Development of a Mathematical Model to Predict Skin to Lumbosacral Epidural Distance in Dogs

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A thesis submitted in the fulfilment of the requirements
for the degree of Doctor of Philosophy,
School of Veterinary Science, Faculty of Science,
The University of Sydney

2024

STATEMENT OF ORIGINALITY

This is to certify that, to the best of my knowledge, the content of this thesis is original and solely my own work.

This thesis has not been submitted for any degree or other purposes. I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged.

Dr Tsim Christopher Sun

30th September 2024

LIST OF PEER REVIEWED PUBLICATIONS AND AUTHOR CONTRIBITIONS

<u>Sun TC,</u> *Makara M, Martinez-Taboada F. Computed Tomography-Derived Occipital–Coccygeal Length and Ilium Wing Distance Correlates with Skin to Epidural and Intrathecal Depths in Dogs. Veterinary Sciences 2020;7:196. <u>https://doi.org/10.3390/vetsci7040196</u>*

This manuscript is presented as chapter three of this thesis. I led the conceptualisation, study design, data retrieval, curation, analysis including statistical analysis, interpretation and writing of the manuscript. Dr Maraka contributed to study design, image analysis, data interpretation and manuscript preparation. Dr Martinez-Taboada was involved in study conceptualisation, study design, data interpretation, statistical anlysis and overall supervision of the manuscrupt. Dr Michelle Pui Yan Lau and Dr Jia Wen Seow aided with image analysis and interpretation.

<u>Sun TC</u>, *Schier M, Lau MPY, Martinez-Taboada F. Mathematical Models for the Skin to Lumbosacral Epidural Distance in Dogs: A Cadaveric Computed-Tomography Study. Animals 2021;11:2974. <u>https://doi:10.3390/ani11102974</u>*

This manuscript is presented as chapter four in the thesis. I led the conceptualisation, methodology, validation, formal analysis, investigation, data curation, writing and editing of the original and final manuscript. Dr Schier contributed to supervision, writing review and editing of the manuscript. Dr Lau contributed to methodology, software and image analysis and final review of the manuscript. Dr Martinez-Taboada contributed to conceptualisation, methodology, formal analysis, data curation and final editing of the manuscript. Mr Gavin Burland assisted with the methodology and Dr Jia Wen Seow aided with image analysis and interpretation.

PEER REVIEWED CONFERENCE PROCEEDINGS

Sun T.C., Computed tomography-derived occipital coccygeal length and ilium wing distance correlates with skin to epidural and intrathecal depths in dogs, ANZCVS College Science Week, Gold Coast 2021

PRIZES AWARDED DURING CANDIDATURE

The Lionel Marcellus Lonsdale Scholarship, The University of Sydney 2023- 2024

The Neil and Allie Lesue Scholarship, The University of Sydney 2023 - 2024

VERIFICATION OF AUTHOR ATTRIBUTATION STATEMENT

As the primary supervisor for the candidature upon which this thesis is based, I can confirm that the author attribution statements above are correct.

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30th September 2024

THESIS ABSTRACT

Epidural anaesthesia is frequently the pillar for pain relief in dogs undergoing surgery of the hindlimb or abdomen, but alarmingly, failure rates have been reported as high as 32% even for experienced veterinary anaesthetists [1]. In human anaesthesia, development of equations to predict the skin to epidural distance has shown promise in improving epidural success alongside the use of conventional epidural techniques. It is therefore feasible that the knowledge of a predictive skin to lumbosacral epidural distance may positively influence failure rates in dogs. This thesis aims to identify correlation relationships of canine external body variables with the skin to lumbosacral epidural distance. Predictive equations were developed based on canine computed tomography images, and dog cadavers were then used to further validate the mathematical equations. Finally, a randomised prospective study was conducted, and a non-inferiority analysis was performed to determine the effectiveness of the mathematical equation in a practical clinical setting.

Identification of clinically relevant external morphometric parameters that correlated with the skin to lumbosacral epidural distance (SLED) was an essential part of producing the mathematical equations. This was performed in chapter three in which 86 canine computed tomographic (CT) images were retrospectively evaluated, and positive moderate correlations between the occipital coccygeal length (OCL: $r = 0.59$, $p < 0.0001$) and ilium wing distance (IWD: $r = 0.61$, $p < 0.0001$) were found with a *ligamentum flavum* surrogate (LFS), to represent the entry point into the epidural space. Multivariable and multicollinear analysis revealed that the addition of the body condition score (BCS) best aligned with the model that predicted the SLED (OCL: $R^2 = 0.6156$; IWD: $R^2 = 0.643$). This chapter further reported six predictive mathematical equations of which two were specifically devised for the lumbosacral epidural space. To examine the validity of the CT derived mathematical equations, chapter four examined the two

mathematical equations involving the lumbosacral region in chapter three with a separate population of 11 dog cadavers. The key finding in this chapter was that while both equations were validated, the equation using OCL (SLEDmm = 7.3 + 0.05*OCL + 16.45 (BCS); $R^2 = 0.5179$) demonstrated a closer fit to the concordance line when compared with gold standard epidurography. Additionally, this chapter found that the cranial extension of the pelvic limbs did not affect the relationship with the LFS as postulated in the previous chapter. The OCL was therefore proposed as the mathematical equation to take forward for clinical evaluation. Chapter five investigated the mathematical equation proposed in chapter four in 78 dogs requiring lumbosacral epidural for abdominal or hindlimb surgery by performing a prospective randomised clinical study. Dogs were divided between anaesthetists who were aware of the mathematical equation prior to epidural needle insertion (AWARE n = 39), and anaesthetists who would perform the epidural without mathematical assistance (UNAWARE n = 39). Epidural success was determined clinically using the Westphal's sign, nociceptive induced cardiorespiratory changes, and overall opinion of the anaesthetist. There were no differences in the procedural failure rate between AWARE group and UNAWARE groups (12.8% and 15.4% (P = 0.7749) respectively), and inexperienced and experienced anaesthetists were no different between groups. Additional non-inferiority analysis showed that being aware of the mathematical equation before epidural needle insertion was no different with conventional epidural techniques alone when compared with a pre-defined margin.

ACKNOWLEDGEMENTS

- I would like to acknowledge the Traditional Custodians of the lands on which this research was conducted, the Gadigal people of the Eora Nation, and to pay my respects to elders past, present and emerging.
- To Mary, I would like to express my gratitude and thanks for your support and kindness throughout this journey. Your dedication and understanding is a sign of a great supervisor.
- To Fernando, I would like to express my deepest gratitude for your patience and help. A mentor and friend, you continue to be a person I look up to.
- To Jan and Sara, thank you for your wisdom and advice throughout the project.
- I would like to thank the School of Veterinary Science at the University of Sydney for the Neil and Allie Lesue Scholarship, and the Lionel Marcellus Lonsdale Scholarship
- To my University of Sydney Veterinary Anaesthesia team or Fernando, Mara, Eduardo, Alex P, Charleyne, Jason, Scott, Michelle, Alex R, Maggie, Alison and other support staff, thank you for your patience and assistance.
- To my wonderful parents, Shirley and James who have been so supportive of me and my sister Grace, I extend my deepest thanks and love.
- To my wife, Katrina, who has been patient and supportive throughout this project, I thank you. You are an inspiration to my life and pillar of my soul. I love you completely.
- To my daughters, Kate and Matilda, your birth into this world provided the push I needed to mature from a man to a father. I am eternally blessed to have you in my life. I dedicate this thesis to you both.
- Finally, thank God for the wisdom and perseverance that he has bestowed upon me during this research project, and indeed throughout my life.

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LIST OF ABBREVIATIONS IN ALPHABETICAL ORDER

ActSLED: Actual skin to lumbosacral epidural distance

BCS: Body condition score

CLED: Computed derived skin to lumbosacral epidural distance

CT: Computed tomography

ITS: Intrathecal space

IWD: Ilium wing distance

KG: Kilograms

LFS: *Ligamentum flavum* surrogate

LOR: Loss of resistance

LSE: Lumbosacral epidural space

Mm: millimetres

MRI: Magnetic resonance imaging

OCL: Occipital coccygeal length

PredSLED: Predicted skin to lumbosacral epidural distance

SCE: Sacrococcygeal epidural space

SLED: Skin to lumbosacral epidural distance

Chapter 1

Introduction of thesis

Epidural anaesthesia is an essential analgesic intervention for dogs requiring hindlimb, pelvic and abdominal surgeries. However, the failure rate has been reported to be 32% [2], and does not seem to correlate with the technological progression in neuraxial anaesthesia over the past few decades. Clinically, inserting the epidural needle is often performed blind without imaging assistance or preconceived distance from the skin to epidural space. This thesis systematically examines the potential of using external morphometric variables and developing mathematical equations to predict to skin to lumbosacral epidural distance.

Chapter two reviews the current literature relating to epidural technique in dogs and corroborates human literature regarding neuraxial anaesthesia with specific emphasis on the role of anthropometric and imaging studies in predicting successful neuraxial anaesthesia.

Chapter three is a retrospective investigation into morphometric variables based on canine computed tomographic morphometric variables that has been published in *Veterinary Sciences MDPI*. Chapter four is a prospective cadaveric study evaluating two potential mathematical equations derived from the study in chapter three against an external population. This study has also been published in *Animals MDPI*. Both papers in chapters three and four have been re-formatted to fit the flow of the thesis.

Chapter five compares anaesthetists who are aware of the predicted depth using the mathematical equation against anaesthetists who perform epidural techniques conventionally.

This thesis concludes with a general discussion of the results and recommends future directions of research. Tables and figures are referred to within the respective chapter. References for published chapters three and four are cited at the end of each chapter respectively, while references for the, chapters two, five and six, are listed in chapter seven.

Chapter 2

LITERATURE REVIEW

2.1. Introduction

The deposition of analgesic and anaesthetic drugs in the epidural space is commonly performed in small animals and is an effective method of providing analgesia or anaesthesia to the regions such as the hindlimb, pelvis, and abdomen [3, 4]. The benefits of a successful epidural anaesthesia are multifactorial, including reduced intra-operative inhalant and opioid requirements, reduced central sensitisation, reduced stress biomarkers during surgery, and decreased post-operative rescue analgesics [5, 6]. Alternatively, failed epidural technique not only results in inadequate analgesia, but may also cause dural sac puncture, total spinal anaesthesia, vascular puncture, spinal cord injury, or death [7, 8].

2.2. History of neuraxial anaesthesia and the birth of common epidural techniques

The first reported epidural injection in dogs was by American James Leonard Corning, a neurologist who injected 1.5 mL of 2% cocaine between two adjoining spinous processes. It was noted that the hind quarters were weakened and resolved within four hours [9, 10]. For decades, much controversy surrounded whether this was an epidural or spinal induced blockade, and a detailed review of the historical literature was undertaken in 1994. Corning's dose of local anaesthetic was eight times higher than confirmed subsequent spinal punctures described by August Bier and Théodore Tuffier, and the analgesia in his patient was slower with ultimate level lower of sensation. Additionally, cerebrospinal fluid was not visualised after needle insertion in Corning's initial work and therefore the first accredited epidural in anaesthesia in a dog was accredited to Corning [11].

In humans, specific epidural techniques were first described in 1921 by Spanish military surgeon Fidel Pagés where anaesthetics could be injected into the lumbar region but avoid the spinal canal. Widely accredited as being the first documented publication of the modern epidural for peri-operative purposes, the technique was published in an article called "*Anestesia Metamérica*" and later used widely in the Spanish Rif war. Further, in 1933, Italian Professor Achille Dogliotti hypothesised the epidural space being a potential space in the body, and uniform pressure was applied to the piston of a syringe as the needle continued downwards and up until a pressure change was detected [12]. Earlier in 1932, and American-Italian physician Angelo Soresi described a technique in which 'a drop of liquid will disappear from the shank, as if it had been sucked away' as soon as the tip of the needle passed the *ligamentum flavum* and entered the epidural space. At a similar time in 1933 in Argentina, another physician Alberto Gutiérrez described a direct technique and applied the description of the hanging drop of liquid to provide episubdural anaesthesia [13]. Both Soresi and Gutiérrez were eventually accredited in developing the hanging drop technique. In 1972, Dr Anis Baraka in Lebanon described access to the epidural space by the use of an infusion drip. The drip set would be wide open, and as the Tuohy needle is slowly advanced through the skin, *ligamentum flavum* and into the epidural space, the flow of the drip would be altered from being completely stopped to actively flowing [14]. This was credited to be the first description of the running drip method.

2.3. Neuraxial anatomy and terminology

'Neuraxial' is the term to describe a combination of the central nervous structures of one or both of the spinal or epidural spaces. The vertebral canal houses the neuraxial structures and additionally encompasses the spinal cord, and dorsal and ventral nerve roots. Generally, the nerve roots provide afferent or efferent information to respective effector organs. The term 'extradural' or 'epidural' anaesthesia refers to the administration of drugs into the epidural space which is outside of the dura (extradural), whereas the administration of drug into the subarachnoid space is known as 'spinal', 'lumbar puncture', 'subarachnoid', or 'intrathecal' anaesthesia. Throughout this thesis, the term 'epidural' will be used to describe the aseptic procedure of needle access into the epidural space as clinically performed for epidural anaesthesia, and the term 'intrathecal' will be used to represent all other forms of puncture that pierces the dura.

In dogs, the lumbosacral space describes the seventh lumbar and first sacral intervertebral space, and is the most common site for epidural anaesthesia [4]. This intervertebral distance of this space further increases over twofold from 7 mm to 16 mm in sternal recumbency with pelvic limbs directed cranially [15], and for some anaesthetists is the preferred position when performing an epidural. When performing a successful epidural at the lumbosacral level, a midline approach is performed and the needle (i.e. a Tuohy needle) passes through skin and subcutaneous fat before contacting the dorsal supraspinous and interspinous ligaments. Then, the needle contacts the thick interarcuate ligament or *ligamentum flavum* before entering into a potential space, the epidural space. The potential space can be explained that at rest, the space only exists as a small volume surrounded by fat, but with the potential to expand and accommodate large volumes of injected solution [16]. The epidural space surrounds the dural sac which contains the spinal cord and cerebrospinal fluid, and if drugs are injected past the epidural space and into the dural sac, may inadvertently cause spinal anaesthesia due to direct contact of the medications with the central nervous system. Epidurals performed at the sacrococcygeal space in dogs avoid dural puncture as the dural sac terminates caudal to the lumbosacral space in more than 75% of small dogs under 10 kg and 50% of all dogs studied with myelography, and may be considered in the event the lumbosacral space is not accessible [17].

2.4. Overview of epidural techniques in dogs

Various methods have been used to identify the epidural space in dogs. Some studies evaluate an individual technique [18] or utilise a combination of two techniques [19, 20]. Agreement on the accuracy of one technique over another is lacking between veterinary anaesthetists and was highlighted in a recent systematic review on the literature by Adami and Gendron [1]. Of the 13 studies which fulfilled the selection criteria, four reported the sensitivity, three on the specificity, three on the positive predictive value, and three on the procedural failure rate [1]. The authors were unable to recommend a reliable method for identifying the epidural space routinely. Furthermore, there was paucity in recommending a technique suitable for both client owned dogs and experimental animals although it was suggested that experimental studies should be performed with epidurography if definitive identification of the needle within the epidural space was desired.

2.4.1. Hanging drop

The hanging drop involves removing the stylet before passing the needle through the *ligamentum flavum* with a drop of saline at the hub of the needle, and, once within the epidural space the fluid would be aspirated into the needle shaft due to sub-atmospheric pressures within the epidural space [21, 22].

A study involving 17 dogs of multiple breeds were placed in lateral or sternal recumbency and the hanging drop technique was used to identity entry into the epidural space with verification performed using radiography with iohexol contrast [18]. In seven of the eight cases (88%) of the sternal group, the saline drop was seen to move into the needle, while no movement was seen in none of nine dogs (0%) in lateral recumbency. All dogs had contrast detected within the epidural space radiographically, leading the authors to conclude that the sternal position was the most successful position when using the hanging drop. The authors also suggested that it was possible for false negatives with the technique as demonstrated by the single dog in sternal recumbency which had the needle tip successfully enter the epidural space but did not result in movement of the saline drop into the shaft of the needle [18].

2.4.2. Loss of resistance

The "loss of resistance" (LOR) refers to the method of using a drop of resistance detected by an ultra-low friction syringe containing saline or air once the *ligamentum flavum* had been pierced and the epidural space is entered. A sudden loss of resistance should be experienced upon injecting into the epidural space [3]. The term "lack" and "loss" of resistance have been used variably within the literature, often with original articles citing the alternative terminology [3, 23], or using both terms interchangeably [24].

The failure rate using LOR ranges widely from 5 to 32 % [19, 20, 25]. The failure rate was reported in seven percent of dogs (16/242) that had received a lumbosacral morphine epidural with or without bupivacaine. In this study, failure of the epidural was reported to be if the anaesthetist was unable to reduce the isoflurane concentration requirement during surgery [25].

