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On the assessment and treatment of pain

The effect of transcutaneous electrical nerve stimulation on dogs with osteoarthritis

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Cover: Dog “Dobby” with activity monitor. (Photo: Anja Pedersen, AI-modified 2026).

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Abstract

Pain is a common clinical sign in dogs and negatively affects animal welfare. Pain is a subjective and multifaceted experience that cannot be measured directly in animals. Instead, pain assessment relies on indirect indicators such as behavioural, physiological, and functional indicators, all with inherent limitations. Osteoarthritis is a prevalent welfare concern in dogs and a chronic, degenerative, and painful condition affecting diarthrodial joints. Despite available pharmacological and non-pharmacological treatments, insufficient treatment response and limited pain relief remain common challenges. Transcutaneous electrical nerve stimulation is used for pain relief in dogs, but scientific evidence supporting its efficacy in dogs is limited.

The aims of this thesis were to investigate the possible pain-relieving effects of transcutaneous electrical nerve stimulation in dogs with osteoarthritis and to develop activity monitoring methodology for assessing physical activity. Using the applied stimulation parameters, transcutaneous electrical nerve stimulation administered as single or repeated treatments did not result in significant changes in pain-related clinical findings, behavioural outcomes assessed by pain questionnaires, gait parameters assessed by clinical examination and pressure-sensitive mat analysis, or physical activity measured using activity monitors and questionnaires. These results should be interpreted with caution due to the small heterogeneous study population. Fast Fourier transform analysis of accelerometry data showed that most physical activity in pet dogs occurs below 25 Hz, exceeding the range captured by commonly used commercial filtering approaches. Signal filtering substantially influenced activity intensity classification. In addition, variance of unfiltered vector magnitude did not distinguish between wear-time and non-wear periods, and human-validated non-wear detection methods were not applicable to canine data. These findings emphasize the need for species-specific validation of accelerometry data processing methods in dogs.

Keywords: TENS, OA, canine, accelerometry, pressure-sensitive mat, HCPI, CBPI, clinical examination, non-wear time, sampling frequency.

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Sammanfattning

Smärta är ett vanligt symtom hos hundar och påverkar djurvälfärden negativt. Eftersom smärta är en subjektiv och mångfacetterad upplevelse kan den inte mätas direkt hos djur. Smärtbedömning baseras därför på indirekta indikatorer såsom beteendemässiga, fysiologiska och funktionella förändringar, vilka alla har begränsningar. Artros är ett vanligt välfärdsproblem hos hundar och en kronisk, degenerativ och smärtsam sjukdom. Trots tillgängliga farmakologiska och icke-farmakologiska behandlingar kan behandlingseffekten vara otillräcklig och smärtlindringen begränsad. Transkutan elektrisk nervstimulering används för smärtlindring hos hund, men det vetenskapliga stödet för dess effekt är begränsat.

Syftet med denna avhandling var att undersöka den möjliga smärtlindrande effekten av transkutan elektrisk nervstimulering hos hundar med artros samt att metodologiskt utveckla aktivitetsmonitorering för bedömning av fysisk aktivitet. Med de tillämpade inställningarna medförde transkutan elektrisk nervstimulering, administrerad som enstaka eller upprepade behandlingar, inga signifikanta förändringar i smärtrelaterade kliniska fynd, beteende bedömt med smärtformulär, rörelser bedömda genom klinisk undersökning och analys med tryckmätningsmatta, eller fysisk aktivitet mätt med aktivitetsmonitorer och smärtformulär. Dessa resultat bör tolkas med försiktighet med hänsyn till den lilla och heterogena studiepopulationen. Analys av fysisk aktivitetsdata med hjälp av Fast Fourier-transform visade att majoriteten av den fysiska aktiviteten hos sällskapshundar sker vid frekvenser under 25 Hz, vilket överskrider det frekvensområde som återges av vanligt förekommande kommersiella filtreringsmetoder. Signalfiltrering påverkade klassificeringen av aktivitetsintensitet. Variansen hos ofiltrerad vektormagnitud kunde inte skilja mellan bärtid och icke-bärtid, och metoder för detektion av icke-bärtid validerade för människa var inte tillämpliga på hunddata. Dessa resultat understryker behovet av artspecifik validering av metoder för bearbetning av fysiska aktivitetsdata hos hund.

Nyckelord: TENS, artros, hund, accelerometri, tryckmätningsmatta, HCPI, CBPI, klinisk undersökning, icke-bärtid, samplingsfrekvens.

Dedication

To my wonderful family, without whom this journey would not have been possible.

“Until one has loved an animal, a part of one’s soul remains unawakened.”
— Anatole France

Contents

List of publications

This thesis is based on the work contained in the following papers, referred to by Roman numerals in the text:

I. Pedersen, A.; Hyytiäinen, H.K.; Rhodin, M.; Forterre, F.; Penell, J.; Bergh, A (2024). Effect of Transcutaneous Electrical Nerve Stimulation on Gait Parameters in Dogs with Osteoarthritis. Animals, 14, 1626. https://doi.org/10.3390/ani14111626

II. Anja Pedersen, Johanna Penell, Emil Olsen, Heli Hyytiäinen, Franck Forterre, Anna Bergh. Effect of transcutaneous electrical nerve stimulation on physical activity and pain evaluation in osteoarthritic dogs. (submitted)

III. Anja Pedersen, Anna Bergh, Marie Rhodin, Johanna Penell, Heli Hyytiäinen, Franck Forterre, Emil Olsen. Activity monitors in dogs: The frequency range of free-living pet dogs and non-wear time classification in canine physical activity monitoring. (manuscript)

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Abbreviations

Activity monitor	
Acceleration (m/s^2)	The change in velocity of an object over time.
Counts per minute, CPM	Summation of acceleration over the epoch 1 minute for this thesis. Can also be defined as average for acceleration over the epoch 1 minute.
Epoch	A defined time period over which the values of the accelerometer is summarized. The length of the period varies and is defined by the researcher.
Frequency (Hz)	How often movement-related changes occurs i.e. how fast the movement is.
Frequency bandwidth	The width of the filtered signal that remains after filtering and can be translated to physical activity measurements such as counts per minute. For example, ActiGraph keeps the full signal that has been recorded with acceleration between 0.29-1.63Hz.
Frequency bins	Frequency bins are predefined frequency intervals used to aggregate signal power or time spent within specific ranges of the frequency spectrum.
High-pass filter	Signal-processing method that allows high-frequency signals to pass while attenuating low-frequency components.
Idle sleep mode	When measuring, ActiGraph activity monitor stops recording after 10s of inactivity and rechecks every second if there is activity.

Low-pass filter	Signal-processing method that allows low-frequency signals to pass while attenuating high-frequency components.
Non-wear time	Time periods where the monitor is not attached to the dog during a trial and therefore is not measuring the acceleration of the dog.
Power (g^2)	The energy of the signal created by the measured movements i.e. how much movement energy is present.
Sampling frequency (Hz)	How many times the accelerometer captures acceleration per second, measured in Hertz (Hz). For example, 50 Hz = the accelerometer measures acceleration 50 times per second. Limits how fast movements the accelerometer can detect.
Sensitivity	Sensitivity is the ability of a test to correctly identify animals with a condition (true positives).
Specificity	Specificity is the ability of a test to correctly identify animals without a condition (true negatives).
Stride frequency (Hz)	The number of complete strides (full step cycle of the same limb) performed per second.
Vector magnitude, VM	Summation of the tri-axal acceleration movement as a single value average over a defined time period (epoch). The formula used is $VM = (x^2 + y^2 + z^2)^{0.5}$
X-axis	Horizontal right-left, side-to-side movement
Y-axis	Vertical, up–down movement, including gravitational acceleration
Z-axis	Horizontal fore-after, forward–backward movement

Pressure-sensitive mat	
Peak vertical force, PVF	PVF is the maximum vertical force exerted by a limb on the ground during the stance phase of gait. Reflects weight bearing.
Symmetry index, SI	Ratio of the PVF or the VI value for different limbs or limb pairs. Used to evaluate weight distribution between limbs.
Vertical impulse, VI	VI is the total vertical force applied over time during the stance phase. Incorporates both force magnitude and stance duration.

1. Introduction

1.1 General background

Pain is officially defined, by the International Association for the Study of Pain, as "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" (Raja *et al.* 2020). Further, it acknowledges that the "inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain" (Monteiro *et al.* 2023). Pain is a common clinical sign of disease in dogs and particularly chronic pain, has a substantial negative impact on quality of life of both the dog and consequently also its owner as well as the owner´s economy (Davis *et al.* 2019; Summers *et al.* 2019; Belshaw *et al.* 2020c; Malkani *et al.* 2024). Further, it is suggested that pain in dogs is under-recognized and thus under-treated (Muir *et al.* 2004; Wright *et al.* 2019; Rousseau-Blass *et al.* 2020). Consequently, the detection and appropriate management of pain is essential to safeguarding animal welfare (Muir *et al.* 2004; Belshaw & Yeates 2018).

Pain is a multifaceted phenomenon, and its clinical manifestations vary considerably between individuals (Reid *et al.* 2018; Brown *et al.* 2025). As a result, pain assessment in dogs is inherently complex (Reid *et al.* 2018; Demirtas *et al.* 2023). Because the subjective sensation of pain cannot be measured directly, assessment is based on indirect indicators such as behavioural, physiological, and functional changes associated with the presence of pain (Lascelles *et al.* 2019b). Outcome measures for pain can therefore be broadly grouped into those targeting behavioural alterations, biochemical markers, and physical dysfunction (Belshaw *et al.* 2016). A variety of outcome measures exist; however, none are without limitations (Belshaw *et al.* 2016; Hernandez-Avalos *et al.* 2019; Lascelles *et al.* 2019b; Chmelíková *et al.* 2020; Sandberg *et al.* 2020; Hyytiäinen *et al.* 2023b). Thus, there is a need for reliable, sensitive, and clinically applicable outcome measures (Lascelles *et al.* 2019a), both for diagnostics, but also for evaluation of treatment effects. There are several pain-relieving treatments for pain, modifying the pain signal at different levels of the nervous system. The most common are pharmaceuticals, but also non-pharmaceutical treatments are used such as nutraceuticals, rehabilitation modalities and physical activity (PA) (Monteiro *et al.* 2023).

Osteoarthritis (OA) in dogs represents a chronic, degenerative, and painful condition that compromises quality of life in a major way. It is reported that 20% of dogs over one year old has OA (Johnston 1997). Thus, it has been identified as one of the most important diseases to treat in dogs due to its prevalence and profound impact on long-term animal welfare (Bonnett *et al.* 2005; Freeman *et al.* 2006; O'Neill *et al.* 2013; Anderson *et al.* 2018; Summers *et al.* 2019). Several treatment options exist for managing OA-associated pain, with pharmaceuticals such as non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and monoclonal antibodies constituting the most commonly used modalities (Gruen *et al.* 2022; Pye *et al.* 2022). Although generally effective, pharmaceutical treatments can produce adverse effects. While many of these are mild, they may nonetheless limit long-term medication use (Lascelles *et al.* 2005; Luna *et al.* 2007; Monteiro-Steagall *et al.* 2013; Hunt *et al.* 2015; Elkholly *et al.* 2020; Mabry *et al.* 2021; Gruen *et al.* 2022). Consequently, management of canine OA-related pain can include both pharmacological and non-pharmacological alternatives.

Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological modality used, for example, to relieve pain in dogs with OA. TENS is proposed to exert analgesic effects primarily via the pain gate mechanism and through endogenous opioid release (Jones & Johnson 2009; Lazarou *et al.* 2009; Leonard *et al.* 2010; Hahm *et al.* 2019; Bi *et al.* 2021). Musculoskeletal pain management with TENS in dogs has been explored in two peer-reviewed studies and one conference abstract (Johnston *et al.* 2002; Krstić *et al.* 2010; Gouveia *et al.* 2025). However, the overall evidence base both for usage in humans and dogs remains weak due to the limited number of studies both in general and for specific pathologies, small sample sizes, and frequent lack of objective outcome measures (Gibson *et al.* 2019; Hyytiäinen *et al.* 2023a). As OA is a major cause for mortality due to locomotor disorders (Bonnett *et al.* 2005; O'Neill *et al.* 2013) and is suggested as one of top three disease to impact animal welfare in dogs (Summers *et al.* 2019), it is of outmost importance that the assessment and treatment of pain, especially in dogs with OA, is proven valid and efficient. Therefore, the focus of this thesis was to use several indirect assessment methods, such as pressure mat, activity monitors and pain questionnaires, to investigate the effect of TENS on pain and physical function in dogs with OA.

1.2 Pain

1.2.1 Pain physiology and pain modulation

Since the late 1970s, pain has been defined as an emotion and therefore it is not solely dependent of physiological activation for neural pathway (nociception), hence nociception is not equal to pain. Pain is a personal experience influenced by biological, psychological and social factors (Raja *et al.* 2020). The definition of pain is derived from human literature, however, painful stimuli in humans has induced similar physiological and behavioural changes in other mammals as well, therefore the same definition is applicable to dogs (Sneddon *et al.* 2014).

Pain can be divided into acute pain and chronic pain:

Acute pain is adaptive and physiological; it announces the presence of a potentially harmful stimulus, serving as an essential protective function. It is provoked by a specific injury or disease and is expected to resolve once the tissue has healed (Liu & Kelliher 2022).

Chronic pain persists beyond the normal expected healing time, commonly persisting or recurring for longer than three to six months (Walsh 2016; Liu & Kelliher 2022). Chronic pain can be referred to as maladaptive pain because it results from an abnormal functioning of the nervous system and it has no clear endpoint and can be without apparent biological value (Woolf 2010).

Further, pain can be classified according to its cause (Wang *et al.* 2025):

Nociceptive pain is the most common type of pain. It is defined by the International Association for the Study of Pain (IASP) as "pain that arises from actual or threatened damage to non-neural tissue and is due to activation of nociceptors" (Raja *et al.* 2020). Nociceptive pain can be acute or become chronic. OA related pain is usually defined as nociceptive pain.

Neuropathic pain has been defined by the IASP as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" (Raja *et al.* 2020). It requires damage to peripheral or central nerves. Neuropathic pain is very often chronic.

Nociplastic pain is defined as "pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain" (Raja *et al.* 2020).

Mixed pain is increasingly used but has not been adopted by the IASP. The common definition of mixed pain is a pain with "an overlap of nociceptive and neuropathic symptoms" (Wang *et al.* 2025).

A general overview of pain states that the pain pathway consists of four phases: transduction, transmission, modulation and perception (Karcz *et al.* 2024). Pain starts with a stimulation of nociceptors activated by thermal, mechanical or chemical stimuli, or all of them. The stimulus is then translated to an electrical signal which transmits through afferent neurons, primarily Aδ fibres and C-fibres. The Aδ are small, myelinated fibres with a conduction velocity of approximately 20 m/s, they convey an acute, well-localized and sharp pain. The C-fibres are larger, unmyelinated and has a conduction velocity of 2 m/s, they convey a more diffuse and poorly localized pain. The nociceptors of type Aδ fibres reacts to thermal or mechanical stimuli of specific intensities and the nociceptors predominantly connected to type C-fibres are polymodal and responds to thermal, mechanical and chemical stimuli (Karcz *et al.* 2024).

The pain signal is then transmitted from the afferent neurons to the spinal cord through a release of neurotransmitters in the dorsal horn. The neurotransmitters activate second-order neurons in the spinal cord, and the signal ascends to the brain stem and thalamus. At the level of the thalamus, third order neurons are activated, and send impulses to the primary and secondary somatosensory cortex. The last phase of the pain pathway, perception, is when the pain signals are integrated in the conscious and the subjective experience of pain is formed (Karcz *et al.* 2024)

Pain can be modulated at different levels throughout the pain pathway: peripheral, spinal, supraspinal and central level. Peripheral pain modulation occurs when pain signals are inhibited at the primary nociceptive afferents, i.e. the nociceptors and the nerve axon. Gate control theory of pain describes a modulation at the spinal level where sensory signals from descending A-β fibres reduces the signals from the Aδ and C-fibres through inhibition of the transmission between primary and secondary nociceptive neurons (Melzack & Wall 1965; Fan *et al.* 2022). Supraspinal modulation is through descending pain regulating pathways, with the periaqueductal grey as an important component in the pain modulation together with the rostral ventral medulla (RVM). The periaqueductal grey (PAG) receives signals from hypothalamus, amygdala and cortex, and has direct contact with RVM. From the RVM, neurons are projected to the dorsal horn, where inhibition of the

pain signal takes place (Williams *et al.* 1995; Karcz *et al.* 2024). Finally, thalamus, hypothalamus, limbic system and cortical areas are responsible for the pain modulation at central level, by affecting the descending pathways that starts at PAG.

There are several neuropeptides engaged in pain modulation. The endogenous opiate system consists of endogenous opioid peptides, such as endorphins, enkephalins, dynorphins, nociceptin and endomorphins, and a network of receptors throughout the central nervous system (Vincler PhD & McIntosh Md 2007; Marshall *et al.* 2012; Bagdas *et al.* 2015). There are primarily three types of opioid receptors: μ (mu, in the brain, spinal cord and peripheral sensory neurons), δ (delta, in the brain and peripheral sensory neurons) and Κ (kappa, in the brain, spinal cord and peripheral sensory neurons), together with the nociceptin receptor. Mu and delta receptors are activated by endorphins and enkephalins, and kappa is activated by dynorphins. Enkephalins are primarily concentrated in the periaqueductal grey, RVM and spinal cord. Endorphins are primarily concentrated in the hypothalamus (Williams *et al.* 1995; Bagley & Ingram 2020). Endorphins and enkephalins inhibit the release of neurotransmitters, such as substance P, which reduces the transmission of pain signals (Nicoletti *et al.* 2012). Endogenous opioids can also induce euphoria and sense of wellbeing which can help coping with pain and increasing the pain threshold.

It is utterly important to treat pain, as prolonged and intense pain signalling can cause malfunctions in the nervous system such as peripheral and central sensitisation (Voscopoulos & Lema 2010; Liu & Kelliher 2022; Karcz *et al.* 2024). Peripheral sensitisation occurs when the nociceptors become more excitable due to chemical changes at the site of injury or inflammation (Voscopoulos & Lema 2010; Karcz *et al.* 2024). This will lead to primary hyperalgesia, i.e. when areas close to the injured site becomes more sensitive. Central sensitisation occurs when the secondary neurons in the dorsal horn of the spinal cord are subjected to an intense and persistent input from nociceptors, which leads to an increase in pain signal transmission and hyperexcitability (Voscopoulos & Lema 2010; Liu & Kelliher 2022). Central sensitisation leads to secondary hyperalgesia, i.e. enhanced pain sensitivity in uninjured tissue and allodynia (pain elicited by a non-noxious stimulus). Central sensitisation has resemblance of the windup phenomena. Wind-up is a frequency dependent increase in the excitability of spinal cord neurones, mediated by afferent C-fibres. It is proposed that wind-up initiates

and maintain central sensitisation, which may lead to hyperalgesia (Herrero *et al.* 2000).

1.2.2 General signs of pain, assessment and treatment

Pain can be organized into multiple behavioural domains — including reflexive/evoked responses, spontaneous behaviours, protective pain-specific behaviours, affective/emotional components, and impacts on function and quality of life — as described in pain assessment frameworks (Gregory *et al.* 2013; Fillingim *et al.* 2016). Thus, pain signals to look for are for example reaction to touch, social withdrawal and vocalization, excessive grooming and mood changes, as well as changes in daily habits. Further, aggression and changes in physical activity, both in the way the activity is preformed but also its intensity, altered sleep patterns and reluctance to exercise.

As previously mentioned, it is not possible to directly assess pain in animals, since they cannot verbally express their experience of pain (Lascelles *et al.* 2019b). Therefore, the assessment needs to be indirect. In a clinical setting, the reflexive/evoked behaviour can be examined by a clinical examination including palpation and analysis of pain mediators. Behaviours may be described from taking a dog owner anamnesis. Further, the identification of mood changes and changes in daily habits can be documented by different pain questionnaires and activity of daily living protocols. Finally, changes in physical function can be examined by visual lameness examination as well as more technically advanced gait analysis techniques such as force plates and high velocity videotaping.

Pain treatment involves modulation of pain at all levels of the sensory system. It is claimed that techniques using peripheral stimulation (manual therapy, different types of stimulation techniques) can, through the gate theory mechanisms, activate A-β mechanoreceptor fibres leading to a stimulation of inter-neurons in the spinal cord dorsal horn, supressing the painful stimuli. Further, counter-irritating techniques such as acupuncture or ice spray may stimulate the release of endogenous opioids. Descending pain supressing systems such as distraction techniques can activate central brain areas with the subsequent release of both opioids and non-opioid substances. For the scope of this thesis, the focus is on OA associated pain assessment and treatment in dogs, further described in section 1.5.

1.3 Canine osteoarthritis

1.3.1 Definitions and prevalence

The Osteoarthritis research Society International (OARSI) has defined osteoarthritis as:

"Osteoarthritis is a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodelling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness." (Kraus *et al.* 2015)

OA is the most common orthopaedic diagnose in veterinary medicine and musculoskeletal disease is the most common owner reported disease in the Unites States and Australia (Freeman *et al.* 2006). It is affecting 2,5% of the United Kingdom dog population (Anderson *et al.* 2018), has been found in 16% of a young dog population (Enomoto *et al.* 2024) and in 20% of dogs over 1 year in the US (Johnston 1997). Based on radiographs, the prevalence in dogs over 8 years old was 39.2%, 57.4%, 35.9% and 36.4% for the shoulder, elbow, hip and stifle, respectively (Roitner *et al.* 2024). Further, it is one of the most common causes for mortality due to locomotor disorders in the Swedish dog population (Bonnett *et al.* 2005).

OA is a chronic and painful condition and has a negative impact on the quality of life for both dogs and their owners (Johnston 1997; Belshaw *et al.* 2020c; Belshaw *et al.* 2020b). It has been identified as one of the top three most important diseases to treat to improve overall quality of life in dogs (Summers *et al.* 2019). Therefore, it is utterly important to manage the clinical symptoms from OA.

1.3.2 Aetiology and pathophysiology

OA is a progressive, degenerative disease that affects primarily articular cartilage in diarthrodial joints (Renberg 2005). OA should be recognized as a syndrome with heterogenous aetiology (Meeson *et al.* 2019), such as trauma, developmental dysplasia such as hip dysplasia and an effect of low-grade inflammation caused by for example obesity (Renberg 2005; Meeson

et al. 2019). Thus, risk factors for the development of canine OA may be obesity, genetics, age and environmental factors such as mechanical overloading (Cachon *et al.* 2023).

Although OA primarily affects articular cartilage, it is also a multifactorial disease affecting the whole joint with its bone, ligaments and muscles (Wieland *et al.* 2005; Hunter & Bierma-Zeinstra 2019; Tang *et al.* 2025). The pathological processes involve joint tissue metabolism abnormalities, anatomical and physiological disruptions such as cartilage degradation, bone remodelling, osteophyte formation and joint inflammation. In humans, the progression of the disease is claimed to be load-, structural-, inflammatory-, metabolic- and systemic factor-driven. Tang *et al.* (2025) states that it is important to distinguish between OA as a disease, with its pathological changes in joints, and an illness marked by pain and disability.

The pathophysiology includes changes in chondrocytes, with an increase in an inflammatory amplifying and a senescent subpopulation of chondrocytes (Zheng *et al.* 2021). The changes induce a reduction in hyaluronic acid, proteoglycan 4 and collagen III which, together with changes in the collagen matrix, result in a reduced capacity for mechanical load. A repair process with synthesis of collagen I and a layer of a weaker fibrocartilage, instead of hyaline cartilage, starts. Further, the changes will affect inflammatory responses (Zheng *et al.* 2021).

Changes will also be seen in the subchondral bone, with a more porous and thinner subchondral bone, and finally subchondral bone sclerosis and osteophyte formation (Tang *et al.* 2025). It will further decrease the joint weight bearing ability. There is an inflammation in the synovium, with changes in its composition and a subsequent release of pro-inflammatory cytokines such as IL-1β, TNF and IL-6. Additionally, it is suggested that inflammatory processes may cause degradation of the meniscus and intra-articular ligaments, which may result in joint instability and further damage (Tang *et al.* 2025). Overview of the changes in the joint can be seen in Figure 1.

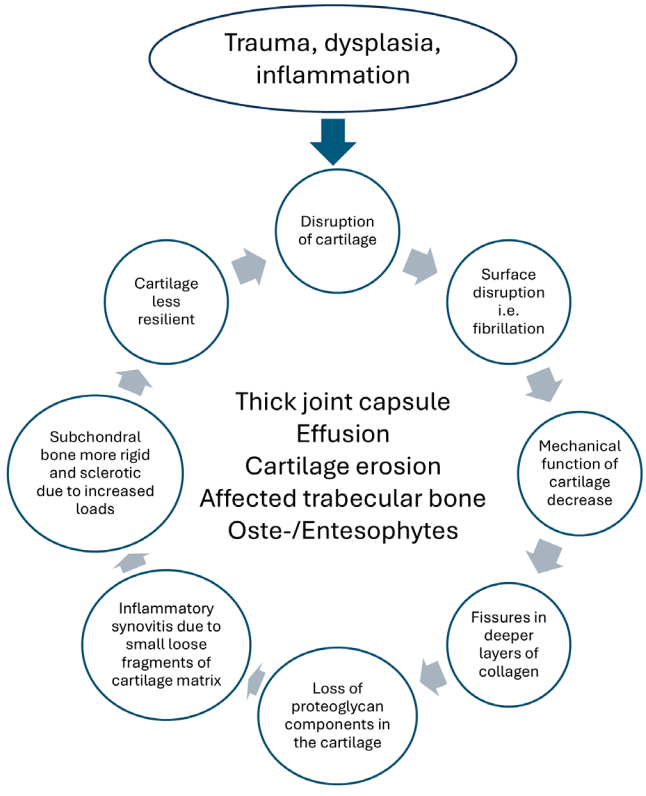

Figure 1. Overview of pathological changes due to osteoarthritis.

The OA changes are seldom restricted to a single joint; it is common with involvement of multiple joints and therefore multiple limbs (Innes *et al.* 2004; O'Neill *et al.* 2020). Due to these pathological changes in the joints the animal experiences pain and discomfort. OA associated pain is derived from activation of peripheral nociceptors in joint tissues, such as subchondral bone, synovium, menisci, tendons, ligaments and periosteum (Tang *et al.* 2025). Action potentials are transmitted to the dorsal root ganglia and then spinal dorsal horn where the second-order neurons are activated. Then the signals go to higher centres and are transformed to perception of pain. The peripheral nociceptors can also express receptors for inflammatory mediators from the macrophages and inflamed tissues and there may be neo-vascularisation of the synovium and sprouting of nociceptors in the subchondral bone. As the nociceptors may become hyperexcitable – non-

noxious stimuli may be perceived as pain. Thus, all changes may contribute to the development of pain (Tang *et al.* 2025).

1.3.3 Clinical signs

Pain and low-grade inflammation are characteristics of canine OA. The clinical signs can be subtle, varied, and often increase in severity as the disease progresses. The pain has an impact on many aspects of the dog's life, including movement, physical state, and behaviour (Belshaw *et al.* 2020b; Malkani *et al.* 2024; Stevens *et al.* 2025). In general, clinical signs associated with OA can be divided into a) mobility and gait impairments; b) functional difficulties/physical dysfunction; c) clinical and physical findings; and d) behaviour and mood changes (Innes *et al.* 2004; Roberts *et al.* 2021; Gildea *et al.* 2024; Stevens *et al.* 2025). For more specific clinical signs in canine OA, see Table 1.

Table 1. Clinical signs associated with canine osteoarthritis.

Clinical signs associated with canine osteoarthritis (OA)			
Mobility and gait impairment	**Functional difficulties/physical dysfunction**	**Clinical and physical findings**	**Behaviour and mood changes**
Lameness (may be intermittent) Stumbling	Reduced willingness to move/exercise/play	Pain on joint manipulation or painful areas upon palpation	Low mood, sadness, depression, or lethargy
Subtle signs of gait abnormalities	Difficulty rising from a resting position or slow to get up and/or lie down	Reduced joint range of motion	Apprehensive/frightened/aggressive
Stiffness (e.g., noted during, after activity, or morning stiffness)	Difficulty jumping up and/or down	Joint thickening or periarticular swelling, effusion	Appearing quiet or unresponsive
Reduced speed at walk or slower movements in general	Reluctance or difficulty climbing stairs or steps	Crepitus	Vocalization (e.g., when moving, or making sounds to show distress)
	Difficulty getting into the right position to urinate/defecate	Muscle atrophy	Restlessness (including nighttime restlessness), panting, licking
	Tiring easily	Abnormal posture	Unsociable behaviour
		Widespread somatosensory sensitivity	Attention seeking or comfort seeking

Clinical signs have been organized into four thematic groups for clarity; the grouping is author-defined and does not appear in the original sources. Information is synthesized and adapted from Innes *et al.* (2004); Roberts *et al.* (2021); Gildea *et al.* (2024) and Stevens *et al.* (2025).

