GHENT UNIVERSITY

FACULTY OF VETERINARY MEDICINE

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DIAGNOSIS OF SUBCLINICAL TENDINOPATHY IN THE HORSE

by

Jacoba Johanna VAN DIJK

Promoters: Prof. dr. F. Pille
Dr. M. Oosterlinck

Literature Review
as part of the Master's Dissertation

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Preface

One day I went running and before I was well on my way, I felt a slumbering pain in my patellar tendon. The pain was not enough to make me stop, so I kept running and my mind wondered off as well. Is this because I have been running too much? Is this similar to what horses feel when they suffer from overload injuries? Is that similar to what I feel now and if so, how long is this present before it is noticed by anyone? Did the inconvenience in my knee alter my running pattern? Could anyone see I was running in a funny way? Do horses alter their movement patterns if they feel a little pain or nuisance somewhere? Obviously what I felt wasn't enough to make me stop running for the day, so I could imagine a horse who is a flight animal is even less inclined to show any signs of weakness. So then I wondered if a clinical tendinopathy is presented, how long has this been going on? Did the horse already notice this long before? Could it have been detected? If it can be detected at an early stage, is it possible to prevent it from becoming a clinical lameness? The more I thought about it, the more I wanted to know. Luckily I was allowed to explore this topic for my master's thesis and I could not have done this without the approval and help of my promotors. I sincerely want to thank prof. Pille for his time and patience, for always being available to answer any questions I had and for his effort in making sense of the lines of thought that I came up with. Secondly I want to thank Dr. Oosterlinck for his time and effort, especially in providing me with suggestions for research articles and most of all, a detailed feedback on my written texts.
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Abstract

Tendinopathies are a common and debilitating condition. Treatment is problematic and the number of horses that return to previous sports levels are limited, therefore there is a need for prevention rather than treatment. It is suggested that there is a subclinical phase prior to the painful and debilitating stage of tendinopathy and the possibilities of diagnosis of this subclinical phase need to be explored. It is thought that overload on the tendon may cause the collagen fibrils to break, inducing microdamage to the tendon. Because repair is not effective the damage to the tendon accumulates which ultimately leads to complete or partial rupture of the tendon. There are also indications that the early stages of tendon overload are hallmarked by increased deposition of proteoglycan. To detect loss of continuity of collagen fibrils or increased proteoglycan deposition, ultrasound tissue characterization is a promising technique. However other techniques such as thermography and magnetic resonance imaging can also be used in certain settings.

Key Words: Diagnosis – Horse – Pathogenesis – Subclinical – Tendinopathy
Samenvatting

Tendinopathie is een aandoening die veroorzaakt wordt door overbelasting en die wereldwijd veel voorkomt bij paarden die in de sport moeten presteren. Bij renpaarden komt dit veelvuldig voor, maar ook in andere disciplines zoals dressuur en eventing wordt het veel gezien. Alhoewel de aandoening al zeer lang bekend is, is het verrassend hoe weinig er geweten is over de oorzaak en pathogenese. Vroeger werd het tendinitis genoemd omdat men er vanuit ging dat het een chronische onsteking van de pees betrof. Echter werd er steeds meer duidelijk dat er van een chronische ontsteking eigenlijk geen sprake is. Er werd steeds meer bewijs gevonden dat wees in de richting van een degeneratieve aandoening en daarom werd de term tendinitis vervangen door tendinose. Recentelijk is men echter gaan inzien dat er toch enige factoren die duiden op ontstekingsprocessen een rol spelen, zoals de aanwezigheid van inflammatoire cytokinen. Daarom is het beter om te verwijzen naar een aandoening van de pezen door overbelasting met de term ‘tendinopathie’ welke neutraal is ten opzichte van de oorzaak van de pathologie.

Veel therapieën en behandelingen zijn bedacht en gepromoot maar enkel het feit dat er zoveel zijn geeft al aan dat er geen één echt succesvol is. Doordat er weinig succesvolle behandelingen zijn die ook nog eens lang kunnen duren en er veelal herval optreedt wanneer de paarden weer in het werk treden, is het een zeer problematische aandoening. Het is daarom evident dat er eerder gezocht zal moeten worden naar mogelijkheden voor preventie in plaats van behandeling. Om de aandoening te kunnen voorkomen is het uiteraard essentieel om de oorzaak en de pathogenese van tendinopathie te kennen. Er wordt algemeen aangenomen dat overbelasting zorgt voor schade aan de collageenvezels van de pees welke scheurtjes gaan vertonen. Dit houdt in dat er zogenoemde microschade optreedt en de pees heeft onvoldoende mogelijkheden om deze schade te herstellen als hij herhaaldelijk te zwaar belast wordt. Door het verlies van continuïteit van de collageenvezels verliest de pees zijn sterkte en gaan de overgebleven collageenvezels blootgesteld worden aan hogere krachten omdat de totale kracht die uitgeoefend wordt bij de locomotie gelijk blijft. Hierdoor gaan ook de overgebleven collageenvezels een hoger risico lopen om beschadigd te worden en ontstaat een vicieuze cirkel. Voordat deze aantasting van de pees tot klinische uiting komt is er al veel schade aan het weefsel toegebracht en herstel van het aangetaste peesweefsel is moeizaam en vaak onvolledig met vorming van littekenweefsel. Er zijn echter ook aanwijzingen dat niet de schade aan de collageenvezels de oorzaak is van de degeneratie, maar dat de degeneratie begint met een toename van proteoglycaan depositie in de extracellulaire matrix als reactie van de tendinocyten op een te hoge belasting.

Doordat er al een langere tijd degeneratie plaatsvindt is het belangrijk om erachter te komen hoe dit opgespoord kan worden. Belasting kan dan al in een vroeg stadium tijdelijk verminderd worden en is er meer kans op een voorspoedig en snel herstel. Hoe dan ook is het belangrijk dat de pathogenese goed opgehelderd wordt in toekomstig onderzoek. Alleen dan is het mogelijk om met de beschikbare technieken te gaan zoeken naar tekenen van beginnende tendinopathie; zonder te weten waar men naar moet zoeken is dit onmogelijk om subtiele veranderingen in de subklinische fase op te sporen. Technieken die veelbelovend zijn, zijn echografie en dan met name de recent ontwikkelde Ultrasound Tissue Characterisation maar ook thermografie en MRI kunnen van waarde zijn in specifieke gevallen. Detectie van subklinische keurpelheid met behulp van de krachtplaat metingen leek een veelbelovende techniek maar is tot nu toe weinig bruikbaar voor het identificeren van deviaties in locomotie die veroorzaakt worden door specifieke aandoeningen.
Introduction

Tendon injuries are very common and impose a serious threat to the wellbeing of the horse and its sports performance. One of the most important injuries both in number and impact on career perspectives is tendinopathy. The reason why these tendon injuries are so problematic is not only the high incidence rate. There is a long recovery period, a lack of effective treatment, a large amount of horses that cannot return to previous levels of work and if doing so, a high incidence of re-injury (Firth, 2000).

Since tendon injuries are such an important cause of losses in sportshorses a lot of effort has gone into determining effective treatment methods. Once a horse is presenting clinical symptoms, the diagnosis of tendinopathy is usually readily made but the difficulty lies in the successful treatment and mostly the lack thereof. Tendinopathy has been known for hundreds of years (Firth, 2000) and after a few decades of intense research on treatment of tendinitis and tendinopathy, the only conclusion is that tendinopathy is problematic to treat. A huge amount of therapeutic regimens exist, but as Firth (2000) and other authors point out, the number of treatments available only serves to illustrate the lack of success of any of them. A lot of research on tendinopathy focusses on specific therapeutic methods or regimens but little is known about the pathology itself. Obviously it is easier to know how to fix something when you know what it is that is broken; for this reason alone more attention should be been paid to the pathological processes involved.

Not only is it crucial to understand the underlying pathology to develop treatment methods, it is thought that subclinical stages preclude a clinically manifest tendinopathy and there are also indications that early pathologic processes might be reversible (Cook and Purdam, 2009). If this is true and these early pathological processes can be detected, prevention and early diagnosis rather than curative medicine will be more likely to solve the tendinopathy problem as is also argued by van Weeren (2012). 'Diagnosis' of a subclinical phase allows to adapt training schedules, thereby preventing the horse from developing a clinical tendinopathy at all. The question is if it will be possible to identify horses that are developing a tendinopathy before clinical symptoms appear and this literature study aims to answer this question. To do so, it is necessary to give an extensive overview of what is currently known about the etiopathology of tendinopathy. Only if early pathological processes and the changes in tissue that it causes are known will it be evident what the diagnostics techniques are that could be used to detect these changes.
1: ETIOLOGY AND PATHOGENESIS OF TENDINOPATHY IN HORSES

1.1 Defining tendinopathy

Tendon injury is a rather unspecific term but yet it is often used when actually referring to tendon overstrain injuries (Clegg, 2012; Dahlgren, 2007; Thorpe et al, 2010a). Not all tendon injuries are due to overload but the majority are. In this paper overload, or sometimes called 'strain-induced' or 'intrinsic tendon injuries', will be discussed. This excludes tendon injuries due to external trauma, defined as 'extrinsic tendon injuries' by Smith (2011). Intrinsic tendon injury caused by overload can affect many different tendon structures but the superficial digital flexor tendon (SDFT) is most often affected (Ross et al, 2011). However, also the deep digital flexor tendon (DDFT), suspensory ligament, and the distal accessory ligament are often seen to develop a tendinopathy (Smith et al, 2000). The definition of intrinsic tendon injuries does not necessarily exclude pathology to an insertional tendon region which should correctly be called desmopathy instead. Despite a lot of research there are no indications yet, that the pathological processes of degeneration due to overload differ between tendons, insertion sites of tendons and ligaments. Hence desmopathies can also be regarded as strain-induced injuries. Ligaments, who connect bone tissues can also be subject to the same overload induced injury (Shepherd and Screen, 2013).

Commonly affected structures differ between the various equestrian disciplines, but large numbers of injured horses are found in many disciplines. Tendon and ligament injuries are very common in racehorses. Data are numerous for incidence rates in various types of racing but in all cases they are a common or sometimes even the most important cause of career endings. In other disciplines numbers are less available but nevertheless known to be high. Tendinopathy is the most important cause of lameness in polo ponies and the most important cause of ending a career in event horses (Bathe, 2011b). In showjumping horses, suspensory desmitis and tenosynovitis are common but tendinopathy can occur as a result of foot pain, which leads the horse to adapt its biomechanical pattern and changes stress patterns on the digital flexor tendons (Boswell et al, 2011). In eventing horses the condition is usually caused by repetitive cyclic loading and not by a single-event injury such as tripping, falling or stumbling. These differences can partly be explained by the fact that showjumping horses do not perform on high speeds, and speed is an important factor for excessive strain on flexor tendons. In dressage horses, proximal suspensory desmitis of the hindlimb is the most common cause of lameness. Due to the to the desired collection in dressage where the horse places more weight on the hindquarters, the hindlimbs are more heavily loaded. Sometimes a tendinopathy of the superficial digital flexor tendon is seen in dressage horses but then mostly in young horses who have been subject to disproportionate pacing and workload (Kold and Dyson, 2011). In general injuries of tendons and ligaments are more common in the forelimb than in the hindlimb (Swor et al, 2004).

It is interesting to know that not only horses are prone to developing these injuries, human athletes are too. A lot of knowledge in the equine field comes from studies in human medicine and vice versa (Lui et al, 2011; Patterson-Kane et al 2012). It may be useful to study results in human medicine to have an indication where research should be directed in equine medicine, but even in human medicine basic reliable studies on the epidemiology of tendinopathy in different tendon structures are not available (Maffulli et al, 2003). To be able to compare studies in both fields it is important to understand what the common
pathological principles are in tendinopathy that apply to all tendon overload injuries and maybe even to
different species. The general mechanism of strain-induced tendon injury is still the topic of a lot of research
and an even larger amount of speculation. However it is important to keep in mind that one should be careful
when extrapolating results of one study of strain-induced injuries to other cases, patients or species (Lui et
al, 2011). Very often, additional research will be necessary to determine if research findings can be
extrapolated. A more or less accepted theory is that tendinopathy is caused by repeated overload which
leads to cumulative microdamage to the collagen fibrils that fails to be repaired. Eventually this leads to
clinical tendon degeneration with loss of function and sometimes partial or complete rupture. This definition is
more or less widely accepted and used by many authors (Goodrich, 2011; Khan et al, 2002; Smith, 2011),
but nonetheless is questioned by Riley (2007) and Cook and Purdam (2009) who propose that the onset of
pathology is at least partially driven by a tenocyte response. A variety of terms are commonly used to refer to
injured tendons but they should be differentiated as follows:

**Tendinitis** describes a histopathologic finding of inflammation where the tendon is the most important
inflamed site, that is, when the term is used in recent humane literature (Fredberg and Stengaard-Pedersen,
2008, Reinking, 2012). Clinical use of this term is no longer accepted to refer to an injured tendon unless a
histopathologic diagnosis is made because usually no inflammatory signs are present on histology. In
previous years, tendinitis was used to describe any injury to tendons because it was thought be a chronic
inflammatory process (Fredberg and Stengaard-Pedersen, 2008). Sometimes the term is still used in
literature while it is clear that the author is actually referring to overstrain injuries (Kasashima et al, 2002a;
Chesen et al, 2009). The term was mostly refuted based on the fact that inflammatory cells are not found in
injured tendon tissue (Fredberg and Stengaard-Pedersen, 2008) and pathology of the painful tendon was
from then onwards referred to as tendinosis to indicate the degenerative nature, but the term tendinosis was
eventually replaced by tendinopathy.

