Patellar and Achilles tendinopathy

Sclerosing injections and ultrasound guided arthroscopic shaving

Lotta Willberg
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Figure 2 and 3 on page 19, Anneli Falck, TMG Stockholm
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To conquer oneself is a greater victory than to conquer thousands in a battle

Dalai Lama

To my beloved family;
Tommy, Emil and Fia.
And to my mother and my late father.
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Abstract
Chronic painful tendinopathy is a common cause for elite- and recreational athletes to stop or decrease the level of their sports activity. Recent research on innervation patterns, histopathology and possible pain mechanisms in tendons has led to an increased knowledge about the chronic painful tendon. Ultrasound (US) and colourDoppler (CD) examination showing localized high blood flow, inside and outside regions with structural tendon abnormalities, has been shown to be of importance for tendon pain. Immunohistochemical analyses of biopsies have shown sensory and sympathetic nerves in close relation to the high blood flow in the painful region of the tendon. These findings have led to new ideas about development of new treatment methods for chronic painful tendinopathy.

In study I, we evaluated the already in use, US-guided sclerosing polidocanol injection treatment of midportion Achilles tendinopathy, using two different concentrations of the substance. This study aimed to find out if there was a faster return to painless activity by using the concentration 10 mg/ml compared to the formerly used 5 mg/ml. There were no significant differences in the clinical results between the groups. In study II - technical note, we aimed to develop a new one-stage surgical treatment method for patellar tendinopathy. This method was based on research concerning the innervation patterns and US/CD findings in patellar tendinopathy/ “jumper’s knee”. Technically we added ultrasound guidance to knee arthroscopy to identify and visualize the region of interest during a surgical shaving procedure. In study III, we tested the newly invented US/CD-guided arthroscopic shaving technique in a pilot study. The short-term clinical results were promising and the majority of the patients returned to painless activity after a short rehabilitation period. In study IV, we compared the US/CD-guided arthroscopic shaving method with the already in use sclerosing polidocanol injection treatment in a randomized study. At short-term follow-up, the patients treated with US/CD-guided arthroscopic shaving had significantly less pain during rest and activity, were significantly more satisfied with the treatment, and had a faster return to sports, compared to the patients in the sclerosing injection group. There were no complications. In study V, at longer-term follow-up (endpoint 46 months) there was a significant decrease in pain during activity in both groups. There were no remaining significant differences in the pain levels during activity between the groups. The tendon structure had improved significantly in both groups. There was a significant decrease in the anteroposterior thickness of the proximal patellar tendon in patients treated with US/CD-guided arthroscopic shaving, but not in the sclerosing injection group. The CD flow had diminished significantly in both groups, and there was a correlation between low CD flow and high patient satisfaction in both groups. The CD flow decreased faster in the surgical group than in the injection group. In conclusion, this newly invented US/CD-guided arthroscopic shaving treatment, focusing on treatment outside the tendon, has shown good clinical results with pain relief and a fast return to sports activity, in patients with patellar tendinopathy.

Keywords: arthroscopy, jumper’s knee, sclerosing injection, tendinopathy, ultrasound
LIST OF ORIGINAL PAPERS

This thesis is based on the following studies

I. **Sclerosing injections to treat midportion Achilles tendinosis: a randomised controlled study evaluating two different concentrations of Polidocanol**
   Willberg Lotta, Sunding Kerstin, Öhberg Lars, Forssblad Magnus, Fahlström Martin, Alfredson Håkan

II. **Ultrasound- and Doppler-guided arthroscopic shaving to treat Jumper’s knee: a technical note**
    Willberg Lotta, Sunding Kerstin, Forssblad Magnus, Alfredson Håkan

III. **Treatment of Jumper’s knee: promising short-term results in a pilot study using a new arthroscopic approach based on imaging and histological findings**
    Willberg Lotta, Sunding Kerstin, Öhberg Lars, Forssblad Magnus, Alfredson Håkan

IV. **Sclerosing polidocanol injections or arthroscopic shaving to treat patellar tendinopathy/jumper’s knee? A randomised controlled study**
    Willberg Lotta, Sunding Kerstin, Forssblad Magnus, Fahlström Martin, Alfredson Håkan

V. **Treatment of patellar tendinopathy with sclerosing injections or ultrasound-guided arthroscopic shaving - a long term follow-up of ultrasound findings and clinical results**
    Sunding Kerstin, Willberg Lotta, Werner Suzanne, Alfredson Håkan, Forssblad Magnus, Fahlström Martin
    *Manuscript submitted 2013*
Abbreviations

ADL activity of daily living
AP anteroposterior
BMI body mass index
CD colour Doppler
cm centimeters
CSA cross sectional area
ESWT extracorporeal shock wave therapy
GAG glucose amino glycanes
GS greyscale
HFP Hoffa’s fat pad
IFP infrapatellar fat pad
JK jumper’s knee
Kg kilograms
kN kiloNewton
m. musculus
MRI magnetic resonance imaging
NP neuropeptides
NSAID nonsteroidal anti-inflammatory drug
PD power Doppler
PGP 9.5 protein gene product 9.5
PRP platelet-rich plasma injection
PT patellar tendon
RCT randomized controlled trial
ROM range of motion
SD standard deviation
SP substance P
SPSS Statistical Package for the Social Science
US ultrasound
VAS visual analogue scale
VMO vastus medialis obliquus
X-ray plain film radiography
Kronisk smärtande patellar- och Achillessena
Skleroserande injektioner och ultraljudsvägledd artroskopisk kirurgi

Bakgrund

Mål
I delstudie I ville vi utvärdera den ultraljudsledda injektionsbehandlingen, gällande mittportions tendinos i hälsenan, genom att jämföra två olika koncentrationer av den skleroserande substansen polidocanol. Avsikten var att undersöka om dubbla koncentrationen av substansen, jämfört med den tidigare använda, kunde medföra en halvering av antalet behövda injektioner. Delstudie 2 syftade till att utföra simultant ultraljud vid knäartroskopi (titthålskirurgi) för att kunna synliggöra det smärtande området i senan och precisera den artroskopiska åtgärden så långt det är möjligt vid sk hopparknä. Vid normal knäartroskopi kan man inte se det smärtande området i patellarsenan. Vidareutveckling av den ultraljudsvägledda artroskopin skulle kunna möjliggöra kirurgisk behandling vid sk hopparknä och därmed sannolikt underlättta för snabbare återgång i idrott än vad tidigare behandlingsmetoder kunnat tillåta (delstudie 3).

Avslutningsvis, var vår föresats att jämföra behandlingsresultaten mellan den helt nya metoden, ultraljudsvägledd artroskopi och den tidigare existerande behandlingsmetoden, skleroserande injektioner med läkemedlet polidocanol hos patienter med sk hopparknä. Avsikten var att med hjälp av ultraljud och
färgDoppler studera hur den smärtande senan förändras över tid efter respektive behandlingsmetod och tiden till återgång i smärtfri idrottsutövning (delstudie 4, delstudie 5).

**Metoder**

I den första delstudien randomiserades (lottades) 47 patienter med 52 kroniskt smärtande hälsenor till två grupper. Båda grupperna fick identisk ultraljudsvägledd injektionsbehandling med den enda skillnaden att den ena gruppen fick 5 mg/ml av läkemedlet polidocanol och den andra gruppen 10 mg/ml. Maximalt tre behandlingar gavs i båda grupperna, innan vi utvärderade om det fanns någon skillnad mellan grupperna avseende effekt på smärta. Såväl patienten, ortopedspecialisten som ultraljudsteknikern var ovetandes om vilken koncentration som gavs vid olika behandlingstillfällen.