1.3.4 Diagnostics

OA is a chronic disease that mostly is diagnosed in older individuals, although radiological changes of OA can be present in younger individuals, but then often underdiagnosed (Smith *et al.* 2006; Enomoto *et al.* 2024). The symptoms of OA can be subtle in the beginning, and it is therefore common

that symptoms are discarded as "old age" (Rychel 2010; Belshaw *et al.* 2020a). This can delay the diagnosis, and a late diagnosis can affect the outcome of treatment (Rychel 2010; Jones *et al.* 2022).

OA diagnostics in clinical practise is primarily based on clinical history, the owner reported symptoms of OA and the findings from an orthopaedic examination (Belshaw *et al.* 2020a; Jones *et al.* 2022). The clinical examination, including joint swelling, effusion, crepitation, skin temperature, is often complemented with diagnostic imaging, primarily radiographs but also magnetic resonance imaging (MRI) or computed tomography (CT) (Widmer *et al.* 1994; Rychel 2010; Jones *et al.* 2022; Clark & Comerford 2023). There is a disparity between clinical signs of OA and radiographic findings, therefore OA cannot solely be based on radiological findings or the absence of findings (Olsson 1971; Gordon *et al.* 2003; Hielm-Björkman *et al.* 2003; Morgan *et al.* 2010). One reason is the inability of radiology to detect early changes, as the main later findings are signs such as a narrowed joint space, osteophytosis and enthesophytosis, subchondral sclerosis, joint effusion, soft tissue swelling and intra-articular mineralisation. Early-stage changes like bone marrow lesions, that usually appears before loss of cartilage, may be detected by MRI (Jones *et al.* 2022). To better predict cartilage damage, diagnosis by arthroscopy can be beneficial (Holsworth *et al.* 2005). With a wider use of more advanced diagnostic imaging techniques, such as CT and MRI, the diagnosis of OA could be improved, allowing confirmation at an earlier stage and potentially leading to a better prognosis (Jones *et al.* 2022). Similarly, an earlier diagnosis of OA could be achieved by screening of dogs by pain questionnaires validated for the use in OA patients and could be incorporated in the overall clinical assessment of dogs (Hielm-Björkman *et al.* 2009b; Rychel 2010). A consensus based diagnostic framework, the Canine Osteoarthritis Staging Tool (COAST), which includes owner questionnaires, orthopaedic evaluation and radiography, has been developed and if applied it could improve the diagnostics (Cachon *et al.* 2023).

1.3.5 Pharmacological and non-pharmacological treatments

Treatment for OA aims to slow down the disease progression and provide analgesia (Rychel 2010; Cachon *et al.* 2023), since OA, at the moment cannot be cured, unless replacing the joint. To achieve this aim, treatment will likely be multimodal and needs to be proven efficient (Mosley *et al.*

2022; Cachon *et al.* 2023). In a meta-analysis study on pain-relieving treatment for OA in humans, 153 different treatments divided into 17 broad categories were included, six of these categories showed clinical significant effect but none of the categories were proven to have high confidence and treatment options could not be ranked, further supporting the multimodal approach (Smedslund *et al.* 2022).

Pharmacological treatment is the mainstay treatment in canine OA (Anderson *et al.* 2018). There are two major pharmacological options: Non-steroidal Anti-Inflammatory Drugs (NSAIDs) and Anti-Nerve Growth Factor Monoclonal Antibodies (Anti-NGF mAbs) (Gruen *et al.* 2022; Pye *et al.* 2022; Michels *et al.* 2023). Systemic use of NSAIDs is aimed to reduce inflammation and provide pain relief. However, NSAIDs can have adverse effects such as gastrointestinal disorders (Luna *et al.* 2007; Hunt *et al.* 2015), and adverse effects are reported in 55% of the studies on NSAIDs (Monteiro-Steagall *et al.* 2013). Anti-Nerve Growth Factor Monoclonal Antibodies is a relatively new drug on the marker with evidence of providing pain relief in dogs with OA (Corral *et al.* 2021; Michels *et al.* 2023; della Rocca *et al.* 2025). Anti-Nerve Growth Factor Monoclonal Antibodies in dogs is suspected to cause musculoskeletal adverse events (Farrell *et al.* 2025), requiring a benefit:risk analysis for concurrent use in dogs (Mosley *et al.* 2022; Cachon *et al.* 2023).

The suggested primary treatment for OA is non-pharmacological and has focus on weight management and nutrition, and exercise and physical therapy (Mille *et al.* 2022; Cachon *et al.* 2023). Obesity increases the pain from OA, due to an increased mechanical load and a low-level inflammation. A weight loss has been shown to significantly reduce lameness derived from canine OA (Marshall *et al.* 2009). Nutritional supplements such as omega-3-fatty acids are recommended and have been shown to improve clinical signs of OA (Hielm-Björkman *et al.* 2009a; Fritsch *et al.* 2010; Roush *et al.* 2010a; Roush *et al.* 2010b; Moreau *et al.* 2013; Rialland *et al.* 2013; Soontornvipart *et al.* 2015; Mehler *et al.* 2016; Vijarnsorn *et al.* 2019). There are several other nutritional supplements, but the evidence for their effectiveness is more sparse- therefore they are generally not recommended (Mosley *et al.* 2022; Cachon *et al.* 2023).

One of the cornerstones in rehabilitation is physical exercise. For a dog with OA, regular and low-impact exercise is beneficial (Mille *et al.* 2022; Mosley *et al.* 2022). Specific therapeutic exercises and hydrotherapy are

commonly conducted at the veterinary clinic. Additionally, it is important that exercises also are performed in the home environment to optimise the amount of training and the prescription of home exercises is thus vital (Mille *et al.* 2022). Further, there are a wide array of therapeutical modalities aimed at decreasing signs of OA. These include manual therapies such as massage and passive range of motion. Further thermotherapy, as well as treatment with different modalities such as low-level laser therapy (LLT), therapeutic ultrasound, (TU), extracorporeal shock wave therapy (ESWT) and different electrotherapies including transcutaneous electrical nerve stimulation (TENS) (Mille *et al.* 2022). Although the different modalities are used by practitioners, the evidence for their effectiveness is sparse, and there is a great need for further research in the area (Boström *et al.* 2022a; Boström *et al.* 2022b; Mille *et al.* 2022; Hyytiäinen *et al.* 2023a; Millis & Bergh 2023).

1.4 Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation is a non-invasive electrophysical modality used globally for the management of acute and chronic pain in humans (Gibson *et al.* 2019; Johnson 2021). It is also used to manage pain in dogs, though evidence is limited (Gaynor & Muir 2015; Hyytiäinen *et al.* 2023a).

Figure 2. Treatment with transcutaneous electrical nerve stimulation.

1.4.1 Mechanism of action and treatment settings

Transcutaneous electrical nerve stimulation delivers electrical currents across the intact surface of the skin via conducting electrodes to stimulate peripheral nerves (Johnson 2021). The possibility of variations in settings is large. Besides setting the mode (constant current, modulation or bursts) and frequency (Hz), the intensity (mA) and pulse duration (μs) are decided. The duration of the treatment can be highly variable: TENS can be used for short sessions (for example 5 minutes) but also for 30-60 minutes sessions depending on the aim of the treatment (Cheing *et al.* 2003; Johnson 2021). Placement of the electrodes are typically over the site of pain but can also be placed over a dermatome (Johnson 2021).

The proposed mechanism of action is that TENS provides hypoalgesia by modulating nociceptive input on multiple levels of the nervous system (Sluka & Walsh 2003; DeSantana *et al.* 2008; Johnson 2021; Patel *et al.* 2025). Which levels to be affected depends on the treatment settings, particularly the frequency and intensity of the applied current (Walsh *et al.* 1995; Walsh *et al.* 1998). Transcutaneous electrical nerve stimulation that utilises high pulse frequencies and low intensities (typically between 50-100 Hz and pulse duration of 50-200 μs) is theorized to work primarily via the gate control theory, and through the release of endogenous opioids, depending on the level of intensity (Jones & Johnson 2009; Lazarou *et al.* 2009; Leonard *et al.* 2010; Bi *et al.* 2021). While the TENS that utilises lower pulse frequencies and higher intensities (typically ≤ 10 Hz and pulse duration of 100- 400 μs) are claimed to work primarily via activation of descending pain inhibitory pathways (Bi *et al.* 2021). The gate theory suggests that stimulation of A-β fibres modulates the nociceptive input from C-fibres and A-δ fibres at the level of the dorsal horn, therefore creating pain-relief (Garrison & Foreman 1996; Sluka & Walsh 2003; Johnson 2007; Hahm *et al.* 2019). Further, it is claimed to activate the periaqueductal grey and initiate a release of endogenous opioids (Johnson 2007; DeSantana *et al.* 2008), as well as activation of delta-opioid receptors. The theory behind descending pain inhibitory pathways suggests that stimulation of A-δ fibres activates the periaqueductal grey (Johnson 2007; DeSantana *et al.* 2009), together with activation of mu-opioid receptors in the brain. It is suggested that repeated exposure to TENS can lead to analgesic tolerance, and alternations in current form or delivery may be beneficial (Pantaleão *et al.* 2011; Avendaño-Coy *et al.* 2019).

1.4.2 Transcutaneous electrical nerve stimulation in animals and humans

Transcutaneous electrical nerve stimulation is used to treat various conditions in dogs. It is primarily used for complementary pain relief in veterinary rehabilitation for both acute and chronic pain. Six studies have evaluated TENS in dogs with various conditions, including OA, ankylosing spondylitis, nerve injury, and postoperative pain, all with more or less positive results (Johnston *et al.* 2002; Mlacnik *et al.* 2006; Sharifi *et al.* 2007; Krstić *et al.* 2010; Srivastava *et al.* 2011; Gouveia *et al.* 2025). For the effect on OA, one study reported increased weight bearing up to 180 minutes after a single treatment in five lame dogs (Johnston *et al.* 2002). Transcutaneous electrical nerve stimulation is also used as pain relief in other species such as horses. There are two studies on TENS in equines, where the treatment of superficial flexor tendon injury and epaxial muscle pain were evaluated with mixed results (Mercado *et al.* 2002; Sharifi *et al.* 2009).

Since there is a lack of animal studies, one may look for evidence in the human literature. Transcutaneous electrical nerve stimulation is used in humans for a wide spectrum of painful conditions, irrespective of the underlying pathology, thus including musculoskeletal, neurological, and acute post-operative pain (Bjordal *et al.* 2003; Gibson *et al.* 2017; Gibson *et al.* 2019; Martimbianco *et al.* 2019; Johnson 2021). Several studies support the use and effectiveness of TENS in chronic conditions. In patients with knee OA, TENS has been reported to reduce pain and/or improve function in several systematic review (Osiri *et al.* 2000; Rutjes *et al.* 2009; Wu *et al.* 2022). However, systematic reviews evaluating the effectiveness of TENS for chronic pain report mixed and often inconclusive results. These inconsistencies are largely attributed to low-quality evidence, small sample sizes, and heterogeneity across studies (Claydon & Chesterton 2008; Gibson *et al.* 2019).

1.5 Pain assessment

Since pain is an emotional experience and cannot be measured directly, its assessment in animals must rely on indirect indicators and observable signs. (Belshaw & Yeates 2018; Hernandez-Avalos *et al.* 2019; Hyytiäinen *et al.* 2023b) When assessing chronic pain, it is important to quantify the impact on physical function and quality of life (Walsh 2016; Lascelles *et al.*

2019b). Today, effective assessment requires a combination of subjective and objective measures, as no single gold standard exists to fully capture all facets of chronic pain (Sharkey 2013; Lascelles *et al.* 2019b; Brown *et al.* 2025).

Semi-subjective outcome measures for pain associated with OA primarily include clinical examinations and pain questionnaires (Belshaw *et al.* 2016; Hyytiäinen *et al.* 2023b). Possible more objective measures encompass analysis of pain mediators, joint range of motion, physical activity monitoring, which quantifies physical activity; gait analysis through kinetic assessments, which measure the force exerted by the paw on the ground; and gait analysis through kinematic assessment, which evaluate joint angles and velocity (Belshaw *et al.* 2016; Sandberg *et al.* 2020; Hyytiäinen *et al.* 2023b). Within the scope of this thesis, the focus is on the following outcome measures: clinical examination, pain questionnaires, gait analysis, and physical activity monitoring. These measures are structured into two overarching themes: (i) clinical findings and behavioural changes, and (ii) gait impairments and physical activity.

1.5.1 Clinical findings and behaviour changes: Clinical examination

Clinical examination, including visual lameness assessment, is the most common outcome measure for assessment of chronic pain derived from OA, and the most used outcome measure in OA research (Belshaw *et al.* 2016). Clinical assessment of the musculoskeletal system should always be the first step in an evaluation of chronic pain (Belshaw *et al.* 2020a; Montalbano 2022). Visual gait assessment is usually done together with the clinical examination, and a numerical rating scale (NRS) or visual assessment scale (VAS) is often used (Sharkey 2013; Belshaw *et al.* 2016). Visual gait assessment is a subjective assessment that correlates poorly with objective measures such as force plate analysis (Quinn *et al.* 2007; Waxman *et al.* 2008). Interobserver reliability is often low and varies considerably between studies, likely due to differences in examiner experience, the degree of examiner calibration, and the severity of lameness, as subtle lameness is more difficult to evaluate accurately (Quinn *et al.* 2007; Waxman *et al.* 2008; Aulakh *et al.* 2020). Based on studies from both human medicine and veterinary medicine variability can be reduced using the same examiner, using an experienced examiner and standardize the dog's movement to a

straight line and standardize the protocol used for the assessment (Quinn *et al.* 2007; Waxman *et al.* 2008; Ridao-Fernández *et al.* 2019).

1.5.2 Clinical findings and behaviour changes: Pain questionnaires

There are several pain questionnaires available to grade the pain derived from OA. The main pain questionnaires are Canine Brief Pain Inventory (CBPI), Canine Orthopedic Index (COI), Helsinki Chronic Pain Index (HCPI), Liverpool Osteoarthritis in Dogs (LOAD), Glasgow University Health-related Dog Behaviour Questionnaire (GUVQuest), Hudson Visual Analogue Scale (HVAS) and the pain questionnaire part of the Bologna Healing Stifle Injury Index (BHSII) (Radke *et al.* 2022; Clark & Comerford 2023; Hyytiäinen *et al.* 2023b). Of these the CBPI, HCPI and LOAD are validated for OA (Brown *et al.* 2007; Hielm-Björkman *et al.* 2009b; Walton *et al.* 2013; Brown 2014a). The CBPI and COI are validated in Swedish and HCPI is translated to Swedish (Essner *et al.* 2017; Andersson & Bergström 2019). All these instruments are owner-reported pain questionnaires, and each assesses somewhat different aspects of the dog's pain. For example, the CBPI mainly describes pain severity, the HCPI mainly focus on behaviour and locomotion, the COI addresses gait, functional ability, and quality of life, and the LOAD specifically measures mobility (Brown *et al.* 2007; Hielm-Björkman *et al.* 2009b; Walton *et al.* 2013; Brown 2014b). Although certain questionnaires may be better suited to particular subgroups of dogs, using a combination of multiple pain assessment tools generally provides a more comprehensive and reliable evaluation (Brown *et al.* 2025). CBPI, COI and LOAD were found to have a sufficient internal consistency in a systematic review according to the Consensus-Based Standards for the Selection of Health Measurement Instruments (COSMIN) guidelines and therefore recommended for clinical usage (Radke *et al.* 2022). Additionally, HCPI and H-VAS has been found to be acceptable for clinical usage based on a review article (Hyytiäinen *et al.* 2023b). As for most of the outcome measures for chronic pain, the usage of pain questionnaire is improved when combined with other pain assessment techniques (Clark & Comerford 2023).

1.5.3 Gait impairments and physical activity: Gait analysis

Objective gait analysis is generally divided into two: kinematic and kinetic assessment (Kieves 2022). Kinematic analysis evaluates gait without considering the forces that generate movement and can be performed using

marker-based motion capture systems (MBS) or inertial measurement units (IMUs). In the future, markerless gait analysis may also be possible (Pahk *et al.* 2026). Kinematic data include upper body movement symmetry, joint range of motion, angular and segmental velocities, stride length, and stride frequency (Rhodin *et al.* 2017b; Sandberg *et al.* 2020). Marker-based motion capture systems use retroreflective skin markers and either 2D or 3D motion capture cameras (Kieves 2022). Three-dimensional MBS is considered the gold standard for kinematic measurements, but the systems are expensive and require specialised expertise. For this reason, 2D systems are more commonly used in clinical settings, although their cost and space requirements still limit routine use (Sandberg *et al.* 2020). Inertial measurement units have the possibility to offer a more space-efficient and cost-effective alternative to MBS (Ladha *et al.* 2017; Sandberg *et al.* 2020). While well-developed for equine gait analysis (Crecan & Peștean 2023), IMUs are not yet fully established for clinical application in dogs (Rhodin *et al.* 2017b; Winkler *et al.* 2025). Inertial measurement units can be attached at various anatomical locations, including limbs, pelvis and head, and may contain accelerometers and gyroscopes or accelerometers, gyroscopes, and magnetometers (Duerr *et al.* 2016; Ladha *et al.* 2017; Rhodin *et al.* 2017b).

Kinetic gait analysis evaluates the forces generated during the stance phase and can be performed using force platforms, instrumented treadmills, or pressure-sensitive mats (Kieves 2022; Clark & Comerford 2023). When a dog is lame, it redistributes its body weight among the four limbs in order to offload the affected limb(s). This redistribution is reflected by reduced peak vertical force (PVF) and vertical impulse (VI) values in the lame limb(s), accompanied by increased values in the remaining limbs (Fanchon & Grandjean 2007; Seibert *et al.* 2012; Abdelhadi *et al.* 2013; Conzemius *et al.* 2022; Park *et al.* 2024). Weight distribution between limbs is influenced by for example the dog's conformation and size (Bertram *et al.* 2000; Voss *et al.* 2010; Carr *et al.* 2015; Kano *et al.* 2016; Fahie *et al.* 2018; Ladha & Hoffman 2018a). Symmetry indices (SIs) can visualise the weight distribution between limbs and are calculated as ratios between limbs (Budsberg *et al.* 1993). Definitive cut off values to distinguish between sound and lame are not established for SIs (Fanchon & Grandjean 2007; Voss *et al.* 2007; Oosterlinck *et al.* 2011; Volstad *et al.* 2017; Brønniche Møller Nielsen *et al.* 2020; Pettit *et al.* 2020). However, in longitudinal

measurement SIs can be of value but they should always be reported together with PVF and VI (Conzemius *et al.* 2022).

Force platforms are considered gold standard and measure ground-reaction forces through piezoelectric elements, strain gauges or load beam cells (Lamkin-Kennard & Popovic 2019; Kieves 2022). The measurements are processed into parameters such as peak vertical force (PVF), vertical impulse (VI) and symmetry indices (SIs). Force platforms are mainly used in research and in movement labs for high-performing athletes and may be arranged as single or multiple plates to capture sequential footfalls (McLaughlin 2001; Kieves 2022).

Pressure-sensitive mats consist of multiple pressure sensors and register at least two continuous gait cycles (Conzemius *et al.* 2022; Kieves 2022). Pressure-sensitive walkway systems measures ground reaction forces, such as PVF and VI, but also temporospatial parameters, including velocity, acceleration, stance time, and stride time, and allow for the calculation of SIs (Besancon *et al.* 2003; Fahie *et al.* 2018; Avendano *et al.* 2023). However, the clinical value of recording many of the temporospatial parameters remains uncertain, and PVF and VI continue to be the most relevant metrics (Conzemius *et al.* 2022). Although pressure mats are more practical in clinical environments than force platforms, cost, calibration requirements and space constraints still limit their use (Conzemius *et al.* 2022; Kieves 2022).

Research has demonstrated a correlation between outcomes obtained using force plates and pressure-sensitive mats (Besancon *et al.* 2003; Lascelles *et al.* 2006). Across all kinetic gait analysis methods, the use of standardised measurement protocols is essential, as variables such as velocity can significantly influence results despite the high precision of the instruments (Conzemius *et al.* 2022).

1.5.4 Gait impairments and physical activity: Physical activity monitoring

Physical activity in dogs can be registered using a collar-mounted activity monitor equipped with an accelerometer. Physical activity can be defined as a change of position of body segments resulting from skeletal muscle contractions. The following physical activity parameters can be derived from an accelerometer: duration, intensity, frequency, volume, type, timing of bouts of activity (i.e. pattern of activity), physical activity energy

expenditure, posture and sedentary behaviour. In dogs, commonly used physical activity domains that are measured by accelerometers are duration, frequency, volume, type, timing of bouts of activity (i.e. pattern of activity) and sedentary behaviour (Thonen-Fleck *et al.* 2025).

The accelerometer measures acceleration (the change of velocity of an object over time) and generates a raw acceleration signal based on the dynamic acceleration of the body segments where it is attached to, static acceleration due to earth's gravity and noise such as movement of the collar around the dog's neck or disturbances from within the accelerometer. The accelerometers consists of two parts; a sensor and a data acquisition system which process and stores data. There are two types of sensors used in physical activity monitors, piezo-electric sensors and inertial sensors (Mico-Electro-Mechanical Systems (MEMS)) (Thonen-Fleck *et al.* 2025). Accelerometers were initially developed as uniaxial devices, measuring acceleration along a single axis. However, the activity monitors most used in contemporary research has triaxial accelerometers, which record acceleration along three orthogonal axes. The raw data from the accelerometer is expressed in m/s^2 and can be analysed as; a time dependant measures, such as sampling frequency (Hz) and vector magnitude (g), or a frequency dependant measures, such as power (g^2) (de Souza *et al.* 2023; Liang *et al.* 2024).

To distinguish biologically relevant movement from noise, filtering procedures are applied to the raw acceleration signal. These procedures typically involve restricting the signal to a defined frequency bandwidth, thereby reducing the signal to frequencies assumed to represent meaningful movement (van Hees *et al.* 2013). A wide range of filtering approaches exists, many of which are proprietary and not openly documented, resulting in limited transparency regarding their effects on the recorded signal (Migueles *et al.* 2017; Thonen-Fleck *et al.* 2025). One of the most widely used activity monitoring systems in research, ActiGraph, applies a proprietary filtering algorithm in post-acquisition processing using the software ActiLife, that is partially described in the literature (Neishabouri *et al.* 2022). The reported bandwidth to retain the full signal with this filtering is 0.29-1,63 Hz, higher and lower frequencies are retained but with a limited amplitude (Neishabouri *et al.* 2022).

Dogs exhibit stride frequencies typically ranging from 2 to 4 Hz, and in some cases up to 6 Hz (Cavagna *et al.* 1988; Heglund & Taylor 1988). For

example, racing Greyhounds demonstrate a mean stride frequency of approximately 3.5 Hz, with frequencies approaching 4 Hz during acceleration phases (Hayati *et al.* 2019). In contrast, healthy Golden Retrievers have a mean stride frequency of around 2.11 Hz when walking four steps and trotting two steps, while Golden Retrievers affected by muscular dystrophy show reduced stride frequencies, with mean values of approximately 1.54 Hz for the same combination of walk and trot (Barthélémy *et al.* 2009). These stride frequencies do not fully correlate to the proprietary bandwidth used by ActiGraph. In human physical activity research, it has been demonstrated that ActiGraph filtering procedures may be too restrictive, affecting the representation and detection of physical activity (Fridolfsson *et al.* 2018; Fridolfsson *et al.* 2019; Arvidsson *et al.* 2024). To date, this issue has not been systematically investigated in dogs.

The ability of an accelerometer to accurately capture movement-related frequencies is also determined by its sampling frequency. In canine physical activity research, commonly used sampling frequencies range from 30 to 100 Hz. However, sampling frequencies below 25 Hz have been suggested to be sufficient, and frequencies as low as 8 Hz have been suggested to be adequate for certain applications (Karimjee *et al.* 2019; Karimjee *et al.* 2024). Higher sampling frequencies increase the number of measurements per time unit but simultaneously reduce feasible monitoring duration due to limitations in battery capacity and data storage. Consequently, optimisation of the sampling frequency is essential (Khan *et al.* 2016). According to the Nyquist–Shannon sampling theorem, the sampling frequency must be at least twice the highest frequency component of interest in the signal to avoid aliasing (frequency misrepresentation) (Nyquist 2002; Shannon 2006; Al Jabri *et al.* 2022). Although stride frequency and specific movement patterns in dogs have been studied (Pillard *et al.* 2012; Hayati *et al.* 2019; Karimjee *et al.* 2019; Reinstein *et al.* 2025), the range of frequencies of pet dogs in their everyday physical activity has not yet been characterised and therefore the recommendations of sampling frequency are inadequate for general physical activity over longer time periods.

For accelerometer signals to be interpreted as physical activity, the raw data are commonly transformed into counts. These counts represent the magnitude of acceleration signals detected by the device within fixed time intervals, typically one-minute epochs, and are widely used as indicators of physical activity duration and intensity. The most common count is counts

per minutes (CPM). Typically, higher physical activity intensity results in higher CPM values. Counts per minutes values allow estimation of total activity levels and classification of time spent in sedentary and various activity intensity categories (e.g. light, moderate, vigorous) using predefined cut-points (Migueles *et al.* 2017). The time a dog spends in each activity level can then be used to describe its overall physical activity pattern. For example, dogs with OA exhibit lower daytime activity and reduced nighttime rest compared with healthy dogs (Rowlison de Ortiz *et al.* 2022; Smith *et al.* 2022), a pattern similar to that observed in humans (Wilcox *et al.* 2000; Power *et al.* 2005; Taylor-Gjevre *et al.* 2011). Physical activity data can also be used to evaluate treatment effects; increased activity levels have been reported in dogs with OA following successful pain-relieving interventions, such as oral nutraceuticals (glucosamine hydrochloride and sodium chondroitin sulfate) and carprofen (Brown *et al.* 2010; Scott *et al.* 2017). In dogs, the classification of CPM into different activity intensities has been validated primarily through observational studies, in contrast to human research where validation relies on measures of energy expenditure, such as respiratory gas analysis using facemask/mouthpiece or a calorimeter (Freedson *et al.* 1998; Swartz *et al.* 2000; Freedson *et al.* 2005; Miller *et al.* 2010; van Hees *et al.* 2011). As a result, the validation of physical activity intensity in dogs remains limited, for example it cannot be used to measure energy expenditure (Sekhar *et al.* 2023). Even though human validation is superior, activity classification with CPM cut-offs is variable and highly dependent on the type/brand of monitor and the filtering procedure applied to the data. There is yet no uniform procedure in place, although there are recommendations on data collection and processing criteria based on a systematic review (Migueles *et al.* 2017).

To measure canine movement, accelerometers must be physically attached to the dog, most commonly via a collar-mounted configuration (Hansen *et al.* 2007; Preston *et al.* 2012). Accelerometers record continuously, and when the collar is removed, the recorded signal reflects handling or storage of the device rather than the dog's movement. These periods are referred to as non-wear time. The amount of non-wear time within a dataset is critical, as failure to correctly identify non-wear can substantially bias the interpretation of physical activity outcomes. In humans, non-wear periods are often shorter than 60 minutes (Jaeschke *et al.* 2017);

however, repeated short non-wear episodes may accumulate and meaningfully affect activity estimates.

In human research, numerous methods for defining and validating non-wear time have been proposed (Migueles *et al.* 2017). One approach involves recording non-wear periods in participant logbooks. Although this method requires additional effort from participants, it can theoretically capture non-wear periods of any duration. Reported performance for logbook-based non-wear detection shows a sensitivity of 76.4% and a specificity of 76.2% (Peeters *et al.* 2013). Automated non-wear detection methods are generally less burdensome for participants and are therefore more commonly applied (Peeters *et al.* 2013). These automated methods typically classify data segments as non-wear based on predefined cut-off values applied over specified time windows (Migueles *et al.* 2017).