**Tendinosis** is currently only used for histopathologic findings of degeneration in the tendon without signs of
inflammation. However, it is also widely used to refer to a painful tendon in which abnormalities are detected
on ultrasound (US), MRI, radiology or histopathology (Fredberg and Stengaard-Pedersen, 2008). Reinking
defines it as a chronic degenerative state of tendon where inflammatory cells are absent on histolopathology.
Evidence of degeneration, such as neovascularisation, proliferation of tenocytes and increased proteoglycan
deposition can be present (Maffulli et al, 2003).

**Tendinopathy** refers to a painful tendon combined with impaired performance and swelling and/or
abnormalities on US and MRI. It is the recommended term for a clinical diagnosis for patients with painful
tendons and it is preferred because it does not make any statement about the histopathologic state of the
structure (Reinking, 2012). Tendinopathy is called acute when symptoms are present less than 6 weeks,
subacute when present for 6-12 weeks and chronic when present for more than 3 months (Fredberg and
Stengaard-Pedersen, 2008). However, in many clinical studies other time frames are used. On top of that,
other definitions are also used. For example tendinopathy is rather vaguely defined as 'condition affecting
tendons' by Riley (2007). Due to confusing use of definitions, one should always be familiar with what an
author actually refers to when comparing research or papers on 'tendinopathy'.

**Tenosynovitis** involves pathology of the synovial tendon sheath around the tendon and should be used when
the damaged tendon is situated within this region (Reinking, 2012).
1.2 Commonly affected structures

1.2.1 Suspensory Ligament (SL)
The suspensory ligament is a strong tendinous structure that contains muscle fibers but the amount seems to vary within breeds. Strength of the SL increases with training, and in horses with high level of training, acute stress overload is more likely to result in a fracture of the proximal sesamoid bone than to cause failure of the SL but these injuries will not be discussed here. When considering injuries to the SL itself, a distinction is made based on location. First there are the injuries to the proximal aspect of the SL also called proximal suspensory desmitis (PSD), secondly there are the lesions in the body (or middle one-third) of the structure and lastly there are the branch lesions that are of course confined to the distal part of the structure (Dyson and Genovese, 2011).

PSD is the also the most common cause of soft tissue injuries to the limbs of sportshorses according to Bertone (2011b). In chronic cases, avulsion fractures, bone resorption and sclerosis can be present around at the origin of the SL. Apparently the origin is most sensitive to overload injuries, since they are most often seen here. Work in deep, soft grounds such as in eventing, or racing on turf places a heavier load on the soft tissues. This can be a reason why all soft tissue injuries, and also PSD, is more often seen in Europe where turf is used on racetracks. Also, conformation is thought to predispose to this trauma; hyperextension of the carpus or tarsus, alone or in combination with hyperextension of the fetlock is thought to predispose to PSD. This dropped fetlock conformation can however also predispose to branch lesions (Dyson and Genovese, 2011) but what is cause and what is result is being debated.

A form of tendon degeneration that is not related to performance is called degenerative suspensory ligament desmitis (DSLDD). It is known to occur in horses that are commonly used for leisure activities and do not perform in sports activities. Its pathogenesis is unknown and there is no treatment; horses with persistent lameness are often euthanized. It causes a progressive degeneration of the SL, but the DDFT and the SDFT can also be affected (Schenkman et al, 2009). It is thought that this disorder is different from overload injuries but as will become clear later, it shows many similarities in histopathological findings in overload injuries.

1.2.2 Superficial Digital Flexor Tendon (SDFT)
While Bertone (2011b) says the SL is the most commonly injured, most other authors (Smith et al, 2000; Butcher et al, 2007; Patterson-Kane and Firth, 2009) refer to the SDFT as the structure being to most often affected. These differences are mainly due to different distribution of affected structures in different types of sports such different types of racing, dressage, eventing and showjumping as well as regional differences due to local conditions such as ground covering on racetracks.

The superficial digital flexor tendon may be rated the first or second most affected structure, but in any case it is one of the most important affected soft tissue of the limbs. Because of its more superficial location, enlargement of the structure is more readily visible and palpable. It is said to develop in size and shape when in training according to Bertone (2011b) but other authors state it does not respond to training and only degenerates onces it has reached maturity (Smith, 2011). The response of tendon to exercise will
be discussed later. Most cases present with injury in the midmetacarpal region, resulting in typical rounding of the contour of the palmar aspect of limb in a lateral view. However the SDFT can also be affected at the distal metacarpal level, at the distal metatarsal level, at the branches in the pastern region or more proximal at the level of the carpus.

The accessory ligament of the SDFT is situated at the caudal radius and attaches the SDFT to it. It serves to support the muscular origin during heavy loading, thereby preventing avulsion of the proximal muscle unit Bertone (2011b). It is not often injured due to overload.

1.2.3. Deep Digital Flexor Tendon (DDFT)

The distal part of the DDFT displays a typical tendon adaptation to increased loading; at the region of the distal interphalangeal joint it has a dorsal zone of fibrocartilage (Blunden et al, 2009). It is clear that the tendon is subjected to high loads in its distal region. It is therefore no surprise that most degenerative lesions of the DDFT are found in the distal phalangeal region, however this is only true in the forelimb (Swor et al, 2004). It is reported that the DDFT is more often injured at the metatarsal level than at the phalangeal region of the forelimb (Swor et al, 2004) but more intense use of MRI imaging may reveal a different distribution of these lesions. These injuries in the phalangeal region are caudal to or at the level where the tendon crosses the flexor cortex of the navicular bone. With the use of MRI it has become clear that many horses with navicular syndrome and absence of radiological abnormalities show degenerative lesions of the DDFT in the foot. They can be considered part of the navicular syndrome (Bertone 2011a). Since these lesions are not commonly visualized by ultrasound, and MRI is only available for a certain group of horses with motivated owners, true numbers of degenerative pathology of the DDFT in this region can only be guessed. However, ultrasonographic evaluation of the DDFT in the phalangeal region is sometimes used and can be succesful (Withcomb, 2009). Only in the last decade when MRI became available for clinical use, has it become clear that injuries of the DDFT are an important factor in causing or contributing to lameness in the foot. Currently it is even the most common diagnosis in horses with foot pain (Schramme, 2011). Lesions in the DDFT in the phalangeal region are primarily degenerative (Blunden et al, 2009).

DDFT strain injuries are less common than strain injuries of the SDFT or SL at the level of the metacarpus, but an injury of the DDFT in the hindlimb is often located at the metatarsal level (Barr et al, 1995; Swor et al, 2004). The tendon can be painful on palpation and the DDFT can show swelling. The clinical findings are similar to the typical SDFT tendinopathy in location and symptoms if the problem is situated at the mid-metacarpal level but the DDFT is of course located deeper than the SDFT.

The digital sheath and annular ligament are in close association with the DDFT at the level of the fetlock. Injury and swelling of the DDFT (as well as that of the SDFT) just above the annular ligament can mimic an annular ligament constriction when in fact the annular ligament is not involved. Therefore a careful examination is needed to assess the involvement of these structures when there is injury at this level. The DDFT is easily injured at the level of the fetlock, when a horse hits itself with another limb (Bertone, 2011a) but this is an extrinsic injury.

The accessory ligament of the DDFT runs from the carpal palmar ligament to the DDFT in the proximal region of the metacarpus. It is thought to provide stability to the carpus in the midstance of the stride, preventing hyperextension of the carpus. Injury to this structure is the third most common cause of
soft tissue injury in the forelimb, after that of the SL and the SDFT. Interestingly, it is quite common in
pleasure horses and ponies and is not that frequently observed in racehorses and event horses. Lameness
is usually seen after work and associated with swelling in the proximal metacarpus. Enlargement and
hypoechogenicity is seen on ultrasound examination. Lameness usually improves with rest but comes back
when exercise is resumed.

1.2.4 Tenosynovitis
The digital flexor tendon sheath surrounds the superficial and deep digital flexor tendons as they curve
around the palmar or plantar aspect of the fetlock joint. When effusion is seen in this structure which normally
only holds a small amount of fluid, it is possible that it is a small harmless blemish called windpuffs. Effusion
can however also be the indicator of injury to one of the tendon structures within it or to the sheath itself, or
of an infectious process causing septic tenosynovitis but the latter is uncommon (Fiske-Jackson et al, 2013).
There are various causes of non-infectious tenosynovitis, such as tendonitis of the SDFT or the DDFT, tears
in the DDFT or the manica flexoria or desmitis of the annular ligament. However the most common cause is
a tear to the lateral border of the DDFT or a tear of the manica flexoria. It is important to differentiate swelling
in this area from swelling of the SDFT or DDFT. Ultrasound can be used to assess the damage of soft tissues
involved as well as the presence of adhesions. However, longitudinal tears in the DDFT are often missed on
ultrasound (Edinger et al, 2005) and lesions in the manica flexoria are even harder to diagnose with
ultrasound (Fiske-Jackson et al, 2013). The possibility of such lesions should always be considered when
ultrasound examination is inconclusive and an explorative tenoscopy or MRI can be used to examine the
presence and extense of such lesions. A recent study (Fiske-Jackson et al, 2013) showed that contrast
radiography may also be valuable to diagnose tears in the manica flexoria and the DDFT, and this contrast
medium can be administered together with intrathecal analgesia which makes it a practical procedure in
clinical settings. A study by Blunden et al (2007) on lesions of the DDFT in the region of the navicular bone,
revealed that 'a significant proportion' of these lesions extented proximally into the DDFT and hence into the
area where the DDFT runs throught the tendon sheath.
1.3 Tendon Properties

1.3.1 Structure and Function

The tendons’ main constituents are collagen type I fibrils, extracellular matrix and tenocytes. The cellular components are tenoblasts and tenocytes. Tenoblasts are more active in the synthesis of extracellular matrix that is mostly composed of collagen, proteoglycans and glycoproteins and after a period of intense synthesis they differentiate into tenocytes which are the predominant cells found in mature tendons. The tenocytes are able to remodel the matrix by synthesizing degrading factors as well as collagen molecules and matrix components (Thorpe et al, 2010a). The number of cells is relatively low as compared to other tissues. The main structural component of the tendon are the collagen I fibrils that make up 75-80% of dry tendon weight. Type III collagen is found mostly in immature and damaged tendon. The tropocollagen I molecules form cross-links and are arranged into fibrils that align to form fascicles. These are considered the structural components since they are moving independently when the tendon is loaded, with a minimal lateral force transmission between them. The fascicles are surrounded by loose connective tissue called endotenon which supplies bloodvessels, lymphvessels and nerves to the tendon. The tenocytes are mostly found between the collagen fascicles within the endotenon and extent long cytoplasmic processes and gap-junctions for intercellular communication (Patterson-Kane and Firth, 2009).

The stress-strain curve was first proposed by Goodship in 1994 to explain what happens to the tendon when load is applied to it and has since then been appreciated by many. It is also discussed by one of the main textbooks on equine lameness, namely ‘Diagnosis and Management of Lameness in the Horse’ edited by Ross and Dyson (2011) from which it is taken here (Smith, 2011).

‘Stress’ is the load, or force per unit area, that is applied to the tendon while ‘strain’ is the elongation of the tendon that the applied stress causes. The curve is devided in four parts that each demonstrate a specific response of tendon at different levels of load (or stress). The collagen fibrils show a wave pattern called crimp when there is no load applied to it. When a load is first applied to the unloaded tendon, the crimp pattern disappears and this is shown in the ‘toe’ region of the graph with number 1. When the crimp pattern has disappeared and more load is applied, the tendon begins to stretch, visualized in the linear increase (2). The increase in load corresponds with a linear increase in tendon lenght. However, when the tendon is maximally stretched it yields to the load that is applied to it; a further increase in load leads to increasing length, however this relation is no longer linear and at this stage the structural integrity of the tendon is lost (3) and microdamage occurs. A further increase in load in the end leads to a macroscopic rupture of the tendon as seen at the level of number 4. It is however not known what the exact damage is that occurs but microrupture of collagen fibrils has been suggested, as well as rupture or slippage of the covalent cross-links between the fibrils (Smith, 2011a).
In humane medicine, a distinction is made between traction tendons and gliding tendons. The former being tendons where the insertion of the tendon and the course of the muscle belly are aligned along the same axis. Gliding tendons have a direction of insertion that is not along the force line of the muscle that is controlling it and course around bony landmarks. As Reinking (2012) points out, the pathogenesis might differ between these because of the compressive and shear forces that are encountered at the level of bony landmarks. The commonly injured human achilles tendon is a traction tendon and it is compared to the SDFT in horses (Patterson-Kane and Firth, 2009). In equine cases, most tendons that are discussed are traction tendons when using this definition (SDFT, DDFT, SL, ALDDFT). However, when considering the aspect of the DDFT that crosses the metacarpo-phalangeal joint as well as the navicular bone, these parts of the tendon are clearly gliding tendon. It is important to consider these functional differences when comparing pathology in different tendon structures.