I den tredje delstudien (pilotstudie), fick 15 patienter med hög idrottsaktivitetsnivå och med diagnosen hopparknä, möjligheten att genomgå en riktad kirurgisk behandling med ultraljudsvägledd artroskopi. En helt ny kirurgisk metod där vi lät ultraljud guida knäartroskopin. Operationen beskrivs i den andra delstudien. Dessa 15 patienter följdes noggrant efter den ultraljudsvägledda artroskopiska metoden tills de återgick till smärtfri idrott. I den fjärde delstudien lottades 45 patienter med 52 kroniskt smärtande patellarsenor, till antingen behandling med ultraljudsvägledd artroskopi eller skleroserande injektionsbehandling med läkemedlet polidocanol. Efter behandlingen följdes dessa patienter över tid. Såväl patienterna från delstudie 4 (45 patienter) som patienterna från delstudie 3 (15 patienter) kallades sedan tillbaka för en långtidsuppföljning med utvärdering av senans utseende (blodflöde, tjocklek och struktur) med hjälp av ultraljud och färgDoppler undersökning och utvärdering av kliniska behandlingsresultat (delstudie 5).

**Resultat i korthet**

Uppföljningen av patienterna i den första delstudien gjordes i genomsnitt efter 14 månader och inga signifikanta skillnader påvisades mellan de två grupperna avseende smärta, antal givna injektioner eller totalt injicerad volym av polidocanol eller antal nöjda och smärtfria patienter. Eftersom vi i enlighet med vår hypotes i den andra delstudien kunde identifiera det smärtande området med ökat blodflöde i patellarsenan, när vi använde ultraljud samtidigt med artroskopi, gick vi vidare med pilotstudien (delstudie 3). Av de 15 opererade patienterna hade 13 efter ca 6-8 veckor återgått till sin idrott med gott resultat avseende smärta. I den fjärde delstudien visade det sig att de patienter som hade opererats med den ultraljudsledda artroskopiska metoden mådde signifikant bättre och var signifikant nöjdare vid korttidsuppföljningen än de patienter som hade genomgått skleroserande injektionsbehandling.
Vid långtidsuppföljningen, efter i genomsnitt 46 månader, upphävade båda grupperna goda resultat jämfört med före start av behandling. Däremot fanns inte några kvarvarande skillnader i behandlingsresultat mellan grupperna avseende smärtan vid aktivitet. Senstruktureren såg finare ut och det tidigare ökade blodflödet hade minskat i båda grupperna. Den enda skillnaden mellan grupperna var sentjockleken, som hade minskat betybigt hos de patienter som genomgått kirurgisk behandling jämfört med de patienter som hade behandlats med skleroserasende injektioner. Även sambandsberäkningar gjordes, vilka visade att det tycks finnas en viss korrelation mellan lågt blodflöde och hög patientnöjdhet.

**Slutsats**

Vid behandling av patienter med kroniskt smärtande mittportions tendinos i Achillesenan verkar ultraljudsledda skleroserasende polidocanol injektioner vara en framgångsrik metod för behandling av smärtan. Det tycks inte finnas några skillnader i effekt på smärtan mellan de två koncentrationerna, 5 och 10 mg/ml. Vår rekommendation är därför att vid behandling med skleroserasende injektioner med polidocanol använda den lägre styrkan och att strikt hålla sig till den ursprungliga metoden, där enbart mycket små volymer (max 2 ml) ges per behandlingstillfälle.

Vid kroniskt smärtande patellarsena, sk hopparknä visas att både behandling med ultraljudsledda skleroserasende injektioner med polidocanol samt ultraljudsledd artroskopisk shaving kan ge goda kliniska resultat. Den ultraljudsledda artroskopin leder dock till mindre smärta, snabbare återgång till smärtfri idrottsaktivitet samt nöjdare patienter.

En intressant iakttagelse är att båda metoderna var associerade med en förbättring av senstruktureren och minskat blodflöde över tid. Det var emellertid bara den kirurgiska metoden som gav en ultraljudsverifierad normalisering av senans tjocklek. Det tycks också finnas en korrelation mellan lågt blodflöde i det patologiska (sjukliga) området och hög patientnöjdhet samt låg smärta vid aktivitet. Denna iakttagelse är mycket intressant men behöver undersökas vidare i större studier.

Resultatet av studierna i föreliggande avhandling visar att ultraljudsledd artroskopisk shaving kan rekommenderas vid behandling av patienter med kroniskt smärtande hopparknä för att uppnå tidig smärtfrihet och snabb återgång till idrottsaktivitet. Avseende kronisk smärtande mittportions tendinos i hälsenan visas att ultraljudsledda skleroserasende injektioner med polidocanol enligt ursprungsmetoden ger god effekt på smärtan.
The normal tendon
Tendons connect muscles and bones. They transmit the force created in the muscle to the bone which enables joint movement. Healthy tendons are glistening and ivory white in colour and fibroelastic in texture and they show great resistance to mechanical loads (Kannus 2000). In the normal painless tendon there are no visible blood flow visualized with US/CD (Öhberg et al. 2001). Tendons are not very tolerant to shearing or compressive forces (Hess et al. 1989), but they have a great capacity to withstand tensile and stretching forces. A tendon with an area of 1 cm² is capable of resisting a weight of 500–1,000 kg (Józsa et al. 1997). Eccentric muscle contractions - such as landing a jump produces the highest stress in the tendon (O’Brien 1992; Kirkendall et al. 1997; Ishikawa et al. 2005). To exemplify; in volleyball, the patellar tendon is exposed to high forces and up to 8 kN have been calculated when landing a jump. Walking on flat ground generates 0.5-2.6 kN load (Komi 1992).

Structure of the tendon
The extracellular tendon matrix is composed of collagen fibers, elastin, ground substance and anorganic components (Kannus 2000). Collagen, mainly type I and elastin are embedded in the proteoglycan-water ground substance. Collagen accounts for 65-80 % of the dry weight and elastin for about 1-2 %. The tendon ground substance consists of 60-80 % water, proteoglycans, glucose-aminoglycans (GAGs) and structural glyco-proteins (e.g. Kannus 2000). Tenoblasts and tenocytes, are elongated fibroblasts and fibrocytes that lie between the collagen fibers in a complex manner (Hess et al. 1989). About 90-95 % of the cellular elements consist of tenoblasts and tenocytes which produce collagen (Kannus 2000). There are two steps in the synthesis of collagen fibrils, an intracellular and an extracellular step. Primarily procollagen is formed and in the next step the procollagen is converted to tropocollagen. Five tropocollagen molecules (microfibrils) are cross-linked to create the insoluble collagen molecule, collagen fibrils (O’Brien et al. 1997). Multiple collagen fibrils then progressively aggregate to form definable groups – collagen fibers, which is the basic and smallest visible (light microscopy) unit of the tendon (Hess et al. 1989; Kannus 2000). There is great variation in terms of collagen content and type of collagen distribution from “tendon-to-tendon” (Fan et al. 1997). It is well documented that the collagen fibrils are oriented not only longitudinally, but also transversely and horizontally and the longitudinal fibrils also cross each other forming spirals and plaits. The complex collagen structure with its crosslinks provides the tendon with tensile strength and enables the tendon to withstand high loads, while the ground substance provides structural support for the collagen fibers and regulates the extracellular assembly of procollagen into mature collagen (Åström 1997).
complex structure of collagen and the elastin may contribute to the recovery after tendon stretch (Butler et al. 1978).

