japan) with a Quicke bevel, the length of which varied (70mm-90mm) depending on the dog’s size.

The study was divided in 2 phases: first a technique study phase was performed, followed by difficulty and accuracy assessment phase.

*Technique study phase:*

The cadavers of a 35 kg neutered male Anatolian shepherd dog and of a 30 kg spayed male cross-breed dog, euthanized for reasons unrelated to the study, were used to establish the technique. The dogs were placed in sternal recumbency with the hindlimbs pulled forward alongside the body of the animal. Hair was clipped. A CT scan examination of the L-S region was performed and abnormalities of the L-S region such as decreased IVD space, disc protrusion, vertebral spondylosis or degenerative joint disease of the facet joints were evaluated and recorded. In each cadaver, transforaminal and translaminar epidural injections were performed, as well as facet joint injections of the caudal lumbar spine. During CT scan survey, bony landmarks for each target were first identified, following published reference (Jones, 1995).For facet joint injections, the target was defined as the most dorsal and largest point of the curvilinear hypoattenuating space between adjacent cranial and caudal articular processes on transverse section (figure 1). Facet joint injections were performed between the cranial and caudal articular processes of the fifth and sixth lumbar vertebrae (L5-L6), sixth and seventh lumbar vertebrae (L6-L7) and seventh lumbar vertebra and first sacral vertebra (L7-S1) (figure 1). Facet joints were chosen randomly for each cadaver. For translaminar epidural access (figure 2), target was defined as the largest and most sagittal point of the L-S epidural space on transverse section and the needle was inserted through the skin and subcutaneous tissue with a dorsoventral direction. For transforaminal access, the most easily accessible and most dorsal point of the L-S intervertebral foramen on transverse section was chosen and the needle was inserted through the skin and subcutaneous tissue with a dorsolateral-ventromedial direction (figure 3) with different angle approaches according to target orientation, which differed on each cadaver. The right or left side of the transforaminal access was chosen randomly for each cadaver. Once the target was identified, biopsy software was used to follow the needle insertion through the subcutaneous tissue and epiaxial muscles. To verify the success of the technique, contrast medium (1 ml in the epidural space, 0.5 ml in the intraarticular facet joint space) was injected and a second CT scan was performed. For epidural injections, the technique was considered successful if contrast medium was noticed in the epidural space. Presence of contrast medium outside the vertebral canal or in an erroneous site, such as subarachnoid space or vertebral venous plexus contamination, were also evaluated and recorded. For intraarticular joint injection, the technique was considered successful if contrast medium was noticed within the intraarticular space. Periarticular spread was also evaluated and recorded.

**Figure 1: Transverse computed tomography image (bone window) of the lumbosacral region showing the needle within the right lumbosacral facet joint space. (Left of the dog to reader's right). (1= sacrum; 2= ilium; * = lumbosacral facet joint space)**

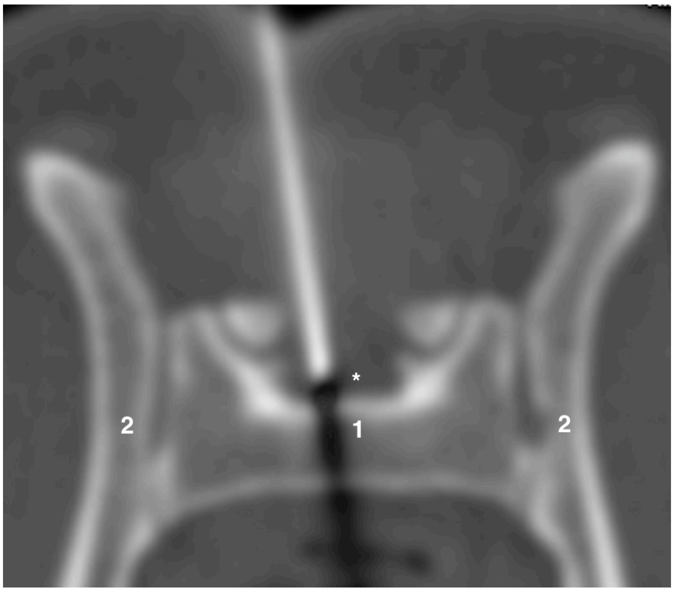

**Figure 2: Transverse computed tomography image (bone window) of the lumbosacral region showing the translaminar epidural access. (Left of the dog to reader's right). (1= sacrum; 2= ilium; * =epidural space)**

**Figure 3: Transverse computed tomography image (bone window) of the lumbosacral region showing the left transforaminal epidural access. Notice the severe vertebral spondylosis. (Left of the dog to reader's right).**

<u>*Difficulty and accuracy study:*</u>

To assess difficulty of the techniques described here above, 8 cadavers, ranging from 5 to 30 kg, euthanized for reasons unrelated with this study, were used. The cadavers were randomly divided into two equal sized groups. Size of the facet joint target in each cadaver, was also retained. The latter was referred to as the measurement on transverse image (bone window) of the largest and most dorsal aspect of the hypoattenuating space between adjacent cranial and caudal articular processes (figure 4). The measurement was made perpendicular to the articular surface of both cranial and caudal articular processes, to measure the entrance point of the needle (figure 4).

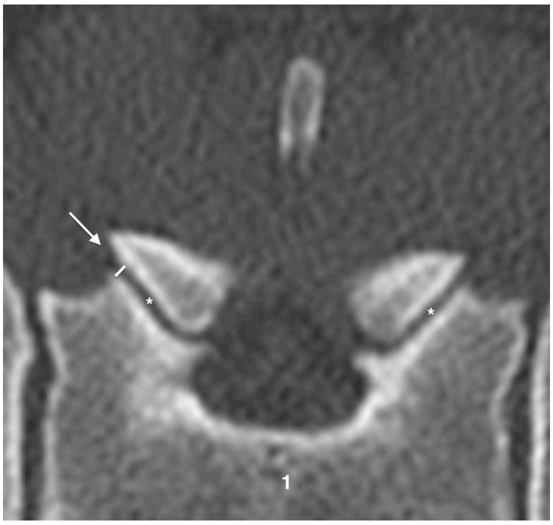

**Figure 4: Transverse computed tomography image (bone window) of the lumbosacral region showing the measurement of the facet joint target (line). The measurement was taken at the largest and most dorsal aspect of the joint, perpendicular to the bony surface of both cranial and caudal articular processes. The aim was to measure the size of the supposed entrance point (arrow) of the needle. (Left of the dog to reader's right). (1= sacrum; * = lumbosacral facet joint space)**

In the first group translaminar epidural access was performed, whilst in second group transforaminal epidural access was chosen. Facet joints injections at L5-L6, L6-L7, L7-S1 of the left and right side were performed on cadavers of both groups. Contrast medium was injected as follows: 5 ml in the epidural space, 0.5 ml in facet joints of the first group, 0.2 ml in facet joints of the second group. Immediately after each injection a CT scan was performed to evaluate the success of the technique. Possible erroneous sites of injection were evaluated and recorded, as previously described. The number of attempts was the number of short-ranging CT scans performed with biopsy software to check the position of the needle until the target was reached. For both epidural and facet joint injections, the number of attempts was recorded to evaluate difficulty. Difficulty in performing procedures was graded as easy, moderately difficult or difficult if the number of attempts was less than 5, between 6 and 10, or more than 10 attempts, respectively. Accuracy percentage values were calculated using the formula: (number of times contrast medium was recorded in the structure of interest divided by the total number of injections) x 100, with a corresponding 95% confidence interval. Each facet joint injection was considered highly accurate (figure 5) if contrast medium was present in the joint space only, and accurate if both periarticular and intraarticular contrast medium was present (figure 6). Each epidural injection was considered highly accurate if contrast medium was present in the epidural space only (figure 7) and accurate if, in addition to a large amount of contrast medium within the epidural space, a minimal amount of subarachnoid contamination, vascular contamination or minimal amount of contrast medium outside the vertebral canal was simultaneously present (figures 8 and 9).

The injections were always performed by the same person (AL), whilst the measurements were performed blindly by another boarded-radiologist (GB).

## ***Results:***

*Technique study:*

No abnormality of the LS region was noticed in the Anatolian Shepherd Dog cadaver, whereas mild L-S spondylosis was observed in the cross-breed dog cadaver.

The insertion of the entire needle through the subcutaneous and muscular tissue could be followed under CT-guidance until the target.

-Facet joint injections:

A total of 5 facet joints were injected: L5-L6 (left) and L6-L7 (left) in first cadaver and L5-L6 (left), L6-L7 (right) and L7-S1 (left) in second cadaver. In 3 out of the 5 injections, the technique was considered successful because of presence of contrast medium in the joint space. Among these three successful injections, one (L6-L7, first cadaver) presented contrast medium in the joint space exclusively, whereas contrast medium was noticed in both intraarticular and periarticular space in the remaining two (L6-L7 and L7-S1 second cadaver). In 2 out of the 5 injections (L5-L6, first and second cadaver), the technique was considered unsuccessful because of the complete absence of contrast medium in the joint space.

-Epidural injections:

A total of 3 epidural injections were performed: 2 translaminar (first and second cadaver) and 1 transforaminal (first cadaver). In all 3 epidural injections, the technique was considered successful because of the presence of contrast medium in the epidural space (translaminar access, second cadaver) and in the epidural space with mild subarachnoid contamination (translaminar and transforaminal access, first cadaver).

### *Difficulty and accuracy study:*

No CT abnormalities were noticed in 3 out of the 8 cadavers. In 4 cadavers, multiple LS disc protrusions were observed. Mild (1) and severe vertebral (1) spondylosis was present in 2 cadavers. Moreover, 2 cadavers presented decreased IVD space. Degenerative joint disease of facet joints (left and right L6-L7) was reported in one cadaver.

-Facet joint injections:

In each dog, each facet joint on both sides, from L5-L6 to L7-S1, was injected. Thus a total of 48 facet joint injections were performed, 16 injections per anatomical site, 24 injections being performed per group. Size of the facet joint target varied from 0.04 cm to 0.12 cm (median 0,07 cm). Success rates were recorded for each target size, with higher success rates recorded for larger facet joints (Table 1). Injection in L7-S1 joint was the most successful site. Of the 48 injections, 30 (62.5%) were considered successful (16 in the first group, 14 in the second group) because of the presence of contrast medium within the joint space (Table 1). In the first group, none of the 16 successful injections were classified as highly accurate, but all 16/24 as accurate (66%). In the second group, successful injections were considered highly accurate in 4/24 (16%) (figure 5), and accurate in 10/24 (41,5%) (Table 1) (figure 6). Injections were classified as easy to perform in 10/48 (21%), as moderately difficult in 28/48 (58%), and as difficult in 10/48 (21%) (Table 1).

**Table 1: Size of Facet Joints and Corresponding Percentage of Success*, Difficulty** and Accuracy***.**

| Facet Joint Size (cm) | Success (%) | Difficulty (%) | | | Accuracy | | | |
|---|---|---|---|---|---|---|---|---|
| | | Easy | Moderately Difficult | Difficult | High Accurate | | Accurate | |
| | | | | | 1° | 2° | 1° | 2° |
| 0.04 (*n*=7) | 0% | / | 85% | 14% | / | / | / | / |
| 0.05 (*n*=3) | 33% | / | 100% | / | / | / | 1/24 | / |
| 0.06 (*n*=6) | 33% | 33% | 66% | / | / | / | / | 2/24 |
| 0.07 (*n*=15) | 73% | 13% | 73% | 13% | / | / | 6/24 | 6/24 |
| 0.08 (*n*=6) | 83% | / | 83% | 17% | / | / | 4/24 | 2/24 |
| 0.09 (*n*=9) | 77% | / | 45% | 55% | / | 2/24 | 5/24 | / |
| 0.12cm (*n*=2) | 100% | / | 100% | / | / | 2/24 | / | / |

**Success was defined as the presence of contrast medium within the target space, visualised on post-injection computed tomography examination; **Difficulty was graded in base of the number of attempts performed during the procedure. *** Accuracy was assessed according to joint space contrast opacification. Each facet joint injection was considered highly accurate if contrast medium was present in the joint space only, and accurate if both periarticular and intraarticular contrast medium was present. In dogs *(n= 24)* of first group (1°) 0.5 ml of contrast medium was injected. In dogs *(n=24)* of second group (2°) 0.2 ml of contrast medium was injected.**

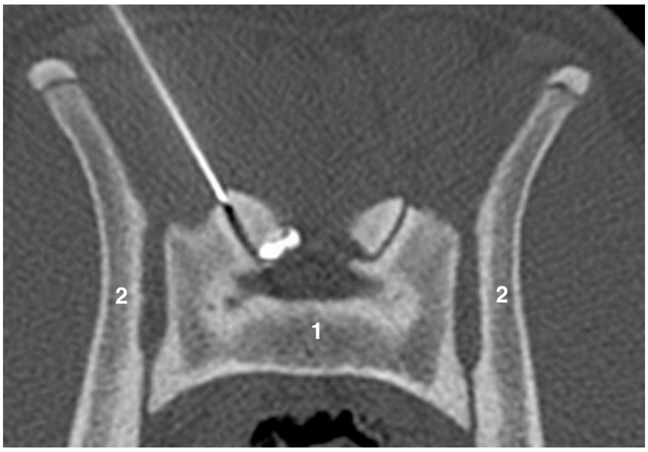

**Figure 5: Transverse computed tomography image (bone window) of the lumbosacral region showing intraarticular contrast medium within the right lumbosacral facet joint. This injection was defined as highly accurate. The needle is still inserted within the joint space. (Left of the dog to reader's right). (1= sacrum; 2= ilium)**

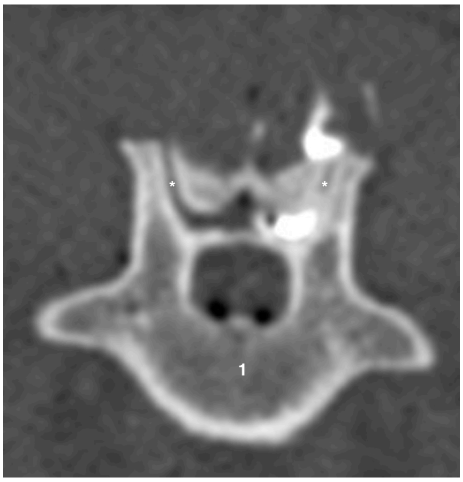

**Figure 6: Transverse computed tomography image (bone window) of the facet joint of sixth-seventh lumbar vertebra. Both intraarticular contrast opacification and periarticular spread are noticed. This injection was classified as accurate. (Left of the dog to reader's right). (1= sixth lumbar vertebra; * = facet joint space)**

-Epidural injections:

Translaminar epidural injections were successful in 4/4 cadavers (100%) because of the presence of contrast medium in the epidural space. In 3/4 cadavers, injections were defined as highly accurate (75%) (figure 7), and in 1/4 as accurate (25%) (figure 8). Injections were classified as easy in 4/4 cadavers (100%).