One of the most widely used automated methods for non-wear classifies periods with zero CPM for 60 consecutive minutes as non-wear, yielding reported sensitivity and specificity values of 98.3% and 89.6%, respectively. Despite its simplicity, this definition fails to detect non-wear periods shorter than 60 minutes and may misclassify periods with brief interruptions, such as when the monitor is moved between locations. When a shorter time window of 20 minutes is applied, sensitivity decreases to 96.2% and specificity drops substantially to 9.6% (Peeters *et al.* 2013). To better accommodate heterogeneous non-wear patterns, the Troiano and Choi algorithms were developed. The Troiano algorithm defines non-wear as 60 consecutive minutes of zero CPM, allowing for up to two minutes of counts between zero and 99 CPM within this interval (Troiano *et al.* 2008; Keadle *et al.* 2014). The Choi algorithm defines non-wear as 90 consecutive minutes of zero CPM, permitting up to two minutes of non-zero counts provided that these interruptions are flanked by at least 30 minutes of zero CPM either upstream or downstream (Choi *et al.* 2011; Keadle *et al.* 2014). Although the Troiano algorithm has been more widely used, the Choi algorithm has been shown to better preserve true wear time (Choi *et al.* 2012; Keadle *et al.* 2014; Migueles *et al.* 2017). These two rule-based algorithms share a fundamental limitation in their inability to reliably detect short non-wear periods. To overcome this limitation, Syed *et al.* (2021) proposed a machine-learning approach that identifies monitor removal and attachment events directly from raw hip-worn accelerometer data, thereby defining non-wear periods independently of their duration. Furthermore, Vert *et al.* (2022)

demonstrated that combining accelerometer data with temperature measurements enables detection of non-wear periods as short as five minutes.

Importantly, all currently available non-wear definitions have been developed and validated exclusively in human populations. In canine populations, the only option for non-wear time is logbooks and non-wear time is not commonly defined or reported in dog physical activity studies (Thonen-Fleck *et al.* 2025). This highlights a clear need for the validation and development of species-specific non-wear detection methods for canine accelerometry.

2. Aims

The general aim of this thesis was to improve pain assessment by providing further information on the use of outcome measures and improve treatment in dogs with osteoarthritis (OA) by providing information on the pain reliving effect of TENS. In the present thesis, indirect pain assessment was conducted by clinical examination, pain questionnaires, kinetic and kinematic techniques and physical activity monitoring.

The specific aims were to:

- Compare the effects of single and multiple TENS treatment(s) to placebo treatment(s) on gait parameters in dogs with OA (paper I).
- Investigate the effects of NSAID treatment on gait parameters in dogs with OA (paper I).
- Compare the effects of single and multiple TENS treatment(s) to placebo treatment(s) on clinical signs of pain, owner-reported pain scores, and physical activity in dogs with OA (paper II).
- Investigate the effects of NSAID treatment on owner-reported pain scores and physical activity in dogs with OA (paper II).
- Compare nighttime physical activity of healthy dogs with that of OA dogs (paper II),
- Compare physical activity outcomes derived from two different data-filtering procedures applied to an identical activity monitor dataset (paper II).
- Determine the frequency range in which physical activity occurs in pet dogs (paper III).
- Investigate the variance of raw data in non-wear periods and compare to wear periods in data derived from activity monitors (paper III).
- Compare outcome from different non-wear validation procedures on activity monitor data (paper III).

3. Hypotheses

The following hypotheses were raised:

- TENS, administered as single and multiple treatment(s), and in comparison to placebo,
  a) reduces lameness both after single and multiple treatments, evaluated by assessing gait parameters applying pressure-sensitive walkway technique.
  b) reduces the number and/or severity of signs of pain detected during clinical examination,
  c) lowers pain scores in owner-reported pain questionnaires, and
  d) increases the amount of daytime physical activity and decreases the amount of nighttime physical activity, registered by physical activity monitors.
- NSAID,
  a) reduces lameness evaluated by assessing gait parameters applying pressure-sensitive walkway technique.
  b) lowers pain scores in owner-reported pain questionnaires,
  c) increases the amount of daytime physical activity and decreases the amount of nighttime physical activity, registered by physical activity monitors.
- Dogs with OA has a higher amount of physical activity during nighttime than healthy dogs.
- The type of data-filtering procedure affects the reported activity levels obtained from the identical activity monitor dataset.
- The frequency range of physical activity represented in raw data is broader than that selected by the commercially available filter used in standard activity monitor processing.
- The variance in non-wear raw data is smaller than wear raw data and can be used to classify non-wear time in activity monitor data.
- The human validated algorithms for non-wear time can classify non-wear in canine activity monitor data.

4. Material and methods

This chapter includes an overview of the material and methods used in the included studies. More detailed descriptions are found in papers I-III. A general overview of the studies is presented in Figure 2.

Written informed consent was obtained from all dog owners prior to participation. Ethical approval was granted by the Ethics Committee for Animal Experiments, Uppsala, Sweden for study 1 (protocols 5.2.18-335/18 and C148/13) and for study 2 (Dnr 5.8.18-15533/2018). Study 3, according to Swedish legislation, did not require ethical approval. The studies were conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (Goodyear *et al.* 2007).

Data collection periods were September 2018 to January 2020 (study 1), August 2021 to October 2021 (study 2) and June 2024-October 2025 (study 3), respectively.

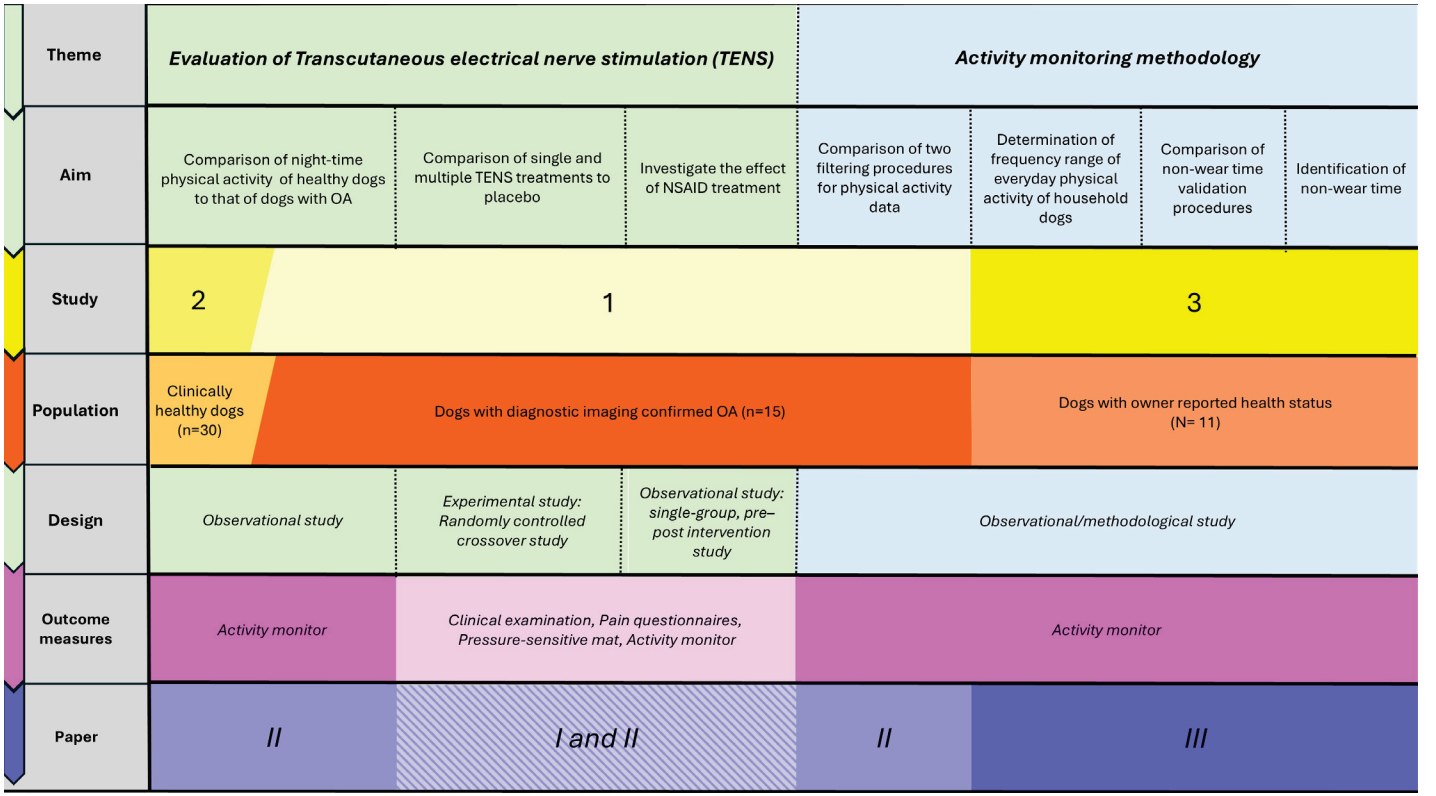

Figure 3. General overview of the studies included in the thesis.

TENS=Transcutaneous Electrical Nerve Stimulation; OA=Osteoarthritis; NSAID= Non-Steroidal Anti-Inflammatory Drug.

4.1 Study design and protocol

4.1.1 Study 1

This study included two sequential phases: Phase 1 evaluated the effects of TENS versus placebo treatment using a prospective, single-blinded, randomised, placebo-controlled crossover design (Figure 4). Phase 2 assessed the response to NSAID treatment using a single-group, pre–post intervention design (Figure 4). A pilot study was conducted and the results from one dog was included in the final data.

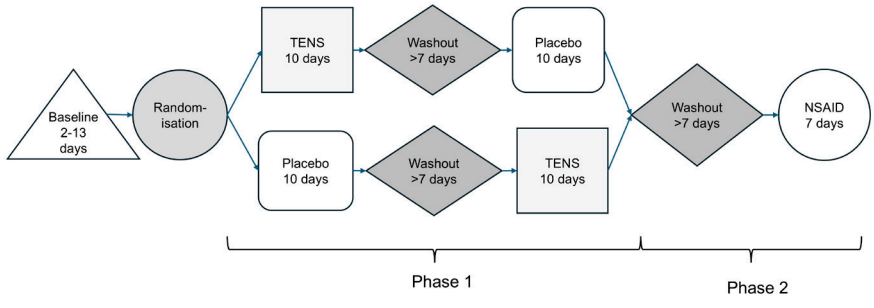

Figure 4. Study design of study 1.

The study protocol for study 1 is presented in Figure 5. The total study duration for dogs participating in both the TENS and NSAID interventions was a minimum of 58 days. The design included three treatment periods: TENS and placebo, each lasting ten days, and NSAID treatment lasting seven days. Washout periods of a minimum of seven days were applied between each treatment period (Figure 4). In the pilot study, the treatment period for TENS and placebo lasted for seven days. Evaluation with pressure sensitive mat were done both for single treatment (one day) and multiple treatments (after full treatment period). Clinical examination and registration on the pressure sensitive mat were done < 1hour before treatment and approximately 15-24 hour after the last multiple treatment. The pressure

sensitive mat evaluation of single treatment was done < 1 hour after treatment.

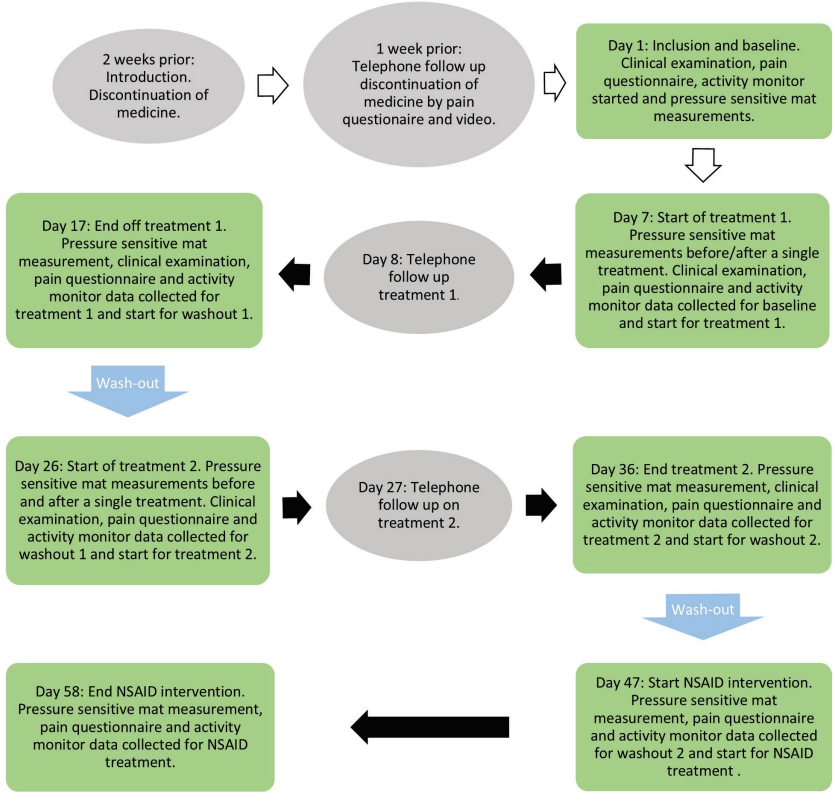

Figure 5. Study protocol of study 1.

4.1.2 Study 2

In this observational study baseline data from healthy dogs participating in an experimental exercise study by Smedberg *et al.* (2024) was used in the study for comparison of nighttime physical activity between healthy and OA dogs. The healthy dogs wore an activity monitor attached to a collar on a 24-hour basis for seven days. The dogs lived their normal life in their own home.

4.1.3 Study 3

In this methodological study physical activity of the pet dogs was measured by an activity monitor attached to a collar on a 24-hour basis for 14 days. The dogs wore the activity monitor for 24 hours continuously for a 7-day period. For the other seven days the collar was taken off in two periods per day, one 30 min period and one 2-hour period. The order of the days and time of interruption of measurements was a convenience decision of the dog owners.

4.2 Study population

In this thesis three study population of dogs are presented; dogs with diagnostic imaging confirmed OA (study 1), clinically healthy dogs (study 2) and dogs with owner reported health status (study 3). Overview of the study populations can be seen in Table 1.

4.2.1 Study 1

Privately owned dogs of any sex or breed and with a clinical diagnosis of OA were eligible for inclusion. Recruitment was conducted via social media (Facebook), email postings, advertisements in local magazines, and through veterinary practices in the surrounding area. Dogs were included if they were older than one year, exhibited lameness of grade 1–3 at trot on a 5-point orthopaedic lameness scale at the baseline clinical examination, and had a history of chronic musculoskeletal pain (> 3 months) previously diagnosed by a veterinarian (Duerr 2019; Møller *et al.* 2021). In cases of multi-limb OA, the most severely affected limb was designated as the “lame limb” and used for study assessments. Exclusion criteria were sensory deficits in the treatment area (assessed by clinical examination), presence of metallic implants that could interfere with treatment, pacemaker, tumour in the treatment area, or known intolerance to NSAIDs. Final inclusion and determination of the most severely affected limb were based on the baseline clinical examination in combination with objective gait assessments performed using a pressure-sensitive walkway on day one of the study. If the lameness and the clinical examination did not match the dog was excluded.

4.2.2 Study 2

The same study population as in study 1 was used together with a convenience sample of clinically healthy privately owned dogs that were recruited as a comparison group for nighttime physical activity recordings (subjects participating in a study by Smedberg *et al.*, (2024)). Health status was confirmed through medical history and orthopaedic examination. Dogs were eligible for inclusion if they were older than one year and physically fit to participate in the lowest level of an exercise programme. Exclusion criteria included any known systemic or orthopaedic disease that could affect physical ability, as well as behavioural or mental conditions that could interfere with safe handling by research personnel (Smedberg *et al.* 2024).

4.2.3 Study 3

Privately owned dogs were recruited through convenience sampling. Eligibility required that dogs lived as a pet dog in Sweden. Dogs were excluded if they were too small to comfortably wear a collar fitted with two activity monitors (e.g. miniature breeds such as Chihuahuas). Dogs were also excluded if they became ill and needed to be confined in a veterinary clinic. Health status of the dogs varied but they were all living in a private home.

4.3 Methods: Outcome measures for clinical findings and behavioural changes

As pain cannot be directly assessed, indirect assessment is conducted by measuring different types of physical dysfunction. In the present thesis, indirect pain assessment was conducted by clinical examination, pain questionnaires, kinetic and kinematic techniques and physical activity monitoring. Detailed description of the study 1-3 can be found in papers I-III.

4.3.1 Clinical examination (Study 1 and 2)

In study 1, clinical examinations were conducted by the same veterinarian following a standardized orthopaedic protocol. Each joint was assessed for pain, crepitation, effusion and thickening, and the dog was assessed for lameness. The spine was palpated for pain reactions across five anatomical regions: cervical, thoracic, thoracolumbar, lumbar, and lumbosacral. Pain

was scored on an ordinal scale from 0 to 4 (0 = no resentment; 4 = attempts to escape or prevent manipulation). Crepitation, effusion, and joint thickening were graded on a 0–2 scale (0 = none; 2 = marked/severe). Lameness was evaluated on a 0–5 scale (0 = sound; 1 = mild lameness with minimal head/pelvic movements, 2 = moderate lameness with normal stride length and partial weight bearing, 3 = moderate lameness with reduced stride length and partial weight bearing, 4 = severe lameness with minimal use of limb, 5 = non-weight bearing lameness) (Møller *et al.* 2021; Carr *et al.* 2023).

In study 2, each dog underwent a clinical examination and a movement assessment prior to data collection. The findings were documented, and the orthopaedic assessment was graded using a binary scale: "with remarks" or "without remarks".

4.3.2 Pain questionnaires (Study 1)

Pain assessment was performed using two validated owner-reported questionnaires: the Canine Brief Pain Inventory (CBPI) and the Helsinki Chronic Pain Index (HCPI) (Brown *et al.* 2007; Hielm-Björkman *et al.* 2009b; Nemery *et al.* 2016; Essner *et al.* 2017). The paper questionnaires were answered by the same individual before and after each treatment period. The language of the questionnaire was either Swedish or English, which one was used was based on the respondent's preference. The respondent was blinded to treatment order and was not involved in the treatments.

The CBPI consists of 11 items. Questions 1–4 assess pain severity on a 0–10 numeric scale, while questions 5–10 evaluate pain interference with physical function on the same scale. Higher scores indicate greater pain or impairment. Question 11 addresses quality of life on a 5-point categorical scale ranging from "poor" to "excellent." The mean of questions 1–4 constitutes the Pain Severity Score (PSS), and the mean of questions 5–10 forms the Pain Interference Score (PIS) (Brown *et al.* 2007; Brown *et al.* 2008). The HCPI includes 11 items related to physical function, each rated on a 5-point descriptive scale, resulting in a maximum total score of 44 (Hielm-Björkman *et al.* 2009b). Higher scores indicate more severe pain.

4.4 Outcome measures for gait impairments and physical activity

4.4.1 Pressure sensitive mat (Study 1)

Kinetic data were collected using a pressure-sensitive mat, Walkway High Resolution HRV4 (Tekscan Inc., Norwood, Massachusetts, United States of America), in combination with the corresponding software, Walkway Research Beta (Tekscan Inc., Norwood, Massachusetts, United States of America). The mat was regularly calibrated, and the measurements were normalised to each dog's body weight. The mat (195 × 45 × 0.57 cm) was placed in a corridor adjacent to a wall and covered with a 1 mm-thick plastic overlay. Video recordings were obtained simultaneously from both lateral and craniocaudal perspectives. Dogs were trotted across the mat at an individually determined pace. The following gait parameters were recorded: stance time, swing time, stride time, stride length, peak vertical force, impulse, and symmetry indices based on peak vertical force. The dog's behaviour on the mat was subjectively evaluated by the examiner and documented in the data collection protocol.

4.4.2 Activity monitor (Study 1, 2 and 3)

Physical activity was continuously recorded using an ActiGraph GT3X accelerometer (ActiGraph, Pensacola, Florida, USA), set to a sampling frequency of 100 Hz and with a dynamic range of ± 6 g. For study 1 and 2 the idle sleep mode (i.e. a battery saving feature) was activated and for study 3 the idle sleep mode was deactivated. The device was attached to a dedicated collar and worn by the dogs 24 hours per day, secured with cable ties and tape, and the collar was only removed during data downloads or when the monitor could be submerged in water (Anastasia *et al.*, 2016). In Study 3, dog owners were additionally instructed to document in a logbook each occasion when the monitor was removed. These logbooks were collected after completion of the measurement period.

4.5 Treatment

4.5.1 Transcutaneous Electrical Nerve Stimulation (Study 1)

Transcutaneous electrical nerve stimulation (TENS) was performed using a Cefar TENS Chattanooga (Enovis, Lewisville, Texas, United States of America) device with 3 × 5 cm CEFAR carbon fibre electrodes (Enovis, Lewisville, Texas, United States of America). The treatment area was clipped, cleaned, and coated with conductive gel prior to electrode placement. Electrodes were applied to intact skin at least 4 cm apart, positioned at the level of the shoulder, elbow, spine, or thigh – depending on the involved joint

Dogs received one treatment per day for ten consecutive days, each treatment lasting 45 minutes and administered by their owners. The TENS settings consisted of asymmetrical biphasic pulses with constant current at a frequency of 80 Hz and a pulse duration of 180 microseconds. Stimulation intensity was gradually increased until a sensory response such as an avoidance reaction was observed. If signs of discomfort occurred, the amplitude was reduced. Intensity was adjusted during the session to maintain an increased sensory stimulus. In the pilot study, treatments were administered for seven consecutive days and performed by animal health personnel.

4.5.2 Placebo (Study 1)

The placebo intervention followed the same procedure as the TENS treatment, including the positioning of the electrodes and 45 min duration of the placements, with the exception that the TENS device was not activated.

4.5.3 NSAID (Study 1)

Following completion of the phase 1 (Figure 1) and a minimum seven-day washout period, dogs eligible for NSAID treatment received firocoxib (5 mg/kg once daily) administered orally for seven consecutive days according to the manufacturer’s guidelines (FASS vet 2024).

4.6 Data management

Data from clinical examinations, pain questionnaires and logbooks for physical activity were transferred from paper to digital format by a researcher blinded to treatment order. Data were organised and analysed in Excel (Microsoft Excel 2016, Microsoft Corporation) and R (version 4.1.2 (2021-11-01)—"Bird Hippie" and all versions in between to RStudio version 2025.09.1+401 (2025-09-23) "Cucumberleaf Sunflower", R Core Team). Samples were double checked to verify that the data transfer was correct.

4.6.1 Clinical examination (Study 1)

Clinical data were grouped by limb: treated (TL), contralateral (CL), ipsilateral (IL), and diagonal (DL), and compared pre- and post-treatment.

4.6.2 Pain questionnaire (Study 1)

Canine Brief Pain Inventory data were analysed per item, as total scores, and as Pain Severity Score (PSS) and Pain Interference Score (PIS). Helsinki Chronic Pain Index data were analysed per item and as total score.

4.6.3 Pressure sensitive mat (Study 1)

For all gait parameters, an average value based on two passages over the mat (minimum four stride cycles/sixteen stances) were used, if two passages were not available, one passage was included. The criteria for an included passage were the dog's correct behaviour over the mat, the number of step cycles (minimum of two step cycles/eight stances), and velocity between 1.5 – 2.2 m/s or an individual variance of < 0.5m/s. If more than two passages met the inclusion criteria, the earliest passage was used.

Three different symmetry indices (SIs) were used; either body quadrants, body sides, or body halves were compared.

SIs were calculated from PVF (%BW) by using the following equations:

$$SI_{limb} = \frac{lame\ limb}{contraleteral\ sound\ limb}$$

$$SI_{sagittal} = \frac{front\ and\ hindlimb\ from\ lame\ body\ side}{front\ and\ hindlimb\ from\ sound\ body\ side}$$

$$SI_{transversefront} = \frac{front\ limbs\ from\ lame\ body\ half}{front\ limbs\ from\ sound\ body\ half}$$

$$SI_{transversehind} = \frac{hindlimbs\ from\ lame\ body\ half}{hindlimbs\ from\ sound\ body\ half}$$

Differences in gait parameter values before and after treatment were calculated for TENS, placebo, and NSAID interventions. For TENS and placebo, comparisons were made both after a single treatment session and following the final day of the treatment period. For NSAID, comparisons were performed between before and after the last day of treatment.

4.6.4 Physical activity monitor (Study 1, 2 and 3)

Study 1 and 2

Physical activity data were downloaded with the software ActiLife (version 6.13.6; ActiGraph, Pensacola, FL, USA) as both raw and filtered files. Data management was performed using two approaches: (i) filtered files exported from ActiLife software, aggregated into 60-second epochs, and (ii) raw accelerometer files processed in R using the Euclidean Norm Minus One (ENMO) filter where gravitational force was removed and negative values is truncated to zero (van Hees *et al.* 2013).

All data were trimmed to full 24-hour periods starting at 22:00 and subsequently summarised into 60-second epochs. Counts per minute (CPM) were calculated for different time windows: (a) hourly values, (b) total 24-hour activity, (c) daytime (06:00–22:00), (d) nighttime (01:00–05:00), and (e) the full treatment period. Total CPM was expressed in three ways: total activity Act (ActiLife-filtered), vector magnitude (unfiltered), and total

activity ENMO (ENMO-filtered). Time spent in different CPM categories was used to describe physical activity intensity patterns (Table 1). These thresholds were defined in accordance with available scientific documentation: resting as lying still with subtle head or leg movements (Hoffman *et al.* 2020); sedentary as ventral or lateral recumbency; light activity as walking; moderate activity as trotting/jogging; and vigorous activity as faster movement in trot or gallop (proprietary filter of ActiLife) (Yam *et al.* 2011). In Hoffman *et al.* (2020) the proprietary filter of ActivityScope was used, and in Yam *et al.* (2011), the proprietary filter of ActiLife was used. Additional physical activity measures were derived from ENMO-filtered raw data. These included maximum and minimum activity across 2-, 5-, 15-, 30-, and 60-minute intervals within each 24-hour period as well as within daytime and nighttime periods (e.g., max2min and min2min, max5min and min5min and so on) (Karimjee *et al.* 2024). Mean CPM per minute and per interval was calculated to represent overall activity levels. The chosen activity measures were based on previously published work and represents different proprietary filters such as ActiLife and also open access filters such as ENMO (Yam *et al.* 2011; Ladha & Hoffman 2018a; Gruen *et al.* 2019; Hoffman *et al.* 2020; Karimjee *et al.* 2024).

For comparisons between ActiLife- and ENMO-derived outcomes, datasets were matched. Periods of zero vector magnitude (VM), attributed to the monitor's idle sleep mode, were interpreted as true inactivity, as any movement would exit sleep mode – consistent with previous findings (Yam *et al.* 2011). In the comparison of nighttime activity between healthy and osteoarthritic dogs, continuous zero activity lasting ≥ 60 minutes was coded as missing (Migueles *et al.* 2017).

Table 2. Example of activity intensities used for physical activity data.

ENMO activity intensities	ActiLife activity intensities	CPM intervall
ENMO Resting100		0-100
ENMO Resting400	Act Resting	0-400
ENMO Sedentary0	Act Sedentary0	0-1352
ENMO Sedentary400	Act Sedentary400	400-1352
ENMO Light		1352-2352
ENMO LightModerate	Act LightModerate	1352-5695
ENMO Moderate		2352-5695
ENMO ModerateVigorous	Act ModerateVigorous	> 2352
ENMO Vigorous	Act Vigorous	> 5695

CPM = Counts per minutes; ENMO = Euclidean Norm Minus One.

Study 3

Raw accelerometer data were downloaded from the activity monitors using ActiLife software (version 6.13.6; ActiGraph, Pensacola, FL, USA) and stored in .gt3x format. Data extraction and preprocessing were performed in R (RStudio version 2025.09.02 [2025-10-20], "Cucumberleaf Sunflower"; R Core Team) using the GGIR package and the readgt3x script set. Raw triaxial acceleration signals were transformed into the frequency domain using the Fast Fourier Transform (FFT). Power range, as well as time spent (minutes), were integrated into frequency bins comprising 0–0.5 Hz and consecutive 1-Hz intervals from 1 to 50 Hz, stratified into 24-hour periods. The cut-off defining a 24-hour period was set to 22:00.