Another distinction can be made between positional tendons and energy-storing tendons. The former have a function in limb placement, or in case of humans, manipulative skills. In the horse these positional tendons are for example the digital extensor tendons who rarely suffer from overload injuries. The minimal elasticity of the tendon ensures efficiency of force transfer from muscle to bone. This is different for tendons such as the achilles tendon and the equine flexor tendons who are known to have higher elastic properties. They are involved in weight-bearing and locomotion and need to have a higher degree of elasticity to serve as an energy store (Reinking, 2012). These tendons are thought to be especially prone to damage due to cumulative load and it is argued that these tendons cannot adapt to mechanical forces after skeletal maturity is reached, which in the horse is after the age of two (Smith et al, 2002). It has been estimated that the amount of work that is recovered due to elastic recoil is around 36% for the equine SDFT during gallop, and even 50% for the human achilles tendon. As said, strain is the change in tendon length due to load and is needed to store energy. However, the need to support limb weight and hence desired tendon strength in both the achilles tendon and SDFT, conflicts with the need to store energy made possible by its elastic properties. This is considered typical for these tendons and results in tendon function within very low safety margins and making it prone to damage if the load is too high (Patterson-Kane et al, 2012). Therefore they are prone to suffer from strain-induced tendinopathy.

1.3.2 Tendon Strength and Adaptation

According to Smith (2011a) the suspensory ligament (SL) strengthens in respond to exercise but the tendons in the adult horse do not. Maybe this adaptive response of the SL is due to the presence of striated muscle fibers in the suspensory ligament; these muscle fibers make up 10-14% of the cross sectional area (CSA) (Firth, 2000). However, the amount of muscle in the SL varies between breeds (Goodrich, 2011). The lack of strengthening in response to exercise might explain why tendons are more prone to accumulate microdamage when trained intensely compared to muscle or bone. Muscle and bone are known to adapt to increased workloads (Goodrich, 2011a). According to Smith (2011a) tendons have been reported to mature and increase strength in response to loading until the horse is two years old and has reached skeletal maturity. After this, tendon tissue quality is thought to degenerate due to ageing as depicted in the graph (adapted from Smith, 2011a).
If this degeneration after skeletal maturity is a natural occurring phenomenon, it is not a pathological degeneration but rather a physiological one. An immediate question that arises, is whether the physiological degeneration (green line) is influenced by demands placed on the tendon due to heavy exercise. In other words; is the demand placed on horses causing a pathological degeneration? The latter is represented by the steeper red line in the curve and this is an adaptation to the original graph by Smith. The answer must be yes, for example when one compares incidence rates of tendinopathy of race- and leisurehorses it is clear the latter group suffers less from tendinopathy (Thorpe et al, 2010a). While many influences have been suggested such as genetic background, conformation and age, it remains largely unclear what causes the balance to tip from normal degeneration to pathology causing the tendon to eventually lose function. Nonetheless, exploring the possibilities of increasing tendon strength by training as also depicted in the graph, offers opportunities for a purely preventive strategy as opposed to early intervention and intense monitoring which, one can argue, is still curative medicine.

The solution to the tendinopathy problem might be to get young horses in a training regimen that allows them to start their sports career with maximally developed and matured tendons. As seen in the graph, Smith (2011a) argues that training before the age of skeletal maturity may increase tendon strength. As can be seen, a horse that starts with a higher level of tendon strength will have a longer racing career while being subject to the same amount of degeneration. One of the parameters of tendon strength is considered to be the cross sectional area (CSA) of the tendon. While one study (Kasashima et al, 2002b) showed that exercise in foals increased cross sectional area (CSA) and thus tendon strength in foals of up to 15 months of age, another study showed that exercise did not increase the CSA compared with foals who were let out at pasture (Moffat et al, 2008). In the first study the foals were confined to pasture only 4 hrs a day, and in the second study they were let at pasture 24 hours a day. It is possible that the difference in time at pasture between 4 hrs and 24 hrs a day accounts for the fact that the first group does not exercise enough whereas the last group already induced a maximal growing response of tendon tissue by being out on pasture 24 hrs a day. If this optimal tendon strength can be achieved in horses while they grow up at pasture, there is no benefit in increasing exercise early in life. More research is needed to determine if there is an optimal exercise schedule for young horses to reach maximal tendon strength during growth. Clearly it can be argued this indicates current sports practices are placing a demand on the horses that is simply too high, however it will still be in the interest of these horses to try to prevent these injuries as much as possible. More studies are needed to confirm this hypothesis, and it would also be good to not only consider CSA as an indicator of tendon strength but also mechanical properties, molecular composition and morphology of tendon tissue (Clegg, 2012).
1.4 Pathogenesis of tendinopathy

1.4.1 Inflammation or Degeneration?

An acute tendinopathic tendon presents with swelling, warmth and painfulness. These are typical symptoms of inflammation and hence the term 'tendinitis' was applied to refer to this clinical presentation. The term tendinitis was also applied to a chronic painful tendon that does not show these inflammation hallmarks any longer, because it was thought to be a chronic inflammation (Abate et al, 2009). Gradually the view shifted away from the inflammatory theory to the appreciation of a degenerative disease, since no inflammatory processes where identified on histopathological examination. This finding long served and still serves to support the degenerative view. It is now widely accepted that a timespan of unnoticed degeneration has already passed before the clinical stage is presented (Smith, 2011a) and the term tendinitis was abandoned to be replaced by tendinosis, implying the absence of an inflammatory component in favour of indicating a purely degenerative process (Smith, 2011a).

Nonetheless, one cannot disregard the fact that the clinical stage with pain, swelling, and warmth is still presenting three out of five inflammatory pillars of rubor, tumor, dolor, calor and loss of function, and four if the injury leads to loss of function. Even if the inflammatory component would be reserved only for histopathological findings, the acute stage of acute tendinopathy could at least be referred to as 'inflammatory-like'. Finnoff et al (2009) say tendonitis can be used to refer to the acute stage of injury, but are not specifying what kind of injury. Campbell and Grainger (2001) explain the inflammatory respons as a result of acute hemorrhage in partial or complete tears after previous degeneration, thus leaving room for the presence of inflammation as well as degeneration.

While the presence of inflammatory cells is generally used as a standard to confirm inflammation of tissue on histological evulation, inflammatory mediators most likely play a role in the early processes of tendon injury and have already proven to be present in early stages of reactive tendinopathy (Abate et al, 2009). Even in affected tendons that have already formed scar tissue, the tenocytes showed positive staining for the proinflammatory cytokines IFN-γ, TNF-α, IL-1α and IL-1β while these were not found in control subjects (Hosaka et al, 2002). Hence it is not correct to consider the process of tendinopathy entirely free of inflammatory processes. Abate et al (2009) propose that initial overstrain induces damage to tendon tissue, and in response inflammatory mediators as well as collagen degrading factors are released. This can be an explanation why corticosteroid injections in the acute phase are effective; they might limit the damage to the tissue in this stage by suppressing the inflammatory respons. However, degeneration has already been present for some time before clinical symptoms appear and it is unclear to what extent these inflammatory mediators are still present at the clinical stage, what their role is in the degeneration that has taken place and what their role is in the onset of the degenerative process. The discussion is an ongoing one, and most likely the truth is both processes of degeneration and inflammation are involved, as is also argued by Abate et al (2009). More research into the pathological mechanisms involved is the only way to find the answer. Most likely it will appear that nature does not let itself be captured within one of the strict definitions of 'degenerative' and 'inflammatory'.

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1.4.2 Pathological findings in equine tendons

1.4.2.1 Superficial Digital Flexor Tendon

Most studies have focussed on changes in the matrix; loss of cellularity and collagen fibrils are the most reported and investigated features of tendinopathy in the SDFT (Smith, 2011a; Patterson-Kane and Firth, 2009). However, proinflammatory cytokines have also shown to be present in the injured SDFT and increase in apoptosis was shown by Hosaka et al (2005). The role of this apoptosis in degeneration of the SDFT is unclear but a loss of cells that are normally active in degrading and synthesizing matrix assumes an alteration in the normal metabolism of the tendon that might result in degeneration. Apoptotic pathways differ from the process of necrosis and the latter is widely accepted to occur. Apoptosis was demonstrated by Hosaka et al and it is not sure to what extent either necrosis or apoptosis are responsible for loss of cellularity in the tendon. Apoptosis may not only result in decrease of collagen synthesis but may also increase collagenase activity as Hosaka et al point out. However, necrosis may also result in leakage of collagenase factors to the tissue. Neovascularisation receives much attention in literature on human tendinopathy and has been shown in the equine SDFT by Kristoffersen (2005). However most studies on vascularization have been performed on the DDFT.

1.4.2.2 Deep Digital Flexor Tendon

In a study by Blunden et al (2009) a comparison was made between horses with less than and more than 6 months of lameness due to DDFT tendinopathy in the foot. They expected to find signs of acute pathological changes in the ‘acute’ cases with less than 6 months of lameness, such as necrosis, hemorrhage or infiltration of inflammatory cells. These changes were not found but necrotic core lesions were apparent in the acute cases. In the horses with more than 6 months of lameness, fibroplasia and fibrocartilaginous metaplasia were seen. In the control group of horse that did not show lameness, some histological changes were also seen but these were not as severe as in the control group. Hence, changes in the matrix structure may be present to a certain extent while not producing pain or other symptoms.

The dorsal part of the DDFT in the phalangeal region shows a poorer vascularization than the palmar regions. Blunden finds that if degenerative changes are seen, the damaged tendon is revascularized from the more vascularized palmar region. However, true neovascularization has only been demonstrated in the SDFT by Kristoffersen et al (2005) and has so far, has not been shown in the DDFT. The involvement of vascularization in the onset and evolution of pathology is unclear. It might be influenced by many factors such as foot conformation and degree of exercise. Exercise can compromise blood supply if it is too strenuous thereby leading to anoxia in regions of the foot. However, the opposite case of too little exercise might lead to lesser blood flow within the foot, thereby also compromising the oxygen supply to the lesser vascularized areas of the DDFT. Blunden et al (2009) conclude that any factor that reduces blood flow in an area of tendon that is placed under considerable loading stress, can lead to matrix changes in the tendon. Proteoglycan deposition around and within bloodvessel walls can then be the cause of vascular degeneration. Proliferation of vasculature is also a common finding in tendinosis in human studies (Maffulli et
In this study by Blunden et al, even horses with a recent and severe episode of lameness did not show any signs of inflammatory response but the presence of inflammatory mediators was not evaluated in this study. Also, all horses included in the study had experienced at least 2 months of lameness and hence the acute phase might have passed. Early changes of core necrosis were characterized by an increase of cellularity central within the fascicles; these cells showed a tenochondrocytic appearance. They seemed to extent to the periphery of the fascicle and ultimately conflated with neighbouring fascicles, causing an area of core necrosis (Blunden et al, 2009). In later chronic stages these the necrotic areas contained fascicles with central chondrocytes and chondroid matrix. This may be caused by an anoxic gradient that causes fibroblasts to migrate in the center of the fascicles.

It is hard to compare research that characterizes distal DDFT pathology, since some include horses with advanced navicular bone pathology, others use the subjective criterion of ‘primary soft tissue injury’ or ‘less advanced navicular bone pathology’ (Blunden et al, 2009) whereas again others only include horses with no radiological abnormalities (Dyson and Murray, 2007b). Distribution of lesions was similar between the study of Blunden and another one by Dyson and Murray, however their inclusion criteria of lame horses differed (Dyson and Murray, 2007a).

Lesions of the DDFT in the foot are most common at the level of the navicular bone and proximal aspect of the navicular bursa. At the insertion to the distal phalanx and the level of the proximal interphalangeal joint they are less common (Schramme, 2011). Various types of lesions occur but the most important distinction is that core lesions and splits are not often seen in combination with changes of the navicular bone, while lesions of the surface of the dorsal border of the DDFT often occur together with degenerative changes of the palmar surface of the navicular bone. In this latter case, it is not known whether lesions in the DDFT lead to adaptation of the navicular bone or vice versa. With sagittal or oblique splits, it is often seen that they run along the septal lines without evidence of presence of inflammatory cells.