Transforaminal injections were considered successful in 3/4 cadavers (75%) and in all cases, the injections were considered moderately difficult to perform. One injection was considered to have failed, because of presence of contrast medium exclusively within the vascular system. All 3 successful injections were classified as accurate (75%) because of simultaneously presence of epidural contrast medium with subarachnoid contamination in 1/3 and vertebral venous plexus in 2/3.

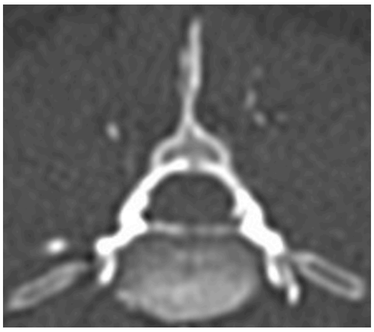

**Figure 7: Transverse computed tomography image (bone window) of mid-body of the sixth lumbar vertebra. Translaminar injection has been performed and epidural contrast medium is noticed. This injection was classified as highly accurate. (Left of the dog to reader's right).**

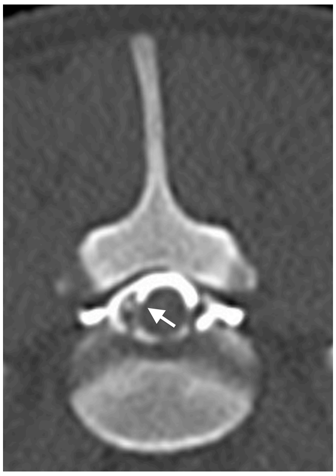

**Figure 8: Transverse computed tomography image (bone window) of seventh lumbar vertebra. Translaminar access has been performed and epidural contrast medium is noticed, as well as mild subarachnoid contrast opacification (arrows). This injection was classified as accurate. (Left of the dog to reader's right).**

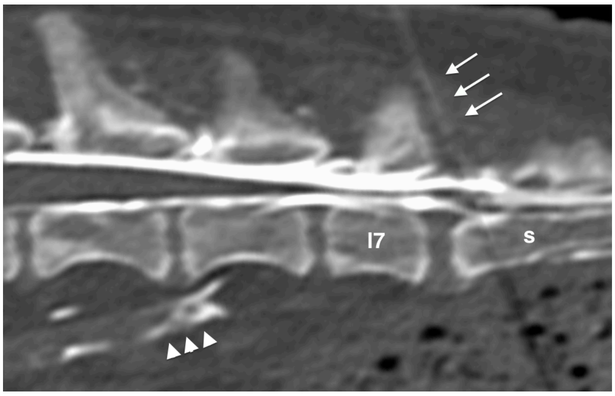

**Figure 9: Sagittal, reconstructed computed tomography image (bone window) of caudal lumbar spine. Contrast medium is visible in epidural space and in caudal vena cava (arrowheads) because of vascular contrast medium contamination. Needle and associated starburst artifact are partially visible (arrows). This injection was classified as accurate. (Left of the dog to reader's right). (l7= seventh lumbar vertebra; s= sacrum).**

## ***Discussion***

CT-guided L-S transforaminal and translaminar epidural injection techniques, as well as CT-guided facet joint injection technique have been described in this study. Translaminar and transforaminal epidural accesses are both feasible and accurate, but according to our results translaminar access is easier to perform and more accurate. Possible incorrect needle position can cause subarachnoid contamination and vertebral venous plexus puncture. Facet joint injections are moderately feasible and accurate, their difficulty depending on facet joint size. Incorrect needle position can lead to periarticular spread.

In human medicine, spinal image guidance comprises techniques like fluoroscopy, US, CT, or MRI. Magnetic Resonance is considered the modality of choice for the assessment of the L-S disease, but CT-guidance is the preferred modality to perform epidural and facet joint injections, because it is considered the most exact procedure with reported accuracy of 94% (Silbergleit *et al.*, 2001; Weininger *et al.*, 2013). Magnetic resonance-guided procedures are indeed limited in both human and veterinary patients by the need of special coils and dedicated non-ferromagnetic biopsy instruments (Vignoli et Sanders, 2011; Westbrook *et al.,* 2011; Mahnken *et al.*, 2013). With CT-fluoroscopy the advantages of both fluoroscopy and CT are obtained and this technique could be used to guide needle placement more precisely (Wagner, 2004), even if in contrast to conventional CT-guidance the operator is exposed to radiations and it is more expensive (Mahnken *et al.*, 2013). In veterinary medicine, the investigation of spinal diseases in dogs is routinely performed by CT or MRI examination (Mai, 2013), however CT-fluoroscopy and MRI are less available compared to CT. Recently, US -guided epidural injection technique have been described in dogs and its use is recommended when performing epidurography or for anesthetic purposes (Gregori *et al.*, 2014; Liotta *et al.*, 2014). However, in diagnosis of spinal disease, CT is a routinely used imaging modality (Mai, 2013) and its use may be concurrently warranted for both diagnostic and therapeutic purposes, such as steroid injections. In human medicine, different advantages and disadvantages have been associated with translaminar and transforaminal epidural accesses (Wilkinson et Cohen, 2013). Advantages of the translaminar technique are the ability to treat bilateral pain with only one injection and the increased likelihood that the injected substance will reach adjacent spinal levels. However, an increased likelihood of dural puncture is also described. The transforaminal epidural technique, on the other hand, is most target-specific, such as in cases of lateralized disc or nerve root compression. It is associated with a lower risk of inadvertent dural puncture (Wilkinson et Cohen, 2013) but with an increased risk of vascular puncture (Watanabe *et al.*, 2002). Controversial literature exists concerning which of these techniques should be considered the most effective (Wilkinson et Cohen, 2013). According to our results, translaminar access was easily performed. This result can undoubtedly be explained by the larger size of the translaminar compared to the transforaminal access.

In our study, accuracy was assessed on cadavers only and we decided to consider successful and accurate the injections even if a small amount of subarachnoid contamination or a small vascular contamination occurred. *Post-mortem* alterations of meninges and other soft-tissues or the inability to assess CSF and blood leakage could have lead to increased complications and therefore could have negatively influenced the accuracy results. In our study, incorrect needle position was found to cause subarachnoid contamination and vertebral venous plexus puncture. This is in accordance with human medical literature, where both subarachnoid and intravascular injections are described as possible and harmful contaminations (Watanabe *et al.*, 2002). Intrathechal steroid administration is associated with possible development of arachnoiditis, whilst intravascular injection of steroids, especially when the arterial system is involved, can potentially result in stroke, seizure or permanent paralysis (Watanabe *et al.*, 2002). In a previous veterinary study concerning US epidural access in dogs, subarachnoid contamination was also described as a complication (Levy *et al.*, 2014). As in this previous study, we postulated that altered permeability of the dural sac in cadavers and accidental dural puncture could be the causes of this complication. Similarly we believe that during clinical procedure erroneous *dura mater* or vascular prickling may occur, without a true intrathecal or intravascular position of the needle. The minimal amount of vascular or subarachnoid contamination compared to the epidural spread of contrast medium supports this hypothesis. In our study, vertebral venous plexus puncture was exclusively recorded with transforaminal access. These results agree with human medical literature, where intravascular injections are described as uncommon using the translaminar approach but are more frequent with the transforaminal access (Watanabe *et al.*, 2002).

In human medicine, facet joint neurolysis is performed in order to control back pain. CT-guided approach is commonly used because it is considered the most exact procedure and allows reliable positioning of the needle by assessing the spread of the contrast medium (Weiniger *et al.*, 2013). Although we did not carry out statistical studies because of the low number of dogs, in our study success of the technique was dependent on the size of the target. Not surprisingly L7-S1 facet joint, which was more commonly of larger size, had the highest success rate. Moreover, as already reported in human medicine (Peh, 2011), despite apparent intraarticular needle placement, intraarticular filling sometimes failed. This result confirmed our theory that success of the technique was dependent on the facet joint size. Our measurements were not meant to measure the overall size of the facet joint, but only the size of the entrance point, *i.e.* where the needle was supposed to enter. However, we did not consider our measurements to constitute true cut-off values, because we did not assess their *inter-* and *intra*-observer repeatability and because the used CT-acquisition algorithms could have staggered the measurements.

In our study, success of the technique was not taken into account in assessing difficulty, which was exclusively meant as an estimation of the technical effort in reaching the target and not as the ability to fill the joint space. The average number of guiding scans needed for the final needle position was higher compared to human medical literature (Weininger *et al.*, 2013). Possible explanations are anatomical and morphological difference between dogs and humans or varying degrees of experience of the operators. According to our results, accuracy of facet joint injections was lower, ranging from 20% (highly accurate) to 40% (accurate), than the accuracy (83%) described in a recent study concerning US-guided access of the cervical facet joint in dogs (Levy *et al.*, 2014). It was also less accurate than the results described in human medicine (Weininger *et al.*, 2013). We may only postulate that this could be, in part, the result of a different grading system. It could also be related to the size of the lumbar joint space compared to the cervical spine or to the human vertebral canal. The amount of contrast medium injected could also be influential. The amount of contrast medium that we injected was superior compared to those studies (Weininger *et al.*, 2013; Levy *et al.*, 2014). Moreover, the degree of periarticular spread was subjectively more important in the first group when more contrast was used. However, because of the small number of facet joint injections, their different sizes and the difficulty in objectively classifying the periarticular spread, no statistical conclusion may be drawn concerning the maximum volume to inject to prevent periarticular spread. In human medicine, rupture of the capsule and periarticular and epidural spread is described as a possible complication (Peh, 2011; Hoeltje *et al.*, 2013). Termination of the injection is therefore suggested when resistance is encountered (Peh, 2011). However, literature is controversial and does not insist on precise intraarticular injection because equivalent results have been described with periarticular injections. In fact, periarticular injection is recommended, especially in case of difficult intraarticular injection (Peh, 2011).

In this study, the time to perform the technique was not recorded. However some information could be extrapolated from the difficulty phase. Indeed, an increased difficulty in performing the technique corresponded with an increased number of short-ranging CT scan used to follow the needle, and therefore with an increased time to reach the target. Approximatively, time to perform translaminar, transforaminal and facet joint injections under CT– guidance varied between 5 and 10 minutes.

We decided to perform our techniques with dogs in sternal recumbency, whilst diagnostic examination of the L-S spine is usually performed on dorsal recumbency and with the hindlimbs caudally extended. Indeed, the extension of the spine is usually associated with a more severe compression of the nervous structures (Lang, 1988). The position of the dogs in our study was chosen because it has been proven that sternal recumbency with hindlimbs pulled forward alongside the body of the animal increases the L-S space (Di Concetto *et al.*, 2012). Therefore we considered this position the most appropriate to perform easily and quickly the CT-guided injections.

The main limitations of our study was the exclusively use of cadavers and the lack of severely pathologic cadavers. Indeed, few cadavers were affected by mild disc protrusion, but none of them was affected by severe foraminal stenosis or severe disc-related extradural compression. In human medicine, lateralized compressions are usually treated by transforaminal access, with an increased likelihood of intravascular puncture (Watanabe *et al.*, 2002). It is as well reasonable to think that the reduction of the access space because of the presence of large amount of discal material could increase the difficulty in performing safely the technique. However, in case of inability to perform a transforaminal access or when this latter is considered too risky, a translaminar injections could be instead suggested. Therefore, further studies are needed to fully assess the safety, as well as the *inter-* and *intra-*repeatability of our technique. However, according to our results, we consider CT-guided translaminar and transforaminal L-S epidural injections and CT-guided intraarticular lumbar facet joint injection in dogs, feasible and variably accurate. Our study may be considered as a preliminary result. Further studies are suggested to evaluate *in-vivo* feasibility and safety of our technique. Clinical trials are as well needed to fully assess the efficacy of ESI in dogs and in which specific conditions they should be suggested as a treatment.

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# COMPUTED TOMOGRAPHY-GUIDED EPIDURAL AND FACET JOINT STEROID INJECTIONS IN DOGS: IMPORTANCE OF CONTRAST MEDIUM INJECTION AND CLINICAL SAFETY

*Adapted from:* LIOTTA A., GIROD M., PEETERS D., SANDERSEN C., COUVREUR T., BOLEN G.; Clinical effects of computed tomography–guided lumbosacral facet joint, transforaminal epidural, and translaminar epidural injections of methylprednisolone acetate in healthy dogs. *American Journal of Veterinary Research,* accepted.