In another study, O and Smith [19] used the combination of hanging drop and LOR to compare the analgesic efficacy between dogs receiving bupivacaine, bupivacaine morphine, and bupivacaine dexmedetomidine as a lumbosacral epidural prior to orthopaedic surgery. The definition for epidural failure was a total pain score of greater or equal to nine using the University of Melbourne Pain Score, or greater or equal to three using the Visual Analogue Score, at any point within the first 24 hour period [19]. The observers were blinded prior to pre-medication and post-surgery. The authors reported that three (5%) of dogs failed at some point of the study, however, there were no overall differences in pain score between all three groups and it was concluded that epidural failure was the most likely reason for the elevated pain scores in these dogs. In contrast, Sarotti, Rabozzi [20] used the LOR technique in 92 dogs requiring pelvic limb surgery. The authors defined failure by incorrect Tuohy needle positioning being outside the epidural space using radiography. In the 47 dogs that received an epidural, fifteen (32%) were reported to be procedural failures. Interestingly, of the 15 cases, only eight were successfully repositioned to achieve a successful epidural. There should be paucity in direct comparison between these studies given the variations in definition for what was considered a procedural failure. Furthermore, both O and

Smith [19] and Troncy, Junot [25] did not provide a reference technique to confirm the needle position of an epidural, while the study by Sarotti, Rabozzi [20] utilised standard radiography to increase sensitivity of correctly identifying the epidural space.

2.4.3. Running Drip

The running drip method describes an increased flow of fluid visualised in the drip chamber as the needle enters from outside to inside the epidural space. This method does not rely on negative pressure of the epidural space, or the subjective feeling of the loss of resistance. The flow of the infusion was observed equally in both lateral or sternal recumbency, whereas the LOR and hanging drop technique may be affected by gravitational hydrostatic pressure. The success rate reported when using the running drip at the sacrococcygeal level was 90.3% and was based on the reduction of patellar reflex five minutes after drug injection [26]. This was recalculated to 90% if methadone use in the postoperative period was taken as the outcome to indicate epidural failure and was identical between lumbosacral and sacrococcygeal epidural groups. No imaging was performed to confirm placement of the needle during that clinical study, although it was acknowledged that tomographic epidurography would be used as an ultimate standard to confirm epidural needle tip placement [27].

2.5. Juxtaposing veterinary and human epidural studies

Epidural procedural failure rates are similar between human and veterinary studies, with lumbar epidural failure reported to be as high as 32% in a heterogenous population of 2114 human surgical patients [28] and similarly, the success or failure of an epidural is limited by user experience and technique sensitivity and specificity [1]. As in veterinary anaesthesia, conventional epidural techniques have remain unchanged in human medicine since their inception almost a century and a half ago and are also considered blind placement [29]. Therefore, translating human epidural research onto veterinary patients may provide a useful framework on how to optimise outcomes of a successful epidural.

The differences in outcomes between human and canine patients requiring epidurals also suggest that caution should exist in directly applying human research. In dogs, general anaesthesia is commonplace due to the dogs requiring surgery in an unconscious state proceeding neuraxial anaesthesia. Therefore, multiple needle insertion attempts, patient reported discomfort and satisfaction may not be considered failure points in comparison with humans where epidurals are performed conscious [30, 31]. There are also anatomical variances in human and canine neuraxial anatomy, sitting versus recumbent positions, and risk of complications [32, 33]. For example, post-dural puncture headache in humans due to accidentally or intentional puncture of the dura does not seem to be a clinical problem in canines [32].

2.5.1. Adjunctive modalities to improve epidural success in human anaesthesia

Adjunctive technological assistance alongside standard epidural techniques may provide solutions in improving procedural failure rates, particular with the use of imaging modalities which are becoming more easily accessible to both referral and general practitioners. Ultimately, the ideal technique(s) will accurately predict the skin to lumbosacral epidural distance, be practical to apply, low cost, and promote efficiency in anaesthetic and surgical time. Below, we briefly examine the use of imaging modalities and other adjunctive techniques available in human literature specific to neuraxial assistance.

2.5.2. Ultrasound guided techniques

Ultrasonography can be used for real-time visualisation and guidance of the procedure. Scanning prior to the procedure can also help identify the most appropriate space in humans particularly those which have increase subcutaneous fat covering which obscure landmarks. First pass needle success rate has shown to significantly increase when used with pre-scanning ultrasound [34-37]. It was proposed that pre-procedural and peri-epidural utilisation of ultrasound may be used in conjunction with conventional epidural techniques or where the epidural was considered to be potentially difficult. However, in a study of 110 patients, pre-procedural ultrasound showed no benefit in first pass epidural catheterisation or the number of attempts for parturient patients when compared with palpable landmarks in patients undergoing caesarean delivery [31]. Additionally, a recent review of ultrasound use in the pre-procedural setting suggested that even for experienced anaesthetists, epidural needle insertion alongside the use of real-time ultrasound is technically difficult, and potentially adds the risk of introducing infection into the epidural space [29]. Ultrasound depth also tended to have a wide limit of agreement that tended to be less than the actual epidural depth [35, 36]. This was in part attributed to probe pressure or the angle of needle introduction which is not visible on ultrasound [38, 39]. As a result, real time ultrasound use for neuraxial anaesthesia in human anaesthesia is still considered at the early stages of development and not currently used as a standard practice.

2.5.3. Computed tomography

Computed tomography (CT) refers to rapid three-dimensional radiographic scans and is commonly used as part of the patient's workup. Some limitations include cost, non-portability and high radiation exposure. CT may additionally assist epidural placement when ultrasound can not be used to visualise narrow interlaminar spaces and where bony vertebrae interfere with normal anatomy. [35]. There is generally good correlation between CT depth and actual skin to thoracic epidural depth, although some studies show that the actual needle depth was 3 – 4 mm deeper on CT images [40, 41]. This could in part be explained by the sitting position and flexion of the spine resulting in the compression of the skin against the vertebral column, or inadvertent Tuohy needle compression during the pass [7]. Conversely, CT images may under-estimate true epidural needle depth depending on approach, with measurements from the paramedian approach exceeding that of the midline approach due to the increase distance caused by needle angulation [42, 43].

2.5.4. Magnetic Resonance Imaging

Magnetic Resonance Imaging (MRI) is a radiation-free imaging modality and is particularly useful for anatomical measurement of the epidural space when imaging quality from ultrasound is not feasible. MRI predictive depths of the cervical epidural space were slightly greater than the actual epidural depth when compared with the LOR technique [44]. In both human and veterinary species, epidurography, using contrast enhancing iodinated or non-iodinated contrast with MRI or CT, is the gold standard for confirming needle position and the spread of the injectate into the epidural space [1]. However, the contrast carries the risks of seizures upon deliberate or accidental injection into the neuraxial spaces, and its clinical use for epidural anaesthesia is further limited by cost and non-portability [45].

2.5.5. Factors which affect skin to epidural distance in humans

Anthropometric measurements refer to measurements and proportional changes in the human body, and studies have examined these relationships against the skin to epidural space distance. Generally, body mass index was found to have a positive correlation with the skin to epidural distance [46-50]. In addition, body weight [51, 52], body surface area [53] and other weight related ratios [54, 55] also had positive correlations. Few studies found no correlation between anthropometrics and skin to epidural space distance [56, 57]. Height with skin to epidural depth had conflicting results with most studies demonstrating no correlations [56, 58, 59]. Differences in correlation may exist depending on level of epidural puncture, for example, weight was a significant predictor at the lumbar level but not at the cervicothoracic level [60].

Epidural depth was also found to have significant correlations with ethnicity, with patients of African origin having the deepest distance while patients of Chinese origin having the most shallow distance [43, 61]. Body composition and vertebral morphology attributed to ethnicity was the likely explanation for the differences in correlation, for example Asian parturients had smaller spinous and transverse processes but larger vertebral bodies compared to Caucasians parturients [62]. Fat distribution attributable to genetics may also explain differences in skin to epidural distance which influence body mass indices [63, 64]. Increases in age was seen to have a decreasing depth for the midline approach but not the paramedian approach [49], and this relationship was demonstrated in both men, parturient and non-parturient woman [43]. Age related changes may include reduction of epidermal and dermal thickness, muscle mass and fat redistribution [65, 66].

2.5.6. Formulas for predicting skin to neuraxial space in humans

Predictive mathematical formulas for the skin to epidural or intrathecal space have been published extensively in the human literature. In particular, equations investigating dural puncture have received interest due to the added benefit of the neuraxial technique also being the site to obtain cerebrospinal fluid, performing myelography for advanced imaging, and diagnosing diseases of the spinal cord and central nervous system for biochemical or microbial analysis. Therefore, the applicability of these equations may be beneficial in assisting multiple subspecialties, including neurology, paediatrics, diagnostic imaging, surgery, internal medicine and anaesthesia. Alternatively, the focus of epidural anaesthesia in human medicine has largely been advocated by anaesthetists administering the technique for the female parturient patient. As such, equations published are of fewer quantity but nonetheless important in the attempts of reducing epidural procedural failure and preventing complications. Table 1 shows studies which report on mathematical formula based on anthropometric measurements and the prediction of the skin to the relevant neuraxial space depth.

Table 1: Mathematical formulas showing the prediction of the skin to neuraxial (epidural or intrathecal) depth in human studies based on anthropometrics

Author and Year	Predictive Equation	Neuraxial space
Luo, Zhang [67]	(0.352 x intervertebral level) + (0.147 x body mass index) + 0.017	Epidural
Singh, Wirth [30]	6.63 – (0.07x height) + (0.02 x weight)	Epidural
Vallejo, Phelps [68]	5.63 – (0.025 x height) + (0.04 x weight)	Epidural
Ravi, Kaul [69]	17.7966 + (0.9777 x body mass index)	Epidural
Stamatakis, Moka [54]	Male = 3.307 + (0.00577 x age) + (0.34 x gender) + (0.02286 x weight) + (-0.00123 x height) + (0.05065 x body mass index) + (0.199 x vertebral interspace)	Epidural
	Female = 8.401 + (0.002949 x age) + (0.0748 x weight) + (-0.0443 x height) + (-0.0802 x body mass index) + (0.0135 x vertebral interspace) + (-0.34 x population type)	Epidural
Grau, Leipold [34]	3+ (0.11 x body mass index) – (0.01 x age)	Epidural
Nair, Gnanasekar [70]	2.522 + 0.031 x weight	Intrathecal
Taman, Farid [71]	2.1 + (0.009 x height) + (0.03 x weight) + (0.02 x body mass index) + (0.15 x body surface area)	Intrathecal
Prakash, Mullick [72]	2.71 x 0.09 x body mass index	Intrathecal
Chong, Chong [73]	10.6 x (weight/height ratio) + 0.93	Intrathecal
Abe, Yamamoto [74]	1 + (17 x weight/height ratio)	Intrathecal
Stocker [75]	0.5 x weight +18	Intrathecal
Craig, Stroobant [76]	0.03 x height	Intrathecal
Bonadio, Smith [77]	0.77x + 2.56 x body surface area	Intrathecal

2.6. Skin to epidural distance in dogs

In contrast to the plethora of studies examining skin to neuraxial distance in human anaesthesia, there are limited studies which examine this relationship in dogs despite similar procedural failure rates of epidural anaesthesia between the two species [1]. Moreover, only one study has examined morphometric correlations with the skin to epidural space in dogs [78]. While newer technological developments have been investigated such as with epidurography [45], electrical nerve stimulator [26, 79], or evaluation of epidural pressure waves [2, 80], their clinical use forms only a small percentage of epidural anaesthesia in dogs, and current veterinary anaesthesia practice still heavily relies on the commonly used techniques as described above [1].

In a prospective, non-randomised, experimental study of 123 dogs involving a variety of breeds, Iseri, Nishimura [78] measured the skin to lumbosacral epidural distance in dogs by demarcating the Tuohy needle once a positive LOR or hanging drop technique was performed. After the epidural medication was injected, a pair of forceps were clamped at the skin to needle interface and removed from the animal. The authors determined three separate equations based on the measurements for dogs considered thin, standard or obese, and found that body weight and body condition score were strongly and weakly associated with the skin to epidural distance respectively in dogs of all groups. However, the epidural techniques used by Iseri, Nishimura [78] were associated with a failure rate of between 12- 32% [1], and was further limited by the lack of clinical confirmation such as a lack of response to surgical stimulation. Therefore, the equations produced by the correlation relationships may have reduced internal validity and limit their interpretation.

Another study compared the difference in ultrasound distance and Tuohy needle distance of the skin to epidural space in seven obese labrador dogs [81]. Once the LOR was performed, the patellar reflexes were tested to visualise a reduction in motor function, and the dogs proceeded to orthopaedic surgery. The depth calculated was 5.95 +/- 0.62 cm and 5.89 +/0 0.64 cm with the Tuohy needle and ultrasonography respectively. Bilateral patellar reflexes were absent after epidural injection in all dogs confirming a successful epidural. A major limitation of this study was that only obese dogs were included and therefore it is difficult to extrapolate the findings to dogs with a variety of other body condition scores.

In contrast to human anaesthesia research, a dearth of information exists in veterinary literature regarding whether morphometric parameters, such as body condition score, correlate with the skin to epidural distance in dogs. Potentially, dogs with a greater body condition score and body weight may possess a deeper skin to epidural space which may make epidural anaesthesia more challenging [78, 81]. In an ideal situation, correlation relationships can facilitate the formulation of predictive information prior to the epidural needle placement to reduce procedural failure rates of epidural anaesthesia.

2.7. Summary

Performing lumbosacral epidurals in dogs is the standard for providing analgesia for hindlimb, pelvic and abdominal surgeries. However, epidural techniques have largely remained unchanged since its inception over a century and a half ago. Progressive developments in the type of epidural techniques have not been matched by corresponding reduction in epidural failure rates. Largely, conventional techniques including the hanging drop, LOR, and recently running drip techniques, are commonly used in clinical veterinary practice, but continue to carry a risk of failure.

In human neuraxial anaesthesia, imaging modalities, anthropometric correlations and predictive mathematical equations have shown promise in reducing procedural failure rates of epidural anaesthesia. In contrast in dogs, the relationship of morphometric correlations and skin to epidural distance, is largely unknown.

The aims of this thesis were to:

a) Determine correlations between morphometric external body landmarks and the skin to epidural and intrathecal distance in dogs with emphasis on the lumbosacral space.
b) Produce clinically relevant mathematical equations derived from morphometric body correlations to predict the skin to lumbosacral epidural distance in dogs.

To accomplish these general aims, there were three specific objectives; perform a large retrospective analysis using CT derived images of dogs to determine which morphometric landmarks are most likely to correlate with the skin to lumbosacral epidural space and thereby derive relevant and practical mathematical equations; validate mathematical equations with an external population against a gold standard; and finally, investigate the effect of the mathematical equation in a clinical setting and to identify whether using predictive equations positively influence the procedural failure rates of existing conventional techniques of epidural anaesthesia

Chapter 3

COMPUTED TOMOGRAPHY-DERIVED OCCIPITAL-COCCYGEAL LENGTH AND ILIUM WING DISTANCE CORREALTES WITH SKIN TO EPIDURAL AND INTRATHECAL DEPTHS IN DOGS

3.1. Background

It was unknown whether any correlations existed between the skin to epidural distance and canine external morphometric variables. A retrospective analysis of computed tomography records provided an opportunity to discover correlation relationships which could be potentially valuable to an anaesthetist in terms of predicting epidural or intrathecal depth.

3.2. Main article

Sun TC, Makara M, Martinez-Taboada F. Computed Tomography-Derived Occipital–Coccygeal Length and Ilium Wing Distance Correlates with Skin to Epidural and Intrathecal Depths in Dogs. Veterinary Sciences 2020;7:196. https://doi.org/10.3390/vetsci7040196

veterinary sciences

Article

Computed Tomography-Derived Occipital–Coccygeal Length and Ilium Wing Distance Correlates with Skin to Epidural and Intrathecal Depths in Dogs

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Received: 4 November 2020; Accepted: 1 December 2020; Published: 3 December 2020.

Abstract: The current clinical techniques for neuraxial needle placement in dogs are predominantly blind without prior knowledge of the depth required to reach the desired space. This study investigated the correlation and defined the relationship between easily obtainable external landmark variables in the dog; occipital–coccygeal length (OCL) and ilium wings distance (IWD), with the skin to epidural and intrathecal space distances using computed tomography (CT). The CT images of 86 dogs of different breeds were examined in this retrospective observational study. Images of dogs in sternal recumbency were optimized to the sagittal view. The distances between the skin and lumbosacral epidural space (LSE) and skin to sacrococcygeal space (SCE) were measured to the *ligamentum flavum* surrogate (LFS) line. The distance between the skin and the intrathecal space (ITS) was measured from the skin to the vertebral canal at the interlumbar (L_5–L_6) space. Measurements of the IWD and OCL were performed on dorsal and scout views, respectively. Linear regression equations and Pearson's correlation coefficients were calculated between variables. Data were reported as mean (standard deviation). Significance was set as alpha < 0.05. After exclusion of four dogs, 82 CT scans were included. The depths were

LSE 45 (15) mm, SCE 23 (10) mm, and ITS 50 (15) mm. There was a moderate correlation between OCL with LSE (=14.2 + OCL * 0.05 ($r = 0.59$, $p < 0.0001$)), and a strong correlation with ITS (=11.4 + OCL * 0.07 ($r = 0.76$, $p < 0.0001$)), while a very weak correlation was found with SCE (=14.0 + OCL * 0.02 ($r = 0.27$, $p < 0.0584$)). Similarly, with IWD, there was a moderate correlation with LSE (=10.8 + IWD * 0.56 ($r = 0.61$, $p < 0.0001$)), and strong correlation with ITS (=9.2 + IWD * 0.67 ($r = 0.75$, $p < 0.0001$)), while a weak correlation was found with SCE (=11.2 + IWD * 0.2 ($r = 0.32$, $p < 0.0033$)). Mathematical formulae derived from the multiple regression showed that the body condition score (BCS) improved the relationship between IWD and OCL and the LSE, SCE and ITS, while the addition of body weight was associated with multicollinearity. Further studies are required to determine the accuracy of the algorithms to demonstrate their ability for prediction in a clinical setting. **Keywords:** epidural; intrathecal; lumbosacral; sacrococcygeal; anaesthesia; computed tomography; ligamentum flavum

3.3. Introduction

Procedural failure rates for neuraxial anaesthesia in dogs have been reported to be up to 32% for epidural [1], and 29.4% for spinal anaesthesia [2]. Failure to access the desired space results in a variety of complications, ranging from inadequate analgesia to potentially fatal total spinal anaesthesia should the intended volume of epidural drug be injected intrathecally [3]. Most clinicians perform these techniques without any radiographic assistance, so they are blindly selecting the needle trajectory and the final target. In these circumstances, they must rely on subjective tactile and audible sensations such as the 'pop' of the *ligamentum flavum* to signal the entry into the epidural space, or the visualization of either the hanging drop or the free flow of cerebral spinal fluid to confirm the correct identification of the epidural or the intrathecal space, respectively [2].