For non-wear identification based on raw data, acceleration signals from each axis and the vector magnitude were summarised from seconds into 1-minute epochs. Processed data were exported as comma-separated value (.csv) files and compiled in Excel (version 2511, Build 16.0.19426.20218; Microsoft Corporation).

Non-wear time identification based on filtered data was performed using ActiLife (version 6.13.6; ActiGraph, Pensacola, FL, USA). Data were filtered using the standard ActiLife proprietary algorithms and converted into counts per minute (CPM) using 1-minute epochs. Five wear-time validation settings (i.e. non-wear time identification filters) were applied:

- Troiano algorithm, a minimum 60-consecutive minutes of zero CPM, with a spike tolerance threshold of 100 CPM for up to two

minutes and a requirement for consecutive epochs outside the activity threshold (Troiano *et al.* 2008);

- Choi algorithm, a minimum of 90-consecutive minutes of zero CPM, allowing up to a two-minute interval of non-zero CPM if the interruption is accompanied by 30 consecutive minutes of zero CPM either up or downstream (Choi *et al.* 2011; Keadle *et al.* 2014);
- 10_0_0, a minimum of ten consecutive minutes of zero CPM;
- 20_0_0, a minimum of 20 consecutive minutes of zero CPM and
- 60_0_0, a minimum of 60 consecutive minutes of zero CPM.

The resulting datasets were exported as .csv files and compiled in Microsoft Excel (version 2511, Build 16.0.19426.20218).

Paper-based logbooks were manually transcribed into Excel (.xlsx) format and compiled in Microsoft Excel (version 2511, Build 16.0.19426.20218). A wintertime correction of –1 hour was applied to data recorded from 26 October onwards; this correction affected three dogs. Non-wear time periods were excluded when wear status was uncertain, which occurred for two dogs. To minimise potential bias related to monitor handling, non-wear intervals were truncated by 5 minutes at both the start and end, and these periods were classified as transition time rather than non-wear, thereby reducing the influence of movement occurring during monitor removal and reattachment.

4.7 Statistical analysis

A statistical significance level of $p < 0.05$ was applied to all analyses, except where adjustments for multiple comparisons were necessary. In Study 1, Bonferoni-corrected thresholds were applied for the pain questionnaire data, with significance set at $p < 0.025$ for the HCPI and $p < 0.0125$ for the CBPI. For the gait parameters in Study 1, Bonferoni-corrected significance thresholds were set at $p < 0{,}003$ for stance time, swing time, stride time and stride length, $p < 0{,}006$ for PVF and VI and $p < 0{,}0125$ for SIs. For physical activity data in Study 1, Bonferoni-corrected significance thresholds were set at $p < 0.0024$ for ENMO-filtered data and $p < 0.0071$ for ActiLife-filtered data. Data were analysed in Excel (Microsoft Excel 2016, Microsoft Corporation) and R (version 4.1.2 (2021-11-01)—"Bird Hippie" and all

versions in between to RStudio version 2025.09.1+401 (2025-09-23) "Cucumberleaf Sunflower", R Core Team).

4.7.1 Clinical examination (Study 1)

Clinical examination data collected before and after each intervention were summarised descriptively.

4.7.2 Pain questionnaire (Study 1)

Pain questionnaire scores were analysed using a linear mixed-effects model with treatment and treatment order as fixed effects and dog as a random intercept. An ANOVA was performed on the fitted model, and estimated marginal means for treatment were derived. The difference in scores before and after NSAID were evaluated using a one-sample t-test to determine whether the mean change differed from zero.

4.7.3 Pressure sensitive mat (Study 1)

Pressure sensitive mat data were analysed using a linear mixed-effects model adapted for a 2 × 2 crossover design in the TENS and placebo interventions. Continuous outcomes included stance time, swing time, stride time, stride length, PVF (%BW), VI (%BW*s) and symmetry indices. For the NSAID intervention, linear regression models were applied to the same gait parameters for the pre- and post-interventions values. In the mixed-effects model, dog was included as a random effect, while age, sex, and body weight were included as fixed effects across all parameters. In addition, simultaneous NSAID treatment and velocity were specified as fixed effects for stance time, swing time, stride time and stride length. Residuals met the assumption of normality.

4.7.4 Physical activity data (Study 1, 2 and 3)

Study 1

Physical activity data were analysed using linear mixed-effects models (function lme, nlme package), with fixed effects for treatment, day (factor), their interaction, weekday versus weekend and concurrent NSAID use. Random intercepts were fitted for each animal-treatment combination and a continuous autoregressive correlation structure (CAR(1)) was included to

account for within-subject autocorrelation. Model assumptions were assessed through residual diagnostics. Fixed effects were tested using Type III ANOVA (lmerTest) and post hoc comparisons were performed using estimated marginal means (EMMs; emmeans package).

Study 2

Night-time activity data were analysed using linear models, with age and body weight included as covariates. Model significance was assessed with ANOVA.

Study 3

All statistical analyses were performed in R (RStudio version 2025.09.02 [2025-10-20], "Cucumberleaf Sunflower"; R Core Team). Data were excluded if they fell outside the predefined study period or if the wear/non-wear status was uncertain.

Signal frequency analysis

Four frequency outcome categories were analysed:

- power distribution across the full frequency range (0–50 Hz),
- power distribution across the active frequency range (0.5–50 Hz),
- time distribution (minutes) across the full frequency range (0–50 Hz), and
- time distribution (minutes) across the active frequency range (0.5–50 Hz).

These outcomes were summarised descriptively as proportions and visualised using histograms generated with the dplyr and ggplot2 packages. For the active frequency range (0.5–50 Hz), the 97.5th percentile of both aggregated and individual-level distributions of power and time was calculated, and the corresponding frequency bin was identified. The range of values across individual subjects was also recorded.

For each of the four frequency-domain outcome categories, a linear regression model was fitted using the frequency corresponding to the 97.5th percentile as the dependent variable. Body weight, height, age, and sex were included as covariates. Models were fitted using the lm function, and regression coefficients with associated statistics were extracted for further evaluation. Statistical significance was defined as $p < 0.05$.

Non-wear identification using raw data

For non-wear detection based on raw acceleration data, variability in each of the three axes (X, Y, and Z) and the vector magnitude (VM) during each confirmed non-wear periods was quantified as the standard deviation (SD) using the dplyr package. The 97.5th percentile of the SD values, excluding outliers, was calculated and used to define a cut-off threshold for non-wear classification.

Wear time data were segmented into periods of 30, 60, and 120 consecutive minutes, and the derived non-wear cut-off was applied to these periods using the data.table package.

Non-wear identification using filtered data

For the filtered data, aggregated as counts per minute (CPM) in 1-minute epochs, non-wear classification results generated by the ActiLife wear-time validation algorithm for each of the five filters were compared with logbook-confirmed non-wear periods using the dplyr package in R. The non-wear classification results were restricted to the study time for each dog. To be classified as a match, non-wear periods identified by ActiLife and the logbooks were required to overlap by at least 75%. Sensitivity was calculated based on the detected non-wear periods in ActiLife and the documented non-wear periods from the logbook.

5. Main results

5.1 Study population and data overview

5.1.1 Study 1

Thirty-eight dogs were assessed for eligibility; 26 met inclusion criteria and were enrolled. Of these, five were excluded due to a lack of radiographic diagnosis of their OA, two were lost to follow-up, and data from two were unusable due to technical issues. Two dogs were withdrawn post-enrolment – one due to a previously undetected cruciate injury and one due to the owner's illness. One dog sustained a traumatic elbow fracture before phase 2 and was only included in the phase 1 analysis. Another was withdrawn during NSAID treatment in phase 2 due to suspected adverse effects. Two dogs did not participate in phase 2 because they were on NSAID medication in phase 1 due to ethical consideration regarding pain management. One dog participated in the pilot study, receiving seven days of treatment administered by animal health personnel. Complete data were available for 15 dogs for phase 1 (TENS/placebo) and 11 dogs for phase 2 (NSAIDs) and were included in the final analysis.

The descriptive data of the 15 remaining dogs are presented in Table 2. The mean age was 6.8 years (SD ± 2.0 years). The mean weight was 22.7 kg (SD ± 9.5kg). There were five mixed breeds; three Labrador retrievers; and one each of Australian Cattle Dog, Beagle, Border Collie, Flatcoated Retriever, Malinois, medium-sized Poodle and Staffordshire Bull Terrier.

Table 3. Descriptive characteristics of the dogs with OA included in study 1.

Dog No/ ID	Age (Years)	Breed	Weight (kg)	Diagnosis and electrode placement	Lameness in trot at inclusion (0-5)	NSAID treatment through the whole study
I*	8	Beagle	13	OA stifle LH. Cruciate ligament injury LH. Placement LH thigh level.	1º LH	No
II	8	Labrador Retriever	31	OA metacarpal joint phalanx 4 and 5 LF, phalanx 5 RF and elbow LF. Placement LF elbow level.	2º LF	Yes
III	6.5	Poodle, medium size	7	OA elbow LF. Placement LF elbow level.	1º LF	No
IV	8	Malinois	27	Moderate OA shoulder LF. Mild OA shoulder RF. Disc herniation L7S1. Placement LF shoulder level.	1º LF	No
V	3	Mixed breed	15	OA stifle LH. Placement LH thigh level.	1º LH	No
VI	8	Mixed breed	41	OA stifle BH. Placement RH thigh level.	2º RH	No
VII	6	Mixed breed	18	OA hip BH. Placement LH thigh level.	1º LH	No
VIII	8	Border Collie	16	OA lumbar spine. OA shoulder and phalanx BF. Placement lumbar spine bilateral.	1º RH	No
IX	8	Labrador Retriever	37	OA carpus and phalanx BF. OA hips BH. Placement RF elbow level.	3º RF	Yes
X	5	Mixed breed	17	OA elbows and phalanx BF. Placement LF elbow level.	3º LF	No
XI	7	Flatcoated Retriever	26	OA carpus RF. Lameness LF. Placement LF elbow level.	1º LF	No

XII	2	Labrador Retriever	30	Fragmentation of processus coronoideus medialis elbow LF. OA elbow LF. Placement LF elbow level.	1º LF	No
XIII	7	Staffordshire Bull Terrier	13	OA stifle LH. Operated cruciate ligament injury BH. Elbow dysplasia grade 2 BF. Hip dysplasia BH. Placement LF elbow level.	1º LF	No
XIV	9	Mixed breed	30	OA hips BH. Placement LH thigh level.	1º LH	No
XV	8	Australian Cattle Dog	20	OA tarsus LH. Placement LH thigh level.	1º LH	No

No/ID= number of each dog as identification; BF = both forelimbs; BH = both hindlimbs; LF = left forelimb; LH = left hindlimb; L7S1 = junction between the seventh lumbar vertebra and the sacrum; OA = osteoarthritis; RF = right forelimb; RH = right hindlimb. *one dog of the 15 dogs had a 7 day treatment instead of 10 day treatment.

All dogs exhibited signs of pain at the baseline visit based on clinical examination and assessment using the pain questionnaire (Table 3). Joint effusion was present on clinical examination in two dogs at inclusion, one dog had missing values so 14 dogs were included in the assessment. One dog did not undergo a baseline pain questionnaire assessment; therefore, data from 14 dogs were included in the questionnaire analysis.

Table 4. Scores of the pain questionnaires at baseline assessment, presented as estimated marginal means and standard error.

Question	CBPI (EMMs ± SE)	CBPI (N)	HCPI (EMMs ± SE)	HCPI (N)
1	4.64 ± 0.59	14	3.14 ± 0.26	14
2	1.36 ± 0.59	14	3.43 ± 0.26	14
3	2.57 ± 0.59	14	3.29 ± 0.26	14
4	2.64 ± 0.59	14	2.50 ± 0.26	14
5	2.86 ± 0.59	14	3.10 ± 0.27	12
6	2.26 ± 0.60	13	2.86 ± 0.26	14
7	3.07 ± 0.59	14	2.98 ± 0.26	13
8	2.29 ± 0.59	14	2.86 ± 0.26	14
9	3.00 ± 0.59	14	2.21 ± 0.26	13
10	2.50 ± 0.59	14	1.64 ± 0.26	14
11	2.29 ± 0.59	14	1.87 ± 0.27	13
Total score	30.90 ± 5.52	13	31.80 ± 1.71	10
PSS	2.80 ± 0.49	14		
PIS	2.66 ± 0.56	13		

CBPI=Canine Brief Pain Inventory; EMMs=estimated marginal means; HCPI= Helsinki Chronic Pain Index; N = number; PIS= Pain Interference Score average of questions 5-10 CBPI; PSS=Pain Severity Score average of questions 1-4 CBPI; SE=standard error; Total= total pain score.

Clinical examination

Clinical examination data were available for a total of 14 dogs (Table 4). Complete pre- and post-treatment datasets were obtained for 11 dogs for the TENS intervention and for seven dogs for the placebo intervention.

Pain questionnaires

For the CBPI, the number of dogs included varied by item and treatment. During the TENS treatment, 10 to 14 dogs were included per question or score. In the placebo treatment, 8 to 15 dogs were included, and during the

NSAID treatment, 5 to 8 dogs were included. For the HCPI, 8 to 14 dogs were included during the TENS treatment, 12 to 15 during the placebo treatment, and 6 to 8 during the NSAID treatment.

Pressure sensitive mat

The data were collected across 108 measurement occasions (visits to the facility). For 105 of these occasions, three trials per dog were included. On the remaining three occasions, only two trials (comprising a minimum of four step cycles or sixteen stances) were available due to incomplete recordings. The mean number of stances per trial across all dogs was 8.8 (range: 8–12), corresponding to approximately two step cycles. The same handler was used for 103 out of the 108 measurement occasions, and the handler was positioned on the same side of the dog in 104 out of 108 occasions. During each measurement occasion, the dogs trotted across the pressure-sensitive mat between 2 and 20 times (trials).

Physical activity monitor

For the ActiLife-filtered data, the number of 24-hour periods ranged from 92 to 116, representing 12 to 15 dogs. For the ENMO-filtered activity data, the number of included 24-hour periods per treatment ranged from 76 to 116, representing 9 to 14 dogs across treatments. Similar ranges were observed for the daytime data: ActiLife-filtered periods ranged from 92 to 116, with 12 to 15 dogs, while ENMO-filtered periods ranged from 76 to 116, with 9 to 14 dogs represented. For the nighttime data, the ActiLife-filtered dataset included 91 to 116 periods from 12 to 15 dogs across treatments, whereas the ENMO-filtered dataset included 76 to 115 periods from 9 to 14 dogs.

5.1.2 Study 2

In total, 30 dogs were included as healthy controls for the comparison of nighttime physical activity with those of the 15 dogs with OA as are described earlier. The mean age of the healthy dogs was 4.7 years (SD ± 2.5), and the mean body weight was 23.1 kg (SD ± 10.4). The cohort of healthy dogs consisted of three German Shepherds, two mixed-breed dogs, two Labrador Retrievers, two Shapendoes, two Flatcoated Retrievers, and two Lagotto Romagnolos. In addition, one dog of each of the following breeds was included: Siberian Husky, Tibetan Terrier, medium-sized Poodle, Småland Hound, Border Collie, Belgian Malinois, Kromfohrländer, Pumi,

Welsh Springer Spaniel, Staffordshire Terrier, Golden Retriever, Icelandic Sheepdog, Whippet, Bullmastiff, Hovawart, and Boxer.

Included in the analysis were 97 nights from OA dogs and 144 nights from healthy dogs.

5.1.3 Study 3

The study population comprised 11 dogs, including three mixed-breed dogs, two Labrador Retrievers, two Alpine Dachsbracke dogs, and one dog each of Fauve de Bretagne, Golden Retriever, Lagotto Romagnolo, and Rottweiler. The median body weight was 21.5 kg (range: 9 – 40 kg), the median age was 5 years (range: 1 – 11 years), and the median height at the withers was 46 cm (range: 34 – 60 cm).

Data from one dog were excluded due to technical difficulties related to the extraction of large .gt3x files in R. For the remaining dogs, a median of 9 monitoring days (range: 4 – 12 days) were included in the analyses. A total of 94 days were included from the whole cohort of dogs. Loss of data was primarily attributable to the same data-extraction limitations associated with large .gt3x files.

5.2 Results: Clinical findings and behavioural changes

5.2.1 Transcutaneous electrical nerve stimulation vs placebo

Clinical examination

In the treated limb, pain on palpation improved in 14% of joints following the placebo treatment and in 4% following TENS. Conversely, deterioration in pain on palpation was observed in 18% of joints after placebo and in 20% after TENS. See Table 5 for complete data.

Table 5. Proportion of change in clinical examination before and after transcutaneous electrical nerve stimulation treatment or placebo for all joints in each limb.

		Pain (%)		**Crepi-tation (%)**		**Effusion (%)**		**Thick-ening (%)**		**Lame walk (%)**		**Lame trot (%)**	
		P	T	P	T	P	T	P	T	P	T	P	T
TL	+	14	4	2	2	0	2	0	2	14	0	29	29
	=	68	77	95	96	98	96	90	92	86	71	71	57
	-	18	20	4	2	2	2	10	6	0	29	0	14
CL	+	7	5	2	0	0	0	0	2	0	0	0	0
	=	71	86	96	95	100	100	98	96	100	100	100	100
	-	13	7	2	5	0	0	2	2	0	0	0	0
IL	+	9	5	2	2	0	0	2	0	0	0	0	0
	=	79	88	98	96	100	98	98	98	100	100	100	100
	-	13	7	0	2	0	2	0	2	0	0	0	0
DL	+	9	5	4	0	0	0	2	0	0	0	0	0
	=	82	86	96	98	100	98	98	98	100	100	100	100
	-	9	9	0	2	0	2	0	2	0	0	0	0

CL= Contralateral limb; DL=Diagonal limb; IL=Ipsilateral limb; P= Placebo; T= Transcutaneous electrical nerve stimulation treatment; TL= Treated limb; + = Improved; = = Unaltered; - = Deteriorated. Transcutaneous electrical nerve stimulation, n =11 dogs. Placebo, n = 7 dogs.

Pain questionnaires

No significant differences were observed in either the total score or single question scores of the HCPI when comparing TENS with placebo. Similarly, no significant differences were found in the CBPI total scores, single question scores, Pain Severity Score (PSS), or Pain Interference Score (PIS) between the two treatments. See Table 6 for complete data.

Table 6. Difference in pain score before and after treatment with transcutaneous electrical nerve stimulation or placebo.

Questionnaire	Section	TENS difference in scores (EMMs± SE)	Dogs (n)	Placebo difference in scores (EMMs± SE)	Dogs (n)	P-value
HCPI	Single	-0.038 ± 0.095	11-14	-0.004 ± 0.091	14-15	0.71
HCPI	Total	0.954 ± 1.883	8	-0.583 ± 1.458	12	0.78
CBPI	Single	0.102 ± 0.278	11-14	0.348 ± 0.274	10-15	0.16
CBPI	PSS	0.583 ± 1.627	13	0.348 ± 1.561	14	0.91
CBPI	PIS	-0.909 ± 3.500	10	1.644 ± 3.366	10	0.88
CBPI	Total	1.147 ± 5.391	10	-2.620 ± 5.965	8	0.66

HCPI= Helsinki Chronic Pain Index; CBPI=Canine Brief Pain Inventory; TENS= Transcutaneous electrical nerve stimulation; Single= single questions score; Total= total pain score; PIS= Pain Interference Score question 5-10; points = score points from the pain questionnaires; PSS=Pain Severity Score question 1-4; EMMs=estimated marginal means; SE=standard error. Bonferoni corrected P-value for HCPI, significance $p > 0.025$. Bonferoni corrected P-value for CBPI, significance $p > 0.0125$.

5.2.2 NSAID intervention

Pain questionnaires

No significant differences were observed in either the total score or single question scores of the HCPI when comparing before and after NSAID. Similarly, no significant differences were found in the CBPI total scores, single scores, Pain Severity Score (PSS) or Pain Interference Score (PIS) before and after NSAID. See Table 7 for complete data.

Table 7. Mean values and 95% confidence interval for the difference in pain questionnaire scores before and after NSAID treatment.

Questionnaire	Section	Difference (score) mean	95% CI	P-value	Dogs (n)
HCPI	Single	-0.036	-0.215 - 0.144	0.70	7-8
HCPI	Total	-0.050	-5.366 – 4.366	0.80	6
CBPI	Single	0.453	0.010 – 0.897	0.05	5-8
CBPI	PSS	3.875	-1.624 – 9.374	0.14	8
CBPI	PIS	0.800	-10.695 – 12.295	0.86	5
CBPI	Total	3.200	- 19.088 – 5.488	0.71	5

HCPI= Helsinki Chronic Pain Index; CBPI=Canine Brief Pain Inventory; PIS= Pain Interference Score question 5-10; points = score points from the pain questionnaires; PSS=Pain Severity Score question 1-4; Single= single questions; Total= total pain score; n=number. Bonferoni corrected P-value for HCPI, significance $p > 0.025$. Bonferoni corrected P-value for CBPI, significance $p > 0.0125$.

5.3 Results: Gait impairments and physical activity

5.3.1 Transcutaneous electrical nerve stimulation vs placebo

Gait parameters

No significant differences were observed between the TENS and placebo treatments for stance time ($p = 0.14 – 0.98$), swing time ($p = 0.07 – 0.86$), stride time ($p = 0.06 – 0.97$), stride length ($p = 0.06 – 0.90$), peak vertical force (% BW) ($p = 0.15 – 0.82$) or vertical impulse (% BW*sec) ($p = 0.26 – 0.99$) in any of the limbs. Bonferoni-corrected p-values were applied: $p < 0.003$ for stance time, swing time, stride time and stride length; $p < 0.006$ for peak vertical force and vertical impulse. Values for PVF and VI can be seen in Table 8.

Table 8. Mean values, number of dogs and p-value for peak vertical force (% BW) and vertical impulse (% BW*sec), before, after a single treatment and after multiple treatments of either transcutaneous electrical nerve stimulation or placebo.

Parameter	Leg	Time	TENS (Mean ± SD)	Placebo (Mean ± SD)	P-value
Peak vertical force (%BW)	Lame	Before	61.15 ± 16.48	62.08 ± 16.56	
		After single	60.47 ± 17.37	58.94 ± 12.03	0.57
		After multiple	62.16 ± 17.73	61.31 ± 17.61	0.70
	Contralateral	Before	71.47 ± 20.97	72.57 ± 20.68	
		After single	68.87 ± 20.03	68.98 ± 15.19	0.79
		After multiple	73.00 ± 20.99	69.49 ± 20.55	0.40
	Ipsilateral	Before	67.33 ± 22.68	69.05 ± 22.84	
		After single	67.60 ± 23.60	69.48 ± 28.22	0.81
		After multiple	72.03 ± 31.30	66.89 ± 22.89	0.26
	Diagonal	Before	68.15 ± 22.52	70.85 ± 23.43	
		After single	67.55 ± 23.25	69.40 ± 28.90	0.82
		After multiple	73.53 ± 30.14	67.84 ± 25.56	0.15
Vertical impulse (%BW*sec)	Lame	Before	7.16 ± 2.70	7.60 ± 3.19	
		After single	7.14 ± 2.71	7.00 ± 2.63	0.72
		After multiple	7.36 ± 2.87	7.09 ± 2.74	0.75
	Contralateral	Before	8.49 ± 3.44	8.90 ± 3.86	
		After single	8.26 ± 3.04	8.24 ± 3.24	0.88
		After multiple	8.89 ± 3.34	8.10 ± 3.27	0.28
	Ipsilateral	Before	7.59 ± 3.16	7.89 ± 3.26	
		After single	7.66 ± 3.20	7.67 ± 3.43	0.97
		After multiple	8.31 ± 4.87	7.36 ± 3.03	0.33
	Diagonal	Before	7.76 ± 3.08	8.18 ± 3.14	
		After single	7.79 ± 3.24	7.76 ± 3.38	0.99
		After multiple	8.54 ± 4.76	7.54 ± 3.55	0.26

TENS= transcutaneous electrical nerve stimulation; SD = standard deviation; N= number of dogs; Sec = seconds; Cm = centimetre; %BW = percentage of body weight; Single = measurement after a single treatment; Multiple = measurement after 10 (7) treatments; *= significant p-value. Bonferoni corrected P-value, significance p < 0,006. All analyses were based on 15 dogs.

No significant differences in the SIs (p = 0.21 – 0.98) were observed between the TENS and placebo treatments, either when analysed for single treatment or for multiple treatments (Table 9). Bonferoni-corrected p-values was applied, $p < 0.0125$ was considered significant.

Table 9. Mean values, number of dogs and p-value for symmetry indices of peak vertical force (%BW) before, after a single treatment and after multiple treatments of either transcutaneous electrical nerve stimulation or placebo.

Parameter	Time	TENS (Mean±SD)	Placebo (Mean±SD)	P-value	N
SI limb	Before	0.87 ± 0.11	0.87 ± 0.11		15
Peak vertical force	After single	0.89 ± 0.11	0.86 ± 0.11	0.38	15
(%BW)	After multiple	0.86 ± 0.12	0.90 ± 0.11	0.21	15
SI sagittal	Before	0.92 ± 0.09	0.92 ± 0.09		15
Peak vertical force	After single	0.93 ± 0.09	0.93 ± 0.09	0.96	15
(%BW)	After multiple	0.91 ± 0.10	0.94 ± 0.09	0.22	15
SI transversefront	Before	1.64 ± 0.21	1.64 ± 0.24		8
Peak vertical force	After single	1.61 ± 0.23	1.63 ±0.24	0.43	8
(%BW)	After multiple	1.61 ± 0.19	1.61 ± 0.27	0.98	8
SI transversehind	Before	0.57 ± 0.06	0.56 ± 0.07		7
Peak vertical force	After single	0.58 ± 0.06	0.56 ± 0.07	0.52	7
(%BW)	After multiple	0.56 ± 0.06	0.57 ± 0.08	0.56	7

TENS= transcutaneous electrical nerve stimulation; SD = standard deviation; N= number of dogs; %BW = percentage of body weight; SI=symmetry index; SIlimb = lame limb /sound contralateral limb; SIsagittal = front- and hindlimb lame side/front- and hindlimb sound side; SItransversefront= lame front limbs/sound hindlimbs; SItransversehind = lame hindlimbs/sound front limbs; Single = measurement after a single treatment; Multiple = measurement after 10 (7) treatments; *= significant p-value. Bonferoni corrected P-value, significance p < 0,0125.

Physical activity

For the physical activity data per whole treatment period, no significant differences in physical activity were detected between the TENS and placebo treatments across any of the evaluated physical activity measures. In the ENMO-filtered dataset, the number of weekend days was identified as a significant covariate in the model for the min2min activity measure ($p = 0.001$).

For the physical activity data per 24 hours, physical activity did not differ significantly between the TENS and placebo treatments. In the ENMO-filtered dataset, the number of weekend days was a significant covariate in the models for the activity measures ModerateVigorous ($p = 0.002$), max15min ($p < 0.001$), and max30min ($p < 0.001$).

For the physical activity data per daytime and nighttime, no significant differences were observed between TENS and placebo during either daytime or nighttime. As no values for vigorous physical activity (ENMO) were

recorded at night in any treatment condition, vigorous physical activity was excluded from the nighttime analysis.

5.3.2 NSAID intervention

Gait parameters

No significant differences were observed in stance time (p = 0.06 – 0.66), swing time (p = 0.33 – 0.80), stride time (p = 0.42 – 0.78), stride length (p = 0.66 – 0.96), peak vertical force (%BW) (p = 0.07 – 0.33) or vertical impulse (%BW*sec) (p = 0.02 – 0.37) when comparing pre- and post-NSAID treatment. Bonferoni-corrected p-values were applied: $p < 0.003$ for stance time, swing time, stride time and stride length; $p < 0.006$ for peak vertical force and vertical impulse. Mean values and corresponding p-values for PVF and VI are presented in Table 10.

Table 10. Mean values, number of dogs and p-value for peak vertical force (% BW) and vertical impulse (% BW*sec) before and after treatment with NSAIDs.