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## ***Summary:***

**In human medicine, corticosteroid injections in the epidural or joint spaces are commonly performed for lower back pain and radiculopathy. A major complication rate of 0.07%, requiring attendance in an emergency room or hospitalization, has been described, while the reported minor complication rate varies between 9.6% and 15.6%. In veterinary medicine, epidural steroid injections (ESI) has been recently suggested as an alternative treatment for stenosis (DLSS) in dogs, but a systematic study evaluating their clinical safety is still lacking. Therefore, the aim of our study was to test the clinical safety of transforaminal epidural, translaminar epidural and facet joint corticosteroid injections in dogs. Fifteen healthy Beagles were randomly assigned to three groups and underwent computed tomography (CT)-guided lumbosacral (L-S) epidural transforaminal, epidural translaminar, and facet joint injections of 0.1mg/kg of methylprednisolone acetate, preceded by contrast medium injection. During the procedures, heart rate, respiratory rate, oxygen saturation of hemoglobin, and rectal temperature were recorded. Finally, steroid injections were performed in 14/15 dogs. In 1/15, vascular puncture occurred and the steroid injection was not performed. No major or minor complications were reported during the procedure. General clinical and specific neurological examinations of the L-S region were performed 1 day, 3 days, 7 days and 10 days after the injections. In the presence of neurological abnormalities, a control neurological examination was performed 24 days after the procedure. Two healthy Beagles were included as control group and underwent regularly general clinical and specific neurological examinations of the L-S region. In the days following the procedure no motor, sensor or postural deficits were noticed in dogs during clinical examinations, but only minimal transient hyperthermia and mildly altered patellar withdrawal, cranial tibial and perineal reflexes. Overall, altered reflex responses were observed during 27/65 clinical examinations in 11/14 dogs of the injections group and in 2/2 dogs belonging to the control group during 2/6 clinical examinations. In conclusion, CT-guidance and contrast medium injection allows to verify the position of the needle and to avoid major complications associated with intravascular steroid injections. Minor complications can be associated with CT-guided corticosteroid injections in the L-S epidural and facet joint spaces. Further studies are necessary to assess the clinical efficacy of these techniques.**

## ***Introduction:***

In human medicine, corticosteroid injections in the epidural or joint spaces are commonly performed for lower back pain and radiculopathy (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002; Peh, 2011). Many theories have been postulated concerning their mechanism of action (Wilkinson et Cohen, 2013). Suppression of prostaglandin synthesis, decreased formation of inflammatory leukotrienes, decreased capillary wall permeability and subsequent decreased edema formation, as well as osmotic dilution and washout of inflammatory cytokines, and local enhancement of the blood flow to ischemic nerve roots are among the proposed mechanisms of action (Wilkinson et Cohen, 2013). A major complication rate of 0.07%, requiring attendance in an emergency room or hospitalization, has been described, (Johnson *et al.*, 1999) while the reported minor complication rate varies between 9.6% and 15.6% (Watanabe et al., 2002). Complications can be related to the procedure itself or be specific to the injected molecules (Wilkinson et Cohen, 2013). Examples of procedure-related complications are spinal infections, such as epidural abscesses or meningitis, inadvertent subarachnoid or intravascular injections resulting in epidural or subdural hematoma (Watanabe et al., 2002; Wilkinson et Cohen, 2013), arachnoiditis (Watanabe et al., 2002; Lima et al., 2010), seizures, and spinal cord injury (Watanabe et al., 2002). The latter is in particularly associated with intra-arterial injections and it is secondary to potential embolic phenomena related to the particulate nature of injected steroids (Watanabe et al., 2002). The consequences can be devastating and tetraplegia and paraplegia have been reported (Wilkinson et Cohen, 2013; Abdelerahman et Rakocevic, 2014).

Allergic reactions or systemic corticosteroid effects, such as hypercorticism or corticosteroid-induced myopathy, have been reported as molecule-related complications (Wilkinson et Cohen, 2013). It has been proven that inaccurate needle placement occurs in 25-30% of “blind” injections and that the loss of resistance test is an inaccurate tool to verify the correct placement of the needle in the epidural space (Bartynski *et al.*, 2005). Therefore, to increase the safety and efficacy of epidural spinal injections (ESI), many imaging-guidance techniques have been developed (Watanabe *et al.*, 2002). Among these techniques, the CT-guided approach is the preferred modality to perform both epidural and facet joint injections in most centers, because it allows safe needle progression and precise positioning at the target (Mahnken *et al.*, 2013). Injection of nonionic contrast medium before the injection of steroids is recommended and is commonly part of the imaging-guided technique protocol (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002). The aim of the contrast medium injection is to confirm the correct position of the needle and to avoid especially inadvertent dural or intravascular puncture (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002). In particular, stroke, seizure or permanent paralysis are described in case of intravascular arterial injection of corticosteroids because of potential embolic phenomena related to the particulate nature of injected steroids (Watanabe *et al.*, 2002).

In dogs, DLSS is considered the most common cause of the *cauda equina* syndrome. It is characterized by IVDD and herniation, as well as by compensatory new bone production and proliferation of surrounding soft tissue, such as hypertrophy of the interarcuate ligament, epidural fibrosis and degenerative facet joint disease (Meij et Bergknut, 2010). These modifications result in a displacement or compression of the sixth and seventh lumbar, first to third sacral, and first to fifth coccygeal spinal nerve roots, with consequent lower back pain and neurological dysfunction (Sharp et Wheeler, 2005; Dewey, 2008; Meij et Bergknut, 2010). The oral administration of nonsteroidal anti-inflammatory drugs, body weight reduction, and change in exercise patterns or decompressive surgery are the suggested treatments (Sharp et Wheeler, 2005; Dewey, 2008; Meij et Bergknut, 2010, Saulnier-Troff *et al.*, 2014). Recently, ESI has been suggested as an alternative treatment for L-S degenerative stenosis in dogs (Janssens *et al.*, 2009). In this study, both clinical and long-term effects were evaluated by the owners, according to a grading scale questionnaire, but no neurological examination results were reported. Moreover, corticosteroid injections were performed under fluoroscopy, whilst according to human medical literature, CT is considered superior to fluoroscopy to guide epidural and facet joint injections (Hoeltje *et al.*, 2013).Therefore, in veterinary medicine, a systematic study evaluating the safety of CT-guided ESI is lacking.

The aim of our study was to test the safety of CT-guided ESI and corticosteroid facet joint injections in dogs and to describe procedure-related complications. Our hypothesis was that ESI and corticosteroid facet joint injections are associated with a low rate of procedure-related complications.

## ***Material and methods:***

Seventeen healthy experimental adult Beagles (fifteen as injections' group and two as control group) were used with the approval of the University's Animal Care and Use Committee (nr. 1637). Each dog was included only if considered clinically healthy and free from orthopedic and neurological deficits, based on history and general and neurological clinical examinations performed 24 hours before the beginning of the study.

The dogs of the injections' group were randomly included in three groups: 5 dogs (3 intact male and 2 intact female dogs, all of them were 8 years old, ranging from 15 to 16 kg) underwent a L-S facet joint injection, 5 dogs a L-S transforaminal epidural injection (1 intact male and 4 intact female dogs, ranging from 2 to 4 years old and weighting from 11 to 17 kg) and 5 dogs a L-S translaminar epidural injection (1 intact male and 4 intact female dogs, ranging from 2 to 8 years old, weighting from 11 to 15 kg). The left or right hand side for transforaminal or facet joint injections was randomly chosen. A 22G over-the-needle type catheter was aseptically placed in the right cephalic vein. Dogs were premedicated with medetomidine (Sededorm, Vetpharma, Belgium) 20 μg/kg intravenously. Five minutes later, propofol (Diprivan, AstraZeneca, Belgium) was injected intravenously to effect until intubation with an 8 mm inner diameter cuffed endotracheal tube became possible. The dogs were then connected to a circle breathing system and allowed to breathe spontaneously a mixture of isoflurane in oxygen. During the procedure, the heart rate, respiratory rate, and oxygen saturation of hemoglobin were monitored permanently and recorded every 5 minutes. Rectal temperature was recorded every 15 minutes. After the procedure, the dogs received 100μg/kg of atipamazole (Atipazole, Vetpharma, Belgium) intramuscularly. Before the injection, a CT scan examination (Siemens Somatom 16-Slices, Germany; Helical acquisition mode, slice thickness of 1 mm, pitch of 0,8; 120–140 kV, 200–300 mA) of the L-S region was performed to evaluate and record the presence of any bony abnormalities or dystrophic mineralization which could be misdiagnosed as contrast medium. Procedures were performed under CT-guidance always by the same operator (AL) and respecting aseptic conditions. A CT scan survey was performed with the dogs in sternal recumbency and the hindlimbs cranially extended to identify bony landmarks. CT-guided injections were perfomed, following published reference (Liotta *et al.*, 2015b). To perform facet joint injections, the needle was inserted to reach the most dorsal and largest aspect of the L-S articular facet joint, identified on transverse section as the hypoattenuating space between caudal articular processes of the 7th lumbar vertebra and cranial articular process of the sacrum and the needle. To perform the transforaminal injections, the angle of the access was variable according to the angle of LS intervertebral foramen, which differed on each dog. The insertion of the needle aimed to reach with a dorsolateral-ventromedial direction the most easily accessible and most dorsal point of the LS intervertebral foramen identified on transverse section. For translaminar epidural access, the injection was performed advancing the needle with a dorsoventral direction to reach the LS epidural space, identified on transverse section as the largest and most sagittal aspect between the lamina of the 7th lumbar and 1st sacral vertebra. Once the target was identified, a routine biopsy software (Biopsy mode software; Sensation Acquisition Workplace, 10 short-ranging CT scans, Kv 120, mAs 50; slice thickness of 0.75 mm), was used to follow the needle insertion and perform the CT-guided injection. Iohexol (Omnipaque, 300 mgI/ml, GE Healthcare, Belgium) was injected with a spinal needle (Terumo Co. Ltd., Japan; 22 gauche; Quicke bevel, length of 70mm-90mm) to verify the correct position of the needle, 0.15 ml in the facet joint space and 2 ml in the epidural space. Immediately afterwards, a second CT examination was performed and contrast medium spread was evaluated. In the presence of contrast medium in the epidural space, transforaminal or translaminar corticosteroid injections were performed. A mild subarachnoid contamination was also accepted. If no contrast medium was visualized, a vascular puncture with contrast medium migration was assumed (figure 1) and the needle was repositioned. Corticosteroid injection was not performed, if after three attempts (six attempts for transforaminal access, three for each side) correct epidural position of the needle was not obtained. Facet joint injections were performed when intra-articular contrast medium was present. Periarticular contrast medium was also accepted. The contrast medium injection was followed by an injection of 1 mg/kg of body weight of methylprednisolone acetate (Moderin long acting, 40mg/ml, Zoetis, Belgium) with a variable amount of saline for a total of 0.5 ml and 5 ml of solution, in facet joint or epidural space, respectively.

Clinical examinations were repeated 24 hours, 3 days, 7 days and 10 days after the procedure. Each clinical general examination was followed by a specific clinical neurological examination of the L-S region, according to a pre-established scheme (Table 1). It was always performed by the same operator (MG). The latter was aware of the aim of the study but was unaware of the specific kind or side of injection each dog had been administered. Any abnormalities or neurological deficits were evaluated and recorded. Each reflex was rechecked at least three times before being considered abnormal. In the presence of abnormalities, an additional clinical examination evaluating only these abnormalities was performed 24 days after the procedure. No other clinical examinations were performed, but regular information concerning the clinical status of the dogs was obtained contacting the person in charge of the dogs.

Two experimental Beagle dogs (intact male and intact female, weighting both 12 kg dogs) were included as control group. These dogs were part of another research project, but underwent clinical general and specific clinical neurological examination following the same pre-established scheme used for the injections group dogs. Clinical examinations were repeated 24 hours, 3, 7 and 28 days after the procedure. The examinations were always performed by the same operator (MG), who was aware of the aim of the original study, but was not aware of the existence of a control group.

**Table 1: Pre-established scheme, summarizing the general clinic and specific neurologic examination of the lumbosacral region, which was used during each clinical examination.**

| Clinical signs and spinal reflexes | Definition |
|---|---|
| Hyperthermia | Increase of the body temperature above 39,4°C |
| Paresis/paralysis: | Partial/complete loss of voluntary movement manifested as decreased/absence range of motion |
| Pain on caudal lumbar spine palpation: | Reaction/vocalization during palpation of the caudal lumbar spine |
| Pain during tail hyperextension: | Reaction/vocalization during hyperextension of the tail |
| Proprioceptive deficit: | Delayed/Absence of normal foot positioning after its dorsal surface was put in contact with the ground |
| Hind limb lameness: | Absence of/painful weight-bearing with consequential shortening of the stride of the painful limb |
| Patellar reflex: | Single, quick extension of the stifle after the patellar ligament was tapped by a reflex hammer |
| Cranial tibial reflex: | Single, quick extension of the hock in response to a sharp tap on the tibial cranial muscle. |
| Withdrawal reflex: | Flexion of the hip, stifle and hock after pitching of the interdigital skin |
| Perineal reflex: | Contraction of the anal sphincter and tail flexion after touching the perineum |
| Urinary incontinence: | Involuntary leakage of urine |

## ***Results:***

-Articular facet group:

All the dogs of this group were affected by L-S spondylosis, 1/5 by mild L-S disc protrusion. None of them had degenerative joint disease of the L-S facet joints.

A total of 5 articular facet injections, one per dog, were performed. Three were administered on the right hand side, 2 on the left hand side. After the injection of contrast medium, a CT examination confirmed the correct position of the needle in 3/5 dogs. In 2/3 dogs, in addition to the intra-articular contrast medium, periarticular contrast medium spread was also noticed. In 2/5 dogs, contrast medium was exclusively periarticular.

During the procedure, no increase of respiratory or heart rate, no alteration of hemoglobin oxygen saturation or of rectal temperature was reported. No major complications requiring hospitalization occurred. Overall, mild clinical abnormalities were observed in 4/5 dogs, in 7/20 clinical examinations (Table 2). During control examinations, none of the dogs were affected by hyperthermia, pain at caudal lumbar spine palpation or tail hyperextension, hind limb lameness or proprioceptive deficits. The patellar reflex was normal in 5/5 dogs at day 1, increased in 1/5 dog at day 3, increased in 2/5 dogs at day 7, and increased in 2/5 dogs at day 10. The cranial tibial reflex was normal in 5/5 dogs at day 1, increased in 1/5 at day 3, increased in 2/5 dogs at day 7, and increased in 2/5 dogs at day 10. The withdrawal reflex was normal in 5/5 dogs at day 1, increased in 1/5 at day 3, increased in 2/5 dogs at day 7, and increased in 2/5 dogs at day 10. The perineal reflex was considered normal in 5/5 dogs at day 1 and day 3, decreased in 2/5 dogs at day 7, and decreased in 1/5 at day 10. None of the dogs were affected by urinary incontinence (Table 2). When the control of the altered reflexes was performed 24 days after the injection in 4 dogs, no changes were noticed compared to the previous abnormal examinations in 3 of the 4 dogs. In the remaining dog, patellar and cranial tibial reflexes were considered normal and the withdrawal reflex was considered to have decreased, whilst in previous examinations it was considered to be increased (Table 2).