Additional knowledge of the required depth and the factors affecting needle placement might be beneficial in increasing operator accuracy and improving the success rate and safety of epidural and spinal anaesthesia [4]. In humans, anthropometric variables affecting the distance from the skin to the lumbar epidural space have been investigated [4–8]. Body mass index and body weight showed higher levels of correlation compared with age, gender and height with the lumbar epidural space in a population of Nigerian adults [9]. In another study, positive correlations were found for body weight, body mass index and body surface area with the same space in Greek men, with differences further seen for obstetric and non-obstetric populations of Greek women [4]. Both studies produced mathematical models to predict the skin to lumbar epidural space distance in their respective populations, and while there were questions regarding the clinical utility of the derived formulae, potential usefulness may lie in a multimodal approach with other techniques, as well as an initial guide for needle placement for less experienced operators.

In dogs, there are limited studies investigating the skin to epidural depth. Only one study investigated the correlation of weight and body condition score with skin to epidural space distance, finding a moderate and weak correlation, respectively [10]. Unfortunately, in that study, the clinical efficacy of the hanging drop technique was not tested, and it was unknown whether successful epidural anaesthesia was achieved. Alternatively, the distance between the skin and other clinically relevant neuraxial structures, such as the sacrococcygeal epidural space and intrathecal space, has not been evaluated, despite being of common interest for several veterinary specialities, such as anaesthesia, neurology, internal medicine, and radiology. It therefore seems prudent and logical to find clinically relevant variables and investigate the potential ability for correlations and predictions of epidural or intrathecal space depth prior to the actual attempt.

The palpation of external landmarks is routinely performed for neuraxial techniques to guide the clinician towards the site of interest, such as palpating the craniodorsal aspects of the iliac wings to identify the lumbosacral space [3]. Other external measurements may not currently be common practice but are gaining popularity, such as calculating the volume of epidural injectate based on the occipital–coccygeal length [11,12]. These relationships between external anatomical landmarks and internal structures have not been fully explored in dogs, but it is plausible that they closely correlate with the skin to epidural and intrathecal space distances.

The aim of this study was to assess the correlation between external anatomical landmarks (occipital–coccygeal length, ilium wing distance), and skin to epidural and intrathecal space depths using CT images, with dog body condition score and body weight. We hypothesized that the measurements obtained would demonstrate a close correlation between all variables.

3.4. Materials and Methods

3.4.1. Case Selection

This experimental study was a retrospective review of dog computed tomography (CT) images and hospital records. Abdominal, lumbar or whole-body CT scans of dogs obtained under anaesthesia as part of the individual clinical management between September 2018 and June 2020 at the University Veterinary Teaching Hospital Sydney, Australia, were included. The scans were performed using a 16 slice multidetector CT scanner (Phillips 16 Slice, Brilliance CT V2.3; Phillips Medical Systems, Eindhoven, The Netherlands) with a 2 mm transverse slice thickness and 512 × 512-pixel matrix dimensions. The scanning protocol at the institution has been described previously [13]. All owners consented to the procedure and general anaesthesia, and, as per the institutional policies, consented to future data use. Dog details, including body condition score (BCS out of 9, with 9 being obese [14]), body weight, and sex (male or female), were retrieved from the patient file or the anaesthetic record on the day of the CT. Leg positioning was recorded from the CT studies and defined as cranial (pelvic limbs extended forward), neutral (pelvic limbs to the side) or caudal (pelvic limbs extended backwards). Dogs were excluded if they were not in sternal recumbency, had incomplete studies, had fractures or obvious distortion of the spine or pelvis, movement artefact, or anatomical deformity such as hemivertebrae or a lack of clearly defined coccygeal vertebrae.

3.4.2. Distance Measurements

All images were analysed by a single observer (TCS) and viewed on three dimensional reconstructions using a bone Hounsfield unit window (Apple Thunderbolt Display, Apple, Cupertino, CA, USA; Mac Mini, Apple; Osirix version 5.7 64-bit, Pixmeo SARL, Bernex, Switzerland). All measurements were made within the software through the bone algorithm from the sagittal plane unless otherwise specified and converted to the nearest millimetre.

3.4.3. Ligamentum Flavum Surrogate

A straight line was drawn from the cranial margin of the dorsal lamina of the cranial lumbar space vertebrae, to the cranial margin of the caudal vertebrae (i.e., from L_5 to L_6). This line was defined as the *ligamentum flavum* surrogate (LFS).

3.4.4. Intrathecal Space Depth (ITS)

The ITS was measured as the distance from the skin to the floor of the vertebral canal using a line drawn perpendicular to the LFS at the L_5 and L_6 intervertebral space, and represented the theoretical distance the tip of the needle should travel before reaching the ventral intrathecal or subarachnoid space (ITS: Figure 1a).

3.4.5. Lumbosacral Epidural Space Depth (LSE)

The LFS was then drawn at the lumbosacral space, and a perpendicular line was drawn. This line was defined as the LSE90. A secondary line was then drawn to the skin with an angle of 60 degrees to the LFS intersection [15], and was defined as the LSE60 (LSE: Figure 1b). Both the LSE90 and LSE60 represented two possible angular approaches to the LFS. The skin to LFS distances were measured for both angular approaches.

3.4.6. Sacrococcygeal Epidural Space Depth (SCE)

The LFS process was repeated at the first to second inter-coccygeal space to represent the sacrococcygeal epidural space due to differences in the curvature of the sacral vertebrae, and the secondary line was measured for the distance at 60° to the skin and defined as the SCE (Figure 1c).

3.4.7. Ilium Wing Distance (IWD)

The most dorsal aspects of the ilium wings were identified on the dorsal plane window where both bony structures were first clearly visible. A straight line was drawn, and the distance was measured between the cranial margins of the dorsal crests (IWD: Figure 1d).

3.4.8. Occipital–Coccygeal Length (OCL)

The OCL was taken from the scout view which was visually optimised to the dorsal line. The open polygon function was used to measure the distance between the base of the occipital bone to the first coccygeal vertebrae following the outline of the dog's body (OCL: Figure 1e).

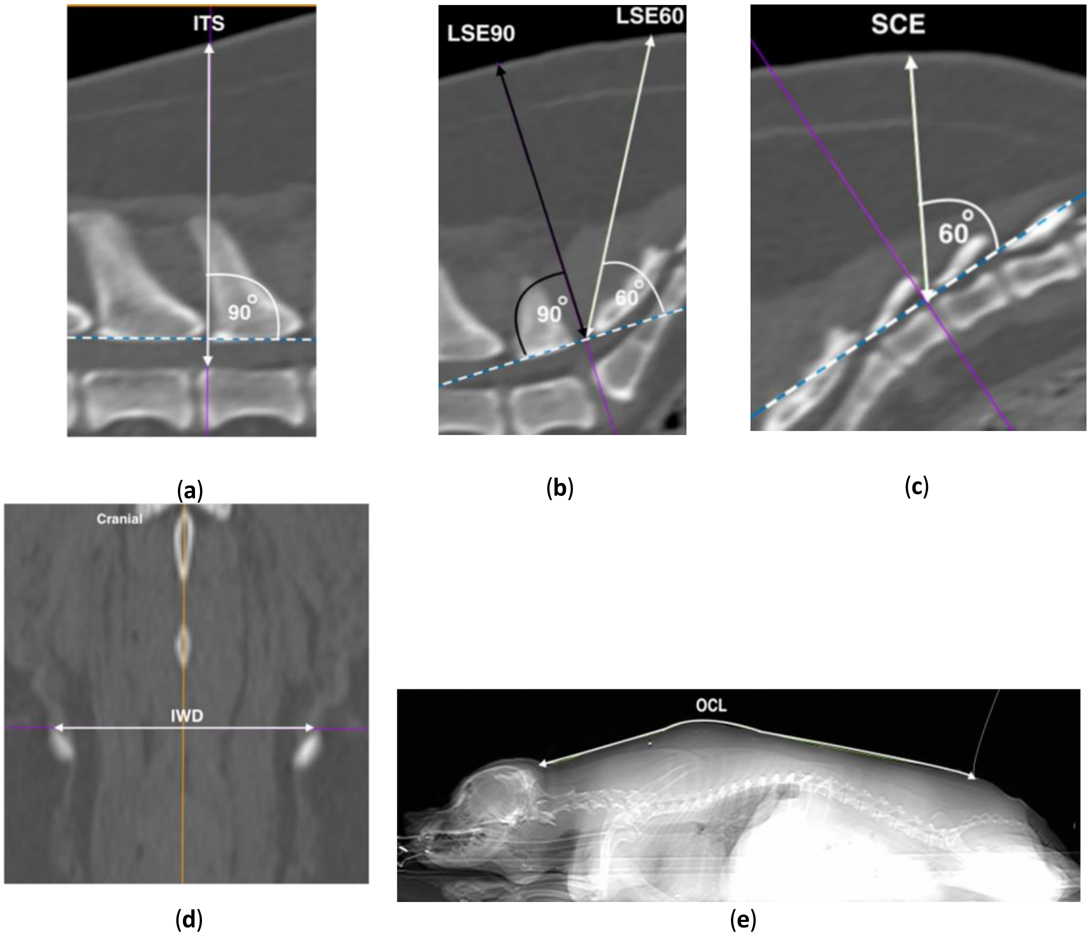

Figure 1. Computed tomographic images representative of measurements performed. Hashed line represents the *ligamentum flavum* surrogate (LFS), with the acute angle depicted by the unidirectional arrow perpendicular to the LFS. Bi-directional arrows represent measured distances of skin to: (**a**) intrathecal (ITS), (**b**) lumbosacral epidural at 90 degrees (LSE90) in black, and 60 degrees (LSE60) in white, and (**c**) sacrococcygeal epidural (SCE) spaces. (**d**) The distance between the most dorsal aspects of the iliac wings (IWD), and (**e**) the occipital–coccygeal length (OCL) on the dorsal and scout windows, respectively. Left is cranial unless specified. All images were from the same dog.

3.5. Statistical Analysis

A sample size of 82 dogs was calculated to be needed based on four predictors with a power of 0.8 and an alpha of 0.05 [16]. Measurements were recorded in a computerized spread sheet (Microsoft Excel 2011; Microsoft Corporation, Redmond, WA, USA), and transferred to the statistical software R, version 3.6.1 for Windows 10 (The R Foundation for Statistical Computing, http:www.Rproject.org, Vienna, Austria). Statistical analysis was performed in three stages and in all sections statistical significance was declared at alpha less than 0.05.

The first analysis involved consolidation of data as appropriate and descriptive statistical analysis. The LSE60 was used as a standardised comparison between leg positions (cranial, neutral, and caudal), sex (male, female), and angulation with LSE90. Data were examined for normality using the Shapiro–Wilks test. When normal data distribution was found, a Student's *t*-test was used. If data were non-normally distributed, non-parametric tests were used. Where there was no statistical significance between groups, further analysis was reported as a consolidated group for leg positions and sex, and for angulation the LSE60 was used for further analyses and redefined as the LSE. If statistical difference existed, then groups were reported individually. Descriptive statistical analysis for continuous data—body weight, LSE, SCE, ITS, IWD, and OCL—were expressed as mean (standard deviation). For categorical data, binomial classification of BCS was performed (less than or equal to BCS 5/9, and greater than BCS 5/9). The reason for the classification was to reduce the subjectivity of a categorical scoring system, and to be able to examine the addition of BCS in the multivariate model.

The second analysis investigated the relationship between depth variables (LSE, SCE, ITS), external landmarks (IWD, OCL), and BCS and body weight. Depth variables were the outcome and estimates were performed by producing linear regression equations and Pearson's correlation coefficients with external variables, BCS and body weight. Correlation coefficients were further calculated between external variables, BCS and body weight. Results were expressed as positive or negative correlation values of Pearson's *r*, where values between 0 and 0.29, 0.3 and 0.49, 0.5 and 0.69, and 0.7 and 1.0 were considered to signify very weak, weak, moderate and strong correlations, respectively. Relationships were examined graphically using crude values, and the linearity of residuals and fitted values were assessed in R. Normality was assessed using Q-Q plots and the D'Agostino–Pearson Omnibus test. Results were further expressed as β coefficients to examine the weight of each variable, $_{adj}R^2$ for the proportion of fit, F statistic and the associated statistical significance for the predictability variable for the outcome. In the third analysis, the best models were selected for the relationship of depth and external variables with the addition of BCS or body weight using multiple regression by determining the model that had the lowest variance inflation factor.

3.6. Results

A total of 86 canine CT scans were examined. Four dogs with incomplete scout views were excluded from analysis, providing a total of 82 dogs for the final analysis. There were 44 dog breeds identified (Appendix A: Table A1). For BCS, there were 47 dogs with BCS ≤ 5/9 (BCS 1/9 = 0; 2/9 = 2; 3/9 = 5; 4/9 = 18; 5/9 = 22), and 35 dogs that had BCS > 5/9 (BCS 6/9 = 18; 7/9 = 11; 8/9 = 6; 9/9 = 0) ($p < 0.0001$). The overall body weight was 19.9 (15.1) kg and the LSE, SCE and ITS were 44 (15), 23 (10), and 50 (15) mm, respectively. The measured OCL was 589 (173) mm and IWD was 61 (16) mm. There were no differences when examining leg positions which were either in neutral ($n = 43$) or caudal ($n = 39$) ($p = 0.0924$), and no dogs had their legs in a cranial position. There were also no differences between males ($n = 42$) and females ($n = 40$) ($p = 0.7760$), and angulations ($p = 0.2148$).

3.6.1. Correlation between Depth Variables Using External Variables

When correlating depth with external variables, the OCL had a moderate correlation with LSE, and a strong correlation with ITS, while the correlation between OCL and SCE was very weak. These variables generated the equations:

$$\text{LSE} = 14.2 + \text{OCL} * 0.05 \ (r = 0.59,\ 95\%\ \text{CI}\ 0.43\text{–}0.71;\ p < 0.0001) \quad (1)$$

$$\text{ITS} = 11.4 + \text{OCL} * 0.07 \ (r = 0.76,\ 95\%\ \text{CI}\ 0.65\text{–}0.84;\ p < 0.0001) \quad (2)$$

$$\text{SCE} = 14.0 + \text{OCL} * 0.02 \ (r = 0.27,\ 95\%\ \text{CI}\ 0.05\text{–}0.46;\ p = 0.0584) \quad (3)$$

The IWD also had a moderate correlation with LSE, and a strong correlation with ITS, while a weak correlation was found between IWD and SCE. This generated the equations:

$$\text{LSE} = 10.8 + \text{IWD} * 0.56 \ (r = 0.61,\ 95\%\ \text{CI}\ 0.45\text{–}0.73;\ p < 0.0001) \quad (4)$$

$$\text{ITS} = 9.2 + \text{IWD} * 0.67 \ (r = 0.75,\ 95\%\ \text{CI}\ 0.63\text{–}0.83;\ p < 0.0001) \quad (5)$$

$$\text{SCE} = 11.2 + \text{IWD} * 0.20 \ (r = 0.32,\ 95\%\ \text{CI}\ 0.11\text{–}0.50;\ p < 0.0033) \quad (6)$$

3.6.2. Correlation between Depth Variables, Bodyweight and BCS

Body weight had a strong correlation with LSE ($r = 0.75$, 95% CI 0.64–0.83, $p < 0.0001$), a strong correlation with ITS ($r = 0.85$, 95% CI 0.78–0.90, $p < 0.0001$), and a weak correlation with SCE ($r = 0.47$, 95% CI 0.28–0.62, $p < 0.0001$). For BCS, there was a moderate correlation with LSE ($r = 0.53$, 95% CI 0.35–0.67, $p < 0.0001$) and a weak correlation with ITS ($r = 0.36$, 95% CI 0.16–0.54, $p = 0.0009$). There was a moderate correlation between BCS and SCE ($r = 0.64$, 95% CI 0.49–0.75, $p < 0.0001$).

3.6.3. Correlation between External Variables, Body Weight and BCS

The OCL strongly correlated with body weight ($r = 0.88$, 95% CI 0.82–0.92, $p < 0.0001$), but no correlation existed with BCS (r = 0.002, 95% CI −0.22–0.22, p = 0.9835). Similarly, IWD strongly correlated with body weight (r = 0.87, 95% CI 0.81–0.92, p < 0.0001), but no correlation existed with BCS (r = −0.005, 95% CI −0.22–0.21, p = 0.9081).