Vascular changes were more often found in horses with foot pain than in control horses, and this may lead to matrix changes (Schramme, 2011; Blunden et al, 2006). Especially the already less vascularized adapted dorsal fibrocartilagenous zone may be prone to degeneration. Intratendinous angiogenesis is associated with degenerative and necrotic processes in the collagen bundles (Crisan et al, 2013) in draught horses suffering from tendinopathy. These blood vessels showed hypertrophy of the vascular wall and all tendons showed neoformation of bloodvessels. Horses with chronic foot pain showed increased vascularity in the DDFT as well as increased proteoglycan deposition (Beck et al, 2011). This increase in vascularization of the distal aspect of the DDFT was also shown by Puchalski et al (2009). Proteoglycan deposition indicates adaptation to stress, since tendon responds to force by increasing proteoglycan deposition (Riley, 2005) and a reduction in proteoglycan synthesis has been associated with tendon failure (Yoon et al, 2004). However, higher proteoglycan levels are also said to suggest beginning degeneration of tendon (Beck et al, 2011). The absence of evidence for inflammation or hemorrhage in the onset of degeneration strengthens the belief that vascular changes may lead to matrix degeneration (Schramme, 2011). In human patients this neovascularisation has been associated with matrix degeneration (Beck, 2011). It is however unclear how vascularization, matrix degeneration and proteoglycan accumulation are related and this will need further investigation.
1.4.2.3 Suspensory Ligament (SL)

Degenerative suspensory ligament desmitis or DSLD is a condition that is not related to level of exercise and it seems to be genetically predisposed. It occurs mainly bilateral or quadrilateral in a familial distribution of horses of the Peruvian Paso breed, but other breeds can also be affected (Bertone, 2011b).

Mero and Pool (2002) studied the histologic lesions seen in DSLD and staged these lesions. Firstly, lesions found in the earliest stages were usually in the branches of the SL and showed clusters of tenocytes or 'ligamentocytes', that had either degenerated, proliferated, where necrotic or were undergoing chondroid metaplasia. Metaplastic chondrocytes were surrounded by amorphous matrix that partially displaced the fibrils. The affected fibroblasts were in the earliest stages mainly found in fascicles in the central region of the branches of the SL. Secondly, in intermediate stages there were enlarged fascicles, loss of vascularity and increase in fibrous tissue. Two types of fascicles where seen between interfascular fibrosis; large paucicellular (hypocellular) fascicles and enlarged hypercellular fascicles with clusters of proliferating fibroblasts. The latter was thought to be indicative of attempts at repair. Thirdly, in the latest stage fibrosis across and between the fascicles was the most dominating observation, with some areas of avascularity, acellularity and mucoid degeneration. In these regions, fibrils were largely replaced with amorphous matrix. On ultrasound, DSLD shows an enlargement that is progressive and continuous. Hypoechogenic lesions are not often seen, but instead there is a diffuse loss of echogenicity and poor fiber pattern.

Recently it has been suggested that the cause of DSLD might be a systemic disorder, where abnormal proteoglycan accumulation in tissue with high collagen content is suggested to be responsible for the onset of DSLD (Halper et al, 2006) and it is hypothesized by Halper et al (2011) that the observed degeneration of collagen fibers is secondary due to proteoglycan accumulation. Halper also suggests that this accumulation is due to proliferation of fibroblasts that secrete proteoglycans. However, Schenkman et al (2009) repeated the study performed by Halper but found no evidence of a systemic proteoglycan deposition. Schenkman et al later reported that a deficiency of aggrecan degradation may lead to accumulation of aggrecan in the affected SL in DSLD (Schenkman et al, 2010). The cause of this condition is clearly not known, but it is interesting that both authors at least agree on the presumption that excessive proteoglycan amount in the tendon tissue is most likely involved in the onset of the disease. Illumination of the pathology might help to understand in what respect it differs from overload pathology, and if there are common pathological pathways in tendon degeneration. It is very interesting that histological characteristics are similar to that of exercise-induced degeneration.
1.4.3 Strain induces damage to tendon

A generally accepted principle is that strain induces damage to tendons when a threshold value is passed. The equine tendon can stretch 12% before damage occurs to individual collagen fibrils. In the human tendon crosslinks are already broken when stressing the tendon to more than 4% of its original length and macroscopic rupture already occurs at a stretch of 8% (Abate et al, 2009). While the incidence rates will likely be different for every individual tendon in different species, the underlying process is likely to be the same. Since speed is an important factor in the amount of strain that is placed on the tendon, work at higher speeds are more detrimental to the tendon. Racehorses performing at high speed are close to this maximum and very prone to accumulating microruptures. Recently it is believed that that cumulative microdamage to tendons may precede clinical tendinopathy (Patterson-Kane and Firth, 2009).

1.4.4 Degeneration is preceding clinical manifestation.

According to (Smith, 2011a) intrinsic overstrain injuries can be caused by single acute overload of the tendon but most clinical manifestations of tendinopathy are believed to be preceded by subclinical degeneration of the matrix. Three reasons to assume subclinical degeneration are given. First, pathology of tendons is found in horses that are euthanised for other reasons than tendinopathy and that have not showed symptoms of tendon injury. Acellular areas, chondroid metaplasia and cyst formation have been observed in these cases and are indicators of tissue degeneration. Another observation is that tendinopathy is often found bilaterally and one limb is usually more affected. This suggests that the pathology was present for some time before a 'sudden' lameness is detected to the more affected limb. Lastly, changes in tendon tissue are found and attributed to aging and exercise and these factors are thought to be the cause of tendon degeneration preceding clinical injury. However, it is still controversial to what extent changes in tendon are adaptation or response to load, and which changes in tendon tissue are pathological.

There are other arguments that support this claim. For example, it is possible after a three-day-event for a subclinical tendinopathy to be develop, but only presenting itself when the horse comes back into training after a period of rest, even if this is 3 to 6 months later. Ultrasonographic followup is advised in these horses to assess if injury is present (Bathe, 2011b). Maybe the most solid indication of preceding degeneration is the fact that various studies have claimed to be able to predict onset of tendinopathy before clinical symptoms are present, for example by use of gait analysis (Dow et al, 1991) or with thermography (Turner, 2001).
1.5 Similarities and differences in humane and equine tendinopathy

The flexor tendons of horses store large amounts of energy when in motion, and have a relatively higher capacity to store energy compared to other animals and humans. Not only horses damage tendon structures due to excessive loading; in human medicine an injury comparable to that of the SDFT is found in achilles tendon overload pathology. The equine SDFT and the human Achilles tendon are functionally and clinically equivalent (Patterson-Kane et al, 2012) and strain injuced injuries share many similarities (Abate et al, 2009). Furthermore, the digital flexor muscles of the horse are situated in a comparable anatomic site as the achilles tendon in humans (Firth, 2000). It is likely that there is a similar response to exercise of the human Achilles tendon and equine SDFT. Both are susceptible to exercise-related injuries while the anatomically opposed extensor tendons hardly ever suffer comparable injury (Birch et al, 2008).

Pathological changes in chronic degenerative tendon disease that are consistent among different tendons and different species are increased tenocyte number and rounding, loss of cellularity, neovascularisation, collagen fibril malalignment, interfascicular matrix accumulation, proteoglycan accumulation and lack of inflammatory cell infiltration. The degenerative changes can be due to alterations in loading or can be the resulting end-stage of a previous injury (Smith and Mcilwraith, 2012).

Human patients often first present with complaints of pain or functional limitations (Kaux et al 2011). However, the first noticed change can also be the gradual onset of morning stiffness (Fredberg and Stengaard-Pedersen, 2008). In equine cases, the first indications of tendinopathy are swelling, warmth and pain. In case of very sensible trainers or owners the first noticed complaints are decreased performance and tenderness on palpation. It is not uncommon that a diagnosis is based on clinical symptoms and clinical examination alone in the human patient (Kaux et al 2011). Veterinarians often use ultrasound to confirm an already suspected diagnosis when clear symptoms are presented. Nonetheless, diagnostic imaging and symptoms have a poor correlation and this is the reason that diagnostic imaging does not play an important role in diagnostics in human medicine. Use of these imaging techniques is often limited to patients in which prescribed treatment is not responsive and symptoms are continuing (Khan et al, 2003). Imaging also has a limited applicability in determining functional recovery after surgery. Ultrasound images are abnormal for up to 12 months after succesful surgery on the patellar tendon, and MRI is not able to differentiate between succesful and unsuccesful outcome of surgery in human patients. The lack of use of imaging techniques in human medicine is in sharp contrast with equine medicine, where imaging techniques are an inherent part of the diagnostic procedure.

Several authors argue that imaging is always needed in followup of recovery and rehabilitation, to determine the pathological state of the tendon when pain has receded (Fredberg and Stengaard-Pedersen, 2008; Cook and Purdam, 2009). The conclusion of Khan et al (2003) is that the appearance of the tendon on imaging should not be used to determine whether or not a patient is fit to return to sport after Achilles tendinopathy. Khan concludes this because abnormalities are still present also when patients have made a good functional recovery and hence no attention should be paid to the structural changes in the tendon. To Cook and Purdam (2009) and Fredberg and Stengaard-Pedersen (2008), loss of pain is not the criteria to resume work but functional recovery seen on imaging should be guiding in rehabilitation and in resuming activities.
1.6 Tendinopathy hypotheses in humane medicine

It is beyond the scope of this thesis to discuss all detailed findings of research on the etiopathology of human tendinopathy. However, based on this research several models or theories have been proposed to explain which pathologic mechanisms are at work in tendinopathy due to overload. Since these are specific to tendon overload injuries and equine and humane tendinopathy show many similarities, it is useful to explore these models. If these models can be applied to tendinopathy in horses that means they can be very valuable in giving an overview of what is currently known and they can be used to direct future research for equine tendinopathy specifically. These models have in common that they are based on overload pathology studies and they include a wide range of tendons (achilles, patellar, rotator-cuff tendons). They also include findings from animal models of both in vivo and in vitro studies. Because of this diversity in background and because the models seem applicable to other tendons and other species, these models leave enough room for the species-specific differences that exist. In fact, these models are suggested in human medicine but often based on results of studies in animals. Therefore these do not serve as a solid explanation, but rather as a guideline of possible hypotheses for future research.

1.6.1 Continuum model

This model was proposed by Cook and Purdam and this entire discussion refers to the paper in which the model was launched in 2009. The goal of the model is to explain why patients with the same pathology of overuse tendon injury represent with such a different degree of pain, irritability and why overuse injuries also result in various levels of loss of function. Another question is why recovery and response to treatment is equally variable. Cook and Purdam address this by proposing three stages in tendon pathology, but these stages should be seen as a continuum rather than as distinct processes. These stages are reactive tendinopathy, tendon disrepair and degenerative tendinopathy. The authors suggest that adding or removing load is the most important stimulus that drives the tendon back or forward along the continuum and that reducing load “may allow the tendon to return to a previous level of structure and capacity within the continuum”.

Fig.3 Taken from Cook and Purdam (2009).
Reactive tendinopathy is a non-inflammatory proliferative response in the tenocytes and matrix, caused by acute overload or burst of unaccustomed physical activity. This results in short-term adaptive homogenous thickening that will reduce stress per force-unit area by increasing cross sectional area (CSA) and this increases stiffness of the tendon. Histologically metaplastic changes in cells and cell proliferation are seen: rounding of cells and increase in cytoplasmic organelles due to increased protein production that are mostly large proteoglycans. Increased levels of large proteoglycans result in matrix changes because of increase in waterbinding. Collagen structure is not changed except for some longitudinal separation. This is a sharp contrast with the previously discussed assumption that microdamage to collagen fibrils is responsible for the onset of tendinopathy. In this stage, neurovascular structures are unchanged. The quick response in large proteoglycan synthesis is thought to be necessary until long-term and slower changes in structure and mechanical properties called 'true adaptation' are made. However, this adaptive response is contesting with the belief that the equine flexor tendon strength cannot increase after maturity as discussed before.

The authors suggest that in this stage, an increased tendon diameter is seen on MRI and ultrasound (US) scans. MRI shows no increase in signal but US shows diffuse hypoechogenicity between intact collagen structures. The change in imaging appearance is caused by increased water binding but one could argue this increased waterbinding should then also show on MRI since this is the imaging modality to evaluate water binding in tissue. It has been shown that an acute bout of exercise results in increased tendon volume and signal seen by MRI in abnormal tendon and tendons that were abnormal with above mentioned changes, where normal at follow-up. This supports the view that transition of reactive to normal stages is possible. The treatment in this stage should be reduction of load to allow the tendon time to adapt. The question is whether this stage is a normal adaptive response to exercise or the onset of pathology.