At the time of writing this manuscript (approximately 5 months after the procedure), the dogs of this group did not show any particular clinical symptom.

**Table 2: Summary of clinical examination results of dogs that underwent lumbosacral facet joint injection on the right (R) or left (L) hand side. The first clinical examination was performed on day 1, the second on day 3, the third on day 7 and the fourth on day 10 after the procedure. A control of the altered reflexes (fifth clinical examination) was performed 24 days after the procedure. (a= absent; n = normal; ↑=bilaterally increased; ↓= bilaterally decreased).**

| | **Dog 1<br>R** | | | | | **Dog 2<br>L** | | | | | **Dog 3<br>L** | | | | | **Dog 4<br>R** | | | | **Dog 5<br>R** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Clinical examination** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **5** |
| **Hyperthermia** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | a | a | a | a | |
| **Pain at caudal lumbar spine palpation** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | a | a | a | a | |
| **Pain during tail hyper-extension** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | a | a | a | a | |
| **Proprio-ceptive deficits** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | a | a | a | a | |
| **Hind limb lameness** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | a | a | a | a | |
| **Patellar reflex** | n | n | n | n | | n | ↑ | ↑ | ↑ | ↑ | n | n | ↑ | n | n | n | n | n | n | n | n | n | ↑ | ↑ |
| **Cranial tibial reflex** | n | n | n | n | | n | ↑ | ↑ | ↑ | ↑ | n | n | ↑ | n | n | n | n | n | n | n | n | n | ↑ | ↑ |
| **Withdrawal reflex** | n | n | n | n | | n | ↑ | ↑ | ↑ | ↑ | n | n | ↑ | n | ↓ | n | n | n | n | n | n | n | ↑ | ↑ |
| **Perineal reflex** | n | n | ↓ | ↓ | ↓ | n | n | ↓ | n | ↓ | n | n | n | n | | n | n | n | n | n | n | n | n | |
| **Urinary incontinence** | n | n | n | n | | n | n | n | n | | n | n | n | n | | n | n | n | n | n | n | n | n | |

-Transforaminal group:

One of the dogs was affected by mild L-S disc protrusion, one by mild L-S vertebral spondylosis and one by mild decreased intervertebral space between the fifth and sixth lumbar vertebrae. Transforaminal access was performed on the left (2 dogs) and right hand side (2 dogs). Presence of contrast medium in the epidural space confirmed the correct placement of the needle in all 4 dogs, with minimal subarachnoid contamination in 1/4 dog. In the remaining dog, transforaminal access was performed three times on both the left and right hand side, but vascular puncture occurred. When the needle is not in the correct position, it can be repositioned changing the obliquity of the insertion's angle. Nevertheless in the dog of our study, although during each attempt the obliquity of the needle was changed to try to avoid the vascular system, vertebral venous puncture occurred every time (figure 1). Therefore, no corticosteroid injection was performed. Nevertheless, this dog underwent regular clinical examinations and no complications were noticed. During the procedure, no increase of respiratory or heart rate, no alteration of hemoglobin oxygen saturation or of rectal temperature was reported. No major complications requiring hospitalization occurred. Overall, mild clinical abnormalities were noticed in 3/4 dogs, in 5/16 clinical examinations (Table 3). None of the dogs were affected during control examinations by pain at caudal lumbar spine palpation or tail hyperextension, hind limb lameness or proprioceptive deficits. Hyperthermia was detected in the same dog at day 3 and 7 (respectively 39.6°C and 39.7°C) and in another dog at day 7. At different others check-up performed on the same days, the body temperature was within normal limits in both dogs. Patellar, cranial tibial and withdrawal reflexes were considered normal in 4/4 dogs at day 1, day 3, and day 7, but mildly unilaterally increased in 1/4 dogs at day 10. The affected side corresponded with the side of injection. Perineal reflex was judged as normal in 5/5 dogs at day 1, decreased in 1/4 dogs at day 3, decreased in 2/4 dogs at day 7, and decreased in 1/4 dogs at day 10. None of the dogs were affected by urinary incontinence (Table 3).

When the control examination of the abnormalities was performed 24 days after the procedure in 3 dogs, no hyperthermia was detected but the perineal reflex was still considered decreased in 2/2 dogs. In one of the latter dogs, the perineal reflex was decreased at all controls from the 3rd day onwards, whereas it was intermittently decreased in the second dog. Indeed, in this dog, perineal reflex was considered decreased at day 7, normal at day 10, and decreased again at day 24 (Table 3). The patellar reflex was considered bilaterally increased in 1 dog, in which it had been considered unilaterally increased during the previous examination. Also, in the latter dog, cranial tibial and withdrawal reflexes, which were unilaterally increased during the previous examination, were considered normal 24 days after the procedure (Table 3). At the time of writing this manuscript (approximately 5 months after the procedure), the dogs of this group did not show any particular clinical symptom.

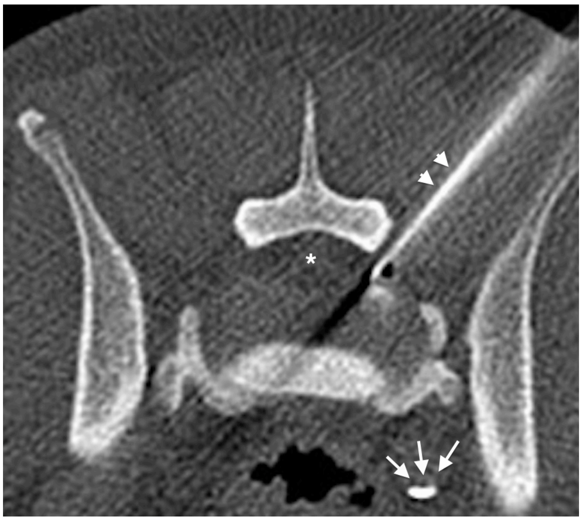

**Figure 1: Transverse Computed Tomography Image (bone window) of the lumbosacral region. In this dog, the needle (arrowheads) was inserted in a dorsolateral-ventromedial direction to perfom a transforaminal access and contrast medium was injected to verify its correct position. Despite the apparent intracanal placement of the needle, contrast medium was not visualized in the vertebral canal (*), but only in left lumbar vein (arrows), suggesting vertebral venous plexus puncture and contrast medium migration.**

-Translaminar group:

Two of them were affected by mild L-S vertebral spondylosis, and one of them by mild disc protrusion. A CT scan after the injection of contrast medium confirmed the correct placement of the needle in the epidural space. In 2/5 dogs a minimal subarachnoid contamination was also noticed. During the procedure, no increase of respiratory or heart rate, no alteration of hemoglobin oxygen saturation or of rectal temperature was recorded. No major complications requiring hospitalization occurred. Overall, mild clinical abnormalities were reported in 4/5 dogs, in 6/20 clinical examinations (Table 4) during control clinical examinations. One dog showed mild hyperthermia with normal temperature at different checks during the same day. No dogs showed pain at caudal lumbar spine palpation or tail hyperextension, hind limb lameness or proprioceptive deficits. The patellar, cranial tibial and withdrawal reflexes were normal in 5/5 dogs at day 1 and day 3, and were unilaterally decreased in one dog both at day 7 and day 10. The perineal reflex was judged normal in 5/5 dogs at day 1 and 3, and judged decreased in 2/5 dogs at day 7, and in 3/5 dogs at day 10. None of the dogs were affected by urinary incontinence (Table 4). When the control of the altered reflexes was performed 24 days after the procedure in 3 dogs, no changes were noticed compared to previous examinations (Table 4). At the time of writing this manuscript (approximately 5 months after the procedure), the dogs of this group did not show any particular clinical symptom.

**Table 3: Summary of clinical examination results of dogs, which underwent transforaminal lumbosacral epidural injection on the right (R) or left (L) hand side. The first clinical examination was performed on day 1, the second on day 3, the third on day 7 and the fourth on day 10 after the procedure. A control of the altered reflexes was performed 24 days (fifth clinical examination) after the procedure. (a=absent; p= present; n = normal; ↑= bilaterally increased; ↓= bilaterally decreased; ↑L = increased on the left hand side).**

| **Transforaminal group** | **Dog 1<br>L** | | | | **Dog 2<br>R** | | | | | **Dog 3<br>R** | | | | | **Dog 4<br>L** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Clinical examination** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** | **5** |
| **Hyperthermia** | a | a | a | a | a | **p** | **p** | a | | a | a | **p** | a | | a | a | a | a | |
| **Pain at caudal lumbar spine palpation** | a | a | a | a | a | a | a | a | | a | a | a | a | | a | a | a | a | |
| **Pain during tail hyperextension** | a | a | a | a | a | a | a | a | | a | a | a | a | | a | a | a | a | |
| **Proprioceptive deficits** | a | a | a | a | a | a | a | a | | a | a | a | a | | a | a | a | | |
| **Hind limb lameness** | a | a | a | a | a | a | a | a | | a | a | a | a | | a | a | a | a | |
| **Patellar reflex** | n | n | n | n | n | n | n | n | | n | n | n | n | | n | n | n | ↑L | ↑ |
| **Cranial tibial reflex** | n | n | n | n | n | n | n | n | | n | n | n | n | | n | n | n | ↑L | n |
| **Withdrawal reflex** | n | n | n | n | n | n | n | n | | n | n | n | n | | n | n | n | ↑L | n |
| **Perineal reflex** | n | n | n | n | n | ↓ | ↓ | ↓ | ↓ | n | n | ↓ | n | ↓ | n | n | n | n | |
| **Urinary incontinence** | n | n | n | n | n | n | n | n | | n | n | n | n | | n | n | n | n | |

**Table 4. Summary of clinical examination results of dogs that underwent lumbosacral translaminar epidural injection. The first clinical examination was performed on day 1, the second on day 3, the third on day 7 and the fourth on day 10 after the procedure. A control of the altered reflexes was performed 24 days (fifth clinical examination) after the procedure. (a= absent; p= present; n = normal; ↓= bilaterally decreased; ↓R = decreased on right side).**

| Translaminar group | Dog 1 | | | | | Dog 2 | | | | | Dog 3 | | | | | Dog 4 | | | | | Dog 5 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Clinical examination** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** | **5** | **1** | **2** | **3** | **4** |
| **Hyperthermia** | a | a | a | a | | a | a | a | **p** | a | a | a | a | a | | a | a | a | a | | a | a | a | a |
| **Pain at caudal lumbar spine palpation** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a |
| **Pain during tail hyperextension** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a |
| **Proprioceptive deficits** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a |
| **Hind limb lameness** | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a | | a | a | a | a |
| **Patellar reflex** | n | n | ↓R | ↓R | ↓R | n | n | n | n | | n | n | n | n | | n | n | n | n | | n | n | n | n |
| **Cranial tibial reflex** | n | n | ↓R | ↓R | ↓R | n | n | n | n | | n | n | n | n | | n | n | n | n | | n | n | n | n |
| **Withdrawal reflex** | n | n | ↓R | ↓R | ↓R | n | n | n | n | | n | n | n | n | | n | n | n | n | | n | n | n | n |
| **Perineal reflex** | n | n | ↓ | ↓ | ↓ | n | n | n | n | | n | n | ↓ | ↓ | ↓ | n | n | n | ↓ | ↓ | n | n | n | n |
| **Urinary incontinence** | n | n | n | n | | n | n | n | n | | n | n | n | n | | n | n | n | n | | n | n | n | n |

-Control group:

No dogs showed hyperthermia, pain at caudal lumbar spine palpation or tail hyperextension, hind limb lameness or proprioceptive deficits. The cranial tibial reflex was considered decreased during the last clinical examination in one dog, which did not show any other abnormalities or neurological deficits. The perineal reflex was considered increased during the second clinical examination in another dog and then normal again during the last clinical examinations in absence of other neurological deficitis (Table 5). At the time of writing this manuscript (approximately 5 months after the procedure), the dogs of this group did not show any particular clinical symptom.