3.6.4. Multiple Regression Analysis

The addition of BCS improved the ${}_{adj}R^2$ and the relationship between the external landmarks and depth variables. Table 1 shows the effects of external, BCS, and bodyweight relationships on depth. Furthermore, a variance inflation factor of 1 suggests BCS and external variables did not possess multicollinearity. Alternatively, when body weight is added to the model, inversely related or statistically insignificant β coefficients suggest that variables may not be independent of one another and do not explain the improved ${}_{adj}R^2$ in the multiple regression model. Multicollinearity was detected between body weight and external variables. The six mathematical formulae derived for this were:

$$\text{LSE} = 7.3 + 0.05(\text{OCL}) + 16.45(\text{BCS}) \quad (7)$$

$$\text{SCE} = 8.4 + 0.02(\text{OCL}) + 13.3(\text{BCS}) \quad (8)$$

$$\text{ITS} = 6.8 + 0.06(\text{OCL}) + 10.88(\text{BCS}) \quad (9)$$

$$\text{LSE} = 3.5 + 0.56(\text{IWD}) + 16.6(\text{BCS}) \quad (10)$$

$$\text{SCE} = 5.3 + 0.20(\text{IWD}) + 13.34(\text{BCS}) \quad (11)$$

$$\text{ITS} = 4.38 + 0.67(\text{IWD}) + 11.05(\text{BCS}) \quad (12)$$

Variables: LSE, SCE, ITS, OCL and IWD in mm; BCS, ≤5/9 = 0, >5/9 = 1

Using Equation (7) as an example, the depth of the LSE can be predicted based on OCL and BCS. A significant regression equation was found (F = 65.86 p < 0.05) with an ${}_{adj}R^2$ = 0.62 (Table 1). The predicted LSE depth is equal to 7.3 + 0.05(OCL) + 16.56(BCS), where BCS ≤ 5/9 = 0, >5/9 = 1, and OCL is measured in millimetres. The LSE depth increased by 0.05mm for each mm of OCL, and dogs with a BCS > 5/9 had an LSE 16.45 mm greater than dogs with BCS ≤ 5/9. Both OCL and BCS were significant predictors of LSE. Details of univariate relationships can be found in the Appendix A (Table A2) and multiple regression analysis in Table 1.

Table 1. Predictors of lumbosacral epidural (LSE), sacrococcygeal epidural (SCE), and intrathecal (ITS) space depth with external and dog variables, using computed tomography of 82 dogs by multiple regression analysis.

Variable		LSE					SCE					ITS				
External	**Dog**	$\beta_{external}$	β_{dog}	$_{adj}R^2$	F_{stat}	**VIF**	$\beta_{external}$	β_{dog}	$_{adj}R^2$	F_{stat}	**VIF**	$\beta_{external}$	β_{dog}	$_{adj}R^2$	F_{stat}	**VIF**
OCL	BCS	0.0524 *	16.4511 *	0.6156	65.86 *	1.0000	0.0156 *	13.2870 *	0.4681	36.64 *	1.0000	0.0658 *	10.8791 *	0.7008	95.87 *	1.0000
	KG	−0.0286 *	1.0613 *	0.5807	57.1 *	4.3715	−0.038 *	0.0709 *	0.2997	18.33 *	4.3715	0.0042	0.8082 *	0.7226	106.5 *	4.3715
IWD	BCS	0.5594 *	1.6594 *	0.643	73.93 *	1.002	0.1979 *	13.3353 *	0.5048	42.29 *	1.003	0.6662 *	11.0524 *	0.6811	87.49 *	1.002
	KG	−0.1926	0.9605 *	0.5675	54.14 *	4.1717	−0.2270	0.5419 *	0.2352	13.46 *	4.1716	0.0034	0.8473 *	0.7221	106.2 *	4.17

OCL: Occipital–coccygeal length; IWD: ilium wing distance; BCS: body condition score; KG: body weight in kilograms; β: standardised coefficients of the variable in subscript within the multiple regression model; *adjR*^{2}: adjusted coefficient of proportion of fit; F_{stat}: test for overall significance in regression; VIF: variance inflation factor test for multicollinearity;

* statistically different for the respective variable ($p < 0.05$), otherwise no statistical difference detected.

3.7. Discussion

The mean measurement of the LSE, SCE and ITS in our study was 45, 23, and 50 mm, respectively, from the skin. Dogs that had a longer OCL and wider IWD had moderate and strong correlations with LSE and ITS, respectively, while the correlation with SCE was weak. Dogs that were heavier or had a BCS of >5/9 had larger LSE, SCE and ITS compared to lighter dogs, or dogs with BCS ≤ 5/9. There was no difference between male or female dogs, the angulation of the LSE line at 60 or 90 degrees, or between neutral and caudal leg positions on CT.

The measurements of LSE, SCE and ITS in this study were a result of CT-derived distances as determined by an artificial line to represent the *ligamentum flavum*. Comparisons to other studies are therefore difficult given differences in the study aim and outcome. Only two other studies have reported on the distance from the skin to the lumbosacral epidural space in dogs, with a mean depth of 26.8 mm reported by Iseri et al. [10], and 59.5 mm by da Silva et al. In this latter study, the authors only investigated the skin to lumbosacral epidural depth in obese Labradors [17]. The distance from the skin to the lumbosacral epidural space reported in our study is noticeably greater than that reported by Iseri et al. Unfortunately, the methodology of both studies was very different, making any comparison difficult. For instance, Iseri et al. identified the epidural space by using the hanging drop, a technique that has been suggested to be insufficiently accurate (in terms of sensitivity and specificity) for research [18]. Additionally, the authors did not provide information regarding the success rate of their epidural techniques (e.g., reporting the number of animals requiring rescue analgesia in the perioperative period). Finally, the skin to epidural space distance was measured by grasping the Tuohy needle with a pair of forceps as close to the skin as possible. Then, the reported distance was measured from the needle tip to the forceps. It is possible that the authors might have unintentionally depressed the skin while grasping the needle, obtaining underestimated results.

Our study found positive moderate and strong correlations between OCL and IWD and the LSE and

ITS, respectively, while both external variables had a weak correlation with SCE. Neither the OCL nor IWD have previously been investigated with regard to their relationship to the skin to epidural or intrathecal space depth. The OCL has primarily been used for the determination of injectate volume into the epidural space [11], but to the authors' knowledge, the iliac wings have been used exclusively as landmark palpation sites of the lumbosacral space in dogs and there is no information regarding any alternative role the IWD may have in practice. Our results may serve as an anchor point for future clinical studies in predicting the skin to epidural and intrathecal space depth using external variables, and whether the knowledge of that information can have an effect on the outcomes of the technique (rate of success and complications). Moreover, the results reported here may be of use for other aims than neuraxial anaesthesia; for instance, the strong correlations with ITS might make them of great interest while performing myelograms or cerebrospinal fluid sampling [19,20].

Our data also confirmed that these positive correlations between OCL and IWD and the LSE, ITS and SCE can be improved with the inclusion of BCS. In the univariate analysis, there was a moderate correlation between the LSE and BCS. Our results also show that this correlation is slightly stronger at the level of the SCE, possibly due to greater accumulation of fat deposits at the base of the dog's tail as BCS increases [14]. Iseri et al. reported a weaker correlation between the skin to epidural space depth and BCS ($r = 0.26$ ($p = 0.004$)) than the one reported in our study [10]. The comparisons between studies are difficult given differences in BCS classification used (Iseri et al. used a 1 to 5 classification, whilst a 1 to 9 classification was used in this study), the subjectivity of the assessment of BCS and study population. The effect of body condition has also been investigated in human studies using body mass index, with correlations also being of a positive direction, possibly due to increased subcutaneous fat between the skin to the desired space [5,8,9].

Our study also showed that weight had positive strong correlations with LSE and ITS, and weak with SCE. A similar relationship was found in the study by Iseri et al. for weight and the skin to the lumbosacral epidural space (r = 0.78, $p < 0.01$) [10]. However, in the multiple regression, body weight was an overall poorer fit for LSE and SCE, and similarly for the ITS when compared with BCS. In addition, multicollinearity was detected with greater variance inflation factors (Table 1). This suggested that collinearity existed between variables, in which independent relationships are actually dependent on each other. A collinear relationship reduces the accuracy of the model and removal of the variable should be considered for further multiple regression analyses [21]. In the presence of external variables such as OCL and IWD, the use of body weight may therefore be inferior to BCS in the prediction of the outcome. Similarly, studies in human anaesthesia have shown that many factors may influence body weight as a variable in predicting skin to lumbar epidural space depth, for example ethnicity [8] or sex [4].

Differences were not observed between sex or leg positioning, although only dogs with legs in neutral and caudal positioning were found in the database. Most radiographers prefer the pelvic limbs of the animals to be extended caudally or resting neutrally so as to not increase beam hardening and noise artefact when acquiring the images. A previous study investigated the effect of limb positioning on the canine lumbosacral anatomy using CT, demonstrated an increase in the lumbosacral and L_6–L_7 distances, when the limbs are extended cranially versus caudally [22]. It is possible that the limbs' position might also influence the skin to epidural and intrathecal space depths. The effect of pelvic limb position might also be an explanation for the difference in the LSE reported in our study and the one reported by Iseri et al. [10]. Further prospective studies should consider the pelvic limbs in a cranially extended direction (given that the majority of epidural procedures in dogs are performed in such a fashion).

The angles used in this study from the skin to the LFS were divided into perpendicular from the skin (LSE90) and the 60 degrees angle (LSE60). Unpublished pilot results from our research group show that the angles for successful lumbosacral epidural needle placement ranged between 60 and 90 degrees, so it was decided to use the extremes of the range. The methodology used for ITS and SCE followed the previously described techniques for needle placement into the sacrococcygeal [12] and intrathecal space [23]. When the measurements obtained for LSE90 and LSE60 were compared, no significant difference was found. It is paramount to point out that distances to any of the studied spaces using different trajectories (e.g., when utilizing the paramedian approach to the intrathecal space), or with angles outside the ones proposed may differ from the ones obtained in this study.

All the measurements in this study were taken from the CT images. This may be of limited clinical value given that a scan would be required to determine the LFS and the relevant depth variables prior to performing the relevant techniques. However, this might not be that uncommon as the use of CT is becoming more popular and accessible in veterinary practice, and the images might have previously been acquired for related or unrelated medical reasons [24].

The skin to epidural distance measured in this study was obtained using the surrogate LFS. The LFS was created as a theoretical representation of the *ligamentum flavum*. Anatomically, the *ligamentum flavum* is not a rigid structure but stretches segmentally between intervertebral spaces [3]. Unfortunately, this ligament is not usually visible on CT in dogs [25], so a representative straight line had to be used to allow a standardised objective comparison between sites of interest. In human adults, the posterior aspect of the spinal cord [26], and the anterior longitudinal ligament at corresponding inter-spinous spaces [27], have been previously used as CT surrogates for entry into the thoracic epidural space. While theoretical in nature, the surrogate was an objective and replicable way to investigate the depth variables and their correlations with other variables of interest.

This study had other limitations derived from its retrospective nature. All the dogs were in sternal recumbency, as this is the most common positioning for this type of radiographic study. Scans with the animals in dorsal are not common in our institution, but occasionally this recumbency might be used to avoid breathing movement artefacts (e.g., CT scans of the spine). They were all excluded, as it was thought that that would greatly impact on the skin-to-epidural distance. Moreover, the dog breeds were reported, but not included in our analyses. The main interest of this study was to correlate external morphometric variables with depth variables. It is reasonable to think that these morphometric variables capture at least some of the breed conformations variations [28–31]. Any attempt to stratify the results by breed would have resulted in extremely underpowered results. Perhaps, a future study with a large sample size might be able to shed further light on this point.

3.8. Conclusions

In conclusion, external variables such as the OCL and IWD correlate positively with LSE, SCE and ITS, and when BCS is also considered, this improves the model. Further investigations are required before this information can be used clinically to assess the skin to epidural space and skin to spinal space depth, prior to attempting the needle placement. Firstly, the LFS must be compared to epidurography to corroborate its validity. Secondly, the morphometric variables values obtained by CT must be compared to the external measuring of such variables, so they can be obtained without the need for advance imaging.

Author Contributions: T.C.S. contributed to study design, image analysis, data interpretation, statistical analysis, manuscript preparation and writing. M.M. contributed to study design, image analysis, data interpretation and manuscript preparation. F.M.-T. was involved in study conceptualisation, study design, data interpretation, statistical analysis, manuscript preparation, and overall supervision of the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

3.9. Appendix A

Table A1. Breed distribution in a study population (*n* = 82) of dogs for computed tomography analysis.

Breed	Number
Beagle	5
Chihuahua	5
American Staffordshire	4
Cross breed	4
German shepherd	4
Kelpie	4
Shih Tzu	4
Staffordshire terrier	3
Husky	2
Jack Russell	2
Maltese terrier	2
Border collie	2
Boxer	2
Cavalier king Charles	2
French bulldog	2
Labrador	2
Pug	2
Retriever	2
Rhodesian ridgeback	2
Samoyed	2
Shetland sheepdog	2
Australian terrier	1
Basenji	1
Bichon frise	1
Boerbol	1
Bulldog	1
Cavoodle	1
Dachshund	1
Doberman Pinscher	1
Great dane	1
Greyhound	1
Havanese	1
Japanese spitz	1
Miniature pinscher	1
Miniature schnauzer	1
Newfoundland	1
Pointer	1
Pomeranian	1

Poodle	1
Rottweiler	1
Schnoodle	1
Terrier	1
Vizsla	1
Wolfhound	1
44 breeds	82 dogs

Table A2. Correlation of predictor and outcome variables using computed tomography of 82 dogs by linear regression analysis.

Predictor	OutCome	*r*	95% CI	Intercept	B	$_{adj}R^2$	F_{stat}	*p* Value
OCL	LSE	0.5884	0.4258–0.7142	1.4236	0.0525	0.3380	42.36	<0.0001
OCL	SCE	0.2646	0.0505–0.4555	1.3988	0.0157	0.0584	6.023	0.0584
OCL	ITS	0.7609	0.6514–0.8393	1.1397	0.0660	0.5737	110	<0.0001
OCL	BCS	0.0023	−0.2148–0.2192	58.8702	0.0812	−0.0125	0.1042	0.9835
OCL	KG	0.8782	0.8169–0.9199	38.7679	1.0101	0.7684	269.7	<0.0001
IWD	LSE	0.6066	0.4487–0.7278	1.0072	0.5568	0.3601	46.59	<0.0001
IWD	SCE	0.3208	0.1115–0.5028	1.1146	0.1958	0.0917	9.174	0.0033
IWD	ITS	0.7453	0.6303–0.8284	0.9200	0.6645	0.55	99.99	<0.0001
IWD	BCS	−0.0053	−0.2221–0.2120	5.9252	0.0165	−0.0150	0.0134	0.9081
IWD	KG	0.8719	0.8078–0.9157	4.2301	0.0974	0.7573	253.7	<0.0001
BCS	LSE	0.5295	0.3530–0.6695	3.8106	1.6494	0.2713	31.16	<0.0001
BCS	SCE	0.6419	0.4936–0.7539	1.7557	1.3300	0.4046	56.05	<0.0001
BCS	ITS	0.3613	0.1566–0.5363	4.5553	1.0933	0.1197	12.01	0.0009
KG	LSE	0.7534	0.6413–0.8341	2.9740	0.0773	0.5622	105	<0.0001
KG	SCE	0.4701	0.2818–0.6235	1.6840	0.0321	0.2112	22.69	<0.0001
KG	ITS	0.8538	0.7816–0.9034	3.3262	0.0851	0.7255	215.1	<0.0001

OCL: Occipital–coccygeal length; IWD: ilium wing distance; BCS: body condition score; KG: body weight in kilograms; *r*: Pearson's coefficient; β: standardised coefficient for the outcome variable; $_{adj}R^2$: adjusted *R*-squared; F_{stat}: test for overall significance in regression.

3.10. References

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Chapter 4

MATHEMATICAL MODELS FOR THE SKIN TO LUMBOSACRAL EPIDURAL DISTANCE IN DOGS: A CADAVERIC COMPUTED-TOMOGRAPHY STUDY

4.1. Background

As discussed in 3.9. the validation of any epidural space in an experimental setting should be conducted with a gold standard, namely with contrast epidurography. Given that the mathematical equations derived in chapter 3 were from a *ligamentum flavum* surrogate, it was imperative to investigate the validity of the formulas in a separate unrelated population of dogs. In this chapter, we reported the validation of two predictive equations of the skin to lumbosacral epidural distance using dog cadavers.

4.2. Main article

Sun TC, Schier M, Lau MPY, Martinez-Taboada F. Mathematical Models for the Skin to Lumbosacral Epidural Distance in Dogs: A Cadaveric Computed-Tomography Study. Animals 2021;11:2974. https://doi:10.3390/ani11102974

Mathematical Models for the Skin to Lumbosacral Epidural Distance in Dogs: A Cadaveric Computed-Tomography Study

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Citation: Sun, T.C.; Schier, M.; Lau, M.P.Y.; Martinez-Taboada, F. Mathematical Models for the Skin to Lumbosacral Epidural Distance in Dogs: A Cadaveric Computed- Tomography Study. *Animals* **2021**, *11*, 2974. https://doi.org/10.3390/ ani11102974

Academic Editors: Angela Briganti and Hamaseh Tayari

Received: 20 September 2021

Accepted: 13 October 2021

Published: 15 October 2021

Simple Summary: Epidural anaesthesia is readily performed in the lumbosacral area in dogs that are undergoing surgery of the hindlimbs or the abdomen. Common techniques that are used to identify the epidural space rely on subtle changes in tactile and audible sensations which are challenging for less experienced clinicians. Research in humans suggest that mathematical equations that are derived from body surface parameters may improve the success of epidural space identification. In a previous study by this research group, we developed two mathematical equations from computed tomography (CT) measurements using dog surface parameters and a body condition score to predict the skin to lumbosacral epidural space. In this study, we aimed to validate the equations in dog cadavers against a gold standard technique (epidurography). For one equation, the use of the occipital-coccygeal length and body condition score resulted in a high degree of correlation and agreement with the skin to

lumbosacral epidural space of the cadavers. Future studies will determine whether the knowledge of the skin to lumbosacral epidural space distance prior to needle placement improves the success of epidural space identification.