Parameter	Leg	Before NSAID (Mean ± SD), N=9	After NSAID (Mean ± SD), N=10	P-value
Peak vertical force (%BW)	Lame	59.33 ± 21.59	55.40 ± 16.09	0.07
	Contralateral	68.03 ± 23.22	61.19 ± 16.90	0.08
	Ipsilateral	70.71 ±18.81	70.55 ± 26.86	0.33
	Diagonal	69.10 ± 18.99	69.85 ± 27.11	0.31
Impulse (%BW*sec)	Lame	6.38 ± 3.07	6.18 ± 2.74	0.28
	Contralateral	7.53 ± 2.80	6.85 ± 2.52	0.37
	Ipsilateral	7.80 ± 3.30	7.98 ± 3.96	0.02
	Diagonal	7.92 ± 3.46	8.05 ± 3.96	0.18

SD = standard deviation; N= number of dogs; Sec = seconds; Cm = centimetre; %BW = percentage of body weight; Single = measurement after a single treatment; Multiple = measurement after multiple treatments. *= significant p-value. Bonferoni corrected P-value for peak vertical force and vertical impulse, significance p < 0,006.

No significant differences were observed in any of the SIs (p = 0.05 – 0.98) between pre- and post-NSAID treatment. Bonferoni-corrected p-values was applied, $p < 0.0125$ was considered significant. Mean values and corresponding significance levels for the SIs are presented in Table 11.

Table 11. Mean values, number of dogs and p-value for symmetry indices of peak vertical force (%BW) before and after treatment with NSAIDs.

Parameter	Before NSAID (Mean ± SD)	N	After NSAID (Mean ± SD)	N	P-value
SI limb Peak vertical force (%BW)	0.87 ± 0.09	9	0.91 ± 0.07	10	0.07
SI sagittal Peak vertical force (%BW)	0.95 ± 0.06	9	0.96 ± 0.06	10	0.52
SI transversefront Peak vertical force (%BW)	1.67 ± 0.21	4	1.69 ± 0.31	4	0.05
SI transversehind Peak vertical force (%BW)	0.55 ± 0.06	5	0.57 ± 0.06	6	0.98

SD = standard deviation; N= number of dogs; %BW = percentage of body weight; SI=symmetry index; SIlimb = lame limb /sound contralateral limb; SIsagittal = front- and hindlimb lame side/front- and hindlimb sound side; SItransversefront= lame front limbs/sound hindlimbs; SItransversehind = lame hindlimbs/sound front limbs. *= significant p-value. Bonferoni corrected P-value, significance $p < 0{,}0125$.

Physical activity

For the physical activity data per whole treatment period, no significant differences in physical activity were observed between the baseline and NSAID treatment periods. All 24-hour periods were included in the analysis.

For the physical activity data per 24-hours, no significant differences were detected for any measure of physical activity between the baseline and NSAID periods.

For the physical activity data per daytime and nighttime, no significant differences in physical activity were observed between baseline and NSAID periods for either daytime or nighttime. In the ENMO-filtered data for nighttime, day 7 had a significant effect on treatment for the activity measures Sedentary0 ($p < 0.001$), Moderate, and ModerateVigorous ($p < 0.001$). As no values of vigorous physical activity (ENMO) were recorded during the night under any treatment condition, this activity measure was excluded from the nighttime analysis.

5.3.3 Comparison of nighttime physical activity

Nighttime activity (measurements between 01:00 to 05:00) at baseline differed significantly in some respects between healthy dogs and dogs with OA. In comparison to healthy dogs, the dogs with OA spent more time in the category Sedentary400 (EMMs ± SE: 13.65 ± 1.1 minutes) than healthy

dogs (9.71 ± 0.8 minutes; p = 0.037) and spent more time in short bouts of Vigourous activity (0.06 ± 0.02 minutes) than healthy dogs (-0.00 ± 0.01 minutes; p = 0.001).

5.4 Results: Activity monitor methodology

5.4.1 Comparison of two filtering procedures for physical activity data

The total activity values (CPM) were higher when filtered using ActiLife compared to ENMO (Tables 12 and 13). When examining activity intensities, ActiLife filtering resulted in lower values in the lower activity ranges (Resting and Sedentary0) and higher values in the moderate-to-high ranges (LightModerate, ModerateVigorous, and Vigorous) compared to ENMO filtering. Consequently, ActiLife-filtered data indicate that dogs spend less time in Resting and Sedentary0 states and more time in LightModerate, ModerateVigorous, and Vigorous activity levels compared with ENMO-filtered data.

Table 12. Results for different activity measures for whole treatment period, comparing filtering in ActiLife and ENMO, for transcutaneous electrical nerve stimulation and placebo.

Activity Intensity	Act TENS (EMMs±SE)	ENMO TENS (EMMs±SE)	Act Placebo (EMMs±SE)	ENMO Placebo (EMMs±SE)
Resting400 (min)	1089.71 ± 40.34	1298.24 ± 32.33	1089.94 ± 40.90	1302.28 ± 32.76
Sedentary0 (min)	1256.64 ± 27.90	1410.65 ± 13.95	1257.64 ± 28.27	1413.82 ± 14.10
Sedentary400 (min)	166.98 ± 22.48	112.61 ± 20.98	167.68 ± 22.85	111.87 ± 21.55
LightModerate (min)	173.33 ± 26.88	23.93 ± 13.47	173.08 ± 27.22	22.18 ± 13.57
ModerateVigorous (min)	118.18 ± 22.65	2.86 ± 1.98	121.30 ± 22.93	1.83 ± 2.10
Vigorous (min)	10.03 ± 4.14	0.04 ± 0.11	9.30 ± 4.19	0.07 ± 0.13
Total Activity (CPM)	754324.72 ± 106269.14	186319.00 ± 44126.23	761886.45 ± 107595.40	180570.80 ± 44656.63
Raw - Vector Magnitude (CPM)	2995742.29 ± 421625.46		3098294.57 ± 426558.19	

Act= ActiLife; CPM=counts per minutes; TENS= transcutaneous electrical nerve stimulation; EMMs= estimated marginal means; ENMO= Euclidean Norm Minus One; min=minutes; raw = unfiltered raw data; SE = standard error.

Table 13. Results for different activity measures for whole treatment period, comparing filtering in ActiLife and ENMO, for baseline and NSAID.

Activity Intensity	Act Baseline (EMMs±SE)	ENMO Baseline (EMMs±SE)	Act NSAID (EMMs±SE)	ENMO NSAID (EMMs±SE)
Resting400 (min)	1099.27 ± 51.12	1293.08 ± 28.28	1084.63 ± 52.01	1309.09 ± 28.77
Sedentary0 (min)	1260.06 ± 33.02	1410.97 ± 10.78	1266.38 ± 33.49	1414.82 ± 10.88
Sedentary400 (min)	160.83 ± 23.57	117.19 ± 23.28	180.63 ± 24.07	105.11 ± 23.80
LightModerate (min)	168.43 ± 31.23	21.42 ± 10.57	162.74 ± 31.63	22.18 ± 10.66
ModerateVigorous (min)	116.60 ± 25.05	2.91 ± 2.69	110.41 ± 25.35	3.63 ± 2.74
Vigorous (min)	11.67 ± 4.64	0.11 ± 0.17	11.00 ± 4.71	-0.04 ± 0.18
Total Activity (CPM)	746756.09 ± 128986.16	183266.01 ± 36691.13	740249.18 ± 131014.81	183633.97 ± 37147.68
Raw Vector Magnitude (CPM)	2967073.67 ± 381899.80		3199541.31 ± 392384.60	

Act= ActiLife; CPM=counts per minutes; EMMs= estimated marginal means; ENMO= Euclidean Norm Minus One; min=minutes; raw = unfiltered raw data; SE = standard error.

5.4.2 Determination of frequency range of pet dogs

Based on the total time of 94 days and total power of 8041961 g^2 included in the analysis, the largest proportion of both time and power was concentrated in the 0 Hz frequency bin, accounting for 83% of the total time and 57% of the total power. The highest time values were observed in the 1 – 5 Hz range, whereas the highest power values occurred in the 2 – 5 Hz range. Compared with power, the time distribution exhibited a sharper peak and steeper slope, indicating a narrower frequency range, while the power distribution was more broadly spread across higher frequencies. For the complete cohort of dogs, the frequency distribution of power and time within the active frequency range (0.5 – 50 Hz) is presented in Figure 6.

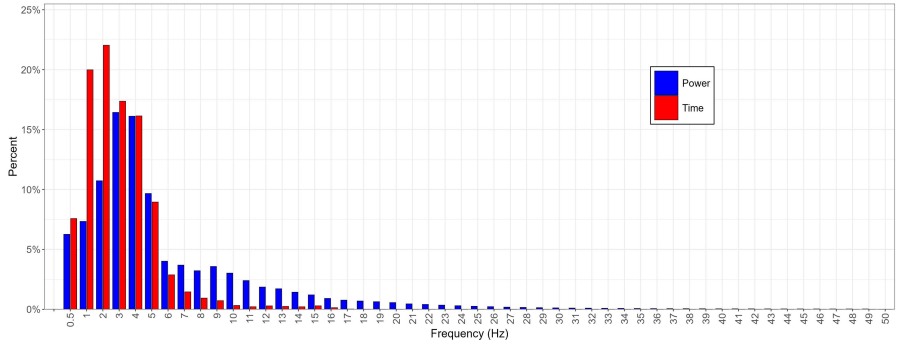

Figure 6. Frequency distribution of power and time for the active range (0.5 – 50 Hz) for the complete cohort summarised.

The frequency distribution of power and time differs between the individual dogs. Examples of the individual frequency distribution of three dogs with different characteristics can be seen in Figure 7.

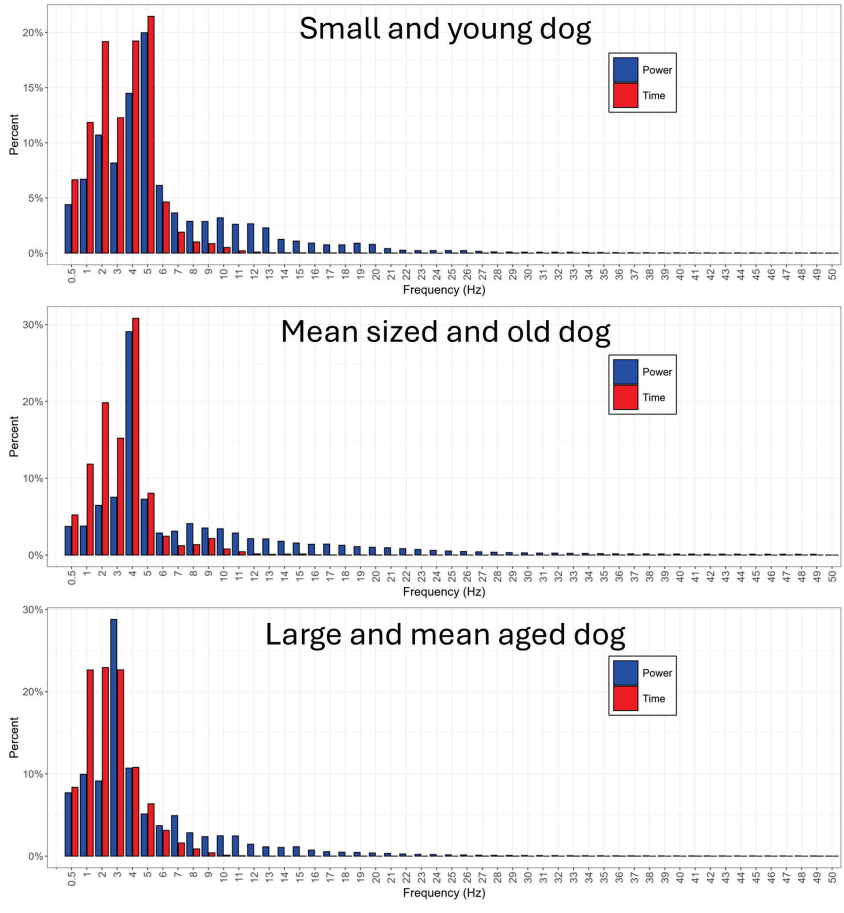

Figure 7. Comparison of individual frequency distribution of power and time for the active range (0.5 – 50 Hz) between three dogs with different characteristics.

For the complete cohort of dogs, analysis of the full frequency range (0 – 50 Hz) yielded a 97.5th percentile cut-off frequency of 17 Hz (range: 14 – 24 Hz) for power and 5 Hz (range: 3 – 5 Hz) for time. When considering the active frequency range (0.5 – 50 Hz), the corresponding cut-off frequencies were 23 Hz (range: 23 – 32 Hz) for power and 9 Hz (range: 7 – 16 Hz) for time. No statistically significant associations were observed between the 97.5th percentile cut-off frequencies and height, body weight, sex or age, indicating that these variables did not influence the frequency cut-off value.

5.4.3 Identification of non-wear time in raw data

The dataset comprised 242 non-wear periods recorded by the logbooks, of which 129 periods exceeded 60 minutes in duration. The total recording time amounted to 340,653 minutes, of which 29,398 minutes (9%) were classified as non-wear. During non-wear periods, the monitors were most frequently placed on a stationary surface (218 periods). Other non-wear placements (miscellaneous placement) included inside a car (12 periods), being moved (9 periods), held in the hand (2 periods), and carried in a bag (1 period).

After removal of outliers (VM and Z; n = 10, X and Y; n = 1), the median SD values for non-wear periods with the monitor placed on a stationary surface were 0.017 g for VM (range: 0.000 – 0.087), 0.228 g for the X-axis (range: 0.000 – 0.447), 0.233 g for the Y-axis (range: 0.000 – 0.718), and 0.157 g for the Z-axis (range: 0.770 – 0.518). The corresponding 97.5th percentile cut-off values were 0.079 g for VM, 0.407 g for the X-axis, 0.650 g for the Y-axis, and 0.460 g for the Z-axis.

When applying the VM SD cut-off value of 0.079 g to wear-time data segmented into consecutive periods of 30, 60, and 120 minutes, 5175 of 5242 periods (99%) were retained for the 30-minute periods, 2518 of 2550 periods (99%) for the 60-minute periods, and 1188 of 1202 periods (99%) for the 120-minute periods.

5.4.4 Comparison of non-wear time validation procedures

For the ActiLife comparison of five different non-wear detection filters the data set comprised of 186 non-wear periods, 97 of these periods were > 60 minutes and 89 periods were < 60 minutes. The total study time included was 254,080 minutes with 22,030 minutes of non-wear.

The sensitivity for non-wear detection for the different non-wear detection algorithms are as follows, 10_0_0 66% (122 periods detected), 20_0_0 66% (122 periods detected), 60_0_0 34% (64 periods detected), Choi 37% (68 periods detected) and Troiano 35% (66 periods detected). Further results of can be seen in Table 14.

Table 14. Sensitivity for five different non-wear identification procedures.

Filter	Period definition (n periods)	Sensitivity (n periods)
10_0_0	Total	66% (122)
	> 60 min	66% (64)
	≤ 60 min	65% (58)
20_0_0	Total	66% (122)
	> 60 min	66% (64)
	≤ 60 min	65% (58)
60_0_0	Total	34% (64)
	> 60 min	66% (64)
	≤ 60 min	0%
Choi	Total	37% (68)
	> 60 min	63% (61)
	≤ 60 min	0%
Troiano	Total	35% (66)
	> 60 min	68% (66)
	≤ 60 min	0%

Total non-wear periods = 186; > 60 min = 97; ≤ 60 min = 89. Non-wear = when the activity monitor is not attached to the dog. Sensitivity = proportion of detected non-wear periods.

6. Discussion

The subject of the present thesis was chosen due to a specific reason, the interest of improving the assessment and treatment of canine pain. The better tools there are to assess pain in dogs, the better diagnostics and possibility to follow the progress of treatment. Additionally, a more reliable way to assess the efficacy of new treatments – thus improving animal welfare. As previously described, there is no way to directly assess pain in animals. Therefore, the focus in this thesis has been on assessing signs of pain including clinical findings and behavioural changes, as well as signs of physical dysfunction, such as gait parameters and functional disabilities. Osteoarthritis constitutes a major source of chronic, degenerative pain and is consistently identified as one of the most important welfare-related conditions due to its long-term impact on mobility, comfort, and behaviour. Osteoarthritis was therefore chosen as the disease of interest, and TENS was investigated as a non-pharmacological complement to standard treatment, particularly for dogs that cannot tolerate pharmacological pain relief.

6.1 Study population, outcome measures in general and treatment protocol

The study population in study 1 consisted of privately-owned dogs with naturally occurring OA, representing the type of patients who would be candidates for TENS in a clinical setting. In the data analysis, only dogs with osteoarthritis confirmed by diagnostic imaging were included. Although additional dogs completed the study, the final sample size was smaller than the number of eligible dogs. While radiographs remain the standard for diagnosing OA in veterinary medicine, human OA diagnostics rely increasingly on other modalities, suggesting that some excluded dogs might have been eligible under criteria more similar to human medicine (Lakkireddy *et al.* 2015; Roemer *et al.* 2022). If MRI could have been included instead of radiography, it is highly likely that more dogs could have had a confirmed OA diagnosis and thus been included.

The dogs pain levels in Study 1 were confirmed through subjective measures as clinical examination and validated canine OA pain questionnaires, and objective measures of secondary pain indicators as lameness and altered nighttime physical activity. All dogs with complete

HCPI data exceeded the pain threshold (> 11), and incomplete datasets still produced estimated marginal means consistent with clinically detectable pain (Hielm-Björkman *et al.* 2003; della Rocca *et al.* 2024). Baseline CBPI scores corresponded to scores shown by dogs with OA from a study by Essner *et al.* (2017) and confirmed pain in all included dogs. This is essential, as TENS targets pain rather than the underlying joint pathology.

Study 1 required substantial owner involvement, which together with covid pandemic, limited recruitment. The requirement for highly motivated owners may have introduced selection bias, as dogs with a longer duration of osteoarthritis may have been more likely to be enrolled in the study due to owners' motivation to seek additional or alternative treatments beyond the existing management regimen. Although the final sample size remains a limitation, it exceeds that of previous TENS studies in dogs with OA (Johnston *et al.* 2002). The earlier study included only five dogs with stifle OA, whereas our study enrolled fifteen dogs with OA in various joints. This heterogeneity may have contributed to variability in lameness patterns and outcomes, yet it also enhances external validity to a wider population of OA dogs, as naturally occurring OA commonly affects multiple joints (Olsewski *et al.* 1983; Innes *et al.* 2004; O'Neill *et al.* 2020; Carr *et al.* 2023). While surgically induced OA allows for more homogeneous samples, its disease progression differs from naturally occurring OA (Meeson *et al.* 2019), making our population more representative of clinical reality despite greater variation. Although clinical signs may vary by joint, OA is inherently painful, and our outcome measures were designed to detect pain-related changes (Brown *et al.* 2008; Hielm-Björkman *et al.* 2011; Muller *et al.* 2018). One proposed mechanisms of action for TENS, the endogenous opioid release, is unlikely dependant of anatomical location of OA therefore a potential analgesic effect should have occurred regardless of the joint treated (Corder *et al.* 2018; van Strien & Hollmann 2025). However, due to anatomical differences it might be easier to apply the electrodes for different joints and therefore the optimisation of the TENS treatment – which could affect the treatment outcome. The difference in OA phenotypes and genotypes have in human research been pointed out as one contributing factor to failure of TENS treatment in clinical trials (Tang *et al.* 2025). Thus, for future studies a more homogenous study population is recommended. Chronic pain is suggested to induce opioid resistance/analgesic tolerance (Ballantyne 2018; Corder *et al.* 2018; Costa *et al.* 2024), which further

supports the usage of a study population with dogs with early signs of OA in future studies.

In Study 2, a cohort of clinically healthy dogs was included based on comprehensive clinical examination and medical history. Although no additional diagnostic imaging was performed to confirm the absence of osteoarthritis, none of the dogs exhibited clinical signs consistent with OA, similar inclusion of healthy dogs has been done in other studies (Essner *et al.* 2017; Braun *et al.* 2019; Brønniche Møller Nielsen *et al.* 2020).

According to the framework outlined by Belshaw *et al.* (2016), our study addresses three of the five major outcome measure categories used in OA research. The remaining categories—advanced veterinary diagnostics and specific behavioural assessments—are partially addressed by pressure-sensitive mat technique and multi-item pain questionnaires employed in the present study. Collectively, the design of Study 1 provides broad coverage of validated OA outcome measures and represents a notable methodological strength compared with earlier TENS studies (Johnston *et al.* 2002; Mlacnik *et al.* 2006; Krstić *et al.* 2010; Gouveia *et al.* 2025). Different measures quantify distinct aspects of the pain expressions, as demonstrated by Brown *et al.* (2013), who showed that CBPI and kinetic gait analysis capture complementary information and improve overall assessment of treatment effects (Brown *et al.* 2013b). When the IMU data captured in the study is analysed, these will provide yet another dimension of objective outcome measures for pain.

While multimodal testing increases the time and resources required from both researchers and participants, potentially limiting recruitment, it enhances reliability and interpretability. Due to the increased time and effort, it is therefore important to apply a study design that entails a higher power and more statistical efficiency (Lim & In 2021), as in Study 1 where a randomized and blinded crossover design was used. Differences between our findings and prior reports may therefore reflect improved methodological rigor as well as variation in underlying pathologies or treatment conditions (Johnston *et al.* 2002; Krstić *et al.* 2010; Gouveia *et al.* 2025). Good internal validity was achieved in Study 1 due to the strength of the study design and the use of multiple validated outcome measures. However, internal validity could have been further strengthened in Study 1 using a randomized study sample rather than a convenience sample.

Transcutaneous electrical nerve stimulation was choosen based on its proposed mechanisms of action, the gate theory and activation of endogenous opioid pathways (Melzack & Wall 1965; Leonard *et al.* 2010; Peng *et al.* 2019; Patel *et al.* 2025). All the dogs in the Study 1 had chronic pain and humans with chronic pain has been shown to develop μ-opioid receptor tolerance (Vance *et al.* 2012; Sluka *et al.* 2013; Patel *et al.* 2025), which can affect the pain-relieving effect of TENS (i.e. the suggested release of endogenous opioids). In this study the settings on the TENS have been chosen as where the main mechanism of action is the usage of gate theory and therefore this bias may be discarded. A human systematic review indicates that frequency settings does not significantly alter analgesic outcomes (Chen *et al.* 2008). However, by choosing a high frequency and low intensity setting, comparability with previous canine studies was ensured. The frequency of 80 Hz aligns with earlier protocols, which used 70 Hz, 85 Hz, or ranges including 80–150 Hz (Johnston *et al.* 2002; Krstić *et al.* 2010; Gouveia *et al.* 2025). To align protocols has been recommended, in human meta-analysis of the effect of TENS, to strengthen the state of evidence for the treatment (Gibson *et al.* 2019).

The intensity was increased to the level of visible muscle fasciculations when tolerated. While this introduced variability in current amplitude, the physiological response was standardized, reducing the risk of tolerance and promoting a comparable analgesic effect across sessions (Sato *et al.* 2012; Sluka *et al.* 2013; Vance *et al.* 2014). Further, two dogs received continuous NSAID treatment during both the TENS and placebo phases. Evidence from a human study suggests that concurrent use of NSAIDs and TENS may increase sensory thresholds, which highlights the need for individualized adjustment of stimulation intensity during TENS treatment (Witkoś *et al.* 2025). The concurrent usage of NSAID was accounted for in the statistical analysis by including concurrent NSAID use as a fixed effect and is unlikely to have meaningfully influenced the results.

Pulse duration was set to 180 μs, a relatively long duration requiring lower current to achieve nerve activation in comparison to shorter pulse width settings (Guillen *et al.* 2025). Since the targeted nerves are superficial, the pulse duration was considered appropriate (Guillen *et al.* 2025). Although shorter pulse durations are more common in human TENS protocols, using higher frequencies can be more painful and animal experiment suggest that differences in pulse duration may not significantly

influence treatment effects (Gopalkrishnan & Sluka 2000). Electrodes were placed near painful joints or at proximal dermatomes when multiple joints on the same limb were affected, following human clinical practice (Johnson 2021; Johnson *et al.* 2022b; Xu *et al.* 2025). The 45-minute session length, longer than in previous canine studies, was chosen based on clinical experience and evidence from human medicine indicating that longer treatment durations may enhance analgesia (Alon *et al.* 1983; Cheing *et al.* 2003). Future studies could benefit from applying similar treatment protocols to facilitate meta-analyses, while focusing on a more homogeneous study population and dogs at an earlier stage of osteoarthritis progression.

To benchmark TENS against a standard analgesic, NSAID treatment was included as a post-TENS intervention in Study 1. To our knowledge, the first such comparison in a canine TENS study. The NSAID chosen for the study was firocoxib based on the indication of osteoarthritis in the safety information for the drug (FASS vet. 2024) and the superior improvement in lameness on induced synovitis in dogs compared to carprofen, meloxicam and deracoxib (Drag *et al.* 2007). The seven-day NSAID treatment period may have been insufficiently to fully address the chronic pain and compensatory movement patterns associated with OA, as some studies employ ≥ 14 days of continuous treatment (Vasseur *et al.* 1995; Brown *et al.* 2008; Hielm-Björkman *et al.* 2009b; Muller *et al.* 2018). In an induced OA synovitis model, firocoxib has been shown to improve lameness up to 24 hours after a single dose (de Salazar Alcalá *et al.* 2019). The insufficient treatment effect cannot be fully discarded based on the study by de Salazar *et al.* (2019) since models of induced OA is not fully comparable to naturally occurring osteoarthritis (Meeson *et al.* 2019), however the importance of treatment length as a confounder is diminished.

6.2 Clinical findings and behavioural changes

When comparing TENS (multiple treatments) with placebo treatment, clinical examination revealed no evidence of a superior analgesic effect of TENS for any of the anatomical structures assessed. Although clinical examination is inherently subjective, it remains one of the most commonly used outcome measures in clinical osteoarthritis research (Belshaw *et al.* 2016). Variability in subjective assessments can be reduced by the use of a single and blinded examiner, an approach that was applied in study 1 (Bello

et al. 2014). Evaluation with clinical examination were conducted 15 – 24 hours after treatment, it is possible that a potential acute pain-relieving effect could have ceased at that time. Although, in humans a cumulative pain-relieving effect > 24 hours have been suggested (Cheing *et al.* 2003; Vance *et al.* 2014; Reichenbach *et al.* 2022; Yamada *et al.* 2025).

A clinical examination shows the level of pain the animal is experiencing at the time of the examination. This is slightly different from pain assessment via pain questionnaires, which can assess pain over a longer period. Both the CBPI and HCPI are validated for assessing chronic OA pain and evaluating treatment responses in dogs, for example carprofen and oral neutraceuticals where a positive treatment affect has been recorded (Brown *et al.* 2008; Hielm-Björkman *et al.* 2009b; Brown *et al.* 2013a; Brown *et al.* 2013b; Webster *et al.* 2014; Alves *et al.* 2020). The use of validated questionnaires distinguishes this study from earlier investigations of TENS, which relied on unvalidated visual analogue scales (VAS) or video behavioural assessments (Krstić *et al.* 2010; Gouveia *et al.* 2025). For the CBPI, neither the Pain Interference Score (PIS) nor the Pain Severity Score (PSS) differed significantly between TENS and placebo treatments. However, the results from estimated marginal means (EMMs) and standard errors indicate individual-level score changes that may be clinically relevant, based on previously proposed thresholds (PSS reduction ≥ 2; PIS reduction ≥ 1) (Brown *et al.* 2013a; Michels *et al.* 2023). This pattern is most apparent for the placebo group's PIS, where the EMM difference exceeds ≥ 2 scores reduction. For TENS (PIS and PSS) and placebo (PSS), EMMs fall below these thresholds; however, the large standard error suggests substantial individual variation, with some dogs possibly achieving results on the pain questionnaire above the thresholds. Since the magnitude of the standard error is similar between TENS and placebo, the clinical implications of this may be regarded as insignificant. In the original study defining these CBPI threshold values, no clinical validation was done and the statistical significance of the cut-off was found when it was applied to dogs in strong pain (Brown *et al.* 2013a). Therefore the usefulness of the cut-off is uncertain, even though it is used in a recent study of the effect bedinvetmab on OA-related pain in dogs (Michels *et al.* 2023). In the Brown *et al.* (2013a) study, when the cut-off was applied to a cohort of dogs, with similar baseline pain scores to the dogs in the present project, that were receiving carprofen treatment, approximately 35% of OA dogs receiving carprofen improved

above the cut-off values, but importantly, 22% of placebo-treated dogs also exceeded these thresholds and the difference between treatments was not significant. The treatment with NSAID in this study did not result in a significant difference in pain scores pre- and post-treatment or above the cut-off values for PIS and PSS which differs from the Brown *et al.* (2013a) study. The difference in response could be attributed to the small size of the study population but also to the stage of OA in the dogs. A requirement to be included in the study was to have disease history longer than 3 months (several of the dogs had longer) and therefore it could be suspected that the main pain component could be due to central sensitisation rather than inflammatory pain which the NSAIDs are directed at (Lluch *et al.* 2014; Knazovicky *et al.* 2016). The dogs were also required to finish their medication before the study and had therefore been without medication for around 2 months, which could enhance a central sensitisation. Although there was no evidence for worsening of symptoms in phase 2 in comparison to phase 1. The low occurrence of distended joints on the clinical examination at inclusion, even though pain were present based on clinical examination and pain questionnaires, can also support the claim that the inflammatory pain might not be the main pain component in the study sample. In horses, NSAIDs have been shown to fail to improve lameness in some cases, despite the presence of pain. In these horses, lameness can nevertheless be alleviated by intra-articular anaesthesia, indicating that pain is present but not adequately managed by NSAID treatment. (Rhodin *et al.* 2022).