Tendon dysrepair is an attempt at tendon healing similar to reactive tendinopathy but with matrix breakdown. Separation of collagen and disorganization of the matrix occurs due to continued increase in proteoglycans. Changes are more focal and matrix changes more varied than in the reactive stage. Increased cell numbers of mostly chondrocytes and myofibroblasts and an increase in protein production, mostly large proteoglycans and collagen, is seen. Increase in vascularity and neuronal ingrowth is detected: neovascularisation. This stage is seen in chronically overloaded tendons across a spectrum of ages and loading environments. It is best detected on imaging when focal structural changes are seen, as opposed to the diffuse changes in the reactive stage and can either be seen with or without increased vascularity. On US discontinuity of collagen fascicles and small focal areas of hypoechogenicity are seen. Increase in vascularity is seen by colour or power Doppler US. MRI shows a swollen tendon with increased signal. The transition from dysrepair to degenerative has not been proven and this is mostly because most studies do not make a distinction between the two phases.

Degenerative tendinopathy is a further progression of both cellular and matrix changes in a chronically overloaded tendon. Areas of acellularity are seen due to cell death. Large areas of matrix are disorganized with breakdown products, show reduced amount of collagen and are filled with vessels. This stage is characterized by heterogenic matrix with islands of degenerative pathology between other pathologic stages and normal tendon tissue. When placed under high load the tendon can rupture and 97% of tendons that rupture show the mentioned degenerative changes. On imaging, extensive compromised matrix and vascular changes are seen. US shows hypoechogenic regions and many larger vessels on
Doppler US. MRI shows increased tendon size and increased intratendinous signal. Changes are also more focal rather than spread throughout the tendon. Large hypoechoic areas remain abnormal and even if tendon function does improve, the normal morphology of the tendon does not return which indicates the irreversibility of this process. Treatment should focus on stimulation of cell activity, protein production and restructuring of the matrix. Exercise is a beneficial treatment in this stage to stimulate tendon healing.

As the authors point out, degenerative tendinopathy has been described a lot in the literature, but the transition from dysrepair to the degenerative stage has not been shown so far. Load of the tendon is here considered as the major influencing factor, but individual factors such as age, genetic background, sex, body composition and biomechanic properties may influence the progression back and forward along the continuum. Stress-shielding or unloading of a tendon can induce the same pathologic changes as overloading a normal tendon and can drive a tendon into the reactive stage, indicated by the red arrow on the side. However, Cook and Purdam are referring to some studies performed in the early 1990’s. In recent years little attention has been paid to the response of tendon to stress-shielding and thus little is known about the effect of stress-shielding on tendon tissue.

Pain is not included in this model. The authors do not incorporate this in the model is because the relation between pain and pathology in tendinopathy is unclear. Tendons that are normal on imaging can be painful. However, it is also common that tendons rupture acutely and show signs of degeneration, while they have not at any stage showed painfulness prior to rupture in the majority of the cases. Pain can occur due to production of cellular substances such as catecholamines, acetylcholine and glutamate and this can be related to the cellular active stages of the model; reactive tendinopathy and tendon dysrepair. Pain has also been suggested to be caused by ingrowth of neurovascular bundles which starts in the dysrepair stage and increases in the degenerative stage. Since pain can occur in all of the proposed stages and in all intensities, this is the reason that pain levels should not be used to base the treatment on. However, pain is the main reason why human patients present themselves. According to these authors, diagnosis and treatment should not only be based on pain but also on imaging of the tendon to understand what stage of pathology is present. Pain is however discussed in the next hypothesis, the iceberg theory.

**1.6.2 Iceberg theory**

Pain is not correlated with symptoms and the cause of pain in tendinopathy has not been defined. Possible mechanisms that induce pain are inflammation, separation of collagen fibers and biochemical stimulation of nocireceptors. Also increased levels of prostaglandins, prostacyclins and thromboxanes can contribute to the development of pain. They increase the excitability of neurons and pain producing stimuli. Neovascularization with nerve ingrowth has been demonstrated extensively and ingrowth of nerve endings might cause pain (Khan and Cook, 2000).

Fredberg and Stengaard-Pedersen (2008) propose to see pain as an iceberg, where pathology is only detected after the pathologic changes have passed the threshold level. When pain is detected a treatment is started which often leads to decrease of pain, causing the pain level to drop below the threshold level again. At this point the human athlete assumes the pathology is over and resumes training, causing a recurring injury. However, the threshold level of pain is high and this means that the majority of pathologic changes remain undetected, as is the larger part of an iceberg which is underwater. Also, when pain resides
after treatment, pathology is still present and painlessness does not mean recovery.

Keeping this in mind when considering the many relapses found when training is resumed, it is easy to conclude that pain had disappeared but the tendon had not yet recovered. Fredberg and Stengaard-Pedersen argue that assessment of the tendon abnormalities should be performed by US. A strong case for his iceberg theory is made by the fact that most ruptured tendons do not display pain symptoms and as mentioned earlier they do display degenerative changes in 97% of the cases. Unfortunately it does not help to understand what the causes are of pain. Fredberg and Stengaard-Pedersen are not agreeing with a solely degenerative pathology but argue for involvement of inflammatory processes.

In a review Abate et al (2009) discuss the iceberg theory but goes even further to give an explanation of the cause of pain. The iceberg that is proposed by Abate et al is an adaptation of the original graphical representation of the iceberg by Fredberg and Stengaard-Pedersen. It proposes a role for neovascularisation and nerve proliferation in the development of pain symptoms.

![Fig.4 Taken from Abate et al (2009).](image-url)
1.6.3 Synthesis and degradation curve

Magnusson et al (2010) discuss the pathogenesis of tendinopathy and conclude that the time span in between exercise bouts is decisive in whether the net result is a healing or degenerative process. Both regeneration and degradation occur in tendon tissue as a response to mechanical loading. This is in contrast with the view that after maturity only degeneration occurs, as was discussed in the paragraph on tendon strength. An acute increase in collagen expression by fibroblasts is seen in animals and human and peaks around 24 hours after exercise. A 2-3 fold increase in collagen expression can be observed at peak values. Degradation of tendon tissue is marked by increase of matrix metalloproteinases (MMPs) and collagen degradation fragments. This response peaks earlier than the regenerative process and results in a net degenerative response 18-36 hours after mechanical loading. After 36 hours up to 72 hours, the net response is a regenerative process with increase in collagen levels (Magnusson et al, 2010).

Before a net increase in collagen levels and thus tendon strength is reached, a certain period of time is needed to compensate for the degradation that was caused, and when this is not respected in between exercise bouts a continuous net loss of collagen results. This is because the tendon is not allowed time to reach the net regenerative stage. This might lead to degeneration of tendon tissue if not enough time is respected in between exercise sessions, because of a dominating catabolic process. There are also indications that the time span of net degeneration after exercise shortens when training status increases.

Another interesting relationship exists with respect to exercise load and responsive collagen synthesis by fibroblasts. Magnusson et al (2010) combined the results of different studies and found that collagen synthesis does not increase with increasing exercise loads once a certain level of exercise is reached, indicating that collagen synthesis by fibroblasts is maximal at this point and cannot increase further. It would be interesting to see if degenerative markes such as MMPs also reach a certain plateau with increasing exercise, or if these levels increase steadily with increasing workload. If this would be the case, increasing workload will be increasingly detrimental after a certain optimal level of stimulation of synthesis has been passed.

Interestingly, Docking et al (2012) studied response of the SDFT to heavy exercise and also proposes that the tendon should not be subjected to heavy load while it is still recovering from a previous heavy bout of exercise. This author also suggests that tendon tissue will not be fully recovered within 72 hours and heavy loads within this period can lead to tendon injury. This argues for a normal adaptive, physiological response to exercise and not that all types of overload at all times lead to degeneration.
1.7 Characteristics of subclinical tendinopathy.

To sum up, there are many changes in tissue that may be indicators of the onset of degeneration. Loss of structural integrity of collagen fascicles is most likely caused by rupture due to too high loads on the tendon, but may also at least to some extent be caused by increased activity of matrix metallo proteinases. Also, increased deposition of proteoglycans by tenocytes can be a response to high load on tendon tissue. Since these proteoglycans cause an increase in water binding and increase in cross-sectional area they alter the properties of the tendon tissue. As early complaints in human patients may involve increased stiffness in the morning or in the beginning of sports activities, this may also be the case in equine patients. Formation of new vasculature may be involved with the onset of pain symptoms and are involved in degenerative processes. While these changes can be detected with common used diagnostic techniques as will be shown in the next chapter, for most of these changes it is as yet unclear what role they play in the pathological processes and probably the most important role of future researchers is to investigate the pathological processes involved in tendon overload injuries.
Tendinopathy of the superficial digital flexor tendon (SDFT) typically occurs at the midmetacarpal level and a horse presenting with acute lameness of the forelimb and signs of swelling, heat and pain to the palmar metacarpal region could be a typical case of acute tendinopathy in the SDFT (O'Sullivan, 2007). Severe, acute tendinopathy often gives rapid development of peritendinous edema, resulting in typical rounding of the normally straight metacarpal palmar contour. In this case a diagnosis can almost instantly be made by taking the history of the patient and a quick glance at its lower limb. The severity of the condition is however not so easy to assess and further examination is usually indicated. Horses that are severely injured can be reluctant to place their hoof fully on the ground, to avoid loading of the tendon (Goodrich, 2011). Many cases will be harder to assess since not all of them will be as typical in their representation (Ross et al, 2011). Sometimes early focal swelling and tenderness on palpation can be found before lameness has developed (Goodrich, 2011). This means the veterinarian can even be confronted with a horse with tendinopathy in the late-subclinical or early clinical stage for reasons other than lameness examination.

Clinical representation of tendon injuries can vary from significant lesions without detectable lameness to large tears that result in severe lameness where the horse is very reluctant to move and takes on a laminitis-like stance. Acute lameness without other clinical signs can also occur; swelling, heat and pain may develop over the course of the following days. In this case it is important to keep a close eye on the horse, especially when acute forelimb lameness is presented and no cause can be identified. Usually a diagnosis can be made but in cases where this is not possible, for example due to lack of equipment, it is useful to keep in mind that typical acute tendinopathy symptoms may appear later (Ross et al, 2011).

As said, SDFT tendinopathy typically occurs at the midmetacarpal region but swelling of the distal metacarpal region can also be due to SDFT tendinopathy, which in turn affects the palmar annular ligament and the digital flexor tendon sheet (DFTS). However, swelling in this region can also be caused by desmitis of the annular ligament, tenosynovitis of the DFTS or tendinopathy of the deep digital flexor tendon (DDFT) and it is important to differentiate what the primary structure is that is affected. Tendinopathy of the SDFT occurs considerably less frequent in hindlimbs and it is most often seen at the plantar hock region and sometimes extends to the metatarsal region if it does affect the hindlimb (Ross et al, 2011).

Desmitis of the accessory ligament of the deep digital flexor tendon (ALDDFT) usually presents as acute onset lameness and can result in moderate to severe lameness; often there is a rapid development of local soft tissue swelling. It is however also possible that no alteration of the ALDDFT is detected on palpation in more chronic cases with recurring lameness (Dyson, 2011).

Desmitis of the suspensory ligament, or proximal suspensory desmitis (PSD) in the forelimb can give rise to lameness of varying degrees that can be intermittent in a more chronic stage. Acute cases may present with heat and edema in the proximal metacarpal region but especially in more chronic cases, there are sometimes no abnormalities are found on palpation. Pressure to the proximal aspect of the suspensory ligament (SL) may be painful, as forced extension and protraction may be, but absence of this pain reaction does not exclude PSD. Sometimes there is only a slight proximal swelling found medially, between the SL
and the DDFT (Bertone, 2011b). Palmar abaxial sesamoid nerve blocks may increase the lameness (Ross et al, 2011). This is explained by the fact that proprioceptive information is partly lost and the loading of the suspensory apparatus is increased, hence increasing the pain. With a lateral palmar nerve block or block of the palmar metacarpal nerves at the subcarpal level, lameness can improve. However in some cases improvement of lameness is only observed by an ulnar nerve block. Desmitis of the body or the branches of the SL is usually visible or palpable because of enlargement of the structure in acute stages. When the lesion has been present longer, the enlargement has a more firm touch (Goodrich, 2011). Usually body and branch lesions show pain on pressure and also respond positive to fetlock flexion. When diagnosed in the chronic stage, it is often seen with fibrosis around the ligament (Dyson and Genovese, 2011).

While forelimbs are more commonly affected by tendinopathies, PSD occurs more often in the hindlimbs than in the forelimbs. In dressage horses PSD is a common cause of lameness of the hindlimbs. PSD in the hindlimb can lead to severe lameness but can also give vague complaints of poor performance, increased stiffness or resistance to the bit without obvious lameness. Clinical symptoms are often absent but in the acute stage heat, swelling and pain when applying pressure to the suspensory ligament (SL) can be present. Palpation is however difficult because of the deep location of the proximal aspect of the SL. Given that obvious lameness is often lacking, and some lesions have a chronic character when first diagnosed, the existence of low-grade unrecognised tendinopathy or subclinical tendinopathy is highly likely. PSD of the hindlimbs is often bilateral and has even been observed in all four limbs (Dyson and Genovese, 2011).