Abstract: This study aimed to validate previously published computed tomography (CT) derived mathematical equations with the true skin to lumbosacral epidural distance (SLED) in dog cadavers. Phase 1: The lumbar region of 11 dog cadavers were scanned in sternal recumbency to determine the effect of cranial, neutral, and caudal pelvic limb positioning on the CT derived lumbosacral epidural distance (CLED). Phase 2: The epidural space was determined using contrast epidurography, and the SLED was analysed against the mathematical equations using a body condition score (BCS) and either the cadaveric occipital-coccygeal length (OCL) (Equation (1): = 7.3 + 0.05*OCL + 16.45*BCS) or the ilium wing distance (IWD) (Equation (2): = 3.5 + 0.56*IWD + 16.6*BCS). There were no differences detected between the pelvic limb positions and the CLED. Both equations demonstrated strong correlations (Equation (1): r = 0.7196; Equation (2): r = 0.7590) with the SLED. The level of agreement was greater for Equation (1) than with Equation (2) (concordance coefficient 0.6061 and 0.3752, respectively). Equation (1) also demonstrated a closer fit to the concordance line compared with Equation (2) (bias correction factor 0.8422 and 0.4960, respectively). Further studies in live anaesthetised dogs will help to determine the usefulness of the pre-procedural knowledge when performing lumbosacral epidurals.

Keywords: epidural; lumbosacral; mathematical; modelling; locoregional; anaesthesia; computed tomography; *ligamentum flavum*; epidurography

4.3. Introduction

Successful epidural anaesthesia relies on the accurate placement of the needle through the skin into the epidural space, but regardless of the method used to identify the epidural space, clinicians are unaware of how far the needle must travel. Most veterinary clinicians performing lumbosacral epidurals do so without any radiographic assistance and instead blindly select the needle trajectory and the final target. Mathematical models have been used in human anaesthesia to predict the distance that is required to enter the epidural space [1,2]. In particular, the relationship between anthropometric variables and the body mass index have been shown to have positive correlations with the skin to lumbar epidural space distance [3–7]. Pre-procedural knowledge of the depth of the epidural space from the skin may serve as a guide for needle placement, particularly for less experienced operators [8,9].

The skin to lumbosacral epidural space distance has recently received similar interest in veterinary anaesthesia [10–12]. A recent study in 82 dogs identified significant positive correlations between external variables (occipital-coccygeal length (OCL) and ilium wing distance (IWD)), and the skin to epidural distance using computed tomography (CT) [12]. Multiple regression analyses have also found that the addition of a dog body condition score further improved the relationship between the external variables and the skin to epidural distance. In that study, however, only dogs with their pelvic limbs in caudal and neutral positions were investigated. It is unknown whether cranial pelvic limb positioning, as is commonly performed in dogs that are receiving an epidural, would influence this anatomical relationship. Furthermore, the derived equations from that study were based solely on correlation relationships from measurements that were obtained from the CT images, and the usefulness of the equations in predicting the true skin to lumbosacral epidural distance that are based on external measurements *in vivo* have yet to be deter- mined. Ideally, a mathematical equation could be used to predict the skin to lumbosacral epidural distance and improve user accuracy in identifying the epidural space before injection in dogs.

The aims of this study were to examine whether the direction of the pelvic limb positioning would affect the skin to lumbosacral epidural distance as determined by CT measurements in canine cadavers. We also aimed to investigate whether external cadaveric measurements would be comparable to the same landmarks on the CT and assess the relationship between the mathematically derived distance and the true skin to lumbosacral epidural distance in canine cadavers. We hypothesised that the pelvic limb positioning would have no effect on the CT derived lumbosacral epidural distance, and that the CT measurements and the cadaveric measurements would be similar. We also hypothesised that the mathematical equations would have close agreement with the true skin to lumbosacral epidural distance.

4.4. Materials and Methods

4.4.1. Cadavers

A prospective experimental study was performed on 11 canine cadavers. The dogs were donated to the Anatomy Department of the School of Veterinary Science for under- graduate veterinary student teaching and were euthanised or died for reasons that were unrelated to the study. The cadavers were thawed in a cold room with a temperature of 18 degrees Celsius for approximately 48 h prior to analysis. The cadavers were fully developed, were not pregnant, and were free of obvious musculoskeletal disease. Any animal that was not amenable to cranial–caudal flexion of the pelvic limbs, suspected to have anatomical defects (i.e., hemi-vertebrae), or had subsequent contamination from the contrast that was outside the epidural space were excluded from analysis. The cadavers were weighed and assigned a body condition score (BCS out of 9 with 9 being obese) [13]. The sex (male or female) and the breed were also recorded.

4.4.2. Procedure

Phase 1

The cadavers were placed in sternal recumbency in the gantry of the CT. In the first phase, three pelvic limb positions were used to determine the effect of positioning on the CT derived skin to lumbosacral epidural distance (CLED) [12], with the pelvic limbs extended caudally (pulled backwards), neutral (placed on the side), and extended cranially (pulled forward). Positioning of the cadavers was performed each time by the same observers (ML and TCS). Scans of the entire lumbar spine and sacrum were obtained using a 16 slice multidetector CT scanner (Phillips 16 Slice, Brilliance CT V2.3; Phillips Medical Systems, Amsterdam, The Netherlands) with a 2 mm transverse slice thickness and 512 × 512 pixel matrix dimensions. For each cadaver, a total of three scans were obtained, one for each pelvic limb position (i.e., lumbosacral epidural cranial, neutral, and caudal positions were $LSE_{cranial}$, $LSE_{neutral}$ and LSE_{caudal}, respectively). For each scan, a first straight line was drawn from the cranial margin of the dorsal lamina of the seventh lumbar vertebra to the cranial margin of the first sacral vertebra. This line was defined as the *ligamentum flavum* surrogate [12]. A secondary line was then drawn to the skin with an angle of 60 degrees to the middle of the first line and was defined as the CLED [12]. Measurements to the nearest millimetre were obtained for each of the three positional scans. The images were analysed by a single observer (TCS) and viewed on three dimensional reconstructions using a bone Hounsfield unit window (Apple Thunderbolt Display, Apple, Cupertino, CA, USA; Mac Mini, Apple; Osirix version 5.7 64-bit, Pixmeo SARL, Bernex, Switzerland).

Phase 2

The second phase of the study investigated whether the surface anatomical measure- ments in dog cadavers could be used as a replacement of CT measurements and predict the true skin to lumbosacral epidural distance (SLED). Surface measurements of the occipital– coccygeal length (OCL) and ilium wing distance (IWD) were manually measured by the same observer (FMT) to the closest millimetre using a flexible measuring tape with the pelvic limbs remaining in cranial extension (Figure 1). CT measurements were subsequently made from the landmarks of the same cadavers by another observer who was unaware of the initial cadaveric measurements (TCS). The OCL was taken from the occipital protuberance to the median sacral crest of the first sacral vertebrae following the dorsal midline of the cadaver, and the same measurement was performed on the CT image from the scout view. The IWD was the distance measured between the most prominent aspects of the dorsal iliac wings on palpation on the cadaver, and between the dorsal aspects of the ilium wings on the dorsal plane window on the CT where both bony structures were first clearly visible (Figure 1). The measurements were recorded on a computerised spreadsheet for data analysis (Microsoft Excel 2011; Microsoft Corporation, Redmond, WA, USA).

For the determination of the SLED, the pelvic limbs of the cadavers remained in a cranial position and hair from the lumbosacral region was clipped. An experienced veterinary anaesthetist (TCS) performed all of the epidural injections on the cadavers. The running drip method [14] was used initially to enter the epidural space. An 18-gauge 80mm Tuohy epidural needle (B Braun, Melsungen, Germany) was inserted into the lumbosacral space. After the needle was placed through the skin, the stylet was removed and the hub of the needle was connected to a three-way tap (Becton Dickinson, Helsingborg, Sweden) attached to a raised 100 mL saline bag (sodium chloride 0.9%, Baxter International Inc., Sydney, NSW, Australia) using a primed giving set ((Vetquip Niki IV infusion set, Amsino International Inc., Pomona, CA, USA). The needle was advanced until an unequivocal increase in the dripping rate was observed, at which point the three-way tap was removed from the hub of the needle and a scan was performed. The location of the tip of the needle was corroborated by a veterinary radiologist (ML), and if the needle tip was determined not to be in the epidural space, another attempt of the above procedure was performed. Each attempt was defined as a positive running drip followed by a CT scan. Epidurography was then performed in situ using diluted iodinated radiographic contrast (Omnipaque 350; GE Healthcare Australia

Pty Ltd., Parramatta, NSW, Australia) with a total of 3 mL solution injected (1 mL contrast and 2 mL saline). Following the contrast injection, a CT scan was performed to confirm the presence of contrast in the epidural space, and the CLED measurement as described above in Phase 1 was later performed with the visible epidural space replacing the first line ($LSE_{epidurography}$) (Figure 2). Once completed, straight forceps were used to clamp the skin–needle interface. A protractor was rested against the skin to measure the acute angle between the Tuohy needle and the skin. The needle and clamp were then removed from the cadaver and the distance from the tip of the needle to the clamp was recorded in mm as the SLED [10]. If epidurography indicated that contrast outside of the epidural space was present, the cadaver was excluded from further analysis.

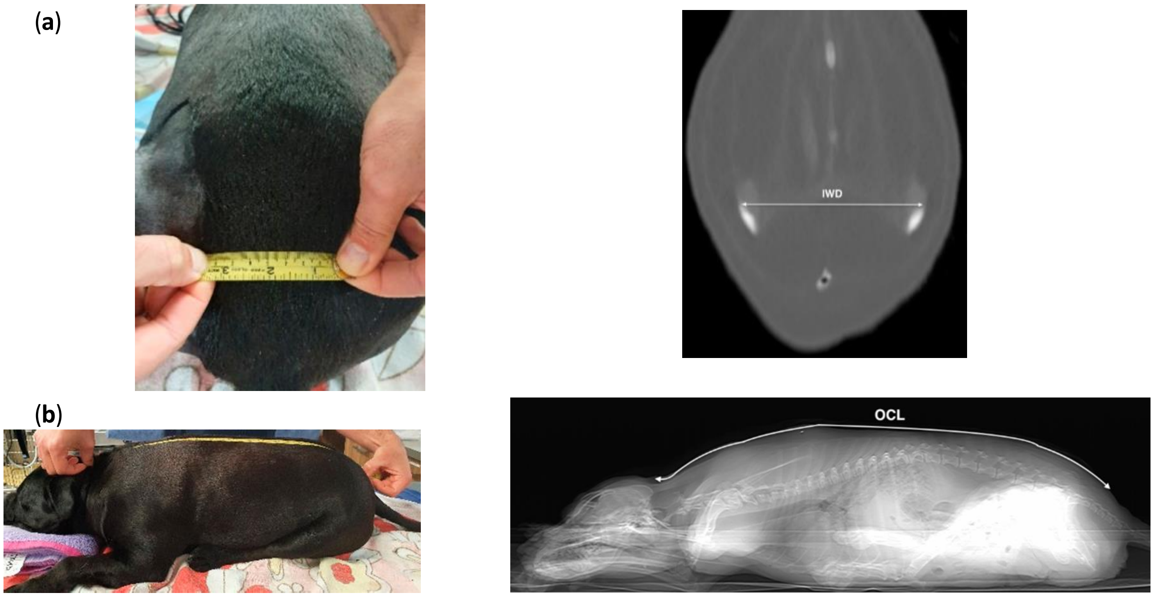
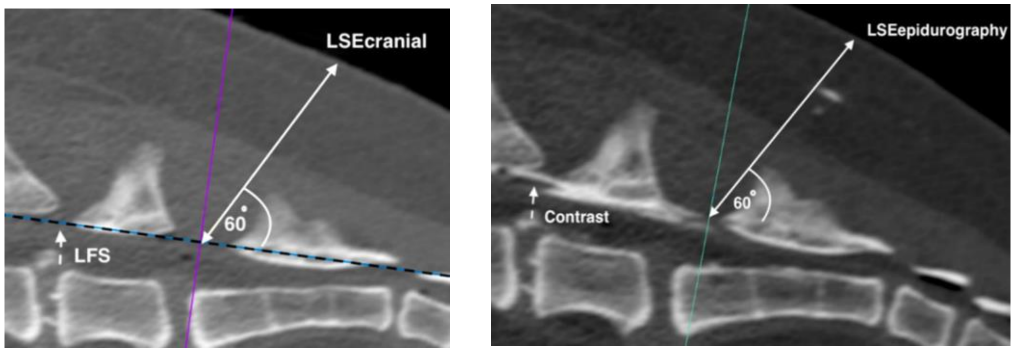


Figure 1. Representative measurements of (**a**) ilium wing distance (IWD), and (**b**) occipital-coccygeal length (OCL) obtained by surface measurements on a dog cadaver (left) and in the same dog on CT (right). Bi-directional arrows depict the landmark sites of the computed tomography (CT) images with the IWD measuring the distance between the dorsal aspects of the ilium wings on the dorsal plane window where both bony structures were first clearly visible, and the OCL from the occipital protuberance to the median sacral crest of the first sacral vertebrae following the dorsal midline of the image from the scout view.



(**a**) (**b**)

Figure 2. Computed tomography (CT) derived lumbosacral epidural distances (CLED) involving pelvic limbs in cranial extension (LSEcranial (**a**)), and contrast epidurography (LSEepidurography (**b**)). Bi-directional arrows represent the measured CLED distance at 60 degrees from either the *ligamentum flavum* surrogate (LFS) (hashed arrow (**a**)), or the epidural space confirmed by contrast epidurography (hashed arrow (**b**)).

4.4.3 Statistical Analysis

A sample size of 10 dogs was estimated for the detection of an 8 mm difference [11] between the SLED and two mathematically derived lumbosacral epidural space distances, with a variance of 25, loss of 15% and power of 90% [15]. The mathematical equation forpredicting the SLED were obtained by using the BCS with the OCL or IWD derived from our previous study [12]:

$$SLED_{equation1} = 7.3 + 0.05*OCL + 16.45*BCS \qquad (1)$$

$$SLED_{equation2} = 3.5 + 0.56*IWD + 16.6*BCS \qquad (2)$$

The BCS was further classified as binominal (0 = less than or equal to BCS 5/9, and 1 = greater than BCS 5/9) as published previously [12]. Measurements were recorded on a computerized spreadsheet (Microsoft Excel 2011; Microsoft Corporation, Redmond, WA, USA), and transferred to statistical software program R, version 3.6.1 for Windows 10 (The R Foundation for Statistical Computing, http: www.Rproject.org, last accessed 18 July 2021, Vienna, Austria).

For Phase 1, the CLED for $LSE_{cranial}$, $LSE_{neutral}$, and LSE_{caudal} were compared. For Phase 2, the cadaveric OCL and IWD were compared with their respective CT measure- ments, and the $LSE_{epidurography}$ was compared with $LSE_{cranial}$ to validate the *ligamentum flavum* surrogate. The crude values were examined for normality using the Shapiro–Wilk test. When a normal data distribution was found, a one-way analysis of variance or Student's t-test was used where appropriate. If the data were non-normally distributed, the Mann–Whitney U test was used. Correlation and concordance relationships were determined to validate the mathematical equations using the cadaveric measurements with the SLED. Correlation was expressed as positive or negative values of Pearson's correlation coefficient (r). Proportion of fit (R^2), F statistic for the predictability variable of the outcome, and β weights for increase in the variable for each standard deviation were reported. Relationships were examined graphically by using the crude values, and the linearity of residuals and fitted values were assessed in R. Concordance was determined by assessing the level of agreement between the predicted variables (Equations (1) and (2)) and a gold standard (SLED) by calculating Lin's concordance coefficient (*CCC*) and concordance line agreement bias (c.b.), where *CCC* = 1 indicates perfect agreement; 0: no agreement; -1: reverse agreement [16]. Values between 0 and 0.29, 0.3 and 0.49, 0.5 and 0.69, and 0.7 and 1.0 were considered to signify very weak, weak, moderate, and strong for both *r* and *CCC*, respectively [17]. Statistical significance was set at $p < 0.05$.

4.5. Results

4.5.1. Phase 1

A total of 11 cadavers met the inclusion criteria, and no cadavers were excluded. Summary descriptive data for sex, weight, and breed are provided in Table 1. Phase 1 analysis of the pelvic limbs in caudal, neutral, and cranial positions demonstrated no effect on the CLED ($p = 0.3084$).

Table 1. Descriptive information for the 11 canine cadavers, the CT derived lumbosacral epidural space distance (CLED) based on three pelvic limb positions (Phase 1), with the predictor and the outcome values for correlation and concordance evaluation (Phase 2).