6.3 Gait impairments and physical activity

Our lack of significant differences in gait parameters measured by pressure-sensitive mat contrast with the only previously published study evaluating TENS as a stand-alone treatment for canine OA, in which five dogs demonstrated significantly increased weight-bearing on the affected limb up to 180 minutes post-treatment, as measured by force plate analysis (Johnston *et al.* 2002). As in the study by Johnston *et al.* (2002), post-treatment measurements in the present study were obtained within one hour of the first TENS session (single treatment). Despite this methodological similarity, the results of the present study do not align with the findings of Johnston *et al.* (2002), nor with human studies in which TENS has been

reported to provide analgesic effects during and shortly after treatment (Johnson *et al.* 2022a). These differences could be attributed to different study populations and different treatment settings between the present and previous studies. The present study population was heterogenous in comparison to the five dogs in the Johnston *et al.* (2002) which all had OA in the stifle. The differences in results are unlikely based on differences in registration technique, since studies have shown a correlation between results from a force plate and the pressure sensitive technique (Besancon *et al.* 2003; Lascelles *et al.* 2006). Ground reaction force measurement using a pressure-sensitive mat is an objective kinetic method capable of detecting asymmetries in weight distribution and considers all four limbs through the use of SIs (Fanchon & Grandjean 2007; Madore *et al.* 2007; Gibert *et al.* 2010; Light *et al.* 2010; Seibert *et al.* 2012; Vassalo *et al.* 2015; Fahie *et al.* 2018; Brønniche Møller Nielsen *et al.* 2020; Rincon Alvarez *et al.* 2020). In a previous study involving 115 lame dogs, the pressure-sensitive mat technique demonstrated a specificity of 84.6% and a sensitivity of 91.1% (Gibert *et al.* 2010). Numerous investigations of pain-relieving treatments for canine OA have evaluated therapeutic effects based on changes in PVF and/or VI, with improvements typically defined as increased weight-bearing on the affected limb and redistribution of weight across the remaining limbs (Budsberg *et al.* 1999; Bockstahler *et al.* 2009; Malek *et al.* 2012; Walton *et al.* 2013; Vilar *et al.* 2014; Belshaw *et al.* 2016; Kano *et al.* 2016; Budsberg *et al.* 2018; Miles *et al.* 2019; Häusler *et al.* 2020; Pavarotti *et al.* 2020; Mejia *et al.* 2021). Peak vertical force and vertical impulse have also been shown to be stable over time in dogs with OA, with changes greater than 5% being uncommon and changes of 10% considered rare over a two-month period (Conzemius & Evans 2012). Thus, an effective OA treatment would be expected to induce changes exceeding 5%, which was not observed for TENS relative to placebo in the present study. This could be indicative of an absence of a pain-relieving effect of TENS but could also be attributed to the study population in the present study. All dogs in this study had been lame for a long period of time and lameness is suggested to persist after pain has been resolved due to for example residual mechanical restrictions or long-term behavioural adaptations that has been discussed in articles by Seymour *et al.* (2023) and Pedersen *et al.* (2025).

In Study 1, some dogs had OA in multiple joints across multiple limbs. Such widespread involvement could have influenced treatment outcomes by

reducing the dog's ability to redistribute weight from an affected limb to other limbs, as would be expected in cases of single-joint OA (Venator *et al.* 2020; Wagmeister *et al.* 2021; Alves *et al.* 2022). Although, dogs with bilateral hindlimb lameness due to orthopaedic disease typically compensate by shifting weight to the forelimbs (Alves *et al.* 2022; Park *et al.* 2024), a change that should be detectable using the SIs. Therefore, gait parameters for all limbs, as well as multiple SIs, were analysed in the present study. Given the precision of the pressure-sensitive mat technique, such analyses would likely have identified changes in ground reaction forces arising from any limb had they occurred (Nordquist *et al.* 2011; Keebaugh *et al.* 2015; Miles *et al.* 2019; Brønniche Møller Nielsen *et al.* 2020). Further, the SIs used in this study compare PVF values between limbs and are therefore less sensitive to variations in gait velocity than PVF alone. Of these indices, the sagittal SI is the most established, with reported variability up to 2 – 3 % in sound dogs (Budsberg *et al.* 1993; Fanchon & Grandjean 2007; Light *et al.* 2010; Oosterlinck *et al.* 2011). Although the transverse and ipsilateral SIs are used less commonly, their application is increasing in canine gait analysis (Adrian & Brown 2022; Conzemius *et al.* 2022). The clinical usage of SIs as an single outcome measure for OA diagnosis can be questioned since an overlap between SI values for healthy dogs and dogs with OA has been shown (Brønniche Møller Nielsen *et al.* 2020). Diagnosis of OA was not the aim of the usage of SIs in this crossover study and as mentioned before the precision of the pressure mat should be able to compare individual dog´s SIs to each other as an indicator of improvement of lameness. There are several approaches for calculating SIs (Budsberg *et al.* 1993; Bockstahler *et al.* 2009; Schnabl-Feichter *et al.* 2018; Brønniche Møller Nielsen *et al.* 2020; Adrian & Brown 2022; Park *et al.* 2024). In the present study, a simple ratio-based equation was selected because inter-individual comparisons were not required; all comparisons were performed within the same dog within an predefined velocity interval (Conzemius *et al.* 2022). Therefore, normalization to the overall magnitude of the measurement was not performed, as body conformation, body weight, and height were considered constant within individuals. In addition, no correction for a fixed reference limb (e.g., left forelimb) was needed, since limb orientation was defined relative to the treated limb. The inclusion of SIs in this study served two purposes: first, to provide a more comprehensive assessment of potential changes in weight distribution across all four limbs; and second, to contribute

to the growing body of methodological research in this field. Taken together, the SIs did not indicate any TENS-mediated effect distinct from placebo.

In addition to kinetic analysis, lameness can also be assessed using kinematic methods such as inertial measurement units (IMUs) and marker-based motion capture (Duerr *et al.* 2016; Rhodin *et al.* 2017; Bergh *et al.* 2018). Evidence supporting the usefulness of IMUs in canine lameness assessment continues to grow (Duerr *et al.* 2016; Rhodin *et al.* 2017). In Study 1, dogs were equipped with IMUs during trot trials over the pressure-sensitive mat, the data from the IMUs is under analysis and results will not be presented in this thesis.

The results from the NSAID intervention showed no significant changes in kinetic gait parameters. This lack of response in kinetic gait parameters aligns with findings from Malek *et al.* (2012), where NSAID treatment improved pain questionnaire scores and reduced nighttime activity, but not force-plate-derived lameness metrics (PVF and VI) in dogs with hip OA. The result from the study by Malek *et al.* (2012) is contradicted by other studies where NSAID has improved lameness in dogs with induced OA and acute synovitis measured by force plate (Vasseur *et al.* 1995; de Salazar Alcalá *et al.* 2019; Vijarnsorn *et al.* 2019). In an equine study, Rhodin *et al.* (2022) found that some lame horses did not alter their gait after NSAID treatment, while diagnostic anaesthesia produced clear improvements. An insufficient NSAID efficacy cannot be discarded but the main limitation of the NSAID intervention is the small sample size in the combination with the pre- and post -treatment evaluation design. Thus, a confounding factor could be the delay between treatment and evaluation (15 – 24 hours). Firocoxib has been shown to have a pain-relieving effect, improved lameness evaluated by force plate, up to 24 hours after administration of a single dose on dogs with surgically induced OA (de Salazar Alcalá *et al.* 2019). Although, surgical models of induced OA are not fully comparable to naturally occurring osteoarthritis (Meeson *et al.* 2019), the importance of timing of evaluation as a major confounder is unlikely.

Increase in overall physical activity and enhanced rest during nighttime can be expected indicators of effective pain management (Gruen *et al.* 2019; Thonen-Fleck *et al.* 2025); therefore, the absence of such changes suggests that TENS did not provide sufficient effect to be detected in this study. Although clinically relevant thresholds for changes in total physical activity remain undefined in dogs (Thonen-Fleck *et al.* 2025), increases of up to 20%

have been reported following effective analgesic intervention (Brown *et al.* 2010). Owner behaviour is known to influence canine activity levels (Katz *et al.* 2017; Belshaw *et al.* 2020c; Lee *et al.* 2021; Stevens *et al.* 2025) and one could argue that for example total activity is more a measurement of the combined human and canine physical activity. For example, in a study by Stevens *et al.* (2025) physical activity patterns were influenced by weekday/weekend and what time of day it was. Although owners in study 1 were instructed to maintain habitual routines, the person administering treatment in each household was unblinded, introducing the possibility of performance bias. The bias can be regarded as reduced due to the crossover design of the study and that also nighttime activity was accounted for, where the impact of physical activity of the owners is less prominent (Stevens *et al.* 2025). Further, the activity registration periods spanned over different seasons and included both weekdays and weekends, randomisation minimised potential confounders, and fixed effects for weekday/weekend were incorporated into the analysis (Lee *et al.* 2021). Weekend effects were observed for a small number of metrics in our study, and since seasonal effects are reported to be minimal (< 1%) in other studies, confounding factors are unlikely to have influenced the results (Katz *et al.* 2017). However, when studying a population of heterogenous OA dogs with different OA localisations, difference in number of OA locations and difference in pain severity, the dog's age, hindlimb muscle atrophy and hindlimb joint pain was shown to significantly influence the level of physical activity (Stevens *et al.* 2025). Since a crossover design was applied in our study, these confounders would likely not impact our results.

Contrary to previous findings that NSAIDs increase physical activity and reduce pain (Brown *et al.* 2008; Muller *et al.* 2018; Gruen *et al.* 2019), NSAID treatment in the present study did not significantly affect physical activity. Similarly, no changes were observed in stance time, swing time, stride time, stride length or peak vertical force (%BW). As been discussed before, the study population had a long-standing history of lameness. Such lameness and associated movement patterns may persist even after pain has been alleviated, for example due to residual mechanical restrictions or long-term behavioural adaptations that has been discussed in articles by Seymour *et al.* (2023) and Pedersen *et al.* (2025). Further, a dog with a long history of OA, the main pain component could be due to central sensitisation rather

than inflammatory pain which the NSAIDs are directed at (Lluch *et al.* 2014; Knazovicky *et al.* 2016), thereby explaining the non-response to treatment.

6.4 Physical activity monitoring methodology

Based on the frequency range representation derived from the fast Fourier transform (FFT) and the 97.5th percentile thresholds for both power (energy of the signal) and time, a sampling frequency of 50 Hz appears sufficient for capturing most physical activity in dogs. This recommendation is grounded in the Nyquist–Shannon sampling theorem, which states that a signal must be sampled at least twice the frequency of its highest relevant component to ensure accurate representation (Nyquist 2002; Shannon 2006; Al Jabri *et al.* 2022). The present findings indicate that the highest frequencies associated to everyday physical activity in pet dogs generally occur below 25 Hz, supporting the adequacy of a 50 Hz sampling frequency. However, individual variability was observed, with 97.5th percentile of the frequency range reaching up to 32 Hz in some dogs, suggesting that higher sampling frequencies, potentially up to 70 Hz, may be required in certain cases. These results differ from a study on a dog model for Duchenne muscular dystrophy where a sampling frequency ≥ 24.2 Hz has been suggested to be proficient (Karimjee *et al.* 2019), although the studies is not fully comparable since the life of a privately owned dog and a dog in research differs. In our data, the majority of both time and power spent in the different frequency bins (predefined frequency intervals) were concentrated in frequencies below 6 Hz, which is consistent with previous reports of canine stride frequencies typically ranging from 2 to 4 Hz, with values up to 6 Hz documented in some contexts (Cavagna *et al.* 1988; Heglund & Taylor 1988; Hayati *et al.* 2019). It is possible that the higher-frequency components observed in the frequency-domain analysis represent disturbances, such as movement of the collar, or non-biological noise rather than meaningful physical activity signals. Minimising the sampling frequency is advantageous (Khan *et al.* 2016), and based solely on step frequency, sampling frequencies as low as 8 Hz have been proposed as sufficient (Karimjee *et al.* 2024). However, if accelerometers are intended to capture more complex information than step counts – such as behavioural patterns or activity intensity – a higher sampling frequency is likely required. That has been shown in humans where different sampling frequencies has affect ed the magnitude of the physical activity

classification for activities such as fast run, walking, vacuuming and washing dishes, where a to low sample filtering excludes data and therefore reduces the physical activity represented in the physical activity classification (Brønd & Arvidsson 2016; Karas *et al.* 2019). It is therefore important to optimize the sampling frequency with respect to battery life, data storage capacity, and the intended physical activity measurements. This needs to be further investigated in dogs.

Compared to the reported bandwidth of the ActiGraph GT3X, 0.29–1.63 Hz (Neishabouri *et al.* 2022), the frequency range analysis of the physical activity of dogs in the present study indicates that a substantial proportion of activity-related signal occurs outside of this range and is therefore attenuated by these filter settings. Given that typical canine stride frequencies extend beyond 2.7 Hz, and that racing Greyhounds exhibit mean stride frequencies of approximately 3.5 Hz, it is likely that this filtering underrepresents higher-intensity physical activity. Further investigation is needed, including FFT-based analyses linked to specific physical activities and the identification of non-biological disturbances. In human physical activity research, a wider bandwidth between 0.29 – 4 Hz has been suggested as more appropriate than the filtering range currently used in the ActiGraph GT3X (Arvidsson *et al.* 2024), similar evaluations are needed in canine accelerometry research.

The non-association between 97.5th percentile of the frequency range and the dog's height and weight contrasts with previous findings demonstrating lower stride frequencies in larger or heavier dogs (Barthélémy *et al.* 2009; Ladha *et al.* 2017; Reinstein *et al.* 2025). The lack of observed differences in our study may be attributable to the limited sample size, and further studies with larger and more diverse populations are required to clarify the influence of body size on frequency characteristics in canine accelerometry.

To compare the effect of filtering procedures, physical activity was analysed using both the proprietary ActiLife software and the open-source ENMO approach implemented in R. In contrast to ActiLife, which applies a high-pass and low-pass filter that limits the bandwidth (Neishabouri *et al.* 2022), ENMO applies minimal filtering (corrects for the gravity and truncates negative values) (van Hees *et al.* 2013). The comparison shows differences in physical activity between the filters when the intensity classification is applied, even though the actual physical activity performed is the same since an identical dataset was used. This is similar to a human study where four different filtering procedures including ENMO and

ActiGraph where compared, the ActiGraph's CPM filtering stood out as the filter with the lowest correlation and type of physical activity influenced that correlation majorly (Olfermann *et al.* 2025). Comparable results between ActiGraph and another commercial accelerometer (VetSens) have been reported in a canine study where the VetSens monitor used open-source filters that were configured to replicate ActiGraph filtering (Westgarth & Ladha 2017); nevertheless, then the problem with limited bandwidth still remains. The intensity classification used in the study is not validated to be used together with ENMO filtering (Yam *et al.* 2011; Hoffman *et al.* 2020) and ENMO's aggregation of low-intensity activity may be caused by this. Presenting ENMO-derived data using minimum and maximum values, rather than intensity levels with predefined cut-off values, may enhance its sensitivity (Karimjee *et al.* 2024). Given the substantial variability observed in raw accelerometer data even when the device was stationary, the suitability of minimal-filtering approaches such as ENMO may also be questioned, as disturbances at all frequencies above 0 Hz are retained. As discussed previously, in human research filtering strategies with bandwidths intermediate between ENMO and the ActiGraph proprietary filter may represent a more appropriate compromise (Arvidsson *et al.* 2024).

While identification of an optimal filtering strategy/method was not the primary aim of this thesis, the results clearly demonstrate that filtering choices critically influence the representation of physical activity. Thus, the filtering procedure needs to be considered when choosing how to present the physical activity intensity. It is also important to note that inconsistent filtering practices and underreporting of filtering procedures in scientific articles hinder meaningful comparisons across studies and the development of accelerometry as a reliable outcome measure for physical activity. Consequently, the frequency characteristics of canine physical activity and behaviour should be further explored, for example by validation using energy expenditure outcome measures, as has been done in human physical activity research (Fridolfsson *et al.* 2019; Arvidsson *et al.* 2024).

Another misclassification bias in physical activity representation from accelerometry data is non-wear time, and non-wear definition of canine accelerometry, except for logbooks, is missing (Thonen-Fleck *et al.* 2025). The initial hypothesis of this study was that non-wear time could be identified using a cut-off value derived from the variance in raw accelerometer data, a practise done in human studies (van Hees *et al.* 2011;

van Hees *et al.* 2013; Ahmadi *et al.* 2020). When comparing variability across the three individual axes and the vector magnitude (VM), VM emerged as the most promising candidate due to its smaller variance, reflected by a narrower range of standard deviation values. However, when applying the 97.5th percentile cut-off derived from non-wear VM data, 99% of the wear time was incorrectly classified as non-wear time, leading to the conclusion that non-wear data and wear data in this study were too similar in variance of the VM therefore rejecting the hypothesis. The resulting cut-off value based on the non-wear data was high (0.079 g), which may be attributable to disturbances present in the unfiltered raw signal. In comparison, human non-wear algorithms for raw data applies a cut-off value of 0,013 g for the SD of VM or 0,013 g SD for all of the three axes, or a combination of 0,013 g for the SD of VM together with a range below 0.150 g for two of the three axes (van Hees *et al.* 2011; van Hees *et al.* 2013; Ahmadi *et al.* 2020), which is substantially less than the variance shown in the present study. The cut-off overlap of 75 % that was set for the non-wear classification derived from raw data variance are compatible with human non-wear procedures (Ahmadi *et al.* 2020) and is therefore not believed to be the reason of the poor performance of the non-wear identification. The reference standard for non-wear classification in this study was the logbook completed by the participating dog owners. In a human study on physical activity with the aim to examine patterns of occupational and leisure time physical activity and sedentary behaviour among office-based government employees, the sensitivity and specificity of wear time validation recorded in logbooks were 76.4 and 76.2 respectively (Peeters *et al.* 2013). If the same sensitivity and specificity were to be expected in this study, it could influence the result in a significant way introducing a misclassification bias in the sensitivity analysis. In contrast to the physical activity study in humans, the participating dog owners in our study were aware that the primary aim was to classify non-wear periods. Consequently, the logbook was considered the most important reference measure. All owners were recruited from the university environment and had prior insight into scientific procedures, as well as an understanding of the importance of accurate and reliable data recording. Therefore, in this study, the sensitivity and specificity of the logbook is suggested to be sufficient.

Non-wear time periods were recorded in a logbook, including information on monitor placement. The VM variance was calculated from periods during

which the monitors were registered as being stationary on a surface; thus, the observed variability likely reflects environmental disturbances or vibrations for example from the furniture they rest on. Such locations are consistent with how non-wear has been tested in a human accelerometry study (Thapa-Chhetry *et al.* 2022). Signal filtering has the potential to attenuate some of these disturbances and thereby reduce variability in the signal, suggesting that filtered data may be more suitable for non-wear identification. Indeed, some of the existing wear-time validation methods, such as those implemented in ActiLife, are based on counts per minute (CPM) derived from filtered data in epochs and have been validated in humans with high sensitivity and would therefore be considered an option also for canine accelerometry (Peeters *et al.* 2013). When the five human-validated wear-time validation algorithms implemented in ActiLife were applied to the present canine data, non-wear identification was likewise unsuccessful. The sensitivity shown in our data is far below performance reported in human studies (Peeters *et al.* 2013). Based on these findings, the use of ActiLife wear-time validation for canine accelerometry data has its limitations.

In a canine study where 0 CPM, according to proprietary algorithm used by the Actical activity monitor, was used as the cut-off for sleep and rest, a sensitivity of 94 % and specificity of 96.1 % was achieved for sleep/rest identification (Straube-Koegler *et al.* 2025). The overlap between cut-off for non-wear and sleep/rest support the notion that algorithms based on CPM and epochs might be unsuitable for canine accelerometry data. Further studies are needed to investigate whether alternative filtering strategies applied to raw data could improve non-wear detection performance based on CPM and epochs. In adult humans, non-wear algorithms based on variance in raw accelerometer data have been shown to outperform algorithms relying on counts per minute and epoch-based methods (Shaheen *et al.* 2020). Therefore, further investigation of raw-data-based algorithms may be warranted. In a study with toddlers – who, similar to dogs, exhibit periods of daytime sleep (naps) (Bastianello *et al.* 2025), the raw-data algorithms described by Ahmadi *et al.* (2020) performed well. In another study by Letts *et al.* (2025), together with the raw-data algorithms used in the study by Bastianello *et al.* (2025), identification of non-wear based on zero counts per minute (CPM) over shorter consecutive time periods (5 – 30 minutes), either alone or in combination with logbook information also performed well in toddlers. Therefore, all these approaches may be worth investigating further.

At present, the most reliable method for wear-time validation in dogs remains the use of a logbook.

In the physical activity data from study 3, wear-time periods with very low variance were present, which contributed to the misclassification of wear time as non-wear. Dogs spend an average of approximately 10 hours per day sleeping, with sleeping periods at an average of 45 minutes (Lucas *et al.* 1977). As diurnal animals, the majority of this sleep occurs between 21:00 and 04:00, with additional periods of inactivity or short naps typically occurring during the afternoon (Lucas *et al.* 1977; Tobler & Sigg 1986; Woods *et al.* 2020). These sleeping pattern can be hard to distinguish from non-wear, which has been discussed previously in this text. Incorporating additional features in the activity monitor, such as a thermometer, may offer a promising approach for identifying non-wear (Zhou *et al.* 2015; Böttcher *et al.* 2022; Pagnamenta *et al.* 2022; Vert *et al.* 2022). Machine learning algorithms in general (Thapa-Chhetry *et al.* 2022) or specifically to detect removal of collar (Syed *et al.* 2021), also poses an interesting candidate for further research.

6.5 Main limitations

The most significant limitation of study 1 is the small sample size, which was largely due to the limited availability of dogs with confirmed OA during the COVID-19 pandemic and the time constraints for completing the study. In addition, as the sample populations were based on convenience (owners voluntarily enrolled dogs in the study) rather than a randomized selection of individuals from a study frame, the external validation were a limitation. While a larger number of dogs participated, many lacked radiographic confirmation of OA. Had diagnostic imaging been extended to include MRI, it is likely that additional OA changes would have been detected, allowing inclusion of these dogs; however, this was beyond the budget of the project. The heterogeneity of the clinical population, although reflective of the broader population of dogs with OA, also increased variability, compounding the challenges associated with a relatively small cohort. The limited sample size may have substantially influenced the results, and consequently, recommendations regarding the overall use of TENS for canine OA cannot be made based on this study alone. Nevertheless, the findings may contribute valuable data for future systematic reviews.

Additionally, only one set of TENS parameters was tested. Because TENS settings vary widely, the results apply only to the specific configuration used here, and no general conclusions about TENS efficacy can be made.

For the NSAID treatment period, although the dosage recommendation according to the manufacturer was followed, the treatment duration may have been a limiting factor. A placebo-controlled randomized trial with a treatment period exceeding 14 days would have been preferable but would have lengthened the study further. Including NSAID treatment in the crossover design would have been ideal, but the required washout period and the already substantial participant burden made this impractical. Given the aims and hypotheses of this study, as well as the conclusions drawn from the results, this limitation is considered minor.

For the comparison of nighttime physical activity between dogs with OA and healthy dogs the suspicion of underrepresentation of vigorous movements by the applied filtering procedures may constitute a limitation, which could have affected this data. Ideally different filtering procedures with different bandwidth could have been applied to the data set to evaluate the vigorous movements. This requires methodological development in canine accelerometry before this is applicable and was therefore not possible in the present study. Therefore, the clinical relevance of this result is limited.

The main limitations of the methodological study of physical activity measurements are the small sample size and data loss associated with the analysis of a large dataset. A larger sample of dogs would be required to detect differences related to body size and height, and additional data would be beneficial for validating non-wear identification against true non-wear periods. Given the aims and hypotheses of this study, as well as the conclusions drawn from the results, the sample size limitation is considered minor. However, to advance the research, further studies with a larger study population are warranted.

6.6 Practical Implications

The combination of outcome measures used in this study captures a broad spectrum of pain manifestations associated with chronic OA, increasing the likelihood of detecting true treatment effects. However, implementing multiple outcome measures demands considerable time and effort from both researchers and participants. Each measure should therefore be selected carefully, and duplicate assessments should be avoided. Here is a list of practical tips based on the experiences from the present study:

6.6.1 Pain questionnaires

- Allow respondents sufficient time and consider a supervised practice round before baseline to improve consistency and to calibrate to reduce subjective interpretation of the questions.
- Review completed forms to ensure answers fall within the scale; some respondents tended to mark between scale points, rendering responses unusable.

6.6.2 Pressure-sensitive mat

- Strict standardization of testing conditions (direction, handler, settings) is essential to minimize variability.
- Determine optimal mat placement during baseline assessments, as some dogs improved performance when walking near a wall, whereas others leaned toward it, creating asymmetry that could be mistaken for lameness.
- Check velocity and other trial parameters immediately after each pass to prevent unusable data.
- Using a single straight pass per trial reduces data-management complexity compared to multiple passes.

6.6.3 Physical activity monitoring

- Provide clear instructions to owners about collar fit and when the device may be removed.
- Standardise the tightness of the collar.
- Remove all leash-attachment points to avoid accidental clipping to the study collar.

- Most data loss resulted from device malfunction or battery limitations. More frequent data downloads could reduce loss and are recommended when feasible.
- Keep in mind that the dog's activity is dependent of the owner's activity and have that in mind for aim and study design.
- A sampling frequency of 50 Hz is probably enough.
- Match the intensity classification with your filtering procedure.
- Record non-wear time in a logbook.
- Be aware of the lacking validation and unoptimized filtering procedures when interpreting your results.

7. Conclusions

With the stimulation parameters applied, transcutaneous electrical nerve stimulation, administered as either a single or multiple treatment(s), did not provide any significant changes on a) pain-related clinical findings assessed by clinical examination, b) behavioural changes assessed by pain questionnaires, c) gait parameters assessed by clinical examination and pressure sensitive mat and d) physical activity assessed by activity monitors and pain questionnaires in this study. These results should be interpreted cautiously given the relatively small and heterogeneous study population. Likewise, NSAID treatment, at the dosage and duration used, did not produce measurable changes in gait, pain behaviour, or activity levels indicative of analgesic benefit in this cohort.

Dogs with OA exhibited significantly different night-time activity patterns compared with clinically healthy dogs; however, the clinical significance of this finding remains unclear.

Fast Fourier transform of accelerometry data indicated that most physical activity in pet dogs occurs at frequencies below 25 Hz and therefore spans a broader frequency range than that captured by commonly used commercial filtering approaches. Data preprocessing in the form of signal filtering, substantially influenced activity intensity classification, highlighting its potential impact on outcome interpretation. The variance of unfiltered vector magnitude did not distinguish between wear-time and non-wear periods, and human-validated non-wear detection methods were not applicable to canine data. These findings emphasize the need for species-specific validation of accelerometry processing methods in dogs.

Taken together, the findings presented in this thesis demonstrate that both therapeutic efficacy and outcome sensitivity in the evaluation of chronic pain remain challenges in dogs with osteoarthritis. Advancing both treatment strategies and measurement techniques will be essential to improve the reliability of pain assessment and to support evidence-based management of osteoarthritis-associated pain in dogs.