Palpation is fundamental in lameness examination and cannot be disregarded when performing a proper examination of the patient. Size, shape, consistency of tendons and ligaments in the metacarpal or metatarsal region should be assessed whilst paying careful attention to pain or sensitivity reactions on palpation, with the limb load-bearing as well as in flexed position. It goes without saying that profound knowledge of anatomy and normal course of involved structures is fundamental. In case of partial or complete rupture a palpable defect may be felt. Often the contralateral limb is used as a reference but one must always be aware that bilateral tendinopathy may be present, and while palpation may reveal symmetrical limbs there is a possibility that both tendons are equally affected and slight enlargement or rounding of the margins is easily missed in this case (Ross et al, 2011).

Diagnostic analgesia can be useful, especially in cases where bilateral tendinopathies are present and lameness is not obvious. Analgesia of one limb may result in a more overt lameness in the other limb but a negative response can be misleading. Bilateral analgesia might improve the gait when both limbs are affected. This does not rule out other causes of lameness and, further diagnostic tests should be performed.

It is clear that clinical examination of tendinopathy cases can be straightforward or extremely hard depending on the structure that is affected, the symptoms that are present and the age of the lesion. This short summary is by no means exhaustive but does illustrate that clinical symptoms have large variation and tendinopathic lameness can present in many different ways. A thorough understanding of clinical representation and a well performed clinical examination can never be replaced by any diagnostic technique; these techniques are always used in addition to a well-performed clinical examination. Depending on many factors such as affected stucture, desired use of the horse, the expertise and equipment available and not in the least, the owners' (financial) motivation, there will often be a need for more intensive examination using additional diagnostic techniques.
2.2 Ultrasound

Ultrasonographic evaluation of an injured tendon is usually the first step in further evaluation of the patient after clinical examination (Redding, 2011). The equipment is also available for most veterinarians and can be performed in the field. The objectives are to confirm the presence of tendon injury and to learn what the exact location and degree of damage is. Parameters that are often measured on a transverse image are cross-sectional area of the tendon (CSA), percentage of the CSA that is taken by the lesion, and echogenicity of the lesion. On a longitudinal image the alignment of the fiber bundles can be visualized. These values are often collected at different, pre-defined levels of the limb (Rantanen et al, 2011). Often the contralateral limb is used for comparison (Pickersgill et al, 2001). It is important to not only observe the suspected area of pathology, but to systematically evaluate the entire lower limb since the lesion might extend beyond the expected area.

Changes that are associated with tendon lesions are seen as loss of intensity of the signal and loss of homogeneity or both, as well as the loss of the alignment of fibers on the longitudinal image (van Schie et al, 2001). In the initial stage of a tendon lesion, echogenicity will decrease due to a loss of structural integrity, loss of collagen content and loss of collagen density. Hence in acute cases of rupture of tendon, anechogenic or hypoechogenic regions are found within the tendon (Micklethwaite et al, 2001). The collagen bundles are absent so they no longer reflect the sonographic beam. In the lesion there is hemorrhage, fibrinolysis and early formation of granulation tissue and because of this the beam is transmitted resulting in hypoechogenicity. When healing progresses, reorientation along the stresslines of the new formed collagen fiber bundles is responsible for gradual increase in echogenicity, because of increasing specular reflection, together with a decrease in areas of hemorrhage and fibrotic tissue. Due to formation of molecular linkage of the new collagen fibers, scatter density also increases.

One example of categories of injury is described by Avella et al (2009). When a focal hypoechogenic area was found on both transverse and longitudinal images, the stage was labelled acute. In case of a heterogenous appearance in the transverse image and disrupted fibre patterns in the longitudinal view, the stage was labelled chronic. Cases were considered recurrent if both acute and chronic stages where present in one horse, and the group normal horses showed no abnormalities on multiple assesments. It may be useful to characterize stages of lesions in this way, but for intense follow-up and to assess an effect of treatment these classifications are not specific enough. When healing progresses the collagen content and density increase but it is important to differentiate between functional tendon tissue and inferior scar tissue and this is impossible with current ultrasonographic methods. The study by Avella et al (2009) was specifically designed to determine if US evaluation could predict a tendon injury when horses where evaluated at a three month interval. However it had to be concluded that US evaluation was not sensitive enough to do so. Advances are being made such as by van Schie et al (2003) with the development of ultrasound tissue characterization.

The major drawback of ultrasonographic evaluation is the large influence the handler has on performing the scan, and the many artefacts that can be present. For example, when one is not familiar with the possible artefacts a site is easily identified as lesion whereas in fact the ultrasound beam angle is slightly adjusted. In a transverse image it is important to have the sound beam perpendicular to the tendon,
otherwise hypoechogenic regions are seen. In a longitudinal image this problem is not seen with a linear array transducer, but with transducers with a divergent ultrasound beam only the part of the image where the beam is at a 90 degree angle can be used for diagnostic information, and where the beam is reflected away the information in the image is lost and cannot be interpreted. On a longitudinal image, it is important to assess the continuity of the fibers of the ligament and this is seen with a longitudinal transducer. However, if the transducer has an oblique orientation towards the fibers, they appear as short segments while in fact no integrity is lost. Gain settings are often referred to as ‘near gain’ ‘far gain’ and ‘overall gain’ and refer to visibility of the structures in the image. When a near gain setting is too high, the superficial structures are seen too bright and information in both the superficial and the deeper tissues is lost because of being respectively too bright and too dark. Proper gain setting should produce images with equal gray scales in the entire image. Also the use of the right frequency transducer, standoff pad, proper recording of images and even preparation of the skin seem straightforward but can in fact have a detrimental effect on the images (Rantanen et al, 2011; Redding, 2011).

While diagnostic ultrasonography has gained immense popularity since it was first introduced in 1982 and is has been used in everyday veterinary practice for a long time, only in recent years have some attempts been made to study qualitative and quantitative repeatability in examination of tissue. For example, variability caused by image analysis performed by different operators when measuring cross-sectional area cannot be neglected (Pickersgill, 2001). This means that one operator should analyse all gathered data to avoid false assumptions on improvement of the lesion, for example in the follow-up in rehabilitation or when performing clinical studies and comparing different subjects. Accurate and reproducible interpretation of the images is still lacking, and improvement is needed in quantifying changes in echogenicity that occur over time. Solutions that have been suggested to this problem are mean gray level statistics (van Schie et al, 2000), quantitative analysis of sonographic brightness (Micklethwaite et al, 2001) and computerized ultrasonographic tissue characterization (van Schie, 2003). The technique was developed by van Schie and is now used by others. A study that illustrates the value of UTC for tendon evaluation is that of Docking et al (2012).

Short terms changes in SDFT tissue after strong exercise such as racing, can be detected with UTC (Docking et al, 2012). Tendon responds to loading as well as to stress-shielding, and changes in expression of various molecules such as metallo matrix proteinases, cytokins en proteoglycans are involved in these processes (Docking et al, 2012). Ultrasound Tissue Characterisation (UTC) uses a standardized setting and collects transverse US images at even distances so that a 3D-ultrasound image is created. The echopatterns can be quantified over the subsequent transverse images by assessing the intensity and distribution of the grey levels of the pixels that correspond in the subsequent images. In this way it is possible to relate the dynamics of the echopatterns to the structure of the collagen matrix, and it was shown by van Schie et al (2003) that this matches the true collagen structure when histologic evaluation of tendon tissue was used as a reference.

Different types of UTC echo patterns are mentioned in the study of Docking et al (2012). They are referred to as intact and aligned tendon fasciculi (type I), less integer or waving fasciculi (type II), fibrillar matrix that is loosened and assumingly has an increased amount of ground substance between the collagenous matrix (type III) and lastly cellular matrix or free fluid (type IV). An increase in either type of echo
pattern compared with a previous UTC evaluation of the tendon is indicative for the associated change in tissue. A reduction in type I echo was seen after racing, while type II and III echo-patterns increased. These changes were seen throughout the tendon and not in a focal area. They were maximal at 48 hours after racing but returned to baseline values (that is, the values before racing) on the third day indicating a response of the tendon to exercise that is transient. This seems to support the Continuum hypothesis that in response to mechanical stimuli, the tenocytes increase proteoglycan deposition in the matrix, resulting in an increase in ground substance. This causes diffuse thickening, or increase in cross sectional area (CSA) which might be an attempt to reduce tendon stress. Docking et al argue that the observed increase in type II and type III is most likely to be due to increase, breakdown and clearance of ground substance. Synthesis and integration of newly formed collagen molecules as a response to microtorn damage is a much more time consuming process and is less likely the cause of the observed echogenic changes. Since all the horses that were included in the study by Docking et al resumed racing and none of them developed any form of tendon injury, this supports the conclusion that the observed changes are a normal response to exercise and are not early signs of tendon injury.
2.3 Magnetic Resonance Imaging

The increasing availability and use of Magnetic Resonance Imaging (MRI) has shown the limitations of US in correctly categorizing lesions of SDFT tendinopathy (Schramme and Redding, 2011). MRI became available for use in horses in the 1990’s and since then has revolutionized the field of equine medicine; it became possible to detect, evaluate and understand conditions in the foot, limbs and head region in a way that was until then unthought of. For example, only with the use of MRI did it become clear that in cases of navicular disease, involvement of DDFT pathology was much more common than was previously assumed. The technique has most application in identification of injuries to the DDFT in the foot where other imaging techniques cannot be used or are not commonly used, but also serves well to visualize lesions of the ALDDFT and the proximal part of the SL where ultrasonographic evaluation is harder compared to ultrasound evaluation of the DDFT and SDFT (Brokken et al, 2011). Because MRI can produce such detailed images, damage to or lesions in tissue can be detected in a very accurate way. Chronic lesions or scar tissue can be better detected and judged by the use of MRI that with US (Kasashima et al, 2002a). By producing an oscillating strong magnetic field around the tissue that is imaged, in combination with a radiofrequency pulse, hydrogen atoms in the tissue are excited and emit a radiofrequency signal that is detected. Contrast between tissues is determined by the rate at which the excited atoms return to their equilibrium state (Bolas, 2011).

Differences in signal detection are referred to as sequences and they produce images of different properties, such as STIR, proton density, T1-weighted and T2-weighted images. The different sequences that are widely used each have their own properties in visualizing the tissue involved. In all cases, the image is produced in a grey scale and changes in tissue structure, biochemical composition or water distribution caused by injury lead to alterations in the image. The differences in tissue are all created by differences in mobility and density of hydrogen nuclei in the observed tissues. In general terms it can be said that in fat and water the hydrogen nuclei are mobile and readily present, hence a strong signal is detected. In tissues such as bone and tendon where there are less hydrogen nuclei or tightly bound ones, there is little or no signal. However differences are large between the different signal sequences and different sequences can be preferred in different situations but sequence of choice is often also influenced by the handlers’ preference (Bolas, 2011).

Tissue of tendons and ligaments usually produce a low signal intensity in proton density, T1-weighted and T2-weighted images. An increase in signal intensity indicates that damage is present in the tissue and acute stages can also be accompanied with swelling. In stages of healing and fibrosis a decrease in signal intensity is observed and but the signal will still be higher than normal on proton density and T1-weighted images. Severe degeneration on necrosis lead to an increase in signal on T2-weighted and STIR images. When an increase in signal intensity is mostly visible on T1-weighted images on not so much on T2-weighted images, this is indicative of degeneration rather than inflammation. However, increase of signal can also be due to cartilage metaplasia but this is a normal observation in the DDFT at the level of the metacarpophalangeal joint. A thinning or discontinuity of the tendon contour can be indicative of an impending tear or a tear that has already occurred. These examples of increase of decrease in signal intensity are by no means exhaustive but only show that lesions or suspected damage to tendon tissue must always be evaluated on all sequences and a lot of experience is needed to interpret the various images.
As the previous paragraph shows, it is not easy to interpret the various images produced and on top of that there are many artefacts that can disturb the image. An artefact is a feature in the image that is not representative of the tissue being imaged. MRI is sensitive to artefacts because the signal to noise ratio is low. That means that of the signal that is detected to produce the image, noise is a large part of the detected signal. Furthermore it takes quite some time to acquire the image and this increases the risk of movement of the patient, which is detrimental to the imaging procedure. The magic angle effect is an artefact that is specifically involved in tendon imaging. It causes a false increase in signal when collagen fibers are aligned at a specific angle of 54.7° to the main magnetic field. This can be seen in different places depending on whether a high- or low-field magnet is used. Another artefact is the chemical shift artefact caused by differences in resonance of fat and water which causes distortion of the boundaries between fat and water. However many other artefacts are known and they cannot all be discussed here (Bolas, 2011).