ID	Sex	Weight (kg)	BCS /9	Breed	Phase 1 (In Millimetres) CLED			Phase 2 (In Millimetres)				
					Caudal	Neutral	Cranial	OCL Cadaver/CT	IWD Cadaver/CT	Equation (1)	Equation (2)	SLED
1	M	15	5	Staffordshire bull terrier	43	43	34	565/510	80/59	35.6	48.3	34
2	F	23.5	7	Staffordshire bull terrier	59	53	46	630/593	90/63	55.3	70.5	49
3	F	20.3	6	Staffordshire bull terrier	57	62	52	580/524	95/61	52.8	73.3	51
4	M	29.9	4	Greyhound	36	36	29	950/941	96/102	54.8	57.3	30
5	F	34.1	7	English bulldog	59	63	56	760/687	85/72	61.8	67.7	61
6	M	14.1	4	Beagle	42	41	36	640/609	70/66	39.3	42.7	41
7	M	9.6	2	Crossbred	22	22	17	560/543	60/56	35.3	37.1	24
8	M	14.1	4	Beagle	34	34	28	670/615	80/66	40.8	48.3	31
9	F	9.2	5	French bulldog	33	33	29	455/454	88/53	30.1	52.8	32
10	M	11.2	5	Kelpie	41	40	32	550/527	65/66	34.8	39.9	33
11	M	17.5	4	Staffordshire bull terrier	40	37	30	730/645	90/63	43.8	53.9	29

ID: Cadaver identification; kg: weight in kilograms; Phase 1—the CT derived lumbosacral epidural space measurements of pelvic limbs in the caudal, neutral, and cranial positioning with the cadavers in sternal recumbency; Phase 2: BCS— the body condition score out of 9; OCL: occipital-coccygeal length; IWD: ilium wing distance; Equation (1)—the lumbosacral epidural space derived from the cadaveric OCL using the equation [= 7.3 + 0.05(OCL) + 16.45(BCS)]; Equation (2)—the lumbosacral epidural space derived from the cadaveric IWD using [= 3.5 + 0.56(IWD) + 16.6(BCS)]; SLED: the true skin to lumbosacral epidural distance confirmed with epidurography.

4.5.2. Phase 2

The individual BCS, SLED, OCL, and IWD (both cadaveric and CT), and the mathe- matically derived lumbosacral epidural distances using Equations (1) and (2) are shown in Table 1. The cadaveric and CT measurements were different for the IWD (p = 0.0150), but not for the OCL (p = 0.3).

The contrast epidurography confirmed the SLED in all dogs. Of the dogs, eight required one attempt, two dogs required two attempts and one dog required three attempts at needle placement, while the final angle of the Tuohy needle projection ranged from 60 to 110 degrees. The CLED for the $LSE_{cranial}$ and the $LSE_{epidurography}$ were not different (p = 0.6037).

The correlation and concordance of mathematical equations using cadaveric measure- ments with the SLED are presented in Table 2. Both demonstrated strong correlations with the SLED (Equation (1): r = 0.7196, p = 0.0125; Equation (2): r = 0.7590, p = 0.0068). However, the level of agreement was greater for Equation (1) (CCC = 0.6061; p = 0.0125) than for Equation (2) (CCC = 0.3752; p = 0.0068). Equation (1) also demonstrated a closer fit to the concordance line (c.b. 0.8422), compared with Equation (2) (c.b. 0.4960).

Table 2. Correlation and concordance relationships between the true skin to lumbosacral epidural distance (SLED), and two mathematically derived lumbosacral epidural distances from 11 canine cadavers.

SLED Prediction	*r*, 95% CI	P_r	R^2	Intercept	β	F	$P_R{}^2$	*CCC*, 95% CI	c.b
Equation (1)	0.7196, 0.2107–0.9217	0.0125	0.5179	19.0621	0.6620	9.668	0.0125	0.6061, 0.1471–0.8503	0.8422
Equation (2)	0.7590, 0.2913–0.9340	0.0068	0.5755	22.7683	0.8225	12.2	0.0068	0.3763, 0.0590–0.6246	0.4960

The two mathematical equations: Equation (1) [SLED = 7.3 + 0.05(OCL) + 16.45(BCS)], and Equation (2) [SLED = 3.5 + 0.56(IWD) + 16.6(BCS)], where (BCS) was (0) for body condition score less than or equal to 5/9 and (1) for greater than 5/9, OCL: Occipital-coccygeal length (mm); IWD: ilium wing distance (mm); *r*: Pearson's correlation coefficient; 95%CI: 95% confidence interval; P_r: *p* value for *r*; R^2: proportion of fit of the variable; F: predictability variable, β: weight for the increase in the variable for each standard deviation; $P_R{}^2$: *p* value for R^2; β: predictability variability of the outcome; *CCC*: Lin's concordance coefficient; c.b: agreement bias for deviation from the best fit line of 45 degrees. No deviation occurs when c.b. = 1.

4.6. Discussion

This study supports the hypothesis that cranial extension of the pelvic limbs in canine cadavers does not affect the CT derived skin to lumbosacral epidural distance when com- pared with neutral and caudal positions. The cadaveric and CT derived measurements were different for the IWD, but not for the OCL. Furthermore, there was no statistical difference in the CT derived skin to lumbosacral epidural distance when using the *ligamentum flavum* surrogate and contrast epidurography. Both Equation (1) (using OCL) and Equation (2) (using IWD) correlated with the true skin to lumbosacral epidural space distance, but Equation (2) had higher agreement.

Dogs undergoing clinical epidural placement are frequently placed in sternal re- cumbency with their pelvic limbs in cranial extension [18,19], and it is possible that the lumbosacral anatomical relationships would be influenced by pelvic limb positioning. Pre- vious studies indicate that dog cadavers with cranially placed pelvic limbs have increased lumbosacral interlaminar distances on the CT when compared with pelvic limbs in the caudal placement [20,21], while the mid-laminar L5-L6 distances in dogs positioned in a sternal kyphotic position with the pelvic limbs extended cranially were greater than in neutral positioning [22]. Our previous research showed that the CT derived skin to lumbosacral epidural distances between pelvic limbs in neutral and caudal positioning were not statistically different [12], and it was unknown whether the pelvic limbs in cranial extension would change this relationship. The results from Phase 1 of this study suggest that cranial extension of the pelvic limbs and the other positions investigated are unlikely to affect the CLED in this population of cadavers. However, there should be caution in extrapolating this relationship to live dogs as the degree of pelvic limb extension may be greater in cadavers than in live dogs. For example, hip extension may be restricted by a disease processes such as osteoarthritis [21]. Additionally, the intrinsic anatomy of the epidural space is maintained by physiological pressures and venous distension, which is lost immediately after death [23]. Further prospective studies in live anaesthetised dogs are necessary to validate the results from this cadaveric study for clinical use.

Epidurography is considered the gold standard method for confirming the epidural space in both dogs and humans [24–26], but the use of contrast agents, the cost, and accessibility to advanced imaging limit its use in clinical veterinary practice [27,28]. Epidurography was chosen as the standard for comparison in this study because this method is the most accurate for confirming the epidural placement of a needle [29]. Correct needle placement was essential in identifying the SLED in the cadavers and corroborating the CT derived mathematical equations. In a previous clinical study, the loss-of resistance method was used to determine the depth of the skin to epidural space in anaesthetised dogs [10]. However, this technique has been associated with a procedural failure rate of up to 32% [30] and was considered inadequate in confirming the epidural space when used alone [29]. The current study used the running drip method as a guide prior to epidurography. The running drip method was associated with a success rate of 90% in the detection of the lumbosacral epidural space, but may not differentiate between the intrathecal and epidural spaces [31]. If an alternative technique to epidurography was used as a confirmation for epidural space placement in cadavers, the internal validity of the results may have been reduced.

The results from this study are limited to cadavers and cannot imply any clinical improvement in the detection of the epidural space of dogs *in vivo*, and the efficacy of performing an epidural was not an aim of this study. Our secondary hypothesis was specific for determining the correlation and agreement between the mathematical equations and the SLED. In humans, predictive mathematical models have been suggested to be beneficial prior to epidural needle placement [6,7,32–34]. In particular, mathematical models have been used for people considered to be at risk of a difficult epidural due to deeper distances [9,35,36]. In morbidly obese parturient women, the combination of an ultrasound with pre-procedural epidural depth equations that are determined from height and weight variables improved the success rate of the epidural catheter placement than with ultrasonography alone [9]. However, the equations that were generated from individual studies have not been validated to other patient populations, therefore, their use is limited to within the same study population [8]. Conversely, the present study validated existing equations by demonstrating good agreement and correlation with an alternative unrelated study population [12]. We hypothesised that our previously reported equations using CT derived external morphometric variables would have a high degree of agreement with the SLED using dog cadaveric measurements. However, the CT derived measurement was statistically different to the cadaveric measurements when the IWD was examined. In our study, the dorsal aspects of the iliac crests were difficult to palpate in dogs with a higher BCS. It is possible that the IWD was overestimated in some cadavers due to extra subcutaneous fat cover over the iliac crests, resulting in a wider distribution of datapoints and the lower concordance reported for Equation (2). Alternatively, the measurements of the OCL in both cadaveric and CT derived distances were not different. The cadaveric measurements were performed over two distinct landmarks, the occipital protuberance and the base of the first sacral vertebrae, both of which were easily palpable in all cadavers regardless of the BCS. The practical ease of measuring the OCL and the higher concordance coefficient suggests that using the OCL (Equation (1)) may be a preferred method in predicting the SLED. Further prospective studies in anaesthetised animals can be used to determine whether mathematical equations to predict depth would truly improve the efficacy in epidural space identification.

There were some limitations to this study. Thawed cadavers were used, and the results should not be extrapolated to live dogs. The SLED in cadavers may be greater due to the absence of epidural pressures that are generated by the lymphatic and circulatory systems in the abdominal and thoracic cavities [23]. The effect of freeze-thawing may also have altered the integrity of epidural anatomical structures due to the collapse of the dural sac after freezing [37]. Another limitation was that this study was designed to validate previous mathematical equations that were only formulated for dogs in sternal recumbency, and the results cannot be applied to other recumbencies. A consideration from the results is the clinical perceptible difference that is acceptable between the mathematical equations and the SLED. The sample size calculations suggested that ten dogs were required to detect an 8 mm difference, and while this number may seem small, it was appropriate for demonstrating a meaningful clinical difference [11] and for concordance analysis [16]. The equations used in this study were derived from multivariable analysis involving two external morphometric variables (OCL, IWD), and the BCS. A moderate proportion of fit was found from both Equation (1) (R^2 = 0.5179) and Equation (2) (R^2 = 0.5755), which showed that some variation was unaccounted for in the models. While increasing the number of variables may improve this relationship, it adds complexity and restricts the clinical applicability of these equations. In addition, while fat content in overweight animals is not evenly distributed, the use of the BCS makes the body fat distribution irrelevant, while the binomial classification further reduces subjectivity of multiple BCS categories and improves the practical use of the equations. Some breeds were over-represented in our study population of cadavers; however, the mathematical equations were originally developed incorporating different dog breeds [12], and it would be reasonable to assume that the external morphometric variables and the body condition score would capture some differences in breed conformation.

4.7. Conclusions

In conclusion, cranial extension of the pelvic limbs had no effect on the CT derived skin to epidural distance. Mathematical equations were highly correlated with the SLED and using the OCL showed a higher level of agreement compared with the IWD. Further clinical studies in anaesthetised dogs are required to determine the usefulness of this information prior to epidural needle placement.

Author Contributions: T.C.S. contributed to conceptualization, methodology, validation, formal analysis, investigation, data curation, and writing and editing of the original and final manuscript. M.S. contributed

to supervision, writing review, and editing. M.P.Y.L. contributed to methodology, software and image analysis, and final review of the manuscript. F.M.-T. contributed to conceptu- alization, methodology, validation, formal analysis, data curation, review, and final editing of the manuscript. All authors have read and agreed to the published version of the manuscript. **Funding:** This research received no external funding.

Institutional Review Board Statement: Ethical review and approval were waived for this study. The cadavers were provided for undergraduate teaching and euthanised for reasons unrelated to the study.

Data Availability Statement: Data provided on request.

Conflicts of Interest: The authors declare no conflict of interest.

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Chapter 5

PERFORMANCE OF A MATHEMATICAL MODEL-ASSISTED VERSUS CONVENTIONAL EPIDURAL TECHNIQUE IN DOGS: A PROSPECTIVE, RANDOMISED, CLINICAL STUDY

5.1. Background

As discussed in chapter 3 and 4, it is possible that the mathematical equation will positively influence anaesthetists who are clinically placing epidurals for dogs requiring surgery of the hindlimb or pelvic region. Additionally, chapter 4 further demonstrated that the formula was validated in a separate unrelated population and that the position of the limbs did not influence the mathematical equation (subsection 4.5.1.). This chapter investigates the use of the mathematical equation in a clinical setting and whether predictive knowledge to anaesthetists would be different to those anaesthetists performing an epidural with conventional techniques.

5.2. Abstract

A prospective, randomised clinical study was performed to determine whether predictive knowledge of the skin to lumbosacral epidural distance (SLED) using a mathematical model would influence procedural failure rates compared with conventional epidurals. Predictive information was generated using an equation: PredSLED (mm) = 7.3 + 0.05 (occipital coccygeal length (mm)) + 16.45 (modified body condition score) from an earlier study. After randomisation, anaesthetists in the AWARE group (n = 39) calculated the PredSLED and used the information while placing the epidural. Anaesthetists in the UNAWARE group (n = 39) placed epidurals using conventional techniques. The Westphal's sign, nociceptive response to stimulation and anaesthetist's opinion of epidural failure were the main outcomes in determining procedural failure rates.

The Westphal's sign was positive in 87% and 84.6% of the AWARE and UNAWARE groups respectively (P = 0.7449). Response to surgical stimulation was 12.8% (5/39) and 15.3% (6/39) in the AWARE and UNAWARE groups respectively (P = 0.7449). Overall procedural failure rate based on anaesthetist's opinion was slightly lower in the AWARE group (12.8%; 5/39) compared with the UNAWARE group (15.4%; 6/39; P = 0.7449). The overall procedural failure rate was compared with a predetermined Δ (-0.22) and non-inferiority was confirmed. Additional predictive information in the form of a mathematical equation did not seem to affect failure rates, and was not shown to be harmful when compared with the use of conventional epidural techniques.

5.3. Introduction

Epidural anaesthesia is commonly performed in dogs undergoing pelvic or hindlimb surgeries, providing perioperative anaesthesia and analgesia [3], reduced opioid consumption [82] and decreased anaesthetic mortality [83]. Conventionally, epidural techniques such as the running drip [24] or hanging-drop [18] methods are used in clinical practice, however, both techniques require training and knowledge of anatomical landmarks surrounding the lumbosacral epidural space. Even for experienced anaesthetists, the procedural failure rate for the running drip and hanging drop techniques were reported to be 10% and 30% respectively [20, 26]. Furthermore, needle placement is blind, regardless of the technique, in that the skin to epidural distance is estimated by the anaesthetist without prior knowledge as to how far the needle must travel to reach the epidural space.

Recently, a mathematical model was developed based on dog morphometric parameters to predict the skin to lumbosacral epidural distance (SLED) [84, 85]. Based on both computed tomographic (CT) and cadaveric measurements of the occipital coccygeal length (OCL) and body condition score (BCS), strong correlations were found with the predicted SLED and the true epidural distance as demonstrated with contrast epidurography. It was proposed that the mathematical model could assist in lumbosacral epidural needle placement particularly for the novice anaesthetist [84]. Certainly, in human anaesthesia, the relative risk of a failed epidural was 2.4 times greater with an anaesthetist in training compared to experienced attending anaesthetists [86]. Additionally, use of mathematical models with predictive variables such as body mass index, height, and weight have been used to facilitate needle placement in human patients with highly variable skin to epidural distance [7]. While there are no known clinical applications of mathematical models in veterinary anaesthesia, the use of predictive models could improve the clinical accuracy for epidural analgesia, or at least be considered no different when used compared with traditional methods [30-32].

The main aim of this clinical study was to examine the influence of a predictive mathematical model on the procedural failure rate of lumbosacral epidural procedures in anaesthetised dogs. Correlation relationships would be determined by the influence of the mathematical model when used by experienced and inexperienced anaesthetists, including the number of epidural attempts and procedural failure rates. We hypothesised that the use of a mathematical model in conjunction with conventional epidural techniques would perform non-inferiorly to current conventional epidural techniques.

5.4. Materials and Methods

5.4.1. Animals and inclusion criteria

The study was a prospective, block-randomised, clinical study conducted at the University Veterinary Teaching Hospital Sydney, Australia and approved by the animal ethics committee at the University of Sydney, Australia (Project number 2021/1999). All owners provided informed consent. Dogs admitted to the hospital for various surgical procedures of the abdomen and/or pelvic limb(s) were considered for the study. Dogs were included in the study if the anaesthetist determined that a lumbosacral epidural was required as part of the anaesthetic plan. Dog breed, age (months), sex (male/female) and body condition score (BCS) out of 9 were recorded. Dogs were excluded if they were younger than six months of age, if there was obvious musculoskeletal disease involving the back or pelvic limb regions, if there was an absolute contraindication for an epidural (coagulopathy, pyoderma around the lumbosacral region, sepsis, neurological disease), or if there was suspicion of anatomical defects (i.e. hemi-vertebrae, lumbosacral stenosis). All dogs underwent a pre-anaesthetic physical examination and blood test analyses including haematology and serum biochemistry profiles.