The tendon is organized in primary, secondary and tertiary bundles (Kannus 2000). The nomenclature might vary in the literature. The basic units of a tendon are the fibrils, and the smallest collagenous structures are the collagen fibers (Hess et al. 1989; Józsa et al. 1997). See figure 1. The length of the collagen fibers varies but they can be as long as the tendon. A fine and loose connective tissue sheet surrounds the tendon; the epitenon, which contains blood vessels, lymphatics and nerves. The epitenon is surrounded by the paratenon. The paratenon is composed of loose randomly organized collagen fibrils, essentially type I and type III. These permit free movement of the tendon against the surrounding tissues, i.e working as an elastic sleeve (Hess et al. 1989; Józsa et al. 1997; Kirkendall et al. 1997). The endotenon is the sheet that surrounds the collagen fibrils in primary fibre bundles. Blood vessels and nerves run inside the endotenon. The vascular system inside the tendon consists of longitudinally oriented vessels localized in the endotenon together with veins and lymphatics (Schatzker et al. 1969). The longitudinal direction of the intratendinous vessels in the normal tendon will be further discussed.

Metabolism
Historically tendon tissue was thought to be metabolically inert, but tendon cells (tenoblasts and tenocytes) have been demonstrated to be more metabolically active than previously believed. The synthetic activity lessens with increasing age though (Józsa et al. 1997). The tendon has a balance between collagen synthesis and degradation when healthy (O’Brien 1997). There are clear circulatory responses and collagen turnover changes related to activity (Vailas et al. 1978; Langberg et al. 1998, 2001, 2007). It appears that it takes 48–72 hours for the collagen type I formation to peak after exercise (Miller et al. 2005). The tendon has a slow metabolic rate and the oxygen consumption is 7.5 times lower than in skeletal muscle (Józsa et al. 1997; O’Brien 1997). Of clinical importance is that
the tendon is allowed to carry loads and maintain tension for a long time, but it has a relatively slow healing response and adaptation to change. The healing after a rupture can take years (Sharma et al. 2006) due to the low metabolic rate. It is likely to believe that these facts are of importance for treating patients with chronic painful tendons.

**General innervation**

Tendons have been described to have innervation deriving partly from the paratenon. Paratenon nerves form rich plexuses that send a few branches penetrating the epitenon, branches that inside the tendon anastomose with branches originating from neighboring muscles and is described to cross the myotendinous junction (Józsa et al. 1997). The number of nerves inside the tendon is relatively few. They follow the blood vessels that run along the axis of the tendon and anastomose via obliquely and transversally oriented nerve endings. Most of the nerve fibers are sensory nerve endings on the surface of the tendon. The mechanoreceptors seem to be concentrated to the myotendinous junction and tendon insertions (Józsa et al. 1997). Four categories of nerve endings are mainly seen in tendons, ligaments and joint capsules. These are type I Ruffini corpuscles (pressure receptors); type II Vater-Pacini corpuscles (activated by movement); type III Golgi tendon organs (mechanoreceptors); and type IV receptors (free nerve endings functioning as pain receptors) (Józsa et al. 1993).

Concerning sensory innervation of the tendon, it has been concluded that large tendons are relatively hyponeural. In recent years there has been a big focus in research in terms of the innervation of tendon tissue. The Achilles tendon and patellar tendon seem to have similar patterns of innervation. These findings are of utmost importance when addressing the pathology and pain when treating patients with chronic painful tendinopathy which is the focus of this thesis. Information and knowledge about the sensory and autonomous innervation has increased (Danielsson 2007; Bjur et al. 2005; Andersson et al. 2007). The innervation found in the tendon is mainly seen in narrow zones of loose connective tissue and blood vessels, zones interspersed between the collagen bundles (Danielsson et al. 2006a). Of these thin nerve fascicles and perivascular nerve fibers only very few display positive reactions for the sensory nerve markers. Most of the nerves are located in the loose paratendinous connective tissue that surrounds the tendon (e.g. Danielsson et al. 2006a). In this tissue, large nerve fascicles, as well as the walls of some of the larger arteries and a few of the smaller blood vessels, display distinct immunohistochemical reactions for the general nerve marker protein gene product 9.5 (PGP 9.5) (Danielson et al. 2006a). Parts of the nerve fibers of the fascicles and perivascular innervation have been shown to correspond to sensory afferents, the sensory nerve markers substance P (SP) and calcitonin gene-
related peptide (CGRP) (e.g. Danielson et al. 2006a). It also contains markers of the autonomous nervous system, both parasympathetic (vesicular acetylcholine transporter) (Danielson et al. 2006b) and sympathetic neuropeptide Y (NPY) and tyrosine hydroxylase (TH) (Danielson 2007). These findings suggest the occurrence of both a sensory and an autonomous innervation. This observation, put together with findings of autonomous nerve markers (Danielson et al. 2006a, 2008) seems to indicate that the innervation of the deep parts of the tendon is mainly autonomous and not sensory in its type.

The general, sensory, sympathetic and parasympathetic (Danielson et al. 2006b, 2007) innervations in the chronic painful tendinotic tendon do not differ particularly from the corresponding innervations of the normal tendon. SP-positive nerve fibers, seen as free nerve endings, have been observed between the collagen fibers in tendons of athletes with or without pain symptoms indicating patellar tendinopathy (Lian et al. 2006). A local production of signal substances within the tenocytes themselves has been shown, signal substances that are traditionally found in the neuronal system. This phenomenon seems to be particularly pronounced in tendinotic tendons (Danielson et al. 2006a, 2008). Evidence of an occurrence of both an acetylcholine production and muscarinic receptors (Danielson et al. 2006b), as well as of a catecholamine production and adrenergic receptors (Danielson 2007), have been shown for the tendon tissue in normal tendons but in particular within tendinotic tendons. Neurokinin-1 (NK-1) receptor (the primary SP receptor) immunoreaction has been demonstrated in the walls of blood vessels and nerve fascicles/nerve fibers (Forsgren et al. 2005).