Not only is image interpretation challenging and can be complicated due to many possible artefacts, there is also variation of normal anatomy in horses to further complicate the matter. Thus, to determine the clinical significance is of a lesion that is found is crucial but not at all straightforward. One can always be sure to find lesions while in fact there is no clinical relevance of these lesions at all; when one wants to detect a developing tendinopathy this will not be different. Horses with a developing tendinopathy and change in or swelling of affected tendons can surely be identified with MRI. While the availability of MRI has increased and has become more or less readily available, the costs are high and the procedure is not easy. It also requires sedation in case of standing MRI, and when a standing MRI cannot be performed general anaesthesia is needed. This rules out the use of MRI for frequent follow-up of horses in training while in itself the technique is probably the most accurate in its representation of tissue properties.
2.4 Gait Analysis

Gait analysis serves to characterize movement of horse locomotion, and to detect deviation from normal locomotion in a quantitative manner. It is not only used for horses but also widely applied in human sports training (Keegan, 2011a). There are several methods available and these have in common that they are all quantitative methods as opposed to the widely applied and more often used method of visual inspection and inherent subjective evaluation of movement. Not only is the subjectiveness of this visual inspection an obvious problem when comparing lameness assessment between different veterinarians, it is also hard to evaluate a horse’s performance over time and to assess whether lameness has improved, stayed the same or has worsened. Another drawback of visual inspection is the incapability of the human eye to observe small deviations during movement and hence the incapability to observe lameness that is subtle or just not visible to the human eye (Oosterlinck et al, 2007). It is obvious that there is a need for a technique that can be widely applied, that serves to give an undisputable grading of lameness and is capable to observe subtle or subclinical lameness before it can be seen by any person. The question is whether any of these quantitative methods is capable of detecting a deviation in locomotion that is specifically caused by a developing tendinopathy before it is clinically apparent. Especially in the case of overload injuries and the important factor of early detection and intervention, one wonders why these methods are not more commonly applied in equine medicine. Promising studies have been performed in the 1980’s and early 1990’s, and it was suggested that it was possible to make a distinction between different types of lameness and that these deviations could already be detected before clinical lameness was apparent (Dow et al, 1991). While many authors refer to the findings of Dow, and few authors are very critical of it, more than twenty year have passed since then. Unfortunately, no considerable progress has been made in establishing disease-specific changes lameness detection.

Quantitative evaluation of movement can be differentiated into kinetic and kinematic evaluation (Oosterlinck et al, 2007). Kinetic techniques measure the forces that act upon bodies which results in movement of these bodies. Kinematic evaluation measures the changes of position of bodies in the space that they move in without considering the forces that act upon it. In this sense, the kinematic evaluation resembles the visual inspection but in addition, it is possible to put a numeric value on the obtained results.

Kinematic analysis is most often used to collect qualitative data but it is also possible to gather quantitative data. Videodata is obtained using a high frequency camera and can be analysed when it is played back on a slower rate. A quantitative analysis can be obtained but is not often done due to higher complexity. Most often symmetry of motion and the pattern of landing of the hoof are evaluated in a qualitative manner. Parameters that can be evaluated are joint angle, stance duration and step duration, length and shape of flight arc and vertical pelvic movement or pelvic rotation (Keegann, 2011b). Changes in body motion that are caused by lameness are more variable than changes seen in ground reaction force. In the literature there is no indication that this can be developed as as tool for detection of specific causes of lameness.

It was suggested by Dow et al (1991) that kinetic evaluation can detect disease specific lameness and the most useful kinetic tools are pressure plates and force plates. Force plates can differentiate the forces that the hoof exerts onto the ground into its vertical, caudocranial and lateral components. Decrease of
vertical force, and to a lesser extent caudocranial force, are seen in lameness. This seems to be obvious because a horse will try to bear less weight on the lame limb, which is mostly represented as decreased vertical ground reaction force. The three vectors can each be visualised in a graph of force over time, to obtain a typical distribution pattern of forces within one stride on the ground. Different parameters can be considered directly on the GRF/time curves but other ways to evaluate gait, for example by evaluation of asymmetry in GRF or statistical manipulation of the data to obtain principal component analysis have also been reported (Williams et al, 1999). The force plate is considered the gold standard of objective lameness evaluation (Keegan, 2011b; Bertone, 2011c) and because it also seems a promising tool for subclinical lameness detection of tendinopathy, this technique will be discussed in further detail.

In a study by Ishihara et al (2005) it was shown that several parameters change significantly in case of lameness but changes in the vertical force peak and impulse are detected in the earliest stages; therefore these may have the highest potential to detect subclinical gait deviations in the forelimb. In case of mild lameness, vertical peak force and impulse already show a significant decrease whereas other parameters such as cranio-caudal peak force or stance time only change in case of moderate and severe lameness. Vertical peak force is here the highest force measured for vertical ground reaction force, while impulse is the total area under the curve. However, changes in vertical peak force and impulse where also noticed in horses where no visual lameness was detected, strongly suggesting presence of subclinical lameness. Another strong asset is that it has the lowest variability both between horses and for the same horse at different testing moments. Various studies have been performed to characterize changes in GRF patterns due to specific conditions such as SDFT tendinitis and navicular disease such as that by Williams et al (1999). The question that is relevant here, is whether these changes can be further characterized such that subclinical lameness specifically caused by a beginning tendinopathy can be detected.

Measurement of vertical ground reaction force using a forceplate is a sensitive and specific method for lameness assessment (Ishihara et al, 2005; Keegan, 2011b). As Ishihara et al mention, it might be possible to determine a cutoff value or reference range for vertical force peak. In this way, clinically sound horses can be evaluated for subclinical lameness. Attention needs to be paid to the fact that different causes of lameness show a different deviation from the normal ground reaction force patterns and the lameness induced in the study by Ishihara may not be representative for other causes of lameness. Hence, cutoff or reference values will need to be determined for specific conditions that cause lameness. The detection of subclinical lameness is valuable but it needs to be established if it is possible to determine in a clinical setting what the underlying cause of the subclinical lameness is, as was claimed by the study performed by Dow et al (1991).

Strain in the SDFT increases in the early stance phase and peaks in the middle of the stance phase, it is at this stage that the greatest reduction of vertical GRF is seen in the lame limbs when SDFT tendinitis is induced (Clayton et al, 2000a). Dow reported in 1991 that changes are seen in the period during which the fetlock extends and in the loading phase in horses with SDFT tendinopathy. Clayton et al (2000a) studied these variables in induced SDFT lameness but found that the method of measurement that has been used does not produce consistent results. Clayton et al (2000a) collected data on induced SDFT tendinitis with both kinematics and GRF to see if these are correlated and showed that changes in vertical GRF were associated with decrease in flexion of the distal interphalangeal joint and decrease in extension of the
metacarpophalangeal joint, while changes in the longitudinal GRF were associated with changes in protraction-retraction angles of the whole limb.

Studies on kinematic data of navicular disease have been performed but the characteristics that are found are the same as that of supporting limb lameness, hence these findings are only general features of lameness and not specific for lameness due to navicular disease (Buchner, 2001). Williams et al (1999) state it is possible to differentiate between navicular disease and SDFT tendinitis because the horses with navicular disease have a deviation from normal patterns for both the beginning of the stride and the end of the stride, whereas horses with SDFT tendinitis only deviate from normal locomotion in the beginning of the stride. Dow et al (1991) reports that it is possible to detect lameness due to SDFT tendinopathy before the onset of clinical lameness, which was found by retrospective evaluation of the data when it was known which horses developed a tendinopathy after the data was collected. When looking back at the GRF recordings of horses that sustained SDFT injury later on, it was seen that small deviations were seen in loading phase in the beginning of the stride and hence it was concluded that subclinical lameness was both present and resulted in a specific gait adaptation.

Net joint moments and joint powers can be calculated from kinematic and GRF adaptations. In humans joint power is the most used variable to describe abnormal gait and it is known that characteristic alterations are caused by specific conditions that cause gait abnormalities (Clayton et al, 2000b). A first study to assess these changes in net joint moments and joint powers in horses with SDFT was performed by Clayton et al (2000b) and found that the net joint moment was decreased in all joints that are crossed by the SDF muscle and tendon, as well as the coffin joint. However, while these data are specifically collected in horses with induced SDFT tendinitis the author does not at any time mention or discuss the question to what extent these parameters can be typical for this specific lameness.

Weishaupt (2008) gives a detailed overview of the adaptation in locomotive patterns that can be observed in lame horses. While gait analysis allows to identify the affected limb, to quantify the degree of lameness as well as to differentiate between supporting and swinging lameness, Weishaupt does not mention the existence characteristic gait patterns that can be used to locate the cause of the lameness. According to Weishaupt, reference data for force plates measurements exist for sounds horses at walk, trot and canter, as well as that of ridden horses at walk and trot, and for take-off and landing when jumping. Most likely recent developments have added some data to this list but while there may be some suggestive reports, no reference values have been determined for any lameness caused by a specific condition.

There are two major drawbacks in determining these reference values as Buchner (2001) points out. The first being the large differences in individual locomotion patterns between horses, and secondly the large amount of orthopedic diseases that exist in combination with the high number of horses that are affected by more than one condition. The latter is an argument against using horses with naturally occuring diseases to study characteristic gait abnormalities, since it is often impossible to guarantee that the horse is free of additional problems. Another reason why it is hard to discern the specific deviations in normal locomotion patterns caused by specific injuries might be that there is no ‘disease-specific’ change in locomotion; horses are rather limited in their locomotive range and respond to different causes of pain with a similar adaptation of locomotion (Buchner, 2001).

To be useful, the data that can be collected with force plates needs to be compared to a standard to
know if there is a deviation from normal locomotion and hence lameness. More importantly, characteristic patterns of lameness due to specific causes need to be further investigated. The presence of a bilateral injury, which is not uncommon in tendinopathy needs to be recognised and limits the use of symmetry evaluation. Asymmetry of locomotion can be caused by many factors, and was even present in all horses that were sound in a study that evaluated gait (Weishaupt, 2001). It is not sure to what extent this is due to ‘handedness’ and to what extent a subclinical lameness is present. In all of these sound horses a ‘lame’ limb could be identified. If the horse is tested before lameness develops these data are a perfect source for comparison at a later stage but these data will most often not be collected in clinical settings. Therefore there is need for a set of reference values, such as are available for many clinical tests that are commonly performed. Some attempts have been made but it is recognised that not only differences between breeds exist (Back et al, 2007) but differences can also be caused by differences in conformation. Velocity or the speed with which the horse moves also influences collected force data so that it needs to be standardized (Khumsap et al, 2001). Until now it is not possible to use this technique to detect subclinical lameness due to tendinopathy but further developments in the field might change this in the future. Even then this is not very userfriendly because the speed of the horse influences force exerted and thus needs to be relatively constant for all measurements, and because the hoof needs to strike the forceplate in a rather small area to be sure of good measurements. Even if it will become possible to detect subclinical tendinopathy and relate it to a specific pathology, it will not be an easy diagnostic procedure and it remains to be seen if it will be available for routine use.
2.5 Thermography

The use of thermography as a diagnostic tool is one of the older methods compared to more recently developed techniques for use in equine medicine such as MRI in the 1990's (Murray, 2011) and ultrasound which was applied for use in equines in the 1980's (Turner et al, 2011). An article written by Stromberg in 1974 that is referred to by Denoix and Audigié (2004) and Soroko et al (2013), is titled 'the use of thermography in equine orthopedics' and is one of the earliest papers on the topic. In this paper it was already claimed that thermographic imaging would be able to diagnose SDFT tendinitis before clinical symptoms were apparent.

These initial thermal imaging systems were not ideal because they were not designed to be used for horses and produced images of rather poor quality. Development has not stood still so fortunately there are now more sophisticated systems specifically designed for use in horses and they are available at a reasonable cost (Bathe, 2011a). Thermography or thermal imaging is a technique that is non-invasive and can be performed without the need to place an instrument on the horse. It seems easy to use in the sense that there is always a pretty colorful picture produced. The images are easy to understand, also by horse owners, and are real time available. Therefore it seems an ideal technique (Denoix and Audigié, 2004). Nonetheless, limitations are plenty. Redealli et al (2014) even point out the paradox that the ease of use is also one of its major drawbacks; a large number of environmental factors can disturb the imaging process while still producing a pretty image. This image still looks like it is showing abnormalities due to pathology while in fact the 'pathological' deviation in temperature is caused by artefacts. When one is not aware of the disturbing factors wrong conclusions are drawn from the erroneous image.