The anaesthetic protocol for each dog was individualised based on temperament, the American Society of Anaesthesiologists physical status categorisation and the attending anaesthetist's preference.

Premedication was performed either intravenously or intramuscularly with a single agent or a combination of acepromazine (0.005 – 0.015 mg/kg; ACP 2 mg/mL, Ceva Animal Health Pty Ltd, Glenorie, NSW, Australia); buprenorphine (0.02-0.03 mg/kg; Ilium Temvet Injection 300 mcg/mL, Troy Animal Laboratories, Glendenning, NSW, Australia); butorphanol (0.3 – 0.5 mg/kg; Ilium Butorgesic Injection 10 mg/mL, Troy Animal Laboratories, Glendenning, NSW, Australia); dexmedetomidine (3 – 5 mcg/kg; Dexdomitor 500 mcg/mL, Jurox Pty Ltd, Rutherford, NSW, Australia); ketamine (0.5 – 1 mg/kg; Ketamine 100 injection Ilium 100 mg/mL, Troy Laboratories Pty Ltd); medetomidine (5 – 10 mcg/kg; Medetomidine injection Ilium 1 mg/mL, Troy Laboratories Ptd Ltd, Glendenning, NSW, Australia); or methadone (0.2 - 0.3 mg/kg; Methadone 10 mg/mL injection Ilium, Troy Laboratories Pty Ltd, Glendenning, NSW, Australia). Five minutes after intravenous premedication, or 15-30 minutes after intramuscular premedication, an intravenous induction of general anaesthesia was performed solely with alfaxalone (Alfaxan Multidose 10 mg/mL, Jurox Pty Ltd, Rutherford, NSW, Australia) or propofol (Propofol lipuro 10 mg/mL, B. Braun Mesungen AG, Mesungen, Germany), or in combination with ketamine (Ketamine 100 injection Ilium 100 mg/mL, Troy Laboratories Pty Ltd, Glendenning, NSW, Australia) or midazolam (Hypnovel 5 mg/mL, Roche Products, Pty Ltd, Sydney, Australia).

After orotracheal intubation, general anaesthesia was maintained using isoflurane (VSO ISO Inhalational Anaesthetic, Veterinary Companies of Australia Pty Ltd, Sydney, NSW, Australia) vaporised in oxygen and delivered via a circle breathing system. The dogs were immediately connected to a multi-parameter anaesthetic monitor with a continuous display (Anitek C50-V, Anitek Pty, Ltd, Sydney, NSW Australia). Depth of anaesthesia and physiological parameters (end-tidal carbon dioxide, non-invasive blood pressure, electrocardiography using lead II, pulse oximetry, respiratory rate and rectal temperature) were recorded every five minutes. The dogs were then placed into sternal recumbency with the pelvic limbs extended cranially. The lumbosacral region was clipped and surgically prepared for the epidural procedure and the patellar reflex confirmed using a Taylor’s hammer on both pelvic limbs, or one pelvic limb if the contralateral limb required surgery. Presence of the patellar reflex was recorded as either present or absent.

5.4.2. Randomisation and groups

Dogs were allocated into two equal groups following block randomisation (www.sealedenvelope.com/simple-randomiser/v1/lists; last accessed 10th December 2021). Based on the group, the anaesthetist was either made aware of the predicted skin to lumbosacral epidural distance (AWARE), or not (UNAWARE).

In the AWARE group, the anaesthetist would measure the OCL in millimetres (mm) as described previously by our research group [84]. The BCS variable was further classified as binomial (0 = less than or equal to BCS 5/9; or 1 = greater than 5/9) [84]. An external observer would then perform the calculation:

$$PredSLED\ (mm) = 7.3 + 0.05 * OCL + 16.45\ (BCS)$$

The PredSLED would then be read out to the attending anaesthetist and recorded on the anaesthetic record to be referenced as required.

In the UNAWARE group, the anaesthetist would perform the epidural technique as per the *status quo* and the PredSLED was not provided.

5.4.3. Epidural technique

Anaesthetists at the institution were categorised as either inexperienced (fewer than ten epidurals performed in the past 12 months), or experienced (ten or greater epidurals performed in the past 12 months), and included non-specialist anaesthetic clinicians and interns employed by the University, and residents and specialists in anaesthesia of the European College of Veterinary Anaesthesia and Analgesia. Anaesthetists were moved from inexperienced to experienced groups if sufficient epidural procedures were performed. The choice of technique for lumbosacral epidural was based on anaesthetist preference and consisted mainly of the hanging drop, or running drip methods. An 18g 80 mm epidural needle with 10mm markings and a Tuohy bevel (B Braun, Melsungen, Germany) was used in all cases.

Details of both epidural techniques have been previously described [3, 24]. Briefly, the hanging drop involves placement of the epidural needle through the skin of the midline of the lumbosacral space before removing the stylet and filling the needle hub with sterile 0.9% saline. The needle is then slowly advanced with the thumb and index finger with both hands until the fluid moves from the hub into the needle and/or a distinctive pop is noted once the *ligamentum flavum* is pierced. If the needle is considered to be in the desired location, the hub is observed for the presence of cerebrospinal fluid or blood before any medication is administered. If the needle encounters bone, it is retracted and redirected either cranially or caudally until the pop is noted or the fluid has moved distally. One motion of retraction-redirection was defined as one attempt and the number of attempts was recorded. This was repeated until the anaesthetist was satisfied that the needle was in the epidural space, at which time the epidural medication was injected gradually over three minutes.

Alternatively, the running drip method involves placement of the epidural needle as described above. After the needle pierced the skin, the stylet was removed and an elevated 100 mL sterile saline bag (sodium chloride 0.9% Baxter International Inc), was connected to the needle hub via a primed giving set (Vetquip Niki IV infusion set, Amsino International Inc, Pomona, CA, USA) and three-way tap (Becton Dickinson, Helsingborg, Sweden). The needle was then advanced until a rapid increase in dripping rate was observed, at which point the three-way tap was removed from the hub of the needle and observed for cerebral spinal fluid or blood. If the dripping rate did not increase, the steps would be repeated as described above for the hanging drop method.

The choice of epidural medication was decided by the attending anaesthetist and dependent on the type of surgery. Lignocaine (Lignocaine injection 2%, Pfizer Global Manufacturing, West Ryde, NSW, Australia) or bupivacaine (Bupivacaine injection BP 0.5%, Pfizer Perth Pty Ltd, Bentley, WA, Australia) were used as single agents, or in combination with buprenorphine (4 - 5 mcg/kg, Temgesic injection 300 mcg/mL, Indivior Ptd Ltd, Ryde, NSW, Australia), methadone (0.1 mg/kg, Physeptone Methadone Hydrochloride 10 mg/mL, Aspen Pharmacare Australia Pty Ltd, St Leonards, NSW, Australia) or morphine (0.1 mg/kg, DBL Morphine Sulfate Injection BP 10 mg/mL, Pfizer, Sydney, Australia). Where required, dilution was performed with sterile 0.9% sodium chloride to achieve the total volume used based on standard normogram calculations for epidural injection [87]. Once the injection of the epidural was complete, straight forceps were used to clamp the skin-needle interface before removing the clamp and needle from the dog. The clamped area on the needle represented the actual skin to lumbosacral epidural distance (ActSLED) and was recorded in mm (Figure 1).

Figure 1: Bi-directional arrows depict the measurement of the actual skin to lumbosacral epidural distance (ActSLED), obtained after the injection of epidural medication and removal of the Tuohy needle from the lumbosacral space. The ActSLED was measured to the closest millimetre from the tip of the Tuohy needle to the clamped forceps.

Cardiovascular and respiratory variables were monitored for any signs of depression or indication of local anaesthetic toxicity (e.g. bradycardia, bradyarrhythmia, hypocapnoea) during and after the epidural medication process. After a period of data recording, the anaesthetic plan continued normally, with the attending anaesthetist having total freedom to adapt the protocol as required. Three outcome measurements were taken after the initial epidural to assess the success or failure of the epidural in both groups:

Westphal's sign: Exactly five minutes after the epidural was performed, the patellar reflex was tested again with a Taylor's hammer on one or both pelvic limbs for determination of the Westphal's sign (reduction of patellar reflex). Presence of a positive (weaker or absent reflex) or negative (intact reflex) sign was recorded. The presence of a positive sign was taken as an indication that the epidural would be successful.

Nociceptive response to surgical stimulation: An increase in heart rate and/ or mean arterial blood pressure 20% above pre-incision baseline values was considered indicative of a failure of the epidural. At any time after the initial epidural was performed, the attending anaesthetist could consider additional rescue analgesics for the dog at their discretion.

Anaesthetist's opinion: At the end of the surgery during recovery, the attending anaesthetist was asked, "In your opinion, was the epidural successful?". This was recorded as success or failure.

5.4.4. Statistical analysis

All data was analysed using R statistical software version 3.6.1. for Windows 10 (The R Foundation for Statistical for Computing, http:www.Rproject.org, last accessed 12th December 2023, Vienna, Austria). Continuous data was assessed for normality using the Shapiro-Wilk test and assessed graphically using a histogram. Normal data was described as mean +/- standard deviation, while non-parametric data was described using the median (interquartile range).

Overall procedural failure rates were determined based on anaesthetists' opinions and were compared between AWARE and UNAWARE groups, as well as between experienced and inexperienced anaesthetists. Crude values and percentages were compared with t-tests for continuous variables and chi squared tests for proportions where appropriate. Where clinically suitable, Pearson's correlation between the procedural failure rates, number of epidural attempts, and anaesthetists' experience were examined within AWARE and UNAWARE groups. Values between 0 and 0.29, 0.3 and 0.49, 0.5 and 0.69, 0.7 and 1.0 equated to very weak, weak, moderate and strong correlations respectively. Correlations were either positive or negative.

Non-inferiority was defined using the predefined non-inferiority margin (Δ) against the 95% confidence interval of the difference between the procedural failure rate means of AWARE and UNAWARE groups. The value of Δ was calculated using the minimum acceptable margin of error of the introduction of the new technique (the mathematical model) when compared with the conventional methods of epidural. The Δ defines how much the conventional methods may exceed the new technique with the new treatment still being considered non-inferior to the conventional methods [88]. This was determined to be to be -0.22, which was a fixed margin of error reported between the procedural failure rate between previously published techniques (loss of resistance; 32% [20] and running drip 10% [24]). If the difference between the AWARE and UNAWARE groups was not statistically different, they would be combined into the calculation against Δ. If statistical significance was detected between the two groups, then the AWARE group would be calculated against Δ. A one proportion z-test to determine the 95% confidence interval was performed between the AWARE and UNAWARE groups based on the anaesthetists' opinion. A *p* value of less than or equal to 0.05 was considered statistically significant.

Table 1: Comparison of demographic, morphometric variables and descriptive epidural data in anaesthetised dogs undergoing lumbosacral epidural performed by anaesthetists AWARE (n = 39) of the mathematical equation, and anaesthetists UNAWARE of the (n = 39) equation.

Variable	AWARE	UNAWARE	P value
Sex			
Male	23	22	1.0000
Female	16	17	
Mean age in months (SD)	81.49 (53.2)	83.44 (50.8)	0.4744
Body condition score			0.6489
1 – 5	23	20	
1	1	0	
2	3	3	
3	2	2	
4	7	9	
5	10	6	
6 – 9	16	19	
6	6	10	
7	4	7	
8	5	1	
9	1	1	
OCL (SD)	676.8 (168.5)	637.4 (132.6)	0.1262
KG (SD)	21.27(11.6)	19.11 (11.5)	0.2116
PredSLED mm (SD)	47.46 (12.3)	N/A	N/A
ActSLED mm (SD)	39 (13.5)	36.74 (8.6)	0.1599
Epidural technique			0.7792
Hanging drop	30	32	
Running drip	9	7	

Table 2: Comparison of anaesthetist experience and epidural outcome data in anaesthetised dogs undergoing lumbosacral epidural performed by anaesthetists AWARE (n = 39) of the mathematical equation, and anaesthetists UNAWARE of the (n = 39) equation.

Variable	AWARE	UNAWARE	P value
Anaesthetist experience over 12 months			0.3625
<10	15	20	
>10	24	19	
ATTEMPTS			0.4307
1	22	19	
2	10	11	
3	3	4	
4	0	2	
5	1	1	
6	2	1	
7	1	1	
Patellar reflex before epidural			0.2024
Absent	5	1	
Present	34	38	
Westphal's sign			0.7449
Positive	34	33	
Negative	5	6	
Response to surgery			0.7449
Required rescue	5	6	
Rescue not required	34	33	
Anaesthetist opinion			0.7449
Fail	5	6	
Successful	34	33	

5.5. Results

Seventy-eight client owned dogs were recruited from clinical cases requiring lumbosacral epidural for surgical treatment of the abdomen or pelvic limbs. No cases were excluded based on the criteria. Thirty-nine dogs were block randomised to each of the AWARE and UNAWARE groups. Table 1 provides the summary of descriptive information and analysis between groups. All dogs recovered from the anaesthetic and were discharged home uneventfully. There were 24 different breeds in the AWARE group with the German shepherd dog being the most common breed (n = 4), while in the UNAWARE group there were 19 different breeds with the cross breed being the most frequent (n = 13). Table S1 lists the different surgical procedures, with tibial plateau levelling osteotomy being the most prevalent in both groups (AWARE n = 6; UNAWARE n = 13).

Table 2 provides information on anaesthetist experience and outcome data between AWARE and UNAWARE groups. The mean number of attempts was 1.9 in the AWARE group compared with 2.0 for the UNAWARE group ($P = 0.4307$). Inexperienced anesthetists and experienced anesthetists between groups were also not statistically different ($P = 0.3625$). Before epidural medication administration, the patella reflex was present in 87% (34/39) and 97.4% (38/39) of dogs in the AWARE and UNAWARE groups respectively ($P = 0.2024$). The Westphal's sign was positive in 87% (34/39) and 84.6% (33/39) of the AWARE group and UNAWARE group respectively after epidural administration ($P = 0.7449$). Response to surgical stimulation was present in 12.8% (5/39) and 15.3% (6/39) of dogs in the AWARE and UNAWARE groups respectively ($P = 0.7449$). Overall procedural failure rate based on anaesthetist's opinion was slightly lower in the AWARE group (12.8%; 5/39) compared with the UNAWARE group (15.4%; 6/39) although this was not statistically different ($P = 0.7449$).

With reference to the correlation between the PredSLED and the ActSLED in the AWARE group, there was a moderate positive correlation ($R = 0.6705$; 95% CI 0.4502 – 0.8138; $P < 0.05$). No correlation was found between achieving a successful epidural (R = 0.1698; 95% CI - 0.1539 – 0.4609; P = 0.3015) and the number of attempts in the AWARE group (R = -0.2126; 95%CI -0.4949 - 0.1103; P = 0.1938). Similarly, there was no correlation between anaesthetist experience and a successful epidural in the UNAWARE group (R = 0.2734; 95% CI -0.0461 – 0.5421); P = 0.0921), but there was a weak negative correlation with the number of attempts (R = -0.3377; 95% CI -0.0461 - 0.5421; P = 0.0355).

Non-inferiority analysis was based on the comparison between the procedural failure rate of the AWARE and UNAWARE group and a predetermined Δ. A chi-squared test showed no significant difference between group means. When compared against the predetermined non inferiority margin of 0.22. assuming that lower failure rates are better, the non-inferiority mean difference was 0.12, and the 95% CI lies to the right of Δ being -0.1808 – 1.000 (Figure 2).

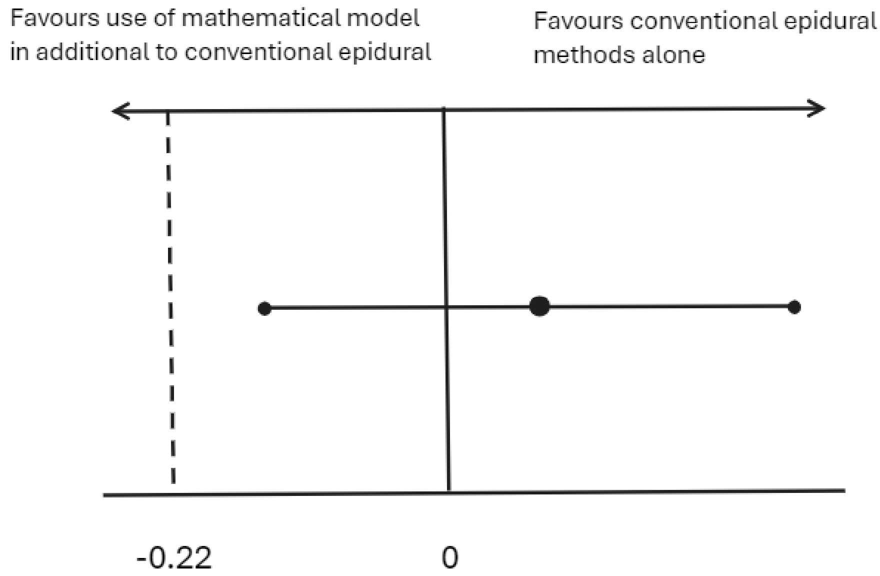

Figure 2: Graph showing the mean difference between the AWARE group against a predetermined Δ. For non-inferiority to be shown the lower 95% CI for the limit should be above Δ (-0.22) and the upper limit should cross zero. The smaller dots indicate the 95% being -0.18 and 1.00 respectively, while the large dot represents the mean difference between the two groups being 0.12.