**Table 5: Summary of clinical examination results of control group dogs. The first clinical examination was performed on day 1, the second on day 3, the third on day 7 and the fourth on day 28 after the procedure (a= absent; n = normal; ↑=bilaterally increased; ↓= bilaterally decreased).**

| | **Dog 1** | | | | **Dog 2** | | | |
|---|---|---|---|---|---|---|---|---|
| **Clinical examination** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** |
| **Hyperthermia** | a | a | a | a | a | a | a | a |
| **Pain at caudal lumbar spine palpation** | a | a | a | a | a | a | a | a |
| **Pain during tail hyperextension** | a | a | a | a | a | a | a | a |
| **Proprioceptive deficits** | a | a | a | a | a | a | a | a |
| **Hind limb lameness** | a | a | a | a | a | a | a | a |
| **Patellar reflex** | n | n | n | n | n | n | n | n |
| **Cranial tibial reflex** | n | n | n | n | n | n | n | ↓ |
| **Withdrawal reflex** | n | n | n | n | n | n | n | n |
| **Perineal reflex** | n | ↑ | n | n | n | n | n | n |
| **Urinary incontinence** | n | n | n | n | n | n | n | n |

## ***Discussion:***

According to the results of our study, CT-guidance associated with contrast medium injection allows to verify the correct position of the needle and to avoid major complications. Minor complications, considered not clinically of concern, have been associated with the CT-guided translaminar and transforaminal ESI and CT-guided facet joint intra-articular injections. In human medicine, because of the high rate of erroneous needle placement associated with the "blind" ESI technique (Bartynski *et al.*, 2005), many imaging-guided techniques have been developed (Silbergleit *et al.*, 2001). Among these, CT-guidance is considered the most accurate (Hoeltje *et al.*, 2013). Nevertheless, subarachnoid contamination or vertebral venous punctures are still reported as possible complications (Watanabe *et al.*, 2002). The former is more commonly associated with translaminar access, while the latter with transforaminal access (Watanabe *et al.*, 2002; Wilkinson et Cohen, 2013; Liotta *et al.*, 2015b). Therefore, we decided to test the safety of both CT-guided accesses. The translaminar technique is usually preferred to treat multifocal pain because there is an increased likelihood to reach adjacent spinal levels with only one injection (Wilkinson et Cohen, 2013). On the other hand, transforaminal access is the most target-specific technique and proves useful in cases of lateralized compression. It is associated with a lower risk of inadvertent dural puncture but with an increased risk of vascular puncture (Wilkinson et Cohen, 2013; Liotta *et al.*, 2015b). In veterinary medicine, subarachnoid contamination was also reported in a study concerning ultrasonographic epidural access (Liotta *et al.*, 2015a). This is in agreement with the results of our study, where we recorded a mild subarachnoid contrast opacification in 2/5 dogs with the translaminar injection, and in 1/4 dogs with the transforaminal injection. However, in our study, vertebral venous puncture occurred on both sides only during transforaminal access in one dog. We decided not to perform the corticosteroid injection when vascular puncture occurred. Computed tomography-fluoroscopy could be used to guide needle placement more precisely, by allowing a dynamic visualization of the needle path and of the contrast medium spread, thus identifying potential intrathecal or vascular puncture (Wagner, 2004). However, this technique was not available in our facility and we assumed vascular puncture in our dog because of the absence of contrast medium at the injection site, showing the utility of contrast medium injection before the injection of corticosteroids. In our study we used an iodinated non ionic contrast medium. The iodinated ionic contrast media are considered more harmfully and contraindicated in case of subarachnoid injection. In human medicine, intravascular injection of corticosteroids is considered harmful, especially when the arterial system is involved because of potential embolic phenomena related to the particulate nature of injected steroid, potentially resulting in a stroke, seizure or permanent paralysis (Watanabe *et al*., 2002; Kozlov *et al*., 2015). Therefore, during daily clinical procedures, corticosteroid molecules are not injected when vascular puncture occurs. In 14/14 dogs that underwent corticosteroid injections, none of these complications were reported during our procedure, supporting our theory that CT-guidance allows a verification of the correct needle placement in dogs. This is in agreement with human literature that considers CT-guidance as the most effective technique to perform ESI (Hoeltje *et al*., 2013). Conversely, we decided to inject corticosteroid when dural puncture occurred. Indeed, we retained that during clinical procedure erroneous *dura mater* prickling may occur, without a true intrathecal position of the needle. In our study, this was confirmed by the minimal amount of subarachnoid contamination compared to the epidural spread of contrast medium. However, in cases of true intrathecal position of the needle, methylprednisolone injection should be avoided because of possible complications that are described in both humans and dogs, such as corticosteroid-induced arachnoiditis (Watanabe *et al*., 2002; Lima *et al*., 2010).

The preferred modality to perform facet joint injections in many human medical centers is CT-guidance, (Hoeltje *et al*., 2013) which allows a high accuracy with a described 94% procedural technical success rate (Weininger *et al*., 2013). However, the literature is controversial and does not insist on precise intra-articular injection because clinical improvements have been described with periarticular injections. Moreover, periarticular injections are recommended when intra-articular injection proves difficult (Peh, 2011). Therefore, in our study, we performed corticosteroid injections even when CT arthrography showed a periarticular contrast medium spread.

According to our results, no major complications occurred. Some altered reflex responses and hyperthermia were noticed in all injection groups, as well as in the control group dogs. Hyperthermia is defined as any increase of body temperature above the generally accepted normal range and a threshold of 39.2°C has been suggested (Miller, 2010). However, the normal range is variable and may be influenced by many factors. In our study, we considered dogs to be hyperthermic when the temperature was above 39.4°C. Some dogs had a body temperature slightly above this threshold, without presenting any other clinical abnormalities. During clinical examination, these hyperthermic dogs behaved in a nervous manner and in all cases their temperature was within normal limits at different checks control during the same day once the dog was at rest. Therefore, we can postulate that this temporary increase in temperature was more likely to be environment- or behavior-related rather than secondary to a true disease. In our study, some altered responses of the patellar, cranial tibial, withdrawal and perineal reflexes were noticed without motor, sensor or postural deficits. Some of these alterations showed a fluctuating nature. For instance the perineal reflex was altered during the third clinical examination, normal at the fourth and altered again at the last clinical examination in one dog (dog number 2, facet joint injection group); and the withdrawal reflex was decreased (third clinical examination), normal (fourth clinical examination) and then increased (fifth clinical examination) in another dog (dog number 3 facet joint injection). The cranial tibial and the perineal reflexes were considered altered in the dogs of the control group as well. These reflexes assess the neurological integrity from the fourth lumbar spinal cord to the third sacral spinal cord segment (Thomas et Dewey, 2008). Reduced spinal reflexes may be caused by a lesion affecting the sensory and motor component of the reflex arch, while exaggerated reflexes are usually caused by a lesion in the upper motor neuron pathways cranial to the spinal segment involved in the reflex (Thomas et Dewey, 2008). Interestingly, even control group dogs showed mild alteration of some reflexes, highlighting the subjective nature of the assessment of these reflexes and reducing the clinical meaning of these findings in the injection group dogs. Indeed, the clinical meaning and underlying etiologies of these reflexes alterations should be interpreted taking into account the absence of motor, sensor or postural deficits, the subjective interpretation and the fluctuating nature of some of these reflexes and the fact that they were noticed even in the dogs of the facet joint groups and in the control group dogs.

In human medicine, paraspinal abscesses and arthritis are sporadically reported as complications following facet joint injections (Hoeltje *et al.*, 2013). Infectious spread into the epidural space and subsequent meningitis has also been rarely described, with a frequency rate of less than 1% (Hoeltje *et al.*, 2013). In our study, it is difficult to believe that the dogs were affected by meningitis with consequential exaggerated patellar, withdrawal, cranial tibial and perineal reflexes in the absence of any other clinical signs or without worsening the following days in absence of treatment. Therefore, among the possible explanations, we can postulate accidental nervous structure punctures, small epidural/subdural hematoma or a behavior-related explanation. Indeed, altered muscle stretch reflexes are described in excited or anxious patients (Thomas et Dewey, 2008). We strongly believe that the latter is the most reasonable explanation for the altered reflexes observed in the dogs of our study. However, limitations of our study are the absence of MRI examinations or histological examinations enabling us to rule out that these altered reflexes were related to our procedure in the injections group dogs, such as the formation of a hematoma or were secondary to a specific neurologic disease in the control group dogs. Even if with the formation of a hematoma, immediate reflexes' alterations would have been expected and not noticed only during late clinical examinations as in some dogs of our study. The absence of other tests, such as urinalysis and blood tests, to rule out abscess, meningitis or other infection could be considered another limitations. However, it is really unrealistic that these dogs could have suffered from these diseases without showing other clinical signs, such as pain at the LS region, and in absence of motor/sensor or postural deficits. The absence of clinical signs should also be evaluated, considering that no antibiotic therapy was administered at any time of the study. Therefore, we strongly believed that the presence of soft tissue of infection, abscess or meningitis can be ruled out in the dogs of our study. Besides the absence of histological, MRI or other complementary examinations, this study has other limitations such as the presence of only two dogs in the control group, the small number of dogs used and the single corticosteroid injection. Even if only two dogs were part of the control group, we considered interesting to include the results of their clinical examinations to show the fluctuating nature of the spinal reflexes in dogs that did not undergo any kind of injections. In human medicine there is no absolute data regarding the number of injections, a series of injections is often suggested if patients are not completely relieved after the first ESI (Watanabe et al., 2002). Moreover, long-term complications were not evaluated. The beneficial effects of corticosteroids on articular cartilage occur especially at low dose and short-duration. At higher dose and long duration, corticosteroids are associated with gross cartilage damage and chondrotoxicity. For instance, steroid arthropathy has been described as complications in horses (Harkins *et al.,* 1993; Mcilwraith CW., 2010). In particularly methylpredinosolone acetate has been associated with deleterious effects, whilst no collateral effects have been found with betamethasone (Mcilwraith CW., 2010). However, in the dogs of our study, only one injection has been performed. To date (approximately 5 month after the procedure) none of the dogs used in this study showed any particular symptom. In human medicine transient worsening of symptoms or emergence of new neurologic symptoms for more than 24 hours after the injection occurred in 4% of patients with a median duration of 3 days and range from 1 to 20 (Watanabe et al., 2002). In the majority of the dogs of our study, the last clinical examination was performed at 24 days. Therefore, the examinations performed in this study were considered by the authors sufficient to assess the presence or absence of infectious disease, and abscess formation, which are among the commonly reported complications in human medicine (Wilkinson et Cohen, 2013).

In conclusion, the results of this study should be interpreted as preliminary research results and suggest that CT-guidance and contrast medium injection allows to verify the position of the needle and to avoid injections into the vascular system causing possible major complications. Furthermore, this study demonstrates that minor neurological alterations can be recorded after corticosteroid injections in the epidural and facet joint space. However, these alterations can be considered clinically irrelevant and the use of these techniques can be suggested for clinical trials.

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# DISCUSSION, CONCLUSIONS AND GENERAL PROSPECTS

# GENERAL DISCUSSION AND SPECIFIC CONCLUSIONS

## ***IV. 1: General discussion and specific conclusions:***

Veterinary interventional radiology is a modern branch of veterinary imaging medicine and it has been predominantly used in the vascular field or as a diagnostic tool, such as imaging-guided FNAs or biopsy (Vignoli *et al.*, 2004; Vignoli et Saunders, 2011). Only recently, it has been an increased interest in developing new-imaging guided techniques with the final aim to reduce the failure rate of techniques, commonly performed blindly, or to guide the injection of molecules within the interest's target for therapeutic intent (Guilherme et Benigni, 2008; Campoy *et al.*, 2010; Echeverry *et al.*, 2010; Etienne *et al.*, 2010; Haro *et al.*, 2011; Gregori *et al.*, 2014; Kneissl *et al.,* 2014; Viscasillas *et al. 2014*). Therefore, it was essential to investigate the feasibility of new imaging-guided techniques and to assess their accuracy and clinical safety.

Theoretically, imaging-guidance can involve a large variety of regions. The leitmotiv of our project was the L-S region. We chose this latter for two main reasons: a variety of "blind" procedures with a variable failure's rate are commonly performed in this region and the absence of highly successful therapies in the treatment of L-S diseases. For instance, among the "blind" procedures epidural anesthesia is commonly performed at the L-S space and itconsists in the injection of anesthetic and analgesic drugs within the epidural space to provides anesthesia for surgical procedures involving the hindlimbs (Torske et Dyson, 2000; Jones, 2001; Valverde, 2008). It is commonly performed blindly, by palpation of the seventh lumbar spinous process and iliac wings. However, failure of the blind technique has been reported, predominantly related to obesity or congenital malformations of the vertebral column (Torske et Dyson, 2000; Jones, 2001; Valverde, 2008).

In old dogs, especially large breed dogs, the L-S region is as well often affected by degenerative changes leading to compression of the *cauda equina* (Meij et Bergknut, 2010). Both medical and surgical treatments have been described. The first is mainly focused on the reduction of the pain perception and tends to be ineffective long-term, whilst the surgical treatment aims to decompress the *cauda equina* nerves, but many intra, early or late postoperative complications have been described with surgical treatment (Sharp et Wheeler, 2005; Dewey, 2008). More recently, a retrospective study suggested ESI as an alternative to surgical treatment (Janssens *et al.*, 2009). However, in this study the absence of systematic neurological examinations to confirm the safety and outcomes of this technique increased the need to carry on further systematic studies concerning the ESI.

In DLSS disc herniation is commonly related to Hansen type II disc degeneration (Meij et Bergknut, 2010). In human medicine, new therapeutic strategies are focusing on the treatment of the IVD degeneration process (Hohaus *et al*., 2008; Yim *et al*., 2014; Wang *et al*., 2015). The basic principle of these new therapies is to use stem cells to regenerate the normal IVD population cells, capable to produce the extracellular matrix (Yim *et al*., 2014; Wang *et al*., 2015). Hypothetically, if these techniques are proved to be effective, they could be suggested for the treatment of chronic IVD degeneration such as in case of DLSS. However, at the moment only few pre-clinical randomized controlled animal trials studies have been conducted on dogs and disc degeneration was created artificially, (Yim *et al*., 2014; Wang *et al*., 2015). Therefore, a systematic study describing this technique on naturally degenerated IVD was still lacking.

For all the aforementioned reasons our research project was more specifically divided in four studies.

In the **first phase** of this project the feasibility of a new US-guided epidural access in dogs was assessed. Recently an US-guided epidural access has been described at the sacrococcygeal space (Gregori *et al.,* 2014), but in small animals epidural anesthesia is more commonly performed at the L-S space (Torske et Dyson, 2000; Jones, 2001; Valverde, 2008). Rate of the "blind" epidural technique has been estimated to range from 7 to 12% (Troncy *et al*., 2002) and different tests, such as "hanging drop" technique or "loss of resistance test" are described to verify needle placement (Torske et Dyson, 2000; Jones, 2001; Valverde, 2008). These tests are based on the negative pressure within the epidural space. This negative pressure attracts the solutions, once that the needle has reached the epidural space. However, several factors including tissue plugs obstructing the needle, increased central venous pressure, or negative pressure associated to suspraspinous fat may induce false tests results (Troncy *et al*., 2002; Valverde, 2008). The most important factors that make this technique difficult to perform "blindly", are obesity, anatomic malformations or degenerative changes in L-S spine. Therefore, to assess our technique we applied it on both normal dogs and dogs with radiographic abnormalities of the L-S spine, normal weighting and overweighting dogs, on cadavers and in live dogs. The technique was successfully performed on all dogs, even if application of the technique was subjectively more difficult in one of the two cadavers with LS radiographic abnormalities and in one of the two overweight cadavers, likely related to the modified shape of the bony surfaces and reduced image quality because of subcutaneous fat. However, the difficulty in performing this technique was not objectively quantified (for instance number of attempts or amount of time were not recorded) and this could represent a limitation of this study.