The thermal camera measures infrared radiation from the surface of the object, in this case the skin with haircoat and transforms it into an electrical signal that produces the image. The camera detects heat that is generated rather than heat that is reflected. Heat differences in the target area are detected, as well as in the surroundings which makes the place where the image is taken an important factor (Eddy et al, 2001). A system with a radiometer can accurately collect absolute temperatures, whereas most systems only visualize temperature differences within the surface that it records. A temperature difference of more than 1°C is usually considered clinically relevant (Bathe, 2011a), but values of 1.25°C (Soroko et al, 2013) and 2°C (Verschooten, 2001) have also been reported. Interpretation is based on comparison between symmetrical areas, such as left and right limbs (Denoix and Audigié, 2004) and this immediately rules out the use of this technique for detection of bilateral overload injuries of the tendons. Recent methods have been developed that omit the use of symmetrical comparison. An image that displays temperature differences instead of absolute temperature does not only give difficulties when comparing different images collected by the same camera over time, it is also limits comparison of images produced by different recording systems due to large variability (Bathe, 2011a). As long as one is familiar with its own thermal imaging system and the images it produces, this will not be a problem but one must be aware of other limitations. The variation between different imaging moments over time can be limited by placing the horse in a room with controlled temperature without draft and to allow it time to acclimatize, as well as preventing any factors that can have an effect such as work or brushing in the hours before imaging or the application of bandages. Variation can also occur because anxious or active horses with increased sympathetic tone show reduced skin temperatures.
(Eddy et al, 2001). When measuring absolute temperatures a difficulty is that there is a variability in the absolute temperature of the distal aspect of the limb in different horses, hence the thermal range needs to be adjusted for each horse and comparison between horses is once again less obvious (Bathe, 2011a).

While the color of the haircoat does not seem to influence temperature measured (Turner et al, 2011), a long hair coat, dirt, topical applications or irregular clipping patterns can disturb the image and make it harder to interpret. The skin temperature directly reflects the underlying tissue metabolism and circulation (Eddy et al, 2001). Normal variations in thermal patterns of the equine body are corresponding to its normal vasculature and a deep understanding of these normal patterns is crucial in interpreting the scans of horses with suspected injury. Increased heat in tissue can be caused by increase of metabolism and by increase in bloodflow, the latter of these occurs in inflammation and allows thermal imaging to identify areas where an inflammatory process is present. Clinical use of thermal imaging is complicated by the fact that intermittent periods of physiological vasodilatation occur and these are not necessarily symmetrical between left and right or front and back limbs. As said, increased bloodflow increases heat in the tissue, but aside from inflammation this can also occur after exercise or after administration of vasodilatators such as acetylpromazine. 'Thermal cutoff' or the restriction of blood flow to the distal limb prevents the horse from losing heat and especially occurs in colder climates. In this case the contrast of the thermal image is reduced and subtle lesions can easily be missed. Nevertheless, severe inflammatory processes will still be identified (Bathe, 2011a) but this can hardly be an argument in favour of the technique; it would be an severe misjudgement if this were not already found on clinical examination, thereby inherently limiting the value of thermography in gathering diagnostic information.

Due to its superficial location, the midportion of the SDFT can be rather accurately imaged and for this reason the SDFT is a candidate for evaluation of subclinical tendinopathy. Injury to structures that are located deeper such as the suspensory ligament and the DDFT are less readily detected or not at all, except for the branches of the SL. Detection of superficial inflammation in the foot showing at the coronary band, is one of the most useful applications of this technique (Bathe, 2011a) however for deeper pathology such as navicular disease and possible pathology of the DDFT, this technique is not applicable. Detection of acute inflammatory processes has received much attention. However it can also be useful for follow-up of horses returning to work after suffering from a tendinopathy (Denoix and Audigié, 2004). Chronic lesions will not be detected but thermal imaging can provide information on activity of lesions in rehabilitation. With ultrasound, it is usually impossible to make a distinction between chronic, scarlike tissue or a preexisting lesions that is again active; thermal imaging can be helpful here.

Detection of early changes in the flexor tendons in training or competition has been reported by Turner in 1991 and 2001 but these texts are not readily available while they are the only sources that are being referred to by recent authors (Eddy et al, 2001; Denoix and Audigié, 2004; Soroko et al, 2013). In another study by Turner et al in 2001, thermographic findings were compared to both the concern of the trainer and assessment of a veterinarian and found a correspondence in 88% and 95% of the cases, respectively. However, if the trainer is worried or the veterinarian is suspicious of injury this is not exactly ‘subclinical’ or ‘before clinical symptoms become apparent’. A later investigation reported in the same paper showed that abnormal tendons were detected in 18% of the scans that were performed on 50 horses, representing 9 horses. Of these 9 horses, 8 horses subsequently developed clinical problems with an
average of detection by thermography 2.3 weeks before clinical symptoms were seen. Eddy et al (2001) also points out that using thermography, it is possible to detect early physiological changes before they cause clinical signs or radiographic abnormalities but he is probably referring to the study by Turner. A more recent study by Soroko et al (2013) concludes to find evidence of both subclinical tendinitis of the SDFT and subclinical inflammation prior to development of bucked shins but this study is not very convincing. Otilia et al(2006) concludes a case study including four injured horses with the statement that 'regular thermographic screening allowed us to find more horses with initial pathological changes in tendons, than those with clinically manifested signs' but this is a rather bold statement when considering the content of the discussed cases. While it seems almost generally accepted that thermographic evaluation allows for diagnosis of subclinical inflammation, Verschooten (2001) is one of the few to state that these claims of early and easy detection of subclinical cases are exaggerations and likewise, that the advantages as well as cost effectiveness of thermography are overrated. According to this author, skin temperature is an important clinical parameter but nevertheless not specific enough for an early exact diagnosis.

Thermal imaging has some major disadvantages. Not only because it is insensitive to deeper structures, insensitive of chronic processes and lacks specificity. Most importantly, there can be interference of many unrecognized artefacts. On top of that the thermographic evaluation of limbs can only indicate a region of interest without defining aetiology or affected structure. (Eddy et al, 2001; Denoix and Audigié, 2004; Bathe, 2011a). With regards to SDFT tendinopathy, there are clues that in the right setting, with an experienced handler and standardized settings as well as standardized moments of data collection, thermographic imaging might be valuable for use in large stables or training centers where risk of midmetacarpal SDFT injuries is high. Data on the practical use of this technique is limited if not to say non-existing and the predictive value of a subclinical tendinitis has not recently been investigated in a convincing research setting. It would be interesting to see if intense follow-up and adjustment of training after thermographic indication of subclinical pathology will lead to lower incidence rates of SDFT injuries.
3: OPPORTUNITIES FOR EARLY DIAGNOSIS?

Pathology in the subclinical phase can consist of loss of continuity of collagen fibrils, increased deposition of proteoglycan in the extracellular matrix, increase in cross-sectional area and formation of new vasculature. These characteristics can be detected with various commonly used diagnostic techniques such as MRI, thermography, US and it is to be expected that UTC will soon become an established method as well. The use of gait analysis unfortunately shows no real opportunities for detection of lameness due to specific causes. While it is a good technique for the detection of subclinical lameness, it is not possible to specify the cause of the lameness and it remains to be seen if this will ever be possible.

An example of a molecular marker that has recently received attention is Cartilage Oligomeric Protein (COMP). It is a molecule that is present in cartilage but also in tendon tissue. It is thought to align collagen fibrils by forming crosslinks and higher COMP levels are associated with stronger tendon tissue (Smith, 2011a). When matrix is degraded this molecule is present in higher levels in surrounding tissue and it is currently used as a marker for cartilage damage and rheumatoid arthritis. Elevated COMP levels in digital sheath synovial fluid, detected by ELISA, could be indicative for tendon injury. However, only significant higher levels were detected when tendon damage was present within the tendon sheet and not when the injury was located in the tendon outside the sheet. (Smith and Heinegard, 2000; Smith et al, 2011). Furthermore, the COMP content of hyaline cartilage and tendon in horses with navicular disease is higher than that in sound horses (Viitanen, 2003) thus questioning the specificity of this marker.

Another and more promising indicator of matrix turnover during tendon injury is PCIP, which is the carboxy-terminal part of the procollagen molecule and it is cleaved off when new collagen is formed. It can be detected in serum and is a quantitative measure of newly formed type I collagen. In a study performed by Jackson et al (2003) it was showed there is a significant change in this serum molecular marker when tendon injury is present. This will be easier to use because blood is easier to collect than synovial fluid. However, the drawback of this marker is that it is not specific for tendon tissue repair but indicates type I collagen formation in any type of healing tissue in the body thus, in this aspect, suffering from the same limitations as detection of COMP.

There is a large variation between mechanical properties such as tendon strength and stiffness in the SDFT and certain horses may be predisposed to injury (Thorpe et al, 2010b). As the mechanical strength of the tendon is derived from the orientation of collagen molecules within fibrils and these fibrils are stabilized by the formation of cross-links between the collagen molecules, differences in crosslinks might be responsible for this variation on mechanical properties. Thorpe et al studied the variation in cross-links levels and found that a certain pyrrole cross-link has the highest correlation with tendon strength and stiffness. It is postulated by Thorpe et al (2010b) that markers for these pyrrole cross-links as well as markers for other matrix components may be developed to identify the horses that have a higher risk of developing tendon injuries, and these markers may also be used to monitor training regimes if they indicate increased turnover of tendon matrix molecules. However, first it needs to be understood how these cross-links are related to tendon properties before it is known what these markers should target.

Future research may provide more information on the chronology of these processes and possibly other processes than have until now been unrecognised. These early processes that are yet to be identified
in the development of tendinopathy are of high clinical relevance if they can be detected early in the process. However, to be useful, these processes should also be easy to measure with current available techniques, it must be possible to measure their presence precisely and accurately, the technique must be available for routine use and the procedure should be fast, cheap and not harmful to the patient. Also, the indicators that will be used to detect the presence of these processes must have a high predicting value. If this will become possible and a developing tendinopathy can be detected, preventive measures can be taken such as adapting the training schedule and temporarily lowering the load. This would truly be a switch from curative to preventive medicine.
Conclusion

The question that needed to be answered with this literature study is whether it is possible to evaluate horses that are subjected to heavy work and to prevent a subclinical overload of the tendon from becoming a clinical manifest tendinopathy.

It can be concluded that there are many techniques available for detection and visualization of a wide scope of physiological and pathological processes. It is mainly dependent on the situation of the individual cases which technique is most applicable. For example, a training center for racehorses could benefit from systematically performing thermography scans as part of their daily or weekly routine. If these are collected in a room that is well-designed so that artefacts are limited, and the procedure is fitted within the activities of normal routine, it may be very useful to collect a database of all horses in training. If deviations in thermographic images are a reason to become suspicious of a developing tendinopathy, the training regime of that specific horse could be adapted by temporarily lowering the load. It would be extremely interesting to perform a study in which it will be assessed whether the previous described thermographic assessment and training adaptation will indeed lead to a lower number of clinical tendinopathies.

In cases of highly valuable individual horses, for example a top-level dressage horse who is usually trained by one very sensitive rider, the situation is different. This rider or trainer may notice a vague change in performance such as increased stiffness in specific circumstances. To rule out beginning damage to tendons in the region of interest, MRI could be indicated to evaluate the involved tendon structures in detail and look for signals of tendon overload such as increased deposition of proteoglycans and increased cross-sectional area. However UTC is only recently developed and seems to be a promising technique in giving a detailed representation of changes in tendon tissue, it will most likely also become one of the imaging techniques of choice these cases. 'Normal' ultrasound evaluation is common practice and the limitations have been discussed, nonetheless it is the most widely used diagnostic aid in assessing tendon damage. UTC is an improvement to these limitations and it is to be expected that it will become a popular tool.

Gait analysis and more specifically GRF patterns are extremely valuable and the technique of choice to detect subtle changes in locomotion. However, it has proven to be hard to determine the specific cause of an irregularity or lameness in horses and it is not at all sure that this will become possible in the future. It can be sure that developments in this field will continue, but most likely the detection of subclinical tendinopathy will not become possible in the near future, if ever. Nonetheless there may still be surprises ahead. In human patients morning stiffness is an early indicator of tendinopathy and it may proof that GFR patterns only show characteristic change in the first strides after stall rest. In the available literature it seems this has never been examined until now.

The use of biomarkers in the evaluation of tendondamage has recently received attention but will also not be available in clinical settings in the near future. If these are to be developed, they will be useful, especially if markers can be detected in the blood, since taking bloodsamples is easy and common practice. However, if these markers are to be screened in synovial fluid of the tendon sheath their clinical ease of use will be lower. Nevertheless, it is sure that these will receive more attention the common years, not only because more attention will be given to unraveling the pathological processes involved, but also because it might be a interesting modality for human medicine.

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Most of all, it needs to become clear to what extent a normal physiological response to load takes place and what the changes in tissue are that mark the onset of pathology. Only if this is known it is possible to have a meaningful discussion about the diagnostic procedures of choice.
References


ground reaction force data documented by use of principal component analysis. American Journal of Veterinary Research 60 (1), 549-555.