5.6. Discussion

This study examined whether predictive information provided to the anaesthetist prior to epidural needle insertion would influence the procedural failure rates of lumbosacral epidurals. It was found that anaesthetist awareness of the predicted distance before epidural administration did not significantly influence the procedural failure rates in dogs. However, the additional knowledge was non-inferior when used in conjunction with conventional techniques and did not worsen outcomes.

The epidural procedure failure rate was 12.8% when the mathematical model was used with conventional techniques (hanging drop or running drip), and 15.4% for conventional techniques alone. This is comparable to studies examining a number of techniques including the loss of resistance technique; 32% [20], hanging-drop at 12% [18], and running-drip 10% [26]. Comparisons between studies are inherently difficult given differences in outcome definition of a successful epidural, study design, sensitivity or specificity of technique in accurately detecting the epidural space, and whether multiple technique were used in conjunction [1]. In the current study, the success of epidural anaesthesia was determined based on three factors to optimise methodology rigour. A positive Westphal's sign provides a strong indication of a successful epidural and signifies an onset of reduced motor function in response to the administration of local anaesthetic causing suppression of a deep tendon reflex [89, 90]. In dogs, the Westphal's sign occurs between 0.5 to 3.0 minutes after successful administration of local anaesthetic into the lumbosacral epidural space, presumably due to a gradual inhibition and abolition of the sensory neuronal synapses of the efferent alpha motor neuron that contract the quadriceps muscle [90]. It is possible that accidental spinal puncture could have also resulted in a positive Westphal's sign in one or more of the dogs in our study, although no cerebrospinal fluid was seen at the hub of the needle in any of the Tuohy needle placements, making this unlikely. Clinical injury to the femoral nerve, concurrent paralysis, muscle atrophy or muscular fasciculations may result in absence of the patellar reflex [91]. It is possible that in our study, some animals may have exhibited one or more of these clinical injuries as co-morbidities which may have resulted in a negative patellar reflex prior to epidural administration. While exclusion of dogs without initial patellar reflexes would have reduced the confounding effect of a negative Westphal's sign, it would have resulted in a greater number of dogs being unnecessarily enrolled in the study given that the Westphal's sign was only one of three components involved in the determination of a successful epidural.

A lack of nociceptive response to incision with either a less than 10 to 30% increase of heart rate and mean arterial blood pressure has been used as a determinant for successful outcome for locoregional techniques in clinical settings [20, 24]. The use of this outcome was used to indicate analgesia inadequacy, and would prompt immediate intervention with analgesics as part of routine clinical practice. In all cases it seemed that response to surgical stimulus was the determinant as to whether the anaesthetist determined the epidural to be successful or a failure.

The influence of the predictive mathematical equation was a novel addition to conventional techniques and had only been validated previously in cadaveric and radiographic studies. It was therefore unknown whether this information may be harmful or beneficial to lumbosacral epidural needle placement, warranting a study design incorporating an evaluation of non-inferiority. The clinical assumption was that additional information may be considered helpful in the successful placement of the epidural needle into the lumbosacral space. This is supported by human studies, in which predictive knowledge showed increased success of epidural puncture when used alone, or in conjunction with other imaging techniques [7, 30, 54, 92]. Alternatively, there are other studies that also demonstrate an insignificant effect between equation groups and controlled groups [31, 33]. At the time of writing, the use of mathematical models seem to be limited to specific patient populations in which the placement of a traditional epidural is considered difficult, for example morbidly obese and parturient patients [33, 50, 93], rather than broad clinical use.

In our study, the confirmation of a non-inferiority result demonstrated that the additional information was not harmful to the dogs when procedural failure rates were concerned. In contrast to superiority studies, non-inferiority studies compare the efficacy of a new treatment with an existing one where the new treatment is expected to have broadly similar efficacy to the existing treatment, but where other benefits might make the new treatment desirable [94]. In this study, the determination of the predictive depth was based on existing calculations determined by easily obtainable measurements and part of normal clinical routine for surgeries requiring lumbosacral epidural at our institution. Therefore, the addition of the mathematical equation was designed as a quick option with little disruption to current clinical practice. Particular emphasis was placed on determining the Δ given the importance to demonstrate meaningful effect based on the anaesthetist's opinion. Alternatively, the non-inferiority margin may be derived from pilot studies, however, this was not possible in our study given we are the first to determine the influence of predictive information and epidurals in veterinary patients. Rather, the difference in procedural failure rates between two common epidural techniques were used as the Δ to demonstrate the minimal clinical margin of safety in addition to expert opinion [95].

The lack of correlation between anaesthetist experience and procedural failure rates could suggest that being aware of the predictive distance was not helpful in the placement of a successful epidural. However, a positive moderate correlation was found between the predictive and actual depth in the AWARE group which suggests validity in the use of the mathematical equation. Due to the design of the study, it was also possible that inadequate sample size at the level of experience could explain the lack of significant correlation. It was interesting that a weak correlation between anaesthetist experience and number of attempts was found in the UNAWARE group, with experienced anaesthetists requiring fewer attempts, but that this correlation was not present in the AWARE group. In this study, experience was defined as having performed greater than ten epidurals in the past 12 months, and anaesthetists could move from the inexperienced to experienced category. It was therefore possible that the experience of having used the mathematical model while learning to perform an epidural would be more familiar, resulting in the results being biased at the level of the anaesthetist. Additionally wide interindividual variability while learning neuraxial techniques suggest that greater than 20 attempts may be needed to gain competency in human anaesthesia [33, 96]. Future studies may examine the impact of mathematical models on the learning curve to identify whether inexperienced veterinary anaesthetists would truly benefit from predictive information in additional to conventional epidural teaching methods.

This study had several limitations. Determination of epidural success by the same attending anaesthetist may have created some misclassification bias, however with randomisation of the groups and using multiple restrictions for epidural success, any confounding effect would have been reduced. The mathematical equation used relied on a limited number of predictors based on previous studies. Additional predictors have been described in human studies, for example body mass index [60], race [69], and ponderal index [97], but in dogs, only body condition score and occipital coccygeal length have been demonstrated to correlate with the true skin to lumbosacral epidural distance. Alternative predictors that contribute to mathematical models may be examined in the future, for example, obese dogs with potentially challenging epidural needle placement [81]. The knowledge of the PredSLED was based on reading aloud the depth derived from the mathematical equation. It was then approximated by the anaesthetist of where the PredSLED was on the Tuohy needle. There was some degree of subjectivity of the PredSLED to the closest cm given the 1 cm demarcations on the Tuohy needle, although it was at the discretion of the anaesthetist of how the PredSLED was utilised in conjunction with either hanging-drop or running drip techniques. While future studies may include sterile marking on the Tuohy needle to record clearly where the PredSLED is, this may incur additional time for demarcation, measurement, and cost with regards to equipment sterilisation, and at this stage considered to be a sharp deviation from routine clinical practice. Additionally, although there are differences between PredSLED and ActSLED measurements as highlighted in Table 1, the differences are between mean values, and even then only represent millimetre differences and an expected limitation of population based mathematical data when compared with individual clinical measurements. Premedication drug choice was not standardised between groups and represented the anaesthetist's preference. It is possible that heavy sedation or increasing anaesthetic depth may have reduced the initial patellar reflex or resulted in a false positive Westphal's sign. Additionally, there were a range of surgical procedures performed on the dogs, which may have confounded the magnitude of nociceptive response at first incision. Surgeons were either Diplomates of the American or European College of Veterinary Surgeons, or senior residents and considered to be highly experienced. Restriction of choice of premedication, surgical experience, or type of surgery would have resulted in significantly greater numbers of dogs used in the study and reduced external validity to a clinical setting.

5.7. Conclusion

This study demonstrated the novel use of a predictive epidural mathematical equation in a clinical setting. Being aware of the predictive distance did not significantly influence the procedural failure rates of epidural but the additional knowledge was non-inferior when used in conjunction with conventional techniques and did not worsen outcomes.

5.8. Appendix

Table S1: List of randomized surgeries in the AWARE group (n = 39) of anaesthetists who were aware of the mathematical equation, and anaesthetists UNAWARE of the (n = 39) equation

AWARE		UNAWARE	
Abscess lavage	1	Adrenalectomy	2
Adrenalectomy	1	Anal sacculectomy	1
Anal sacculectomy	1	Caesarian	1
Arthrodesis tarsus	1	Caudectomy	2
Caesarian	2	Combination	1
Caudectomy	1	Cystotomy	2
Cholecystectomy	2	Exploratory laparotomy	3
Cystotomy	5	Femoral fracture	2
Double pelvic osteotomy	1	Hernia repair	1
Exploratory laparotomy	2	Hip toggle surgery	2
Ileal fracture	1	Ileal fracture	1
Iliopsoas tenotomy	1	Limb amputation	1
Insulinoma	1	Liver lobectomy	2
Juvenile Pelvic Symphysiodesis	1	Liver shunt surgery	1
Limb amputation	1	Lumpectomy	1
Lumpectomy	1	Medial patellar luxation	1
Mastectomy	1	Perineal surgery	1
Nephrectomy	2	Tibial fracture	2
Penile amputation	1	Tibial plateau levelling osteotomy	13
Perineal	1		
Rectal Prolapse	1		
Splenectomy	1		
Tarsal arthrodesis	1		
Tibial fracture	2		
Tibial plateau levelling osteotomy	6		

Chapter 6

General discussion and future perspectives

This thesis examined multiple morphometric variables in dogs to determine whether correlation exists between the skin to epidural space distance in dogs. It was found that the morphometric variables that best correlated with the skin to lumbosacral epidural distance (SLED) were the occipital coccygeal length (OCL) and body condition score (BCS), and determination of these variables were also quick, easily obtainable and often required as part of routine anaesthesia practice. The derived mathematical equation from the OCL and BCS also arose from a variety of breeds which may increase the formulas external validity to a clinical setting. The mathematical equation was further validated in cadaver and clinical populations to investigate whether additional predictive knowledge would influence procedural failure rates in epidural placement compared to conventional techniques.

Chapter three retrospectively examined 86 canine computed tomography (CT) images and found moderate positive correlations between the OCL ($r = 0.59$, $p < 0.0001$) and ilium wing distance (IWD) ($r = 0.61$, $p < 0.0001$) with a *ligamentum flavum* surrogate (LFS). The LFS was used to represent the *ligamentum flavum* which indicates the entry point into the epidural space but was not visible on CT imagery at the lumbosacral level. Multivariable and multicollinear analysis revealed that the BCS was an additional variable that best aligned with the model that predicted SLED (OCL: $R^2 = 0.6156$; IWD: $R^2 = 0.643$). This was in agreement with a previous study that identified a positive correlation between BCS and skin to epidural distance [78]. This chapter further reduced the literature gap by producing six predictive mathematical equations of which two were specifically devised for the lumbosacral epidural region using OCL and IWD as predictive variables in addition to BCS to predict the SLED in dogs.

Chapter four examined the validity of the previous two mathematical equations from chapter three in a separate population of 11 dog cadavers of varying ages and breeds. Contrast epidurography was used as the gold standard to definitively detect the epidural space for the purpose of objectively measuring the actual SLED [98]. The key finding in this chapter was that while both equations were validated, the equation using OCL (SLEDmm = 7.3 + 0.05*OCL + 16.45 (BCS); R^2 = 0.5179) demonstrated a closer fit to the concordance line. Additionally, cranial extension of the pelvic limbs (the most frequent position for lumbosacral epidural) did not affect the relationship with the LFS as had been postulated in the previous chapter. The OCL was therefore proposed as the mathematical equation to take forward for prospective analysis given that it was easy to perform, commonly used at our institution to calculate epidural injectate volume, and unlikely to impact anaesthesia time efficiency.

Chapter five further investigated the mathematical equation proposed in chapter four in 78 dogs of varying breeds and ages requiring lumbosacral epidural anaesthesia for abdominal or hindlimb surgery by utilising the equation in a prospective randomised clinical study. Dogs were randomly allocated to an anaesthetist and one group was made aware of the predicted SLED as calculated using the mathematical equation prior to epidural needle insertion (AWARE n = 39). The other group of anaesthetists performed the epidural as per standard procedure in the absence of the knowledge of the predicted SLED (UNAWARE n = 39). Epidural success was determined clinically using the Westphal's sign, nociception during surgery, and overall anaesthetist's opinion. There were no differences in the procedural failure rates between AWARE and UNAWARE groups (12.8% and 15.4% (P = 0.7749) respectively), or between the failure rates of inexperienced and experienced anaesthetists. Additional non-inferiority analysis further showed that being aware of the mathematical equation before epidural needle insertion was no different with conventional epidural techniques alone when compared with a pre-defined margin of the difference between two epidural techniques.

The findings of this thesis can be broadly organised into two distinct themes, namely the potential benefits of predictive knowledge in the at-risk patient, and the potential educational benefit for the learning clinician. With reference to the first point, the additional knowledge provided by the mathematical equation proposed has been validated by two separate study populations (Chapters 4 and 5), demonstrating moderate correlation with the actual SLED. Furthermore, no differences in epidural success rates were detected between anaesthetists who were aware of the mathematical model versus those who were not (conventional epidural group). This is in contrast to human studies investigating depth prediction, in which the proposed benefits of a predictive equation are counteracted by unmeasured factors, confounders and study design, thereby limiting mathematical equations to experimental studies [43]. Moreover, equations were suggested by some reviews that, despite high internal validity within the study population, should be applied with caution to new patient groups and should not replace current epidural methods used in human anaesthesia [7, 29].

Indeed, if the mathematical equation from this thesis is solely relied upon, what would be the consequence? The results depicted earlier demonstrate a moderate correlation between the predicted and actual lumbosacral epidural distance (Chapter 5 section 5: $R = 0.6705$; 95% CI 0.4502 – 0.8138; $P < 0.05$) in the group that was aware of the predicted depth. It is therefore possible that a large proportion of dogs would have had a successful lumbosacral epidural from the use of the equation alone. However, the prediction of our mathematical equation was limited by the data availability of CT derived measurements, a relatively simple multivariable regression, and assumptions which excluded extremes in body conformation and physical deformities relative to lumbosacral space. It is therefore possible that this model would not fit individual dogs with difficult lumbosacral epidurals, and an extended interpretation may be that a mathematical model would be unsuitable in those dogs given high levels of epidural variability. However, that was not the intention of this thesis nor the aim to investigate individual levels of epidural success, but rather to propose an alternative add-on method to lumbosacral epidural medication administration which would be easy to perform in a broad population of dogs. A greater number of ActSLED measurements may be collected in the future to improve the dataset and refine the mathematical equation and at the very least provide an accurate predictive measurement for subsequent lumbosacral epidurals for that individual patient. Currently, the predicted mathematical equation created from our research is not intended to be a replacement for conventional techniques as reiterated in chapters three and four, but rather, an additional tool-in-the-toolbox that potentially can provide a scaffold to prevent under or over-shooting of the epidural needle, such as inadvertent intrathecal medication injection.

Although limited studies have examined some canine groups considered to be at greater risk of epidural failure [81], future research into predictive mathematical assistance can be also honed into at-risk patient groups such as brachycephalic dogs. In these breeds, epidural anaesthesia can be difficult due to breed-related anatomical anomalies in the lumbosacral space. This would require a greater number of breed-specific measurements and adjustments to the predictive variable, for example, the iliac wings are usually not palpable in brachycephalic breeds due to their tendency to have greater subcutaneous fat overlying this anatomical structure.

It has been highlighted in numerous human anaesthesia studies that some personnel groups may benefit from additional predictive information prior to epidural needle placement, namely resident anaesthetists at all levels or junior anaesthetic clinicians [46, 86], physicians in developing countries with limited resources [70, 72], and increasingly after the COVID-19 pandemic, certified registered nurse anaesthetists [99]. A potential benefit of using a mathematical equation, as alluded to in chapter 3, is that it may provide a minimum margin of safety between the epidural and intrathecal space junction, as injection of the epidural volume of medication through the dural sac may result in potentially catastrophic consequences. Indeed, this has been recently highlighted in a study that utilised machine learning using epidural simulation. The simulator study investigated the risk of incorrect epidural needle placement related to epidural technique, and the skin to loss-of-resistance (LOR) plane distance (the equivalent of the *ligamentum flavum*) in a variety of anaesthesia practitioners at different experience levels [100]. Gradual technique with the LOR needle advancing incrementally (as may be done cautiously in the case of inexperienced anaesthetists), along with a more shallow LOR plane resulted in the greatest risk of overshoot translating to inadvertent dural puncture and greater risk of debilitating post-dural puncture headache in people [100]. Machine learning is a subset of artificial intelligence that can make predictions from novel datasets [101]. This may potentially be the point at which mathematical models add benefit and potentiate the learning epidural techniques. Additionally, there are recent non-animal based alternatives used as practical teaching models in the context of veterinary education to teach epidural anaesthesia [102], and together, these two innovations may lead to a positive trajectory in continual research in the prediction of successful epidurals in both human and veterinary anaesthesia.

The overall outcome in this thesis was the novel investigation of correlation relationships and the subsequent development and clinical application of a mathematical equation to predict the skin to lumbosacral epidural distance in dogs for the purposes of increasing the success rate of epidural anaesthesia. The increased knowledge represents a valuable contribution to the advancement of clinical veterinary anaesthesia and an ongoing endeavour to reduce failure rates in dogs requiring epidural anaesthesia for optimal relief from pain related to a variety of surgeries.

Chapter 7.

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