To verify the correct needle's position, contrast medium was injected, followed by a CT examination. Interestingly, beside the large amount of contrast medium in the epidural space confirming the success of our technique, a various amount of subarachnoid contamination in dogs of all groups was noticed. This contamination was considered more important when spinal needles were used compared to epidural catheters. In live dogs the injection of contrast medium was as well preceded by the "hanging drop" technique or "loss of resistance test", which are commonly performed during "blind" technique to verify the correct position of the needle (Jones, 2001; Valverde, 2008). In all cases, the results of these tests were in agreement with ultrasonographic images, confirming the epidural position of the needle. Therefore, given the large amount of epidural contrast medium, the epidural position assessed during the ultrasonographic technique and the positive "hanging drop" and "loss of resistance" tests, three hypotheses concerning the subarachnoid contamination can be postulated. According to the first hypothesis the subarachnoid contamination was related to the permeability of meninges. Epidural leakage due to increased meningeal permeability was reported in a dog, following myelographic examination (Carstens et Kitshoff, 2007). The epidural leakage was noticed far away from the injection site and histologically no communication between the injection site and the leakage site was noticed. Instead *the dura mater* was affected by severe inflammatory changes with degenerated collagen. For this reason, the authors assumed an increased permeability of the *dura mater* as the primary cause of the leakage. Among the spinal meninges the *arachnoid mater* has been identified as the principal diffusion barrier. The physical and chemical properties governing the diffusion process have been studied with a biphasic relationship between hydrophobicity and meningeal permeability coefficient (Bernard et Hill, 1990; Bernard et Hill, 1992). However, to our knowledge, no study evaluating the possible diffusion process of iohexol through the meninges has been conducted. Therefore, permeability of the meninges as cause of communication between the subarachnoid and epidural space is only one hypothesis that could be supported by the fact that subarachnoid contamination in our study was considered more important in cadavers than in live dogs. According to the second hypothesis, the subarachnoid contamination was related to a particular vascular drainage of the *dura mater*. For instance, in a cadaveric study (Kneissl *et al.*, 2015) subarachnoid contamination was noticed during perineural infiltration, although direct application in the subarachnoid space was not expected given the position of the needle tip. The authors postulated the likelihood of a retrograde passage of contrast medium trough the puncture of postmortally collapsed periforaminal veins. A drainage system of the CSF into the perispinal veins is described in the rabbits and the authors based its hypothesis on the assumption that this pathway could be present in dogs. According to the third hypothesis a dural puncture occurred in our dogs during needle insertion in the vertebral canal. This hypothesis is partially supported by the fact that a greater amount of subarachnoid contamination was recorded with spinal needles compared to the epidural catheters, which are considered less harmful. In human literature, dural puncture is a well-known complication during epidural anesthesia, resulting in postdural puncture headache (Norris *et al.*, 1989; Macarthur *et al.*, 1993; Reynolds, 1993; Bezov *et al.*, 2010; Waise et Gannon, 2013). In parturients receiving epidural anesthesia, the incidence of dural puncture is reported to be between 0% and 2.6% (Reynolds, 1993) and incidence is reported to be inversely related to the anesthetist's experience, to be correlated to size and shape and needle used, and to be reduced by orientation of the needle bevel parallel to the dural fibers (Norris *et al.*, 1989; Macarthur *et al.*, 1993; Reynolds, 1993; Bezov *et al.*, 2010; Waise et Gannon, 2013). It is reasonable to think that these factors can influence the degree of subarachnoid contamination even in veterinary medicine. Nevertheless, for our project we used the same kind of spinal needle that is commonly used at our institution when performing subarachnoid or epidural access. Therefore, the use of other kinds of needle, for instance with a larger gauche, should be suggested for the future.

Histological examinations that could have confirmed our hypothesis were not performed and therefore it is another limitation of our study.

Eventually, we demonstrate that the US-guided epidural injection technique at the L-S space was feasible in dogs. This technique could be a valid aid during anesthetic procedures, especially in obese dogs or in dogs with anatomic degenerative changes of the L-S spine. However, this study had some limitations. First of all, a low number of overweight and abnormal dogs were included in the study. Moreover, this technique was always performed by the same operator with experience in the US field. Theoretically this technique would be potentially helpful in daily clinical activity during difficult anesthetic procedures and should be therefore used by anesthetists with limited experience in performing US. Therefore, it would have been interesting to assess its feasibility in normal clinical activity. In human medicine the usefulness of US-guidance *vs* “blind” technique has been studied. According to the majority of the studies the imaging-guidance helps in reducing the number of attempts, number of complications and overall the failure rate concerning many procedures (Verghese *et al.*, 1999; Miller *et al.*, 2002; Milling *et al.*, 2005; Tran *et al.*, 2010; Nassar et Abdelazim, 2015), involving the epidural access too (Grau *et al.,* 2001; Bauer *et al.*, 2012). In veterinary field, two recent studies focused on this topic. In the first study it has been shown that the US-guidance improves the success rate when subarachnoid access is performed by inexperienced veterinarians (Etienne *et al.,* 2014) and the second demonstrated a higher total success rate and a decreased number of attempts for the US-guided technique when the subarachnoid access was performed by last year students (Etienne *et al.*, 2015). These studies were focused on subarachnoid puncture technique, but given the similarities between the two techniques we can postulate similar results for our epidural technique. However, the true usefulness of this technique for experienced anesthetists has still to be studied, especially on obese patients or on dogs with malformation of the L-S spine. In the future, further studies are therefore needed to completely validate the use of the US-guided technique in daily clinical activity.

In the **second phase** of our project new CT-guided epidural and facet joint injections techniques were developed and their difficulty and accuracy were assessed.

In human medicine, epidural injections with corticosteroids are commonly performed to treat low back pain and radiculopathy (Watanabe *et al.*, 2002; Wilkinson et Cohen, 2013). Theoretically, different imaging modalities can be used to perform interventional imaging. Three-D reconstructions typical of cross-sectional imaging modalities such as CT or MRI, in contrast to 2-D techniques such as fluoroscopy or US, allow a better visualization of the target and therefore a better planning of the path to the target (Mahnken *et al.*, 2013). MRI is considered the modality of choice for the assessment of the L-S disease, but CT-guidance is the preferred modality to perform epidural and facet joint injections, because it is considered the most exact procedure with reported accuracy of 94% (Silbergleit *et al.*, 2001;Weininger *et* *al.*, 2013). MRI-guided procedures are indeed limited in both human and veterinary patients by the need of special coils and dedicated non-ferromagnetic biopsy instruments (Vignoli et Sanders, 2011; Westbrook *et al.,* 2011; Mahnken *et al.*, 2013). With CT-fluoroscopy the advantages of both fluoroscopy and CT are obtained and this technique could be used to guide needle placement more precisely (Wagner, 2004), however this technique is rarely available in veterinary medicine and it is more expensive. In the anesthetic field, US-guided procedures are widely used to perform epidural anesthesia (Grau *et al.*, 2001; Karmakar *et al.*, 2009; Bauer *et al.*, 2012) or local plexus blocks (Marhofer *et al.*, 2005; Mejia-Terrazas *et al.*, 2015; Sehmbi *et al.*, 2015; Seidel *et al.*, 2015). In the previous phase of our project we described the US-guided technique to perform epidural access and we suggested its use for anesthetic purposes. This previously described US-guided epidural access can be performed to administer different kind of molecules. However, in veterinary medicine, the investigation of spinal diseases in dogs is routinely performed by CT or MRI examination (Mai, 2013). For the aforementioned reasons, we decided to develop a CT-guided technique, warranting that CT could be used concurrently for both diagnostic and therapeutic purposes in a clinical setting, such as steroid injections as treatment of DLSS.

Two different epidural accesses can be performed: translaminar (synonymous= interlaminar) or transforaminal (Watanabe *et al.*, 2002; Wilkinson et Cohen, 2013). The first usually chosen in case of multifocal, the second in case of lateralized compressions (Watanabe *et al.*, 2002; Wilkinson et Cohen, 2013). Literature is controversial concerning which access should be considered the most efficacious. The majority of the authors considered the transforaminal access the most efficacious. Indeed it seems that the direct deposit of the injectate over the affected area is associated with the best outcome. A possible explanation is the presence of particular septa in the epidural space of humans that could prevent spread of the molecules (Wilkinson et Cohen, 2013). In our study both accesses were described and assessed. According to our results, translaminar and transforaminal epidural accesses are both feasible and accurate, but translaminar access is easier to perform and more accurate. Possible incorrect needle position can cause subarachnoid contamination and vertebral venous plexus puncture, respectively more likely with translaminar and transforaminal access. These results were in agreement with human literature. Advantages of the translaminar technique are the ability to treat bilateral pain with only one injection and the increased likelihood that the injected substance will reach adjacent spinal levels. However, an increased likelihood of dural puncture is also described (Watanabe *et al.*, 2002; Wilkinson et

Cohen, 2013). The transforaminal epidural technique, on the other hand, is most target-specific, such as in cases of lateralized disc or nerve root compression. It is associated with a lower risk of inadvertent dural puncture but with an increased risk of vascular puncture (Watanabe *et al.*, 2002; Wilkinson et Cohen, 2013). This latter can be very harmful and in particularly, stroke, seizure or permanent paralysis are described in human literature in case of intravascular arterial injection of corticosteroids (Watanabe *et al.*, 2002). In our study, accuracy was assessed on cadavers and we decided to consider highly accurate the injection if contrast medium was visualized only within the target, and accurate if the majority of, but not all, the contrast medium was visualized within the target. Therefore even if a small amount of subarachnoid contamination occurred, the epidural injections were still considered accurate. This grading system could be criticized, but on the other hand it should be considered that postmortem alterations of meninges and surrounding soft tissues could have negatively influenced the accuracy results and contribute to the subarachnoid contamination. *In-vivo* accuracy studies are therefore necessary to validate these results.

The second part of this study was focused on facet joint injections. According to our results, CT-guided facet joint injections are moderately accurate and their difficulty depends on facet joint size. In our study, accuracy of facet joint injections was negatively influenced by periarticular spread and was lower than described in a recent study concerning US-guided access of the cervical facet joint in dogs (Levy *et al.*, 2014), cervical and thoracolombar facet joints in horses (Nielsen *et al.,* 2003; Cousty *et al.,* 2009) and it was lower compared to human medicine (Weiniger *et al.*, 2013). However, in another study focused on accuracy of US-guided thoracolumbar facet joint in horses, the intra-articular injections were only 27% (Fuglbjerg *et al.,* 2012). We may only postulate that this discrepancy could be, in part, the result of a different grading system and in part be related to the size of the lumbar joint space compared to the cervical spine or to the human articular processes. In our study, size of facet joints seemed to play an important role in the success and accuracy of the technique. Indeed, even if we did not carry out statistical analysis because of the low number of dogs in our study, success of the technique was dependent on the size of the target. Not surprisingly L7-S1 facet joint, which was more commonly of larger size, had the highest success rate. The amount of contrast medium injected could also have been influential. In human medicine, rupture of the capsule and periarticular and epidural spread are described as a possible complication (Peh, 2011; Hoeltje *et al.,* 2013). Termination of the injection is therefore suggested when resistance is encountered (Peh, 2011). However, literature is controversial and does not insist on precise intraarticular injection because equivalent results have been described with periarticular injections. In fact, periarticular injection is recommended, especially in case of difficult intraarticular injection (Peh, 2011). Even in equine medicine, precise intraarticular infiltrations are not considered mandatory and paraspinal and periarticular injections are suggested for the treatment of synovial intervertebral arthropathy (Denoix and Dyson, 2001). Dogs of our study were divided in two groups and two different volumes of contrast medium were injected. However, given the low number of injections, the different sizes of the facet joint space and the difficulty in objectively classifying the periarticular spread, no statistical conclusion may be drawn concerning the maximum volume to inject to prevent periarticular spread. Eventually we could postulate that periarticular spread is a possible complication of incorrect needle position but it could be related as well to the amount of contrast medium and secondary rupture of the capsule. For this reason, the success of the technique was not taken into account in assessing difficulty, which was exclusively meant as an estimation of the technical effort in reaching the target and not as the ability to fill the joint space. The average number of guiding scans needed for the final needle position was higher compared to human medical literature (Weininger *et al*., 2013). Possible explanations are anatomical and morphological difference between dogs and humans or varying degrees of experience of the operators.

In conclusion, this *ex-vivo* study can be considered a preliminary result and showed that CT-guided epidural and facet joints injections are feasible and variably accurate techniques. Theoretically, their use can be suggested to administer locally analgesic and anti-inflammatory drugs for the back pain treatment. However, the dogs of our study did not suffer from severe spinal or foraminal compressions or from severe degenerative joint disease of the facet joints. Therefore to apply these techniques in the daily clinical activity, our results need to be confirmed by further studies, assessing the *in vivo* feasibility and safety, on both normal and pathologic dogs.

In the **third phase** of our project we assessed *in vivo* safety of CT-guided corticosteroid injections within the epidural and facet joint space.