The Achilles tendon – gross anatomy
The Achilles tendon is the strongest and longest tendon in the human body (Komi et al. 1992). The gastrocnemius and the soleus muscles (triceps surae muscles) merge to form the Achilles tendon. The tendon of gastrocnemius is 11–26 cm long and the length of the soleus tendon portion is 3–11 cm (Curvin et al. 1984). The cross sectional area (CSA) of the tendon is 0.8–1.4 cm² (Koivunen-Niemala et al. 1995) and it may vary according to activity (Magnusson et al. 2003). The most proximal part is rather flat but during its descent towards its insertion into the calcaneus, it becomes narrower and more circular until it inserts in the form of a delta into the calcaneus (Reynolds et al. 1991). The plantaris tendon, if present, normally runs between the triceps surae muscles and does not normally merge with the Achilles tendon (Josza et al. 1997; Doherty et al. 2006). The Achilles tendon may rotate up to 90 degrees laterally during the descent. This means that fibers originally posterior become lateral, the lateral fibers become anterior and so on. The degree of rotation has been found to correlate with the described variation in fibers from gastrocnemius and soleus respectively and at what level
the fibers from soleus fuses with the fibers from gastrocnemius (Józsa et al. 1997). This facilitates elongation and elastic recoil within the tendon and stored energy can be released during locomotion (McNeill 2002). Another important factor of the rotation is that concentrated stress might occur when the fibers from soleus and gastrocnemius merge. This is most prominent at 2–5 cm proximal to the calcaneus insertion, and corresponds well with the region of the tendon that according to some authors has the poorest vascular supply (Reynolds et al. 1991). In the literature the ventral aspects of the Achilles tendon is unclear but dorsally, laterally and medially there is a paratenon (loose connective tissue) (Kvist et al. 1987; Franklyn-Miller et al. 2009). In this thesis the ventral aspect of the Achilles tendon is of utmost interest. We know that the dorsal boundary of “Kager’s fat pad” (Kager’s triangle) is the Achilles tendon (Ly et al. 2004). Kager’s fat pad consists primarily of adipose cells, but also some elastic fibers and type I collagen (Shaw et al. 2007). Kager’s fat pad is said to protect and stabilize the bloodvessels entering the tendon (Theobald et al. 2006). In studies on rats, the Kager’s fat pad has been shown to be supplied by sensory nerve fibers (Ackermann et al. 2003, Shaw et al 2007). Whether there is a “paratenonlike structure” or not ventral to the Achilles tendon still needs to be clarified.

**The Achilles tendon – blood supply**

By some authors, the main blood supply of the Achilles tendon is considered, to be the paratendinous network of blood vessels, which originates from the anterior and posterior tibial arteries, as well as the peroneal arteries. But it is also considered to come mainly from the muscles and is usually divided into the following three regions, the musculotendinous junction, the length of the tendon, and the tendon bone junction. The main blood supply of the midportion of the tendon takes place through the paratenon (O’Brien 1997; Chen et al. 2009). Most of the paratendinous vessels can be found on the ventral side of the tendon, and less are seen on the dorsal side of the tendon (Zantop et al. 2003).

**The Achilles tendon – innervation**

The nerve supply to the Achilles tendon originates mainly from the sural nerve, via nerve fascicles that occur subcutaneously. The innervation is quite sparse inside the tendon tissue, with just a few small nerve fibers following the endotenon septa (Józsa et al. 1997). The main part of the innervation of the Achilles tendon is found in the paratenon (Stilwell 1957; Andres et al. 1985). Formerly, the innervation within the Achilles tendon has been sparsely studied although it has been of great interest in recent studies. The innervation pattern has been somewhat clarified by findings of a general (PGP9.5), a sensory (SP/CGRP) and an autonomic nervous system in the Achilles tendon (Bjur et al. 2005; Andersson et al. 2007).
The patellar tendon – gross anatomy

The patellar tendon is sometimes referred to as the ‘patellar ligament’ when definitions are used correctly. But it is suggested to refer to it as a tendon since its macroscopical and microscopical appearance more resembles tendon tissue and its function is directly controlled by the quadriceps muscle (Peers et al. 2005). The patellar tendon is an extension of the quadriceps tendon in which the patella is embedded as a sesamoid bone (Moore et al. 1999). See figure 2. The quadriceps muscle consisting of, m. rectus femoris, m. vastus medialis, m. vastus lateralis and m. vastus intermedius, is the strongest extensor in the knee joint. The vastus muscles have their origins at different sites of the femur, and they insert at the tibia via the patella and the patellar tendon. They also function as flexors of the hip joint. The m. rectus femoris, originates in spina iliaca anterior inferior and inserts into tuberositas tibiae. It has been shown that the tendon fibers of m. rectus femoris generally are the only tendon fibers of the quadriceps muscle that actually continue over the anterior surface of the patella to form the patellar tendon (Reider et al. 1981). The patellar tendon is a flat tendon and the normal width is approximately 30 mm (frontal plane) (Peers et al. 2005), and the thickness 4-5 mm (sagittal/cross sectional plane). The patellar tendon can be broader at its attachment to the tip of the patella than at the insertion to the tibial tubercle (Andrikoula et al. 2006). The average length of the patellar tendon is reported to be 46 mm (range 35-55 mm) (Reider et al. 1981).

The patellar tendon – blood supply

The arterial blood supply has been thoroughly mapped in a study of 20 specimens of human patellar tendons (Soldado et al. 2002). The arterial blood supply to the medial patellar tendon originates from the descending and inferior medial
genicular arteries, branches of the femoral and popliteal arteries, respectively. The lateral side is supplied by the lateral genicular arterioles from the main anastomotic arches. It also obtains blood supply directly from the medial and lateral arteries (Soldado et al. 2002). The level of blood vessels seen within the tendon tissue is low and consists of branches of the popliteal artery and the recurrent tibial anterior artery; a branch of the the anterior tibial artery. For simplicity; the patellar tendon can be divided into two parts concerning the blood supply, the lower and the upper segment. The lower segment is supplied by superficial vessels from the supratubercular arch and the upper segment receiving deep vessels from the retropatellar arch. In the middle third of the tendon these intratendinous vessels anastomose resulting in a bipolar pattern of tendinous arterial supply (Soldado et al. 2002; Andrikoula et al. 2006). See figure 3. In contrast to the tendon, which is only supplied by blood in the way described above, the loose paratendinous connective tissue (paratenon), receives arterioles from the main anastomotic arches and also obtains blood supply directly from the medial and lateral arteries (Soldado et al. 2002). The level of blood vessels seen within the tendon tissue is lower than that seen in the paratendinous tissue (Soldado et al. 2002).

The patellar tendon – innervation

The nervous system of the patellar tendon and surrounding loose connective tissue consists of sensory and autonomic nerve fibers (Ackermann et al.1999; Bjur et al. 2005; Danielson et al. 2006 a, b; Lian et al. 2006). They derive from neighbouring muscular, cutaneous, peritendinous and deep nerve trunks (Stillwell 1957). The loose paratendinous connective tissue of the patellar tendon is richly innervated, but the tendon itself has a limited innervation. However, recently the tenocytes themselves were shown to produce signal substances, normally associated with neurons (Danielson 2007). Of special interest in this thesis is the proximal and dorsal part of the tendinotic tendinopathic patellar tendon. In a study of patients with chronic patellar tendinosis, it was shown that there was an existence of free myelinated nerve fibers in the proximal osteotendinous zone of the patellar tendon, and a periadventitial innervation of arteries, particularly in the IFP (Hoffa’s fat pad) adjacent to the inferior pole of the patella (Sanchis-Alfonso et al. 2001). Furthermore, sympathetic free nerve endings were found to be present in the tendon tissue, a majority of these, in contrast to the sensory fibers, being clearly related to blood vessels (Lian et al. 2006).