8. Future considerations

In both veterinary and human medicine, the evidence regarding the efficacy of TENS for chronic pain remains inconclusive, as highlighted in several systematic reviews (Brosseau *et al.* 2003; Rutjes *et al.* 2009; Gibson *et al.* 2017; Gibson *et al.* 2019; Martimbianco *et al.* 2019; Hyytiäinen *et al.* 2023a). Key limitations in the current literature include small sample sizes, low study quality, and substantial heterogeneity in TENS treatment protocols. Future veterinary studies should therefore adopt standardized treatment protocols and rigorous study designs, incorporating multiple validated outcome measures to strengthen the level of evidence. Consideration should also be given to using study populations that are homogeneous in terms of disease progression.

Additional research is needed to refine canine accelerometry methodology. This includes:

- Characterizing the frequency range of dog movements and behaviours and using these findings to optimize filtering procedures for accelerometry data.
- Investigating the influence of dog size and conformation on frequency distributions and assessing the potential need for individualized filtering strategies.
- Validating physical activity intensity classifications in dogs against objective measures such as energy expenditure.
- Developing and validating a robust definition and algorithm for identifying non-wear periods in canine accelerometry data.
- Creating an open-access template or script for standardized filtering of canine accelerometry data to promote methodological harmonization and enable meta-analyses across studies.

These steps will provide a stronger methodological foundation for future studies and improve the reliability and comparability of canine physical activity research.

Finally, to process IMU data into a clinical useful tool for a kinematic outcome measure that can be used to measure pain-related motion asymmetry.

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Popular science summary

Pain is common in dogs and can seriously affect both their wellbeing and the lives of their owners. Unlike a broken bone or a visible injury, pain is a sensation that is personal, which makes it hard to measure directly. To understand if a dog is in pain, we rely on measurement of indirect signs such as changes in behaviour, movement, and body responses — but none of these measurements are perfect.

One of the biggest causes of chronic pain in dogs is osteoarthritis, a degenerative joint disease that affects the dog's ability to move and causes long-term pain. There are many treatments available, from medications to physical therapies, but even with these, pain is not always fully relieved. One non-drug approach is transcutaneous electrical nerve stimulation, which uses mild electrical pulses to reduce pain. Transcutaneous electrical nerve stimulation is used in both humans and dogs to relieve pain. However, solid scientific evidence of its effectiveness in dogs is limited.

This research aimed to test whether transcutaneous electrical nerve stimulation gives pain-relief in dogs with osteoarthritis and to develop better ways of measuring physical activity, which is one of the indicators of pain in dogs.

Using the settings applied in this study, transcutaneous electrical nerve stimulation — whether given once or repeatedly — did not significantly change clinical signs of pain, behaviour, gait, or physical activity. Results should be viewed with caution due to the small and varied group of dogs studied.

The project also investigated physical activity monitoring using activity monitors containing accelerometers. Accelerometers measures the movement of a body and transforms it into a signal that can be translated to different representations of physical activity. In our study most physical activity in pet dogs occurs at frequencies as high as 25 Hz. The commercial activity monitors do not record frequencies that high, therefore is suspected to not record certain physical activity correct. Physical activity representation in the form of intensity classification is also affected by how the data, derived from the signal, is filtered, therefore further misrepresents the physical activity recorded. The activity monitor needs to be worn on the body to be able to measure movements. If the activity monitor is removed (non-wear) and this is not recognized when making the physical activity

representation, the physical activity is misrepresented. In this study different methods of identifying human non-wear time were tested and methods designed for humans do not work reliably for dogs. These findings highlight the importance of using dog-specific methods when studying their movement and activity. The dog-specific methods are missing at the moment, and more research needs to be done to establish such methods.

Populärvetenskaplig sammanfattning

Smärta är vanligt hos hundar och kan påverka både deras välbefinnande och livet för deras ägare. Till skillnad från ett brutet ben eller en synlig skada är smärta en subjektiv upplevelse, vilket gör den svår att mäta direkt. För att avgöra om en hund har ont används indirekta tecken, såsom förändringar i beteende, rörelse och kroppsliga reaktioner – men inga av dessa mått ger en komplett bild.

En av de största orsakerna till kronisk smärta hos hundar är artros, en degenerativ ledsjukdom som påverkar hundens rörlighet och orsakar långvarig smärta. Det finns många behandlingar, från läkemedel till fysioterapi, men även med dessa blir smärtan inte alltid lindrad till en komfortabel nivå. Ett alternativ är transkutan elektrisk nervstimulering, som använder milda elektriska pulser för att minska smärta. Metoden används både hos människor och hundar, men det finns begränsat vetenskapligt stöd för dess effekt hos hund.

Syftet med detta projekt var att undersöka om transkutan elektrisk nervstimulering kan lindra smärta hos hundar med artros, samt att utveckla bättre sätt att mäta fysisk aktivitet, som är en indikator på smärta. Transkutan elektrisk nervstimulering, med de använda inställningarna, påverkade inte kliniska smärttecken, beteende, rörelser eller fysisk aktivitet hos de undersökta hundarna, varken vid enstaka eller upprepade behandlingar. Resultaten bör tolkas med försiktighet, eftersom studien omfattade en liten och heterogen grupp hundar.

Projektet undersökte också mätning av fysisk aktivitet med aktivitetsmonitorer som innehåller accelerometrar. Accelerometrar mäter kroppens rörelser och omvandlar dem till en signal som sedan kan omvandlas för att beskriva den fysiska aktiviteten. Hos sällskapshundar sker de flesta rörelser vid frekvenser upp till 25 Hz, vilket är högre än vad många kommersiella aktivitetsmonitorer kan registrera. Detta gör att aktivitetsmonitorerna missar att registrera viss fysisk aktivitet. Hur signalerna filtreras påverkar också hur aktiviteten klassificeras, vilket också kan ge en missvisande bild av den fysiska aktiviteten. Om monitorn tas av (icke-bärtid) och detta inte upptäcks, blir den övergripande fysiska aktiviteten felaktig. Det finns metoder som är utvecklade för människor för att upptäcka icke bärtid och dessa testades i detta projekt. Metoderna för att identifiera icke-bärtid för människor fungerar dåligt för att identifiera icke

bärtid hos hundar. Dessa resultat visar att artspecifika metoder behövs för att på ett mer korrekt sätt kunna mäta hundars aktivitet med aktivitetsmonitorer, och att mer forskning krävs för att utveckla sådana metoder.

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And finally, if you are still reading this paragraph, you have likely supported me in some way—through good company in the stable, knitting or weaving sessions, fika in the lunchroom, fun times at travels and conferences, a phone call, or professional guidance. Thank you all for your invaluable support!

I

animals

MDPI

Article

Effect of Transcutaneous Electrical Nerve Stimulation on Gait Parameters in Dogs with Osteoarthritis

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Simple Summary: Although scientific evidence for treatment efficacy is lacking, transcutaneous electrical nerve stimulation is used in dogs as a pain-relieving treatment. This randomised single-blinded cross-over study aims to investigate whether treatment with transcutaneous electrical nerve stimulation will affect gait parameters in dogs with osteoarthritis. Fifteen dogs were included in the study, and all dogs were over one year of age, lame, and had chronic pain for more than three months. The dogs were treated with transcutaneous electrical nerve stimulation for seven or ten days, and their gait pattern in trot was evaluated with a pressure-sensitive mat. In the present study, no significant differences were seen between transcutaneous electrical nerve stimulation and placebo treatments for any of the gait parameters evaluated by the pressure-sensitive mat. Further studies are needed to confirm the observations.

Abstract: Osteoarthritis is a common degenerative disease in dogs, often manifested as pain, joint swelling, and lameness. Despite the lack of scientific evidence for its treatment efficacy, transcutaneous electrical nerve stimulation (TENS) is used in dogs as a pain-relieving treatment. This randomised single-blinded cross-over study investigated the effect of TENS on gait parameters in fifteen dogs with osteoarthritis. Stance time, swing time, stride time, stride length, peak vertical force (%BW), vertical impulse (%BW*sec), and symmetry indices were obtained using a pressure-sensitive mat. TENS treatment of 80 Hz and 100 µs with an individually selected amplitude was conducted for 45 min once daily for a treatment period of seven or ten days. No significant differences were seen between TENS and placebo for any of the gait parameters. Hence, in this study, TENS did not affect gait parameters, compared to placebo. Further studies are needed to confirm the observations.

Keywords: TENS; pressure sensitive mat; locomotion; lameness; electrotherapy; kinetic; canine; pain; rehabilitation; musculoskeletal system

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1. Introduction

Osteoarthritis (OA) is a common degenerative disease in dogs, with a possibly long-term need for therapy [1–4]. It is usually manifested as pain, joint swelling, and reduced joint mobility, causing varying degrees of lameness [5–7]. Joint pain may lead to pain-induced functional impairment, regarded as one of the clinical signs of OA [8]. There are several treatment strategies for OA, including pharmaceuticals, nutraceuticals, weight reduction, regenerative medicine, therapeutic exercises, and different rehabilitation modalities [9–14]. It is likely that the management of canine OA may benefit from an integration of both pharmacologic and non-pharmacologic treatments. Common pharmaceuticals for OA are nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and monoclonal antibodies [11,15–17]. However, in 55% of the studies on NSAIDs, adverse effects are reported [18]. Even if the majority of adverse effects are mild, they may restrict long-term

use of medication [15,17,19–22]. Further, concurrent disease may also restrict the use of corticoids [15,16,20]. Untreated pain causes suffering for the dog and has a negative impact on its welfare, as well as on the wellbeing of the owner, since managing a dog with chronic pain negatively affects their life [23]. Therefore, it is relevant to study non-pharmacologic treatments, such as different rehabilitation techniques, as complementary treatments, but especially as stand-alone treatments for those dogs that do not tolerate NSAIDs or corticosteroids and where treatment with monoclonal antibodies is not feasible.

Veterinary rehabilitation has attracted increased interest from dog owners and animal health staff in recent decades. Rehabilitation is considered an important component of an overall long-term treatment strategy for OA. Among different rehabilitation modalities, there is an increasing use of transcutaneous electrical nerve stimulation (TENS). TENS is a device that uses electric current, delivered though electrodes on the skin, to stimulate nerve fibers for therapeutic reasons, i.e., as pain relief. The specific treatment settings include adjustable parameters such as pulse frequency, pulse duration, and intensity. TENS is claimed to provide pain relief through either endogenous opioid release (low-frequency TENS) or on a segmental level by the use of the pain gate theory (high-frequency TENS) [24,25]. The latter is believed to be effective by applying stimuli to large diameter non-noxious afferents (A-beta), which subsequently reduces pain via decreased nociceptor activity [24,25]. Further, studies have shown an increase in β-endorphins and methionine-enkephalin in human subjects, a release of glutamate and substance P in animals with inflammation, neuropathic, or incisional pain, a reduction in pressure pain thresholds at the site of TENS and at sites outside the area of application, and a reduction in microglia and astrocyte activation in the spinal cord in both osteoarthritic and neuropathic pain animal models [26–29].

In humans, TENS is used as a pain-relieving treatment and a complementary or single treatment for OA [24,30–32]. A systemic review and meta-analysis of TENS for acute and chronic pain in humans, based on 381 studies, concluded that there was moderate-certainty evidence that pain intensity was lower during or immediately after TENS treatment compared to placebo [33]. The review included studies that used participant-reported strong but comfortable TENS sensation stimulation, with electrodes at the site of pain or over nerve bundles proximal to the site of pain. The effect was evaluated directly after treatment and with different types of pain scales [33]. However, other studies report no effect on pain compared to control [34–37]. Conflicting results and, thus, inconclusive evidence are explained by the low quality of relevant studies as well as the diversity in treatment protocols [37]. Regarding animal studies, studies report that TENS produced an analgesic effect in rodents with experimentally induced OA [38,39]. The scientific documentation on the effect of TENS in dogs is even sparser than in humans and laboratory animals. Thus, several authors report that there is a need for more canine studies [40–43]. The results from the few existing studies indicate that treatment with TENS may increase weight bearing on the affected limb in dogs with OA for up to 180 min, with the greatest significant difference immediately after treatment [42]. A study on dogs with canine ankylosing spondylitis showed a decrease in signs of pain evaluated by visual analogue scale and clinical examination after TENS treatment [40]. Further, a weight-reduction study on dogs with OA examined the difference in lameness in two treatment groups, both with dietary protocol, but with two different physical therapy programmes, one of which included TENS treatment. Results indicate that dogs that received an additional TENS treatment showed significant improvement, evaluated with force plate and changes in peak vertical force (PVF) and vertical impulse (VI), whereas dogs with no TENS treatment showed only significant improvement after 4 months [41,44]. Two of the previous studies have evaluated the effect of TENS by the use of kinetic techniques, i.e., pressure-sensitive mats and force plates; the latter is regarded as the gold standard for measuring ground reaction forces [45–53]. Recent studies have compared the results from these two kinetic techniques and report that they are equally reliable but not interchangeable [54–57]. Further, studies have shown a high agreement between repetitive measurements in individual dogs [58].

The use of these techniques enables the registration of different gait parameters, such as temporospatial parameters, peak vertical force (PVF), vertical impulse (VI), and symmetry indices (SIs) [7,56,59–62]. PVF and VI adjusted to bodyweight (% BW) show a low variability [56,60,61]. Thus, the kinetic techniques contribute, together with an orthopaedic examination, to a more objective lameness evaluation.

In OA, mild to moderate lameness is often seen, and kinetic studies show alterations in PVF and VI, as well as symmetry indices [7,47,63–66]. Studies on pain-relieving treatment of dogs with OA have used changes in PVF and/or VI as outcome measures, showing therapeutic effects such as an increase in load on the lame limb but also redistribution of weight to other limbs [45,67–74]. Further, registration of temporospatial parameters has been used, but results are rarely described [59,60,75].

Due to the increasing clinical use of TENS, together with the lack of research on its possible effects, the present cross-over study investigates the effect of TENS on canine gait parameters, evaluated with a pressure-sensitive mat. The null hypothesis is that, for dogs with OA, treatment with TENS will not affect gait parameters differently than placebo treatment.

2. Materials and Methods

The study consisted of two parts—part 1 (TENS and placebo intervention) and part 2 (an NSAID intervention)—see Figure 1. For the comparison of TENS and placebo treatment effect, a prospective, single-blinded, randomised, placebo-controlled, and cross-over design was utilised (Figure 1). A pilot study was conducted in order to test the study design (study part 1), consisting of seven days of treatment with TENS or placebo performed by animal health personnel, and the pilot data were included in the final data. For the evaluation of the effect of NSAIDs (study part 2), a one-group pre-test–post-test study design was used (Figure 1).

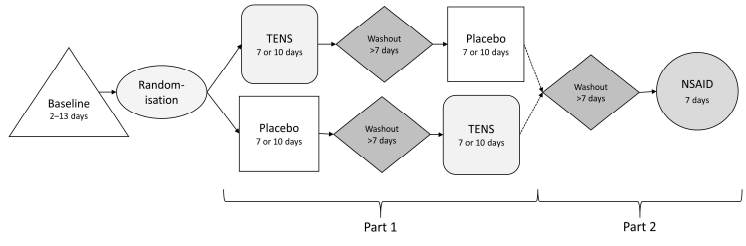

Figure 1. Schematic view of the study. The difference in length for the TENS and placebo treatment (7 or 10 days) depends on whether the dog participated in the pilot study (7 days).

Client-owned dogs of any sex or breed with confirmed OA were eligible for the study. Recruitment of dogs was conducted through social media (Facebook), through email posting and advertising in magazines, and at veterinary practices in the local area. Dogs were included if they were over 1 year of age, were 1–3 degrees lame in trot on a 5-degree scale at an orthopaedic examination, had an OA diagnosis confirmed by diagnostic imaging and had had chronic musculoskeletal pain (>3 months), diagnosed by a veterinarian before the study [76]. If the dog was diagnosed with OA in multiple joints, enrolment was based on the worst affected limb (referred to as the "lame limb") based on the dog's clinical history together with a clinical assessment and baseline/preintervention performed kinetic measurements.

Dogs were excluded if they had a metallic implant that interfered with treatment, a pacemaker or a tumour in the treatment area, or a sensory deficiency in the treatment area. The latter was assessed by palpation of the whole body and by manually stroking the skin at the selected localisations of the electrodes. Dogs were excluded from part 2 (NSAID intervention) of the study if they had a history of adverse reactions to NSAIDs.

Informed consent from the owners was signed and an ethical permit was granted by a source (information withdrawn as a result of blinding), and the study was performed according to guidelines established in the Helsinki Declaration [77]. The study included five to seven visits (measurement occasions) to the research facility, depending on participation in the NSAID part of the study (Figure 2). Registration on the pressure-sensitive mat was performed at each visit to the research facility. Data collection took place between September 2018 and January 2020.

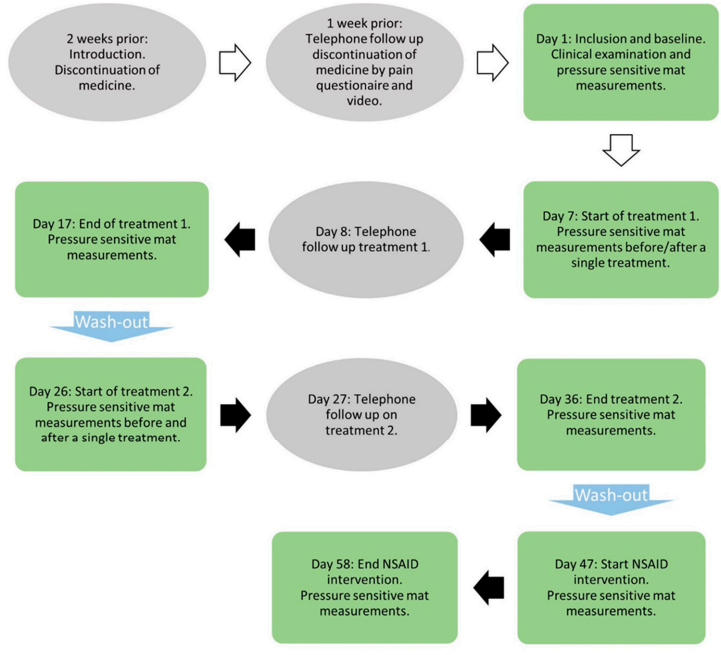

Figure 2. Study design and protocol. Grey ellipse = telephone contact. Green rectangles = physical visit. Black arrows = treatment period. Blue arrows = washout period.

2.1. Evaluation Methods

The dogs were evaluated via clinical examination, pressure-sensitive mat measurement and pain assessment questionnaires (Helsinki Chronic Pain Index and Canine Brief Pain Index). The pain index assessments were used during the baseline and throughout the study period to ensure animal welfare, especially after an eventual discontinuation of medication. In this article, results from the pressure-sensitive mat are presented.

2.1.1. Pressure-Sensitive Mat

A pressure-sensitive mat "Walkway High Resolution HRV4" (Tekscan Inc., Norwood, MA, USA) and software "Walkway Research ver. 7.60-31" (Tekscan Inc., Norwood, MA, USA) were used to collect the kinetic data. The measurements were made within an hour after the first treatment session (from now called "single treatment") and within 12–24 h after the last treatment of the whole treatment period ("multiple treatments"). The mat was regularly calibrated, and the calibration files used were coherent with each dog's weight.

The mat (195 × 45 × 0.57 cm) was placed in a corridor next to a wall and was covered with a 1 mm-thick non-slip plastic mat. Cameras filmed the dogs from a lateral and a craniocaudal aspect. The dogs trotted over the pressure-sensitive mat at a comfortable

individual pace. The same handler and handler side was used in the absolute majority of measurements. A valid trial was defined as the dog's correct behaviour over the mat and the number of step cycles (a minimum of two step cycles/eight stances). Correct behaviour was defined as the dog trotting at a constant pace in a straight line, looking straight ahead with minimal intervention from the handler. It was subjectively assessed by the author(s) and noted in the data collection protocol. The criteria for successful kinetic data collection were three trials in trot (a 2-beat gait with left front (LF)/right hind (RH)-suspension-right front (RF)/left hind (LH) steps), with a velocity of between 1.5 and 2.2 m/s and an individual variance of <0.5 m/s.

The following gait parameters were registered: stance time, swing time, stride time, stride length, peak vertical force (%BW), vertical impulse (%BW), and symmetry indices based on peak vertical force.

2.1.2. Clinical Examination

To investigate if the dog met the inclusion criteria, a clinical examination was conducted by an experienced veterinarian.

2.1.3. Pain Questionnaires

Helsinki Chronic Pain Index and Canine Brief Pain Index were used as a control for animal welfare, especially after the discontinuation of pain-relieving medication [78–81]. The two pain questionnaires were answered by the owner or another person who had daily contact with the dog. The respondent was instructed to fill out the forms once a week to keep track of the dog's pain score and to contact the authors if the dog showed signs of deterioration.

2.2. Study Protocol

Telephone contact with eligible dog owners was made at both two weeks and one week before the start of the study. The suitability of the dogs was determined by the information the owners sent in when they expressed interest in the study. The first call focused on the retrieval of the dog's status and medication (Figure 2). Owners were asked to send in videos of their dog's locomotion from a lateral and cranial view in trot for an initial lameness assessment. Based on the video and the phone information, the study veterinary surgeon assessed if the dog's pain medication could be discontinued. Pain medication was reinstated before baseline if deemed necessary by the same veterinarian, based on pain questionnaires and owner information. For these dogs, pain medication was given throughout the study. If the medication was needed later in the study (i.e., after baseline), the dogs were excluded. The dog's status was checked one week prior to the start of the study via the second telephone call, pain questionnaires, and new videos. Owners could make additional contact with the study team when needed.

In part 1 of the study, each dog was allocated randomly into either TENS or placebo treatment for the first treatment period. The treatments were reversed during the second treatment period (Figure 1). A washout period of a minimum of ten days was used between the two treatment periods in study part 1. Part 2 of the study started after a washout period for those dogs that could withstand NSAID treatment. The NSAID intervention consisted of a seven-day treatment.

2.2.1. Transcutaneous Electrical Nerve Stimulation and Placebo Treatment

Treatment was administered with either one of two TENS machines—Profile TENS (Body Clock Health Care Limited, London, UK) or a Cefar TENS Chattanooga (Enovis, Lewisville, TX, USA)—using CEFAR coal fibre electrodes (3 × 5 cm) (Enovis, Lewisville, TX, USA). The treatment programmes of the two TENS devices were synchronised so that the settings were identical. The skin was clipped precisely where the electrodes were situated during treatment, soaked with water and ultrasound gel was used as a transmitting substance. Two electrodes, a minimum of 4 cm apart, were placed on intact skin, with

electrodes at the site of pain (distal placement) or over nerve bundles proximal to the site of pain (proximal placement).

The first treatment was conducted partly by animal health staff and partly by the owner under the supervision of the animal health staff. During the following treatments, the dogs were treated by their owners, except for the pilot study, where the treatments were conducted by animal health personnel. The treating person, mainly the owner, received instructions both verbally and in writing before each treatment period (TENS and placebo) regarding how to perform the treatment. Optional additional supervision was offered by one of the authors.

The TENS device was set to a constant current with a frequency of 80 Hz and a pulse duration of 100 µs based on previous studies and clinical experience. The intensity (amplitude, unit milliampere (mA)) was increased until muscular fasciculation in the treatment area's muscles occurred and was lowered if the dogs expressed discomfort. The intensity was then gradually increased during the treatment session to maintain sensation throughout. The treatment sessions were 45 min once daily. The treating person kept a diary of each treatment session, including treatment duration, electrode placement, used intensity, and behaviour of the dog. The placebo treatment protocol was identical to the TENS treatment, with the exception that the device was not switched on. Each treatment period's length was ten days, except for the pilot study, where the dogs were treated for seven days.

2.2.2. NSAID Treatment

Firocoxib was administered orally by the owner once daily for seven days after the finalisation of the TENS part of the study. A dosage of 5 mg per kg body weight was subscribed based on the recommended dosage by the manufacturer [82]. Owners were instructed to start the medication eight days before the final measurements of the NSAID treatment.

2.3. Data Management and Statistical Analysis

For all gait parameters, an average value based on three trials over the mat (a minimum of six step cycles/twenty-four stances) was included. If there were not three trials that met the inclusion criteria, the average value of two trials was used.

Three different symmetry indices (SIs) were used; either body quadrants, body sides, or body halves were compared. For the commonly used SI_{limb}, the quadrant containing the lame limb was compared to the contralateral quadrant, i.e., the sound limb, and the $SI_{sagittal}$ was compared to the left and the right sides of the body. The additional $SI_{transversefront}$ compared front limbs from front limb lame dogs with their sound hindlimbs, and the $SI_{transversehind}$ compared hindlimbs from hindlimb lame dogs with their sound front limbs.

SIs were calculated from peak vertical force (%BW) by using the following equation:

$$SI_{limb} = \frac{\text{lame limb}}{\text{contralteral sound limb}}$$

$$SI_{sagittal} = \frac{\text{front and hindlimb from lame body side}}{\text{front and hindlimb from sound body side}}$$

$$SI_{transversefront} = \frac{\text{front limbs from lame body half}}{\text{hindlimbs from sound body half}}$$

$$SI_{transversehind} = \frac{\text{hindlimbs from lame body half}}{\text{front limbs from sound body half}}$$

Differences in gait parameter values before and after treatment with TENS and placebo, respectively, were compared. The comparison was made on data collected before and after the first treatment session and before and after the last day of the whole treatment period for TENS and placebo; hereafter, the terms "single treatment" and "multiple treatments" are used. Further, differences in gait parameters were compared before and after the last day of NSAID treatment.

The data were compiled in Excel (Microsoft Excel 2016 (16.0.5443.1000), Microsoft Corporation, Redmond, WA, USA), and the statistical analysis was made in R (version 4.1.2 (2021-11-01)—"Bird Hippie", R Core Team, Vienna, Austria). The individual data

and history of disease of the participating dogs are presented descriptively. The pressure-sensitive mat data were analysed in a linear mixed-effects model for a 2 × 2 cross-over design for the TENS and placebo part, with gait parameters (stance time, swing time, stride time, stride length, peak vertical force (%BW), vertical impulse (%BW*sec), and symmetry indices) as continuous outcomes. For the NSAID intervention, a linear regression model was used with gait parameters (stance time, swing time, stride time, stride length, peak vertical force (%BW), vertical impulse (%BW*sec), and symmetry indices) as continuous outcomes. In the linear mixed effects model, dog was set as a random effect, and age, sex, weight, simultaneous NSAID treatment, and velocity were set as fixed effects for all parameters except for the symmetry indices where age, velocity, and simultaneous NSAID treatment were excluded from the fixed effects due to restriction of numbers of factors in the model. Residuals were normally distributed. The significance level was set to $p < 0.05$.

3. Results

3.1. Descriptive Statistics

A total of 38 dogs were initially selected for the study. Of these, 26 matched the inclusion criteria and were enrolled in the study, and data from 15 of these dogs were finally used in the study. Of the 26 enrolled dogs, two were lost to follow-up, five were excluded due to unconfirmed diagnostic imaging diagnosis of OA, and two had to be excluded due to data corruption. Furthermore, two dogs had to be excluded: one due to an aggravated caudal cruciate ligament injury noted during baseline and the other due to the illness of the owner after one treatment period. One dog did not participate in part 2 of the study (NSAID intervention) due to a traumatic fracture of the elbow, so data from part 1 of the study were used. During part 2 (NSAID intervention), one dog needed to end the medication after five days due to suspected adverse reactions to the treatment, so the data from the NSAID intervention were excluded from the study.

The descriptive data of the dogs are presented in Table 1. The mean age was 6.8 years (±1.9 years). The mean weight was 22.7 kg (±9.4 kg). There were five mixed breeds: three Labrador retrievers and one each of Australian Cattle Dog, Beagle, Border Collie, Flatcoated Retriever, Malinois, medium-sized Poodle, and Staffordshire Bull Terrier. In part 1 (TENS and placebo intervention), one of the dogs received 7 days of treatment, and 14 dogs received 10 days of treatment. Two of the dogs were treated with NSAIDs during the whole study. Electrodes were placed at the site of pain (distal placement) in 14/15 dogs; in one dog, a placement over nerve bundles proximal to the site of pain (proximal placement) was made.