In human medicine, a major complication rate of 0.07%, requiring attendance in an emergency room or hospitalization, and a minor complication rate varying between 9,6% and

15,6% has been described with ESI and steroid facet joint injections (Johnson *et al.*, 1999; Watanabe *et al.*, 2002). In a previous study in dogs, ESI has been suggested as treatment for the DLSS (Janssens *et al.*, 2009). However, in that study dogs did not undergo a specific neurological examination but were evaluated by the owners according to a pre-scheduled exam. In our study we decided to assess clinical safety during and after the injections. No major or minor complications were recorded during the procedure, but because of the intravascular position of the needle following a transforaminal access, the corticosteroid injection in the epidural space was not performed in one dog. Corticosteroids intravascular injection is among the described complications in human medicine and can be associated with severe side effects such as stroke, seizure or permanent paralysis (Watanabe *et al.*, 2002). Therefore, injection of non ionic contrast medium before the administration of steroids is recommended and is commonly part of the imaging-guided technique protocol (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002). This is in agreement with the results of our study, where CT-guidance allowed the transforaminal access but only contrast medium injection confirmed the true position of the needle and avoided intravascular injections. Our results highlighted therefore the importance of contrast medium injection. Considering these results we could also suggest to perform a Doppler examination in case the injections are performed under US-guidance if DLSS is diagnosed by MRI examination. In the days following the procedures we assessed *in vivo* safety of the technique, performing regular neurological examinations according to a pre-scheduled clinical examination focused on the L-S region. With our clinical examinations we aimed to assess specifically the function of the peripheral nerves originating from the *cauda equina* by means of spinal reflexes. Reduced spinal reflexes may be caused by a lesion affecting the sensory and motor component of the reflex arch, while exaggerated reflexes are usually caused by a lesion in the upper motor neuron pathways cranial to the spinal segment involved in the reflex (Thomas et Dewey, 2008). More specifically, in the dogs of our study we assessed the integrity of the *n. femoralis* originating from the L4-L6 spinal segment by means of patellar reflex, with the cranial tibial and withdrawal reflex we assessed the *n. ischadicus*, originating from the L6-S1 spinal segment, whilst the *n. pudendus* originating from the S1-S3 spinal segment was assessed by means of the perineal reflex. During our clinical examinations we assessed not only the presence or absence of the spinal reflexes, but also we tried to quantify their possible increased or decreased entity. Retrospectively this choice is quite debatable. Indeed, even if the exams were performed always by the same person, it is quite difficult to define objectively their possible decreased or increased entity in comparison with a previous examination. In our dogs, the spinal reflexes were always present, but a mild alteration (increase or decrease) was recorded in absence of motor, sensor or proprioceptive deficits in many dogs of the study. Interestingly, even control group dogs that did not underwent any kind of injections showed mild alteration of some reflexes. These results highlighted the subjective assessment of these reflexes and instilled doubt on the “true” clinical meaning of these findings in the injection group dogs. Indeed, the clinical meaning and underlying etiologies of these reflexes alterations should be interpreted taking into account the absence of motor, sensor or postural deficits, the subjective interpretation and the fluctuating nature of some of these reflexes. It should also be considered that these alterations were noticed in all dogs of our study. Indeed, it appeared unrealistic that some dogs of our study, for instance dogs that underwent facet joint injections, could have suffered from a so large spinal lesion (extending from the spinal segment L4-S3) without other neurological deficits. It appears as well unrealistic that this hypothetical large lesion could have been caused by our injections that were always performed at the L-S level. For the aforementioned reasons we considered these minor complications clinically not of concern and we postulated that they could have been more behavior-related than true complications secondary to our injections. However, the results of our study highlighted the biggest limitation of our study design. No other complementary examinations, such as MRI, electromyography or histological examinations, were performed to objectively rule out other possible etiologies. Recently, in human medicine, a motion analysis software has been used to assess the patellar reflex (Tham *et al.,* 2013). According to the result of this study, this new reflex quantification method is a valid and reliable method to assess objectively deep tendon reflexes.

In human medicine, different molecules can be injected when performing ESI. Commonly injected substances in epidural space and facet joints are betamethasone, triamcinolone, and methylprednisolone (Watanabe et al., 2002; Peh, 2011; Wilkinson et Cohen, 2013). Sometimes, local anaesthetics such as lidocaine or bupivacaine can be added to ESI. Even if according to some authors there may be some long-term benefit with the addition of local anaesthetics, the origin of this benefit is not completely understood (Watanabe et al., 2002). Moreover, among the possible complications associated with the epidural use of anaesthetic molecules there is their possible absorption by the spinal cord causing sympathetic or motor blocakge. Therefore, when performing epidural anesthesia in veterinary medicine it has been suggested that epidural injectate should not exceed 6 ml, to prevent the absorption by the thoracolumbar or cervical spine when epidural anaesthesia is performed (Valverde ,2008). This aspect should be taken into account if anesthetics are used in conjunction with corticosteroids when performing ESI in dogs. The use of methylprednisolone in human medicine has been associated with arachnoiditis in case of intratechal administration; therefore triamcinolone is often the preferred molecule (Silberlgleit et al., 2000; Watanabe et al., 2002). In a control animal trial, methylprednisolone was injected intratechally in experimental dogs. Even if no neurological deficits were noticed in these experimental dogs, histological examinations confirmed the presence of histological changes in the dogs of this study, predominantly meningeal thickness (Lima et al., 2010). For the injections in the dogs of our study, methylprednisolone was used. This choice was made because the other molecules that are commonly used in human medicine were not commercially available for dogs in Belgium.

In conclusion after assessing the feasibility and accuracy of CT-guided epidural and facet joint injections, in this third phase of our project we assessed the *in vivo* safety of corticosteroids injections in epidural and facet joint space. Our results showed that no major or minor complications were recorded during the procedure and that the injection of contrast medium is essential to verify the position of the needle before steroid injections. Minimal neurological alterations of unknown etiology can be recorded in the days following the corticosteroids injections, but they can be considered not clinically significant. Therefore, the use of these techniques can be suggested for clinical trial.

# FINAL CONCLUSION AND GENERAL PROSPECTS

## *IV. 2. Final conclusion and general prospects:*

Our project has to be considered as a valid contribution to interventional radiology of the L-S region. Its aim was to develop and assess new imaging-guided procedures that could be useful in daily clinical activity. Firstly, these techniques could potentially reduce the failure rate of commonly performed "blind" techniques, and, secondly, they could be used to treat common diseases of the L-S region by means of precise and safe molecule injections within the target of interest. Therefore, we focused on the description of the imaging-guided techniques and on the assessment of their feasibility, accuracy, and safety. This study represents a preliminary step and further validations of these techniques still have to be performed. Indeed, we assessed the techniques on cadavers and experimental dogs and only a small number of pathologic dogs were included in our study. Moreover, the repeatability of these techniques was not assessed.

More specifically concerning the first study of our project, it would be interesting to assess the usefulness of the US-guidance in performing epidural anesthesia in pathological or obese dogs in comparison with the "blind" technique. Recent studies on the comparison between "blind" and US subarachnoid accesses showed an increased success rate when imaging-guidance was used (Etienne *et al., 2015*; Etienne *et al.*, 2016). These results need to be validated for the epidural access. Hypothetically, in a clinical setting our US-guided epidural access should be performed by anaesthetist to perform epidural anaesthesia in difficult patients, such as obese patients or in patients with anatomic malformation. Therefore the usefulness of the US-guided technique should be still evaluated studying the comparison between failure rate of "blind" *vs* "Us-guided" technique when performed by anesthetists. The comparison of the success rate of epidural access performed by experienced and non-experienced anesthetists should also be evaluated. Simultaneously, the learning process of the US-guided technique by experienced and non-experienced anesthetists should be taken into account and should be compared among experienced and non-experienced anesthetists using pathological and obese dogs.

In our study subarachnoid contamination was recorded. It would be therefore interesting to compare the degree of subarachnoid contamination among "blind" and US-guided technique, or among different spinal needles.

In human medicine, US-guidance is used to perform epidural anesthesia at any level of the spine, such as high lumbar or thoracic vertebral canal (Chin *et al.,* 2011). Therefore, in veterinary medicine, further studies could be performed to assess the use of US-guided epidural anesthesia at other levels than the L-S spine, such as thoracic or cervical spine.

The use of US-guidance by radiologists for therapeutic aims could also be hypothesized, for instance to inject corticosteroids within the epidural space if CT is not available.

Interesting ideas for the future concerning the treatment of the DLSS arise from the second and third phases of our project.

Firstly, clinical trials should be performed to study the effects of ESI and corticosteroid facet joint injections in dogs affected by L-S discal herniation, or degenerative joint disease of the articular processes, or in dogs affected by multiple diseases and multiple neural compressions at the L-S junction, and to compare these results with the current medical or surgical treatment. It could also be postulated that in presence of multiple diseases the local administration of corticosteroids or anaesthetics could also be used as a test to localise more precisely the site of pain. Moreover, multiple molecules, different doses or injection series should be assessed. Indeed, in human medicine, different substances are injected into the epidural space and facet joints, such as betamethasone, triamcinolone, methylprednisolone and bupivacaine (Watanabe *et al*., 2002; Peh, 2011; Wilkinson et Cohen, 2013). However, human literature is controversial concerning the different amounts that can be injected and no absolute recommendations are established about the frequency of injections. Repetition of the series can also be performed with different suggested intervals varying from 2 to 6 months (Watanabe *et al*., 2002; Peh 2011). All these parameters need to be estalished in dogs.

Secondly, transforaminal and translaminar epidural accesses should be compared to assess which one should be considered the most effective. As in human medicine, we can postulate that the interpretation of data concerning epidural steroid injections could be quite difficult because of the multiple, sometimes subtle, differences in patient pathology, region, and injection route. Therefore, multiple cross-sectional studies on large cohort of dogs are necessary to fully evaluate the usefulness of the epidural corticosteroid injections. Thirdly, injections of corticosteroids to treat spinal pain should not only be considered for the treatment of DLSS, but also for spinal pain secondary to disc compression at any level of the spine. For instance, it could be suggested for the treatment of Hansen type II disc herniation at the thoracic or cervical level. Indeed, in human medicine, thoracic and cervical epidural steroid injections are commonly performed with variable efficacy results (Benyamin *et al.,* 2012; Diwan *et al.,* 2012), and to reduce serious complications the use of imaging-guidance is considered essential to ensure appropriate delivery of medication into the epidural space (Diwan *et al.,* 2012).

Finally, steroid injections could be performed when surgical procedures, such as hemilaminectomy, are not technically advisable. Indeed, in veterinary medicine, it has been demonstrated that the extension of a hemilaminectomy up to 3 adjacent sites or bilaterally up to 2 adjacent sites does not increase the risk of injury to the lumbar vertebral column (Corse *et al*., 2003). However, beyond 3 adjacent sites, hemilaminectomy is not performed in daily clinical activity. Therefore, in cases of multiples (more than 3) and bilateral neural compressions (more than 2), the use of imaging-guided steroid injections could be suggested. Moreover, if surgical procedures are declined by the owners for financial reasons, ESI could be considered a less expensive alternative.

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# SUMMARY/RESUME

## ***V. 1: Summary:***

Interventional radiology is a branch of the modern medicine, which encompasses many diagnostic and therapeutic procedures and nowadays imaging-guided procedures are commonly performed in different fields, including cardiovascular, oncological, anesthetic and pain medicine (Mahnken *et al.*, 2013).The key of imaging-guidance procedures is the good visualization of the surrounding anatomical structures, with the intrinsic advantage of avoiding critical anatomical structures, compared to the " blind" techniques, allowing to reach the target with an increased precision and therefore reducing failure rate of the blind techniques (Mahnken *et al.*, 2013).For instance, in the human anesthetic field the reported success rate for blind epidural catheter placement at first attempt is approximately 60% (Bauer *et al.*, 2012). Therefore, many image-guided epidural injection techniques have been described (Silbergleit *et al.*, 2001; Watanabe *et al.*, 2002) and the use of ultrasound (US)-guidance is well established during anesthetic procedures (Karmakar *et al.*, 2009; Brinkmann *et al.*, 2012). Computed tomography (CT)-guidance is instead the preferred modality to inject corticosteroids epidurally or within the facet joint space to treat low back pain and radiculopathy (Hoeltje *et al.*, 2013).In veterinary medicine, epidural access is commonly used for anaesthetic purposes or more recently in the orthopaedic/neurological field to treat DLSS (Janssens *et al.*, 2009). Epidural analgesia is commonly performed "blindly" to provide intra- and post-operative pain control and reported failure rate technique ranges from 7 to 12% (Heath, 1992; Troncy *et al.*, 2002).

Degenerative lumbosacral stenosis is considered the most common cause of lumbosacral neurological dysfunction in old large-breed dogs (Sharp et Wheeler, 2005; Thomas et Dewey, 2008; Meij et Bergknut, 2010). Conservative and surgical treatments have both been described, but the first can be to be long-term ineffective and early or late postoperative complications have been described with the latter (Sharp et Wheeler, 2005; Thomas et Dewey, 2008; Meij et Bergknut, 2010). More recently, a retrospective study suggested epidural steroid infiltration as an alternative to surgical treatment (Janssens *et al.*, 2009).

The general aim of this project was to develop new interventional radiological procedures of the lumbosacral spine in dogs that can be used in the daily clinical activity to improve the success rate of the corresponding "blind" techniques or that can be applied with a therapeutic/diagnostic aim. Our hypothesis were that:

- It is possible and safe to perform US-guided epidural access at the L-S space;

- It is possible to perform CT-guided facet joints injections and different accesses of CT-guided epidural injections; the difficulty to perform these techniques and their accuracy is variable according to the access;
- CT-guided facet joints injections and CT-guided epidural injections can be considered clinically safe;

In the first phase of this project we described the feasibility of the US-guided epidural access at the L-S space in dogs. We assessed this technique with both spinal needle and epidural catheter on 20 cadavers divided in normal weight and overweight group, with and without radiographic abnormalities of the lumbosacral spine. Eventually, we applied this technique on 5 live dogs to assess clinical safety. Sonographically, the vertebral canal at the L-S junction was easily visualized and the epidural access was performed using as bony anatomic landmarks the seventh lumbar vertebra, the first sacral vertebra and the iliac wings. The target for directing the needle was the trapezoid-shaped echogenic image between the contiguous articular facets of the lumbosacral vertebral canal visualized in a parasagittal plane. The visualization of the deep structures varied depending on size of the dog, amount of subcutaneous fat and skin's hydration of the cadaver. CT examinations confirmed the presence of contrast medium in the epidural space of all cadavers and live dogs, but a various amount of contrast medium was noted in the subarachnoid space.