Autonomic innervation is mainly related to the blood vessels and both sympathetic and parasympathetic neuropeptides are implicated in the dynamic regulation of blood flow during exercise (Hannukainen et al. 2005). The sympathetic NP mediate vasoconstriction (decreased blood flow) and the parasympathetic NP mediate vasodilatation (increased blood flow).
The Hoffa’s fat pad – infrapatellar fat pad
Dorsal to the patellar tendon the infrapatellar fat pad (IFP) is located. Also known as Hoffa’s fat pad, named by the orthopedic professor Albert Hoffa, 1859-1907. IFP is an intracapsular, extrasynovial structure that fills the anterior knee compartment, and is richly vascularized and innervated. Although the precise function of the IFP is unknown, studies have shown that it may play a role in the biomechanics of the knee or act as a store for reparative cells after injury. Its degree of innervation, the proportion of substance-P-containing fibers and close relationship to its posterior synovial lining implicates IFP pathologies as a source of infrapatellar knee pain (Dragoo et al. 2012). A variety of traumatic mechanisms can lead to haemorrhage and inflammation including acute injury, repetitive microtrauma and iatrogenic injury (Murakami et al. 1997; Ellen et al. 1999; Steadman et al. 2008). Acute injury or microtrauma to the IFP may occur from blunt impact, shear injury with cruciate ligament tearing patellar dislocation, torsion and impingement. (Ogilvie et al. 1994; Tang et al. 2000; Kumar et al. 2007; Abreu et al. 2008, von Engelhart et al. 2010). Examples of iatrogenic injury include fibrosis due to the creation of arthroscopy portals, scarring due to tendon harvest during anterior cruciate ligament reconstruction and fat pad resection (Rosenberg at al. 1992; Paulos et al. 1994; Murakami et al. 1995; Bayar et al. 2008).

Photos showing size and location of the Hoffa’s fat pad. At top left, patellar tendon released from its insertion at the tibial tuberosity. To the right, patellar tendon with Hoffa’s fat pad, view from the dorsal aspect. At bottom left, Hoffa’s fat pad resected from its insertion at the patella, view of the patellar tendon from the dorsal aspect.
BACKGROUND
Epidemiology

**Midportion Achilles tendinopathy**
All patients in this thesis, paper I, were diagnosed as “midportion Achilles tendinotic tendinopathy”. This type of pathology is considered to be involved in 55-65% of all Achilles tendon injuries (Järvinen et al. 1997, 2005).

Despite all overuse theories, Achilles tendinopathy has recently been found in people with relatively sedentary lifestyles. Some studies reporting up to almost a third of the patients not participating in any sports/physical activity on a regular basis (Rolf et al. 1997; Alfredson et al. 2000). Some common activities that can lead to Achilles tendinopathy include middle- or long distance running, badminton, track and field activities etc (Fahlström et al. 2002). It is considered that 7-9% of professional athletes participating in sports consisting of a high frequency of running and jumping present with Achilles tendinopathy (Lysholm et al. 1987; Almekinders et al. 1998; Cook et al. 2002; van Gent 2007). For recreational runners the condition is found in up 6-18% of the runners (Alfredson et al. 2000; Schepsis et al. 2002). Studies have shown that up to 30% suffer from bilateral symptoms (Paavola et al. 2002; Öhberg et al. 2004). Midportion Achilles tendinopathy is most common in the age group from 30 to 60 years (Paavola et al. 2000). The distribution of males and females varies in studies. A range between 45% and 89% of males has been reported in the literature (Paavola et al. 2000; Öhberg et al. 2002; Alfredson et al 2005b).

**Patellar tendinopathy**
In one of the few epidemiological studies on elite athletes in different sports, the overall prevalence of patellar tendinopathy was reported to be 14%. The prevalence was lower in females 5.6%, compared to 13.5% in males (Lian et al. 2005). Other clinical studies also show that the condition is more common in males (Myllymäki et al. 1990). However, no difference between males and females was found in a prospectice study on 138 physical education students (Witvrouw et al. 2001). The highest prevalence (40–50%) has been reported in male volleyball players (Ferretti et al. 1984; Gisslén et al. 2005). Patellar tendinopathy is most commonly seen in sports with high demands on speed and power from the leg extensors (Lian et al. 2005). Other sports than volleyball, where the condition is seen are for instance basketball, soccer, football and track and field (Blazina et al. 1973). The long-term prognosis for male athletes has been shown to be poor and 53% of the athletes abandoned their sports career due to pain symptoms (Kettunen et al. 2002). Patellar tendinopathy is rarely, if ever seen, in physically inactive people in contrast to midportion Achilles tendinopathy.
Aetiology
The aetiology and pathogenesis of chronic painful tendinopathy is still unclear. The aetiology is believed to be multifactorial, involving both intrinsic and extrinsic risk factors. It should be stressed that scientific evidence of the role of intrinsic and extrinsic risk factors is still lacking. Several different theories have been presented (Åström 1997; Kannus et al. 1997; Khan et al. 1998b). The knowledge about the pain mechanisms is scarce and the condition in many ways still constitutes a pathological mystery (Cook et al. 2004a; Hamilton et al. 2004; Alfredson 2005b; Peers et al. 2005; Danielsson 2009). Chronic painful tendinopathy is considered to be a degenerative condition, or at least one with a failed healing response with a lack of a true inflammatory infiltrate and response. In summary tendon overload/overuse is the most commonly accepted hypothesis concerning the etiology of tendinosis (Józsa et al. 1997; Cook et al. 2004a; Hamilton et al. 2004; Alfredson 2005b; Peers et al. 2005).

Histopathology
The histopathological changes can be correlated to those of an incomplete healing of the tendon, which very well corresponds to the widely accepted theory that an incomplete healing could be the basis for tendinosis.

The lack of inflammatory lesions and granulation tissue has become a hallmark in the tendinosis field (Denstad et al. 1979). It is, however considered that inflammation may be an important first step in development of tendinosis. In animal studies on tendon healing, the inflammatory infiltrates appear to disappear after 18 days post tenotomy with suturing of the Achilles tendon (Enwemeka 1989). When patients seek medical care after a long time of pain symptoms, they are not likely to be in a primary inflammatory phase anymore, but the condition has entered a “chronic” stage (Khan et al. 1999).

Tendinotic tendons show a degeneration of the extracellular matrix (Riley 2005) with disordered arrangement of collagen fibers, increased vascularity (Khan et al. 1999) and an increase of tendon cells, especially cells with rounded nuclei (Åström et al. 1995). The vessels, which are considered neovessels, are by some authors described to be randomly oriented (e.g. Khan et al. 1999), while others have noted an increase also in the number of vessels aligned parallel with the tendon fibers (Maffulli et al. 2000). These contradictory findings concerning blood vessels are of importance when developing new treatment methods. I would like to challenge the later finding in the discussion of this thesis. The collagen component of tendinotic tendons, also display changes compared to the normal tendon. There is an increase in collagen type III (Jarvinen et al. 1997; Riley 2005). Accumulation of GAG:s and lipids as well as calcification of the tendon tissue has also been described in tendinopathic tendons (Riley 2005).
**Midportion Achilles tendinopathy – Clinical symptoms**
Patients commonly have a history of a gradual onset of tendon pain, often related to a change in activity level or recurrent episodes of pain. Initially, the patients often experience stiffness, pain or discomfort at the beginning of an activity, followed by less pain during activity, and a return of the stiffness and pain afterwards (Rogers 1996). When becoming chronic, pain increases during activity and becomes functionally impairing. The patients often complain about postfunctional and morning stiffness and sharp intolerable impairing pain during activity, sometimes also at rest. This characterizes chronic Achilles tendinopathy. It is suggested; the more pain during activity and stiffness, the poorer stage of the tendon condition (Cook et al. 2002). The later is also discussable since sometimes increased stiffness is seen when the sharp pain is decreased.

**Midportion Achilles tendinopathy – Clinical findings**
Inspection and palpation will reveal a swelling in the midportion of the tendon. When palpating the thickening a remarkable sharp tenderness will be found. There may be some pain during palpation even if there is no injury (Cook et al. 2001b). The tonus of the tendon will be normal and Thompson’s test negative. Range of motion in the ankle joint should also be checked.

**Patellar tendinopathy – Clinical examination**
The clinical symptoms of patellar tendinosis is chronic tendon pain, onset of or increased pain during tendon-loading activity and impaired function (Alfredson et al. 2005b). Sometimes the patients also describe a feeling of instability of the knee joint and muscle fatigue of the lower extremity. Symptoms often start gradually, and relate to changes in sports activity; duration and/or intensity and/or frequency (Peers et al. 2005). Most often, patients complain of pain after strenuous activity, leading to impaired performance and sometimes augmented by prolonged knee flexion, for example driving a car or going to the movies. Severe cases present with pain during activity of daily living and/or at rest (Cook et al. 1998). The area of the patellar tendon most frequently affected by tendinosis is the proximal part, involving the tendon-bone junction at the inferior pole of the patella, and the pain symptoms are described to be well localized to this area (Peers et al. 2005)

**Patellar tendinopathy – Clinical findings**
Intense tenderness, when palpating the proximal patellar tendon at the apex of patella, is always present in patients with patellar tendinopathy. Palpation should be performed with the knee fully extended and the quadriceps muscles relaxed. When the knee is flexed to 90°, the tension in the tendon increases and tenderness
often decreases. Keep in mind that a tendon may be tender even though no injury exists (Cook et al. 2001b). The only finding when examining the tendon should be the sharp pain, if crepitus or swelling is found, another diagnosis should be suspected. Atrophy and hypotonia of the quadriceps muscles is a common clinical sign. A sudden and fast contraction of the quadriceps with the knee joint in extension will often provoke pain which the patient often recognizes as the pain experienced during a tendon loading activity. Intrarticular findings should be absent.

**Radiographs – x-ray and Magnetic Resonance Imaging – MRI**

Historically, x-ray and MRI have been used as diagnostic tools as complements to the patient history and clinical findings in patients with anterior knee pain. During recent years, imaging is used in acute trauma, and for the assessment of cases of anterior knee pain resistant to non-operative measures. The role of the radiograph is now largely restricted to cases of suspected fracture. US is the most recommended technique for suspected tendon and bursal pathology (Soila et al. 1999; Ostlere 2013). When using MRI a common finding in tendinopathies is a local widening of the tendon and high signal intensity in the affected region of the tendon (Johnson et al. 1996; Schmid et al. 2002). These imaging findings might sometimes be difficult to distinguish from partial ruptures in the tendon. Another difficulty could be the variability of the normal/asymptomatic tendon in MRI, which could be a potential source of diagnostic interpretation (Soila et al. 1999).

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*MRI images showing the same knee sagittal view. To the left normal findings, to the right tendinotic findings in the patellar tendon at the apex with oedema dorsally in the central part.*
Ultrasound and colourDoppler – US/CD
US has been used for clinical musculoskeletal examinations for a long time (Fornage 1986) but not focused on tendon pathology. In the past, US was considered a complement to MRI for the imaging of tendons. Modern high-resolution US is highly competitive, and it is today the preferred choice when imaging tendon injuries (Rasmussen 2000). It is proven to be accurate, cost-effective (Jacobson 1999) and a valid method (Martinoli et al. 1993). It is recommended to be the most suitable method when it comes to investigating superficially located structures such as tendons, for example Achilles and patellar tendons (Soila et al. 1999; Ostlere 2013). US is a dynamic examination which is an important advantage compared to MRI. There are studies comparing the accuracy of MRI and US when confirming clinically diagnosed patellar tendinopathy. US/CD and interestingly also grey scale (GS) ultrasound proved to be more accurate than MRI (Warden et al. 2007; Garrick et al. 2008).

In tendinosis, GS/US reveals a thickening of the tendon, irregular organisation of collagen fibers and also hypoechoic areas (Khan et al. 1996)

In the midportion tendinotic Achilles tendinopathy, the hypoechoic areas are seen on the ventral side of the tendon where the tendinotic tendon is the thickest. In the tendinotic patellar tendinopathy these areas are seen in the dorsal side of the tendon near the apex patella.

ColourDoppler is another advantage of ultrasound. CD shows visible blood flow and this gives us a possibility to study the blood flow within the tendon (Weinberg et al. 1998; Öhberg et al. 2001).
Treatment methods of the chronic painful tendon
There is a large variety of different treatments. However, very few have been adequately scientifically studied. This field is advancing very fast trying to find new treatment methods, which might explain why there is so sparse scientific evidence for many of the existing treatment methods used today. Eccentric training is the most evidence based treatment today (Bahr et al. 2006; Gaida et al. 2011; Nilsson-Helander et al. 2012).

Rest
Rest and avoidance of painful activities are usually recommended. Hence, this can be adequate in an acute injury (Angermann et al. 1999). But it is not the case in chronic painful tendinopathy. It is said that since we are dealing with an overuse “injury” (Józsa et al. 1997) activity could worsen the condition. However, patients who have tried to rest still seek help for their chronic painful condition. Immobilization of the tendon may cause tissue atrophy (Peers et al. 2005). Rest may reduce the symptoms. While, recovery is not to be expected since the symptoms usually reoccur (Ferretti 1986; Colosimo et al. 1990). There are some recommendations but no clear protocol in the literature about partially resting from tendon loading activity and adjusting activity when experiencing pain in the tendon (Wilson et al. 2005; Rees et al. 2009). This has not been scientifically investigated in patients with chronic painful patellar tendinopathy, though.

Non steroidal anti-inflammatory drugs and steroid injections
Considering the modern research findings that a “traditional inflammation” is not present in these tendons, it seems contradictory to treat the chronic painful tendon addressed in this thesis with any NSAID or injection. In the literature, NSAIDs have been shown to reduce pain during medication but have not being able to heal this chronic painful condition (Almekinders et al. 1998, 1999). Steroid injections seem to give pain relief in the short run but then the symptoms often reoccur (Almekinders et al. 1998). There are studies suggesting that steroid injections may predispose for spontaneous tendon ruptures (Józsa et al. 1997; Wilson et al. 2005). The injection of steroids are heavily questioned nowadays (Andres et al. 2008).

Extracorporeal shockwave treatment
The use of extracorporeal shockwave has exploded in popularity during the recent years and is often used as a complement to eccentric training. Most often, the diagnosis is obtained solely by clinical examination. There is sparse evidence and no treatment protocol has been suggested in the literature. It is concluded that further studies are needed when using ESWT as a treatment in patients with a chronic painful tendon (Rompe et al. 2008; Foldager et al. 2012).
**Physiotherapy**

Painful eccentric muscle training has shown good long term results when treating the chronic painful tendon. Eccentric contractions seem to be superior to concentric ones (Mafi et al. 2001; Jonsson et al. 2005). Moreover, it is suggested that eccentric training should be carried out with pain/some discomfort and with a heavy load (Stanish et al. 1986). For the midportion Achilles tendinopathy there are a lot of studies and importantly the results are reproducible (Alfredson et al. 1998, Fahlström et al. 2003; Rompe et al. 2007). When it comes to patellar tendinopathy the studies are fewer and they often have small sample sizes and relatively short follow-up times (Cannell et al. 2001; Jonsson et al. 2005; Young et al. 2005; Bahr et al. 2006). Better results are achieved if adding a decline board (Purdam et al. 2004; Jonsson et al. 2005; Young et al. 2005). During the period of rehabilitation the patients should avoid sporting activities (Purdam et al. 2004; Visnes et al. 2005).

**Sclerosing injections**

Sclerosing therapy is widely used for treating varicose veins of the lower extremities and oesophagus, haemorrhoids and teleangiectases of the skin. Polidocanol (aethoxysclerol) was first developed as a local anaesthetic. It is used as a sclerosing agent with very few side effects (Conrad et al. 1995; Winter et al. 2000; Öhberg et al. 2002). Polidocanol is used in different concentrations 5, 10 and 30 mg/ml. The active substance is an aliphatic nonionised nitrogen-free surface anaesthetic. Polidocanol has a selective effect on the vascular intima causing thrombosis of the vessel (Guex et al. 1993). It can act indirectly by compressive effects on vessels by tissue expansion. It is used both for intravasal and perivascular injection. The perivascular effect is an important property when very small vessels are being targeted. It is plausible that the sclerosing effect of polidocanol on the vessels also might affect nerves adjacent to the neovessels, either directly (by destruction) or indirectly (by ischaemia). Polidocanol has a sclerosing effect and a local anaesthetic effect.

The hypothesis behind the treatment is to target the areas in the tendon with increased blood flow associated with pain (Öhberg et al. 2002; Alfredson et al. 2003b; Alfredson et al. 2005a; Cook et al. 2004b). Treatment with injections of the sclerosing substance polidocanol 5 and 10 mg/ml have shown promising clinical results and no side effects (Öhberg at al. 2002; Alfredson et al. 2005 a, c; Hoksrud et al. 2006; Hoksrud et al. 2011).

**Other injection treatments**

There are a variety of models of injections with different theories about their mechanisms. Most injections are given blindly; without US guidance. Both
extratendinous and intratendinous injections are given. Injecting platelet rich plasma (PRP) as well as ESWT has become very popular. However, a recent randomized study showed no differences between saline injections and PRP injections (de Vos et al. 2010). Other substances in use are hyperosmolar dextrose, autologous blood and MMP-inhibitors (Maxwell et al. 2007; Orchard et al. 2008; de Almeida et al. 2012; Pascual-Garrido C et al. 2012; Wiley et al. 2013).

**Surgery in general**

When reviewing the literature it is striking how difficult it is to compare different studies, according to the method used and clinical outcome, since it is difficult to tell what conditions of the patients that really have been included. The diagnostics and indications for surgery differ considerably.

If non-operative treatment fails, surgery is often recommended, although it is the “last attempt of treatment” (Colosimo et al. 1990; Maffulli et al. 1999; Panni et al. 2000; Alfredson et al. 2007a). A surgical approach is also usually only to be considered after at least 3-6 months non-operative treatment (Angermann et al. 1999; Khan et al. 1998; Bahr et al. 2006). There are numerous different surgical methods described in the literature, which may reflect the lack of randomized clinical trials comparing different procedures (Khan et al. 1998b; Peers et al. 2005). Concerning surgical treatment of Achilles tendinopathy and patellar tendinopathy critical reviews show that studies with a poor scientific design generally have reported good clinical results, whereas studies with a good design have reported poor clinical results (Coleman et al. 2000; Tallon et al. 2001; Bahr et al. 2006). In conclusion, it seems as if the results after surgery are varying and unpredictable.

**Surgery in Achilles tendinopathy**

The variety of surgical approaches to treat chronic Achilles tendinopathy has been grouped into four different approaches. These are (1) open tenotomy with removal of abnormal tissue, paratenon not stripped; (2) open tenotomy with removal of abnormal tissue, paratenon stripped; (3) open tenotomy with longitudinal tenotomy, with or without paratenon stripping; and (4) percutaneous longitudinal tenotomy (Tallon et al. 2001). Surgical resection involves excision of what is macroscopically found to be pathological tissue and is an intratendinous procedure. The result of surgical treatment is reported to have a success rate around 70% or better (Schepsis et al. 1994; Morberg et al. 1997). However, as discussed above this success rate may be doubtful since the diagnoses and indications vary and sometimes include partial ruptures. Recently, a minimally invasive surgical procedure has been described, based on the same idea as the sclerosing injections, where the newly formed vessels and accompanying nerves,
ventral to the Achilles tendon, are targeted and no tendon tissue is excised (Alfredson et al. 2007b).

**Surgery in patellar tendinopathy**
Methods available are either open surgery or arthroscopic surgery. Surgical techniques involve for example; osteotomy, resection of the distal patellar pole (Pecina et al. 2010), open patellar tenotomy to remove macroscopically abnormal tissue, arthroscopic patellar tenotomy with or without removing the tip of the patella, and US-guided percutaneous longitudinal tenotomy (Coleman et al. 2000a). There is a long recovery for the different surgical methods used to treat chronic painful patellar tendinopathy. In one retrospective study, “traditional” open surgery, rendered a median time to return to preinjury level of activity of about 10 months and for arthroscopic tenotomy about six months. The success rate with both treatments was about 50% and there were no significant differences between the open and the arthroscopic procedure (Coleman et al. 2000b).

In a review of 23 studies, Coleman et al. (2000a) evaluated the success rate of surgical outcome, showing varying results, 46–100% good results. When comparing the non-operative treatment eccentric training with “traditional” open tenotomy, no benefits were shown with surgery (Bahr et al 2006). In a recent systematic review comparing minimally invasive arthroscopically assisted procedures and open surgery in the treatment of chronic proximal patellar tendinopathy (Muccioli et al. 2013), they did not see any statistically significant differences in the treatment results according pain. Nor were any differences shown concerning painless (or with minor pain) return to preinjury activity level. The methodology of studies in this field has improved over the past 15 years, but well-designed RCTs using validated patient-based outcome measures are still lacking (Muccioli et al. 2013).
General definitions

There is a lack of consistent terminology relating to chronic painful conditions in tendons and the terminology can be confusing with the consequences that scientific studies are difficult to compare. In the past different terms have been used in order to describe the chronic painful tendon. These are, for instance, tendinitis, tendonitis, tendinosis, tendinopathy, peritendinitis, paratendinitis, insertional and non-insertional tendinopathy, partial rupture, calcified tendinopathy, apicitis and chronic painful tendon.

Tendinitis and tendonitis have been widely used, assuming that there was a true inflammation within the tendon. Tendinitis is primarily involving the tendon showing an inflammatory response within the tendon and is often associated with reactive paratendinitis (Józsa et al. 1997). Research in this area has evolved during the years, several observations, including histological and biochemical studies (Khan et al. 1996) and intratendinous microdialysis (Alfredson et al. 1999; Alfredson et al. 2001), have shown an absence of a true prostaglandin-mediated inflammatory process inside the chronic painful tendon (Kannus et al. 1991; Åström et al. 1995; Alfredson et al. 1999; Alfredson et al. 2003a). This is why this term will not be used in the present thesis.

Tendinosis has been proposed to describe the findings interpreted as being degenerative in this chronically painful state of the tendon (Khan et al. 1999; Peers et al. 2005). The term tendinosis can be used regardless of pain or symptoms and it refers to intratendinous histopathological changes which can be visualized and objectively verified by US, MRI or biopsies (Maffulli et al. 1998; Alfredson et al. 2005b).

Tendinopathy is widely recommended to describe a condition with tendon pain, swelling and impaired function, thereby not assuming any information of the underlying pathology (Khan et al. 1998; Maffulli et al. 1998; Peers et al. 2005; Riley 2005).

Peritendinitis is characterized by a true inflammation in the paratenon (Åström 1997).
Midportion Achilles tendinopathy
The most common tendinopathic conditions in the Achilles tendon can be found at three different locations along its length, (1) insertional – at the calcaneal insertion (Carmont et al. 2007), (2) midportion – at 2-6 cm above the insertion, and (3) myotendinous – at the muscle-tendon junction (Movin 1998). In paper I of this thesis, all patients included had a chronic painful midportion tendinotic Achilles tendinopathy, location number 2 according to above. Subjectively, all patients had to have experienced disturbing pain during activity for a longer period than three months, (to consider it chronic) (Kettunen et al. 2002). No acute onset of pain was allowed. Objectively, a distinct and sharp tenderness in the midportion of the Achilles tendon, a noticeable midportion swelling was necessary, but a normal tonus and a negative Thompson’s test. Pathological GS/US findings in the ventral part of the thickened midportion Achilles tendon with hypoechoic areas had to be present. CD findings of increased blood flow in a transversal direction was also mandatory. These US/CD findings had to strictly correspond to the tender and painful area of the tendon. If any of the above mentioned signs were missing we choose not to call it midportion Achilles tendinopathy, and those patients were not considered for inclusion in any study of the present thesis. To follow all the definitions in the literature we could describe our included patients to suffer from “chronic painful impairing tendinotic midportion Achilles tendinopathy”.

Patellar tendinopathy/jumpers knee
In the literature there are many definitions of patellar tendinopathy and jumper’s knee. Since the nomenclature and suggested treatments often varies considerably it is difficult to make comparisons between different studies.

Jumper’s knee is usually a clinically verified condition with exercise related pain and tenderness to palpation in the patellar tendon at the inferior pole of the patella (Blazina et al. 1973; Khan et al. 1998; Maffulli et al. 1998). The clinical diagnosis of jumper’s knee does not require verification by imaging findings.

For inclusion in all studies of this thesis the definition of jumper’s knee has been narrowed. A very strict definition of tendinopathy has been used when including the patients in order to make sure that the same sort of condition was treated in all pathological patellar tendons.

Subjectively, all patients had to experience disturbing pain during activity, and they had to have experienced the sharp typical pain during a longer period than three months, to consider it chronic (Kettunen et al. 2002). No acute onset of pain was allowed nor any subjective intra articular symptoms. Objectively, distinct tenderness at the apex of the patella was necessary, but no swelling or other signs of intra articular pathology when examining the knee was allowed. Pathological greyscale US findings in the proximal, dorsal part of the tendon with tendon
thickening and hypoechoic areas had to be present, CD findings of increased blood flow in a transversal direction was also mandatory. These US/CD findings had to strictly correspond to the tender and painful area of the tendon. If any of the above mentioned signs were missing we did not define the condition as jumper’s knee, and those patients were not included in any of the studies presented in this thesis. To follow all the definitions in the literature we could describe our included patients to suffer from “chronic painful impairing tendinotic proximal patellar tendinopathy”. In summary, in the present thesis, jumper’s knee, consists of multiple findings both subjective and objective and will be referred to as PT/JK.
Aims and hypothesis

I. The aim of this double-blind randomized controlled trial was to evaluate whether there were any differences in the clinical effects between injections of polidocanol in the two different concentrations, 5 and 10 mg/ml, in patients with chronic painful midportion Achilles tendinopathy/ tendinosis. The hypothesis was that the use of higher concentration (polidocanol 10 mg/ml) would lead to a less number of treatments and lower volumes needed for good clinical results.

II. The aim was to visualize the area with increased blood flow in patients with jumper’s knee/proximal patellar tendinopathy during arthroscopic surgery. Therefore, we wanted to evaluate the possibility of performing knee arthroscopy with simultaneous ultrasound and colour Doppler guidance and present it in a technical note.

III. The aim of this pilot study was to evaluate the effects of a more radical destruction of the area with neovessels and nerves on the dorsal side of the tendon by using US guided arthroscopic shaving.

IV. The aim of this randomized study was to compare the clinical results after treatment with ultrasound and colour Doppler-guided sclerosing polidocanol injections and US-guided arthroscopic shaving to try to clarify whether either treatment, both performed outside the tendon, is significantly superior to the other. The primary outcome measure was to evaluate the clinical effect of the treatment by having the patients to score the level of patellar tendon pain during their specific sport or recreational activity, and at rest, and evaluate patient satisfaction with the results of the treatment.

V. The aim of this study was to compare the US/CD findings, pain and clinical outcome, before and after treatment between US/CD guided sclerosing injections and US/CD-guided arthroscopic shaving, in a longer term follow-up. Our hypothesis was that a tendinotic tendon treated with US/CD-guided arthroscopic surgery, including shaving outside the dorsal side of the tendon, would sonographically show signs of a better recovery than a tendon treated with US/CD-guided sclerosing polidocanol injections.
MATERIALS & METHODS
Subjects
All patients in this thesis were referred to the Capio Artro Clinic AB, Stockholm, Sweden for possible treatment of their chronic painful tendinopathy, i.e. pain for more than three months and no acute onset.

Study I
Forty-seven patients (52 tendons) were consecutively referred to the Capio Artro Clinic with chronic painful midportion Achilles tendinopathy. They were randomized to treatment with polidocanol 5 mg/ml or 10 mg/ml. The majority of the patients were recreational athletes but had a rather sedentary lifestyle. BMI was in the upper level of normal (>25). For more information about the patients, please see summary of papers (Table 1).

Studies III-V,
All patients were active, ranging from recreational to competition level and they all had painful proximal patellar tendinopathy. They were younger than the patients suffering from Achilles tendinopathy and they were dominantly males. They were all examined with US/CD to confirm the tendon changes described above in definitions for this thesis. They all had a long duration of tendon pain during activity. For more information, please see summary of papers.

Study III
Fifteen elite and recreational athletes with a long duration of pain symptoms from 15 patellar tendons were included. All patients were referred to the Capio Artro Clinic in Stockholm, Sweden, or the Sports Medicine Unit in Umea, Sweden, for evaluation (Table 2).

Study IV
Forty-five patients (52 tendons) were included. All patients were referred to the Capio Artro Clinic in Stockholm, Sweden, with the diagnosis chronic painful patellar tendinopathy and a long duration of pain. Seven patients had bilateral tendon changes (Table 3).

Study V
Patients included in this study were the 45 former participants in study IV and an additional 9 patients from the pilot study – study III. A total of 43 patients (41 males/2 females) with 57 treated tendons chose to participate. For more basic data see table 2, table 3 and table 5.
General inclusion and exclusion criteria
All patients referred to the Capio Artro Clinic AB, Stockholm, Sweden with chronic painful tendinopathy in either midportion Achilles tendon or proximal patellar tendon were considered for inclusion.

Study I, inclusion criteria, midportion Achilles tendinopathy
- Chronic pain during activity in the Achilles tendon for more than three months, no acute onset of pain
- Clinically noticeable swelling and tenderness when palpating midportion Achilles tendon
- Thompson’s test negative and normal tonus