Table 1. Descriptive data of the dogs. OA = osteoarthritis, LF = left front limb, LH = left hindlimb, RF = right front limb, RH = right hindlimb, BF = both front limbs, BH = both hindlimbs, DP = distal placement electrodes, PP = proximal placement electrodes, L7S1 = 7th lumbar vertebra and sacrum.

Dog	Age (Years)	Breed	Weight (kg)	Lameness at Inclusion	Diagnosis and Electrode Placement	Number of Days of Treatment	NSAID Treatment through the Whole Study
Dog 1	8	Beagle	13	1° LH	OA stifle LH. Cruciate ligament injury LH. DP.	7	No
Dog 2	8	Labrador Retriever	31	2° LF	OA metacarpal joint phalanx 4 and 5 LF, phalanx 5 RF and elbow LF. DP.	10	Yes
Dog 3	6.5	Poodle, medium size	7	1° LF	OA elbow LF. DP.	10	No
Dog 4	8	Malinois	27	1° LF	Moderate OA shoulder LF. Mild OA shoulder RF. Disc herniation L7S1. DP.	10	No
Dog 5	3	Mixed breed	15	1° LH	OA stifle LH. DP.	10	No

Table 1. *Cont.*

Dog	Age (Years)	Breed	Weight (kg)	Lameness at Inclusion	Diagnosis and Electrode Placement	Number of Days of Treatment	NSAID Treatment through the Whole Study
Dog 6	8	Mixed breed	41	2° RH	OA stifle BH. DP.	10	No
Dog 7	6	Mixed breed	18	1° LH	OA hip BH. DP.	10	No
Dog 8	8	Border Collie	16	1° RH	OA lumbar spine. OA shoulder and phalanx BF. PP.	10	No
Dog 9	8	Labrador Retriever	37	3° RF	OA carpus and phalanx BF. OA hips BH. DP.	10	Yes
Dog 10	5	Mixed breed	17	3° LF	OA elbows and phalanx BF. Spondylosis spinal cord. DP.	10	No
Dog 11	7	Flatcoated Retriever	26	1° LF	OA carpus RF. Lameness LF. DP.	10	No
Dog 12	2	Labrador Retriever	30	1° LF	Fragmentation of processus coronoideus medialis elbow LF. OA elbow LF. DP.	10	No
Dog 13	7	Staffordshire Bull Terrier	13	1° LF	OA stifle LH. Operated cruciate ligament injury BH. Elbow dysplasia grade 2 BF. Hip dysplasia BH. DP.	10	No
Dog 14	9	Mixed Breed	30	1° LH	OA hips BH. OA lumbar spine. DP.	10	No
Dog 15	8	Australian Cattle Dog	20	1° LH	OA tarsus LH. DP.	10	No

3.2. Gait Parameters

The data were collected from a total of 108 measurement occasions (visits to the facility). Three trials per dog were included from 105 of the 108 measurement occasions. For the remaining three occasions, two trials (a minimum of four step cycles/sixteen stances) were used due to incomplete registrations. The mean value for a trial for all the dogs was 8.8 (range 8–12) stances, which corresponds to two step cycles. The same handler was used for 103 of 108 measurement occasions, and the handler was on the same side of the dog in 104 out of 108 occasions. The dogs trotted over the pressure-sensitive mat between 2 and 20 times (trials) on each measurement occasion.

No significant differences were seen between TENS and placebo treatments for stance time, swing time, stride time, stride length, peak vertical force (% BW) and vertical impulse for (% BW*sec) for any of the limbs. Similarly, no significant differences were seen, comparing before and after NSAID treatment, for stance time, swing time, stride time, stride length, and peak vertical force (% BW). However, the results show a significant increase in vertical impulse (% BW*sec) for the ipsilateral limb ($p = 0.02$). Estimated mean values and p-values for the gait parameters can be seen in Table 2.

No significant differences were seen for the SIs, either for single or multiple treatments, between TENS and placebo treatments. The NSAID treatment period showed no significant difference between before and after for any of the SIs. The mean values and significance for the symmetry indices can be seen in Table 3.

In order to further visualise the individual differences between TENS and placebo, the individual SI values are presented in spaghetti plots in Figure 3.

Table 2. Estimated mean values, number of dogs and *p*-value for the different gait parameters. SD = standard deviation. N = number of dogs. Sec = seconds. Cm = centimetre. %BW = percentage of body weight. Single = measurement after a single treatment. Multiple = measurement after multiple treatments. ** = significant *p*-value ($p < 0.05$).

Parameter	Time	Leg	TENS (Mean ± SD)	N	Placebo (Mean ± SD)	N	*p*-Value	NSAID (Mean ± SD)	N	*p*-Value
Stance time (sec)	Before	Lame	0.19 ± 0.04	15	0.20 ± 0.04	15		0.18 ± 0.04	9	
		Contralateral	0.20 ± 0.04	15	0.20 ± 0.04	15		0.19 ± 0.03	9	
		Ipsilateral	0.19 ± 0.04	15	0.20 ± 0.04	15		0.19 ± 0.05	9	
		Diagonal	0.20 ± 0.04	15	0.20 ± 0.04	15		0.19 ± 0.05	9	
	After single	Lame	0.20 ± 0.04	15	0.19 ± 0.04	15	0.80			
		Contralateral	0.20 ± 0.04	15	0.20 ± 0.04	15	0.87			
		Ipsilateral	0.20 ± 0.04	15	0.19 ± 0.04	15	0.14			
		Diagonal	0.20 ± 0.04	15	0.19 ± 0.04	15	0.19			
	After multiple	Lame	0.20 ± 0.04	15	0.19 ± 0.04	15	0.67	0.19 ± 0.04	10	0.66
		Contralateral	0.20 ± 0.04	15	0.19 ± 0.04	15	0.42	0.19 ± 0.03	10	0.36
		Ipsilateral	0.19 ± 0.04	15	0.19 ± 0.04	15	0.98	0.19 ± 0.04	10	0.20
		Diagonal	0.20 ± 0.04	15	0.19 ± 0.04	15	0.35	0.19 ± 0.04	10	0.06
Swing time (sec)	Before	Lame	0.25 ± 0.04	15	0.25 ± 0.04	15		0.25 ± 0.04	9	
		Contralateral	0.25 ± 0.04	15	0.25 ± 0.04	15		0.25 ± 0.04	9	
		Ipsilateral	0.26 ± 0.03	15	0.26 ± 0.03	15		0.25 ± 0.03	9	
		Diagonal	0.25 ± 0.03	15	0.26 ± 0.04	15		0.24 ± 0.04	9	
	After single	Lame	0.25 ± 0.03	15	0.26 ± 0.03	15	0.26			
		Contralateral	0.25 ± 0.04	15	0.25 ± 0.04	15	0.19			
		Ipsilateral	0.26 ± 0.03	15	0.26 ± 0.03	15	0.86			
		Diagonal	0.26 ± 0.03	15	0.26 ± 0.03	15	0.08			
	After multiple	Lame	0.25 ± 0.03	15	0.25 ± 0.04	15	0.58	0.26 ± 0.04	10	0.80
		Contralateral	0.25 ± 0.04	15	0.25 ± 0.05	15	0.07	0.25 ± 0.04	10	0.33
		Ipsilateral	0.26 ± 0.03	15	0.25 ± 0.04	15	0.25	0.25 ± 0.03	10	0.63
		Diagonal	0.25 ± 0.03	15	0.26 ± 0.04	14	0.19	0.24 ± 0.03	10	0.39
Stride time (sec)	Before	Lame	0.44 ± 0.06	15	0.45 ± 0.07	15		0.43 ± 0.06	9	
		Contralateral	0.45 ± 0.06	15	0.45 ± 0.06	15		0.44 ± 0.07	9	
		Ipsilateral	0.45 ± 0.06	15	0.45 ± 0.06	15		0.44 ± 0.08	9	
		Diagonal	0.45 ± 0.06	15	0.45 ± 0.06	15		0.44 ± 0.07	9	
	After single	Lame	0.45 ± 0.06	15	0.45 ± 0.05	15	0.34			
		Contralateral	0.45 ± 0.06	15	0.45 ± 0.05	15	0.06			
		Ipsilateral	0.46 ± 0.06	15	0.45 ± 0.06	15	0.47			
		Diagonal	0.45 ± 0.06	15	0.45 ± 0.05	15	0.97			
	After multiple	Lame	0.45 ± 0.06	15	0.44 ± 0.06	15	0.28	0.44 ± 0.07	10	0.78
		Contralateral	0.44 ± 0.06	15	0.45 ± 0.07	15	0.25	0.44 ± 0.06	10	0.59
		Ipsilateral	0.45 ± 0.06	15	0.44 ± 0.06	15	0.29	0.44 ± 0.06	10	0.46
		Diagonal	0.45 ± 0.06	20	0.45 ± 0.07	15	0.24	0.44 ± 0.07	10	0.42

Table 2. *Cont.*

Parameter	Time	Leg	TENS (Mean ± SD)	N	Placebo (Mean ± SD)	N	*p*-Value	NSAID (Mean ± SD)	N	*p*-Value
Stride length (cm)	Before	Lame	88.96 ± 14.37	15	89.17 ± 13.80	15		87.36 ± 14.20	9	
		Contralateral	88.90 ± 14.35	15	89.07 ± 13.91	15		86.05 ± 14.90	9	
		Ipsilateral	89.23 ± 14.09	15	88.94 ± 13.52	15		87.71 ± 13.86	9	
		Diagonal	89.57 ± 14.46	15	89.38 ± 13.95	15		87.44 ± 14.54	9	
	After single	Lame	88.22 ± 14.09	15	90.47 ± 14.77	15	0.52			
		Contralateral	87.84 ± 14.06	15	91.04 ± 15.19	15	0.13			
		Ipsilateral	88.70 ± 14.31	15	90.38 ± 14.53	15	0.90			
		Diagonal	88.41 ± 14.05	15	90.76 ± 14.75	15	0.49			
	After multiple	Lame	88.86 ± 13.45	15	90.14 ± 15.18	15	0.50	87.90 ± 14.36	10	0.96
		Contralateral	88.40 ± 13.41	15	92.60 ± 16.00	15	0.06	87.39 ± 14.24	10	0.66
		Ipsilateral	89.03 ± 13.56	15	90.68 ± 15.52	15	0.67	87.98 ± 14.17	10	0.96
		Diagonal	88.53 ± 13.32	15	93.04 ± 16.37	15	0.07	87.97 ± 14.26	10	0.81
Peak vertical force (%BW)	Before	Lame	61.15 ± 16.48	15	62.08 ± 16.56	15		59.33 ± 21.59	9	
		Contralateral	71.47 ± 20.97	15	72.57 ± 20.68	15		68.03 ± 23.22	9	
		Ipsilateral	67.33 ± 22.68	15	69.05 ± 22.84	15		70.71 ± 18.81	9	
		Diagonal	68.15 ± 22.52	15	70.85 ± 23.43	15		69.10 ± 18.99	9	
	After single	Lame	60.47 ± 17.37	15	58.94 ± 12.03	15	0.57			
		Contralateral	68.87 ± 20.03	15	68.98 ± 15.19	15	0.79			
		Ipsilateral	67.60 ± 23.60	15	69.48 ± 28.22	15	0.81			
		Diagonal	67.55 ± 23.25	15	69.40 ± 28.90	15	0.82			
	After multiple	Lame	62.16 ± 17.73	15	61.31 ± 17.61	15	0.70	55.40 ± 16.09	10	0.07
		Contralateral	73.00 ± 20.99	15	69.49 ± 20.55	15	0.40	61.19 ± 16.90	10	0.08
		Ipsilateral	72.03 ± 31.30	15	66.89 ± 22.89	15	0.26	70.55 ± 26.86	10	0.33
		Diagonal	73.53 ± 30.14	15	67.84 ± 25.56	15	0.15	69.85 ± 27.11	10	0.31
Vertical impulse (%BW*sec)	Before	Lame	7.16 ± 2.70	15	7.60 ± 3.19	15		6.38 ± 3.07	9	
		Contralateral	8.49 ± 3.44	15	8.90 ± 3.86	15		7.53 ± 2.80	9	
		Ipsilateral	7.59 ± 3.16	15	7.89 ± 3.26	15		7.80 ± 3.30	9	
		Diagonal	7.76 ± 3.08	15	8.18 ± 3.14	15		7.92 ± 3.46	9	
	After single	Lame	7.14 ± 2.71	15	7.00 ± 2.63	15	0.72			
		Contralateral	8.26 ± 3.04	15	8.24 ± 3.24	15	0.88			
		Ipsilateral	7.66 ± 3.20	15	7.67 ± 3.43	15	0.97			
		Diagonal	7.79 ± 3.24	15	7.76 ± 3.38	15	0.99			
	After multiple	Lame	7.36 ± 2.87	15	7.09 ± 2.74	15	0.75	6.18 ± 2.74	10	0.28
		Contralateral	8.89 ± 3.34	15	8.10 ± 3.27	15	0.28	6.85 ± 2.52	10	0.37
		Ipsilateral	8.31 ± 4.87	15	7.36 ± 3.03	15	0.33	7.98 ± 3.96	10	0.02 **
		Diagonal	8.54 ± 4.76	15	7.54 ± 3.55	15	0.26	8.05 ± 3.96	10	0.18

Table 3. Estimated mean values, number of dogs, and *p*-value for symmetry indices of peak vertical force (%BW). SD = standard deviation. N = number of dogs. %BW = percentage of body weight. SI = symmetry index. SI_{limb} = lame limb/sound contralateral limb. $SI_{sagittal}$ = front- and hindlimb lame side/front- and hindlimb sound side. $SI_{transversefront}$ = lame front limbs/sound hindlimbs. $SI_{transversehind}$ = lame hindlimbs/sound front limbs. Single = measurement after a single treatment. Multiple = measurement after multiple treatments.

Parameter	Time	TENS (Mean ± SD)	N	Placebo (Mean ± SD)	N	*p*-Value	NSAID (Mean ± SD)	N	*p*-Value
SI limb Peak vertical force (%BW)	Before	0.87 ± 0.11	15	0.87 ± 0.11	15		0.87 ± 0.09	9	--
	After single	0.89 ± 0.11	15	0.86 ± 0.11	15	0.38			--
	After multiple	0.86 ± 0.12	15	0.90 ± 0.11	15	0.21	0.91 ± 0.07	10	0.07
SI sagittal Peak vertical force (%BW)	Before	0.92 ± 0.09	15	0.92 ± 0.09	15		0.95 ± 0.06	9	--
	After single	0.93 ± 0.09	15	0.93 ± 0.09	15	0.96			--
	After multiple	0.91 ± 0.10	15	0.94 ± 0.09	15	0.22	0.96 ± 0.06	10	0.52
SI transversefront Peak vertical force (%BW)	Before	1.64 ± 0.21	8	1.64 ± 0.24	8		1.67 ± 0.21	4	--
	After single	1.61 ± 0.23	8	1.63 ± 0.24	8	0.43			--
	After multiple	1.61 ± 0.19	8	1.61 ± 0.27	8	0.98	1.69 ± 0.31	4	0.05
SI transversehind Peak vertical force (%BW)	Before	0.57 ± 0.06	7	0.56 ± 0.07	7		0.55 ± 0.06	5	--
	After single	0.58 ± 0.06	7	0.56 ± 0.07	7	0.52			--
	After multiple	0.56 ± 0.06	7	0.57 ± 0.08	7	0.56	0.57 ± 0.06	6	0.98

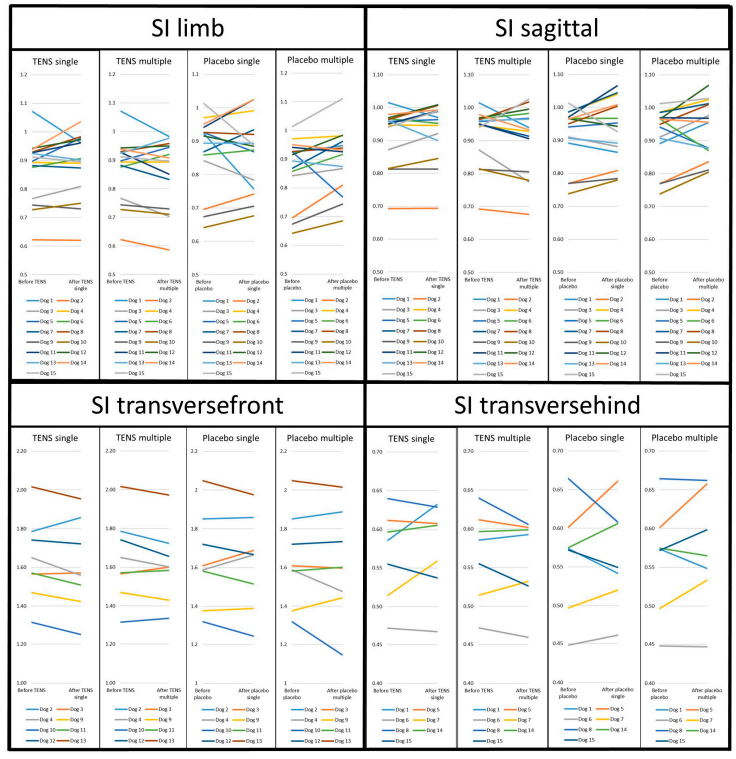

Figure 3. Individual symmetry indices of peak vertical force (%BW) for TENS and placebo. SI = symmetry index. SI_{limb} = lame limb/contralateral sound limb. $SI_{sagittal}$ = front and hind limb from lame body side/front and hind limb from sound body side. $SI_{transversefront}$ = front limbs from lame body half/hindlimbs from sound body half. $SI_{transversehind}$ = hindlimbs from lame body half/front limbs from sound body half. Single = single treatment. Multiple = multiple treatments. The suggested reference values are the following: SI_{limb} = 1.0, $SI_{sagittal}$ = 1.0, $SI_{transversefront}$ = 1.5, and $SI_{transversehind}$ = 0.66.

4. Discussion

Our results show no significant differences in peak vertical force (%BW), vertical impulse (%BW*sec), or SIs of osteoarthritic dogs when treated with TENS compared to placebo. Nor were there any significant differences in temporospatial parameters, such as stance time, swing time, stride time and stride length. Accordingly, our null hypothesis was accepted for this study protocol and population.

Our result differs from the only previous study on TENS as a stand-alone treatment for OA in dogs, where five dogs significantly increased weight bearing on the affected limb, evaluated by a force plate, indicating a positive pain-relieving effect of TENS [42]. The dogs were treated with a single treatment, at 70 Hz for 20 min, and the largest increase in weight bearing on the affected limb was seen immediately post-treatment and with changes remaining up to 180 min [42]. Similar to the Johnston et al. (2002) study, our measurements after a single treatment were made within an hour post-treatment [42]. Thus, the results from the present study are not in accordance with the Johnston et al. (2002) study nor with human studies indicating a pain-relieving effect during and shortly after TENS treatment [30,42].

The present study called for dog owners with a large commitment since it required a high degree of involvement from the owners, which narrowed the availability of possible candidates. Still, the study population in the present study was larger than in the previous study. It consisted of dogs with various locations of arthritic joints, thus representing the diverse patient population with OA. However, the five dogs in the Johnston study (2002) had OA in the stifle and the fifteen from our study in various joints, which may have had an effect on the lameness pattern and thus the inconsistent results [42,53,83].

Even though there are similarities in study design between previously conducted studies and the present study, there are also differences. A cross-over design was used to study the effect of the TENS and placebo interventions. This design entails a higher power and more statistical efficiency than the parallel design without control groups that have been used in previous studies on TENS in dogs [40,42,84]. An additional difference between our study and the previous ones was that two dogs were treated with NSAIDs throughout the TENS and placebo intervention. This was accounted for in the statistical analysis, with concurring NSAID treatment set as a fixed effect, and should not have affected the results significantly.

Our treatment sessions were longer than the treatment in the studies by Johnston et al. (2002) (20 min), Mlacnik et al. (2006) (15 min) and Krstić et al. (2010) (15 min) [40–42]. The decision to have a longer treatment session was based on clinical experience and from studies on humans, indicating, for example, an optimal treatment length of 40 min in knee OA [32,33,37,85]. In our study, a frequency of 80 Hz was used, a setting in between the frequency used in the studies by Krstić et al. (2010) (85 Hz) and Johnston et al. (2002) (70 Hz) [40,42]. A low degree of consistency in treatment settings was highlighted as one major limitation of TENS-related studies in a systematic review by Gibson et al. (2019) and Hyytiäinen et al. (2023) [37,43]. Therefore, our study aimed to have similar settings for frequency as the previous studies in dogs, and 80 Hz was used [37,40,42]. Further, the use of the strongest comfortable intensity possible is critical for pain relief with TENS; therefore, the intensity in the present study was increased until muscular fasciculation occurred as long as the dogs would withstand it [24,37]. Also, increasing intensity during the treatment compared to keeping the intensity fixed has been shown to decrease analgesic tolerance after five days in rats [38]. Since our study lasted longer than five days, the intensity was increased during treatment. As recommended by the literature, the most common electrode placement in our study was at the painful site; however, in one dog, this was not possible due to a limited area for electrode placement [25,86,87]. A transferred analgesic effect has been shown to happen in humans, and therefore, the placement over proximal nerve bundles is regarded as a suitable electrode location [88].

High-frequency TENS is claimed to alleviate pain through the pain gate theory and endogenic opioid release [24,38,39,89,90]. Studies on other pain-relieving treatments of dogs with OA have used changes in PVF and/or VI as outcome measures, evaluated with kinetic techniques [44,45,67–72,75]. Thus, therapeutic effects have been evaluated as an increase in weight on the affected limb and as a redistribution of weight to other limbs [59,60,74,75,91]. Measurement of ground reaction forces with a pressure-sensitive mat technique is an objective method for detecting asymmetries in weight distribution and takes all four limbs into consideration by using SIs [50,58,63,83,92–96]. In a previous study, when measuring 115 lame dogs on a pressure-sensitive mat, a specificity of 84.6% and a sensitivity of 91.1% were determined [50]. However, whether the technique can be used in the diagnosis of OA in dogs is discussed since studies have shown an overlap in the values for ground reaction forces of sound dogs and dogs with OA [58]. Further, there are several suggested cut-off values for the distinction between lame and not lame, indicating the difficulties in using the technique for the determination of a diagnosis [58,63,97,98]. The kinetic registrations in the present study were used to detect eventual changes in gait parameters within an individual dog and not for diagnosing OA; therefore, no cut-off values have been used.

Peak vertical force is considered an accurate variable for detecting weight distribution between limbs and is often used together with vertical impulse in gait analysis [56,58,63]. Peak vertical force and vertical impulse have been shown to be consistent in dogs with OA over time. Over two months, a change of 5% in these values is unusual, and a change of 10% is rare. Therefore, an effective treatment for OA could be expected to provide more than a 5% change in PVF and VI, which was not the case for TENS treatment compared to placebo in our study [56,68,99]. Besides ground reaction forces, temporospatial parameters such as stance time, swing time, stride time and stride length may be used to evaluate lameness; however, the documentation is limited [58,92,100]. The temporospatial parameters were included in the present study as the data can form a basis for future research in the area.

In the present study, some of the dogs had OA in multiple joints of multiple limbs. In these cases, the most affected limb (i.e., lame limb) was determined based on clinical history, clinical examination and kinetic data as in the studies by Moreu et al. (2003), Madore et al. (2007) and Roush et al. (2010) [83,101,102]. However, the involvement of multiple locations of OA could have influenced the results based on the reasoning that the dog would not shift as much of its weight from the affected limb to other limbs as if there was a single joint involvement [103–105]. However, in our study, gait parameters for all limbs and SIs were analysed, which most likely would have detected a difference in the exerted pressure on the ground from any limb based on the sensitivity of the pressure-sensitive mat [41,58,71,104]. The SIs in the present study are indices comparing the PVF between limbs and, thus, less vulnerable to the influence of velocity than solely reported PVF data, with SI sagittal showing a low variability of 2–3% in sound dogs [56,95,106]. The use of SIs to complement other parameters is becoming more common [41,56,61]. There is an increasing body of evidence from equine studies and some from canine regarding the influence on weight distribution and motion symmetry from compensatory lameness [74,91,100,103,107–109]. Thus, the reasons behind the inclusion of additional SIs, SI transverse and SI ipsilateral, were twofold: first, to get a better picture of eventual changes in the weight distribution between all four limbs, and second, to supply information for further research in the area. Based on the SIs, the results from the present study are not indicative of a TENS treatment effect different from that of a placebo.

As previously stated, velocity has a major effect on all gait parameters except for the SIs [110]. Therefore, the velocity was set as a fixed effect in the analysis for the TENS and placebo's effects on the gait parameters, with the exception of SIs. Furthermore, a fixed velocity interval was specifically used for the selection of trials [56,111]. Three trials were included for each measurement occasion, which is considered the gold standard, and this was possible most of the time [56]. In the three remaining occasions, the registrations were cancelled after two valid trials due to the risk of deterioration in lameness [56,112]. It is unlikely that the lack of three missing trials out of over three hundred had any major influence on the results. Mickelson et al. (2017) showed a mild alteration in weight bearing with repeated measurements in 61 dogs with mild to moderate lameness; the variance was <5% [112]. Therefore, in our study, the three missing trials should not have influenced our results drastically.

The handler may affect the outcome of the pressure-sensitive mat measurements by his placement in relation to the dog and through his general behaviour [113,114]. In the present study, the majority of trials had the same handler and leash side. According to Jevens et al. (1993), a variation between 0 and 7% of the total variance in gait parameters is to be expected when changing handlers [113]. However, due to the small portion of measurements that was affected by the change of handler and side, this should not have influenced the results significantly.

All the dogs included in the present study had OA and pain from the musculoskeletal system as determined by clinical history and clinical examinations. Medication with NSAID is used as the gold standard when investigating the effects of new pain-relieving treatments [115]. The NSAID intervention, i.e., study part 2, was performed to test whether a standard pain relief medication would change the gait parameters of the dogs. No

significant differences were seen before and after NSAID treatment for stance time, swing time, stride time, stride length, and peak vertical force (%BW). However, the results show a significant increase in vertical impulse (%BW*sec) for the ipsilateral leg ($p = 0.02$) after treatment with NSAID. Previous studies on weight redistribution have not shown an isolated increase in VI for the ipsilateral leg without any other changes in gait parameters for the other limbs [74,100,107]. Our result is, therefore, not consistent with the current documentation on weigh redistribution in lame dogs and can, therefore, be suspected to be a false positive value. Firocoxib has an indication for pain relief in OA, with the dosage per kg body weight given in the study; however, the length of the treatment for sufficient pain relief is not specified [82]. The treatment period might have been too short to ensure increased efficacy in dogs with chronic pain [21,116,117]. It is also possible that the discrete change in VI (%BW) is explained by the time (12–24 h) between the last medication and the measurement occasion [82]. Further, in a study by Rhodin et al. (2017), horses with lameness did not change their gait pattern in response to NSAID treatment; however, after diagnostic anaesthesia, the lameness improved, so the minor response in the present study may also be due to the insufficient treatment effect of the NSAID [118].

In both veterinary and human medicine, the evidence of the effect of TENS on chronic pain is inconclusive, reported in systematic reviews [35,37,43,119–121]. The major deficits in the scientific material are small studies of low quality and a large variety of settings used for the TENS treatment. Future studies in veterinary medicine should, therefore, ensure similar treatment protocols and study designs to be used to increase the level of evidence.

5. Conclusions

To the author's knowledge, our study is one of the few that measures the effect of TENS treatment in dogs with OA. The results of our study provide preliminary evidence that TENS, with the settings used, did not cause significant changes in gait parameters in dogs with OA. Thus, the null hypothesis that TENS treatment of dogs with OA will not change gait parameters differently than placebo treatment was accepted. However, further studies are needed to confirm the clinical efficiency of TENS as a treatment for OA in dogs.

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This thesis investigated whether transcutaneous electrical nerve stimulation reduces pain in dogs with osteoarthritis and developed methods to monitor physical activity. Using the applied settings, treatment with transcutaneous electrical nerve stimulation did not significantly change pain. Accelerometer data indicated that most pet dog activity occurs below 25 Hz, exceeding the range captured by common monitors. Signal filtering influenced activity classification, and human-based non-wear detection was unreliable, highlighting the need for dog-specific data processing methods to accurately assess physical activity in dogs.

Anja Pedersen received her postgraduate education at the Department of Clinical Sciences, Swedish University of Agricultural Sciences (SLU). She obtained her veterinary degree at SLU.

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