In the second phase of our study we described the technique and we assessed the difficulty and accuracy of CT-guided epidural and lumbar facet joint injections in dogs. More precisely, we evaluated two different epidural techniques at the L-S space, respectively the translaminar (synonymous interlaminar) and the transforaminal access. A total of 6 translaminar and 5 transforaminal epidural and 53 joint injections were performed. Translaminar injections had a high success rate (100%), were highly accurate in 75% of dogs, and easy to perform in all the dogs (100%). Transforaminal injections had an inferior success rate (75%), were accurate in 75% of dogs, and moderately difficult to perform in all the dogs. Therefore, translaminar and transforaminal epidural accesses are both feasible and accurate, but translaminar access is easier to perform and more accurate. Possible incorrect needle position can cause subarachnoid contamination and vertebral venous plexus puncture. Success rate of facet joint injections was 62% and was higher for larger facet joints, such as the L-S facet joints. Accuracy of facet joint injections ranged from accurate to highly accurate depending on the volume injected. In 58% of cases, injections were moderately difficult to perform.

In the third phase of this project we assessed the clinical safety of corticosteroids injections in the epidural space and in the lumbar facet joint space, performed under CT-guidance. Seventeen experimentally healthy dogs were included in this study: 2 as control group and 15 as injections groups, randomly divided in transforaminal, translaminar and facet joint group. Before each steroid injection, contrast medium was injected to verify the correct position of the needle. Vital parameters were recorded during the procedures and general and specific neurological examinations were performed in the days following the procedure to assess clinical safety. Finally, steroid injections were performed in 14/15 dogs. In 1 dog, contrast medium injection showed the intravascular position of the needle and steroid injection was not performed. No major or minor complications were reported during the procedure. In the days following the procedure no motor, sensor or postural deficits were noticed in dogs during clinical examinations, but only minimal transient hyperthermia and mildly altered patellar withdrawal, cranial tibial and perineal reflexes. Overall, altered reflex responses were observed during 27/65 clinical examinations in 11/14 dogs of injections groups, and in 2/2 dogs belonging to the control group during 2/8 clinical examinations. These neurologic alterations were considered clinically not of concern.

In conclusion our project has to be considered as a contribution to the interventional radiology of the L-S region in dogs. We aimed to develop and assess new imaging-guided procedures that could be useful in the daily clinical activity. First of all, these techniques could potentially reduce the failure rate of commonly performed "blind" techniques and secondly they could be used to treat common disease of the lumbosacral region by means of precise and safe molecules injections within the target of interest. Therefore we focused on technique's description and on the assessment of feasibility, accuracy and safety. Going into the detail, findings from our project indicated that:

-US-guided epidural access in normal weight and overweight dogs with and without abnormalities of the L-S spine is feasible, but subarachnoid contamination can be recorded as possible complication.

- CT-guided translaminar and transforaminal accesses at the L-S epidural space are both feasible and accurate, but translaminar access is easier to perform and more accurate. Possible incorrect needle position can cause subarachnoid contamination and vertebral vascular puncture. CT-guided lumbar facet joint injections are moderately feasible and accurate and their difficulty depends on facet joint size. Incorrect needle position can lead to periarticular spread.

- Minor neurological alterations, clinically not of concern, are associated with epidural steroid injection and corticosteroids injections in the lumbar facet joints. CT-guidance and injections of contrast medium allows avoiding major complications associated with intravascular corticosteroid injections.

However, our project represents only a preliminary step and the use of these techniques on daily clinical activity has still to be done. Many interesting studies focusing on this subject could be carried on. For instance, it would be interesting to assess the usefulness of the US-guidance in performing epidural anesthesia in pathological or obese dogs in comparison with the "blind" technique. Moreover, clinical trials should be performed to compare the useful of ESI and corticosteroids facet joint injections with the current medical or surgical treatment.

## V. 2: ***Résumé:***

L'imagerie interventionnelle est une branche de la médecine moderne qui inclut plusieurs procédures diagnostiques et thérapeutiques. Actuellement, les procédures assistées par l'imagerie sont fréquemment réalisées dans différentes disciplines, incluant la médecine cardiovasculaire, l'oncologie, l'anesthésie et la gestion de la douleur (Mahnken et Ricke, 2009). L'avantage des procédures assistées par l'imagerie est d'avoir une bonne visualisation des structures anatomiques environnantes et d'éviter les structures anatomiques critiques, contrairement aux techniques « à l'aveugle », permettant ainsi d'atteindre la cible avec une précision accrue et de réduire le taux d'échec des techniques « à l'aveugle » (Mahnken et Ricke, 2009). Notament, en anesthésie humaine, le taux de succès rapporté pour la pose de cathéter épidural à l'aveugle à la première tentative est approximativement de 60% (Bauer *et al.*, 2012). Plusieurs techniques d'injection épidurale assistées de l'imagerie ont été décrites (Silbergleit *et al.*, 2001 ; Watanabe *et al.*, 2002) et la technique écho-guidée est fréquemment utilisée dans les procédures d'anesthésie (Karmakar *et al.*, 2009 ; Brinkmann *et al.*, 2012). La technique scan-guidée est préférée pour l'injection de corticostéroïdes en épidural ou dans l'articulation intervertébrale en cas de traitement des douleurs dorsales basses ou des radiculopathies (Mahnken et Ricke, 2009). En médecine vétérinaire, l'accès épidural est fréquemment utilisé en anesthésie et plus récemment dans le domaine orthopédique et neurologique pour traiter la sténose dégénérative lombo-sacrée (DLSS) (Janssens *et al.*, 2009). L'analgésie épidurale est fréquemment réalisée « à l'aveugle » pour prévenir la douleur intra- et post-opératoire et le taux d'erreur rapporté de cette technique varie de 7 à 12% (Heath, 1992 ; Troncy *et al.*, 2002). La DLSS est considérée comme la cause la plus fréquente d'atteinte neurologique lombo-sacrée chez les chiens de grande race âgés (Sharp et Wheeler, 2005 ; Dewey, 2008 ; Meij et Bergknut, 2010). Plus récemment, une étude rétrospective a suggéré d'utiliser l'infiltration épidurale de stéroïdes comme alternative au traitement chirurgical (Janssens *et al.*, 2009).

L'objectif final de ce projet était de développer de nouvelles techniques d'imagerie interventionnelles de la colonne lombo-sacrée chez le chien pouvant être utilisées dans la pratique clinique quotidienne afin d'augmenter le taux de réussite des techniques « à l'aveugle » ou d'aider à la démarche diagnostique ou thérapeutique. Nos hypothèses étaient :

- Qu'il est possible et sans danger de réaliser une ponction épidurale écho-guidée dans l'espace lombo-sacré ;

- Qu’il est possible de réaliser des injections scan-guidées dans les facettes articulaires et d’utiliser différents accès pour les injections épidurales scan-guidées ; la difficulté de réaliser ces techniques et leur exactitude est variable en fonction de l’accès ;
- Que les injections de corticostéroïdes dans les facettes articulaires et les injections épidurales scan-guidées peuvent être considérées comme cliniquement sans danger ;

Dans la première partie de ce projet, nous avons décrit l’échoanatomie et la faisabilité de l’accès épidural écho-guidé dans l’espace lombo-sacré chez le chien. Nous avons évalué cette technique en utilisant une aiguille spinale et un cathéter épidural sur 20 cadavres de chiens divisés en un groupe de chiens de poids normal et un autre groupe de chiens en surpoids, avec ou sans anomalies de la colonne lombo-sacrée détectées radiographiquement. A la fin de cette première étape, nous avons appliqué cette technique sur 5 chiens vivants pour évaluer sa sureté clinique. Echographiquement, le canal vertébral à la jonction lombo-sacrée était facilement visualisé et l’accès épidural a été réalisé en utilisant comme points de repère anatomique la 7ième vertèbre lombaire, la 1ière vertèbre sacrée et les ailes de l’ilium. La cible pour diriger l’aiguille était une image échogène trapézoïde entre les facettes articulaires adjacentes du canal vertébral lombo-sacré visualisée dans un plan para-sagittal. La visualisation des structures profondes variait en fonction de la taille du chien, la quantité de graisse sous-cutanée et l’état d’hydratation de la peau du cadavre. Des examens tomodensitometrique ont confirmé la présence de produit de contraste dans l’espace épidural de tous les cadavres et des chiens vivants, mais une quantité variable de contraste a été notée dans l’espace sous-arachnoïdien.

Dans la seconde partie de cette étude, nous avons décrit la technique et nous avons évalué la difficulté et la précision des injections scan-guidées épidurales et dans les facettes articulaires en région lombaire chez les chiens. Plus précisément, nous avons évalué deux accès épiduraux différents au niveau de l’espace lombo-sacré, respectivement translaminaire (synonyme d’interlaminaire) et transforaminal. Un total de 6 injections épidurales translaminaires, 5 injections épidurales transforaminales et 53 injections articulaires ont été réalisées. Les injections translaminaires avaient un taux de succès élevé (100%), étaient très précises dans 75% des cas et faciles à réaliser sur tous les chiens. Les injections transforaminales avaient un taux de succès inférieur (75%), étaient précises dans 75% des cas et modérément faciles à réaliser sur tous les chiens. Donc, les accès épiduraux translaminaire

et transforaminal étaient realisables et précis, mais l'accès translaminaire était plus facile à réaliser et plus précis. L'imprécision était secondaire à une contamination sous-arachnoïdienne et à une ponction du plexus veineux vertébral qui pourraient être dues à une position incorrecte de l'aiguille. Le taux de succès des injections dans les facettes articulaires était de 62% et était plus élevé pour les facettes articulaires plus larges, telles que les facettes articulaires lombo-sacrées. La précision des injections dans les facettes articulaires variait de précise à très précise (25%) en fonction du volume injecté. Dans 58% des cas, les injections étaient modérément difficiles à réaliser.

Dans la troisième partie de ce projet, nous avons évalué la sureté clinique des injections de corticostéroïdes dans l'espace épidural et dans les facettes articulaires lombaires, réalisées de manière scan-guidée. Des chiens d'expérience sains ont été inclus dans cette étude et divisés aléatoirement en 3 groupes : injection transforaminale, injection translaminaire et injection dans les facettes articulaires. Deux chiens supplémentaires ont servie de contrôle. Avant chaque injection de stéroïdes, du produit de contraste a été injecté afin de vérifier la position correcte de l'aiguille. Les paramètres vitaux ont été enregistrés pendant la procédure et des examens généraux et neurologiques spécifiques ont été réalisés dans les jours suivant les injections afin d'évaluer la sureté clinique. Finalement, des injections de stéroïdes ont été réalisées chez 14 chiens sur les 15 inclus dans l'étude. Chez un chien, l'injection du produit de contraste a montré une position intravasculaire de l'aiguille et l'injection de stéroïde n'a donc pas été réalisée. Aucune complication majeure ou mineure n'a été rapportée pendant la procédure. Dans les jours suivants la procédure, aucun déficit moteur, sensitif ou postural n'a été noté chez les chiens durant l'examen clinique, mais seulement une hyperthermie transitoire et une légère altération des réflexes patellaire, tibial crânial et périnéal. Globalement, les réflexes altérés ont été observés chez 11 chiens sur 14, au cours de 27 examens cliniques sur un total de 65. Les deux chiens utilisés comme groupe de contrôle ont également montré des réflexes altérés et ceci lors de 2 des 6 examens cliniques réalisés. Ces altérations de réflexes ont été considérées comme non préoccupantes cliniquement.

En conclusion, notre projet d'étude a apporté une contribution à l'imagerie interventionnelle de la région lombo-sacrée chez le chien. Nous avons réussi à développer et évaluer de nouvelles procédures sous assistance de l'imagerie pouvant être très utiles dans

l'activité clinique journalière. Premièrement parce que ces techniques peuvent potentiellement diminuer les taux d'erreur des techniques « à l'aveugle » fréquemment réalisées, et deuxièmement parce qu'elles peuvent être utilisées pour traiter les maladies communes de la région lombo-sacrée en permettant l'injection précise et sûre des molécules actives au site d'intérêt. Cependant, nous nous sommes concentrés sur la description des techniques ainsi que sur leur faisabilité, leur justesse et leur sureté clinique. Sur base de ces résultats, nos découvertes ont démontré que :

- L'injection épidurale échoguidée chez les chiens normaux et en surpoids avec ou sans anomalies de la colonne lombo-sacrée est faisable, mais que la contamination sous-arachnoïdienne peut être une complication possible.
- Les injections translaminaire et transforaminale scan-guidées dans l'espace épidural lombo-sacré sont faisables et précises, mais que l'accès translaminaire est plus facile à réaliser et plus précis. Une position incorrecte de l'aiguille peut être la cause d'une contamination sous-arachnoïdienne et d'une ponction d'une structure vascularisé. Les injections scan-guidées des facettes articulaires lombaires sont modérément faisables et précises et leur difficulté dépend de la taille de la facette articulaire. Une position incorrecte de l'aiguille peut causer une contamination péri-articulaire.
- Des altérations neurologiques minimes, sans impact clinique, sont associées à l'injection des corticostéroïdes dans l'espace épidural et aux injections de corticostéroïdes dans les facettes articulaires lombaires. L'utilisation du scanner et l'injection du produit de contraste permet d'éviter les complications majeures associées aux injections intravasculaires de corticostéroïdes.

Cependant, notre projet représente seulement une étape préliminaire et l'utilisation de ces techniques dans l'activité clinique journalière doit être réalisée. D'autres études se concentrant sur ce sujet devraient être réalisées. Par exemple, il pourrait être intéressant d'évaluer l'utilité de l'assistance échographique lors des anesthésies épidurales chez les chiens pathologiques ou obèses en comparaison des techniques « à l'aveugle ». Des essais cliniques devraient être réalisés pour comparer l'utilité des injections épidurales et articulaires de corticostéroïdes par rapport aux traitements médicaux ou chirurgicaux habituels.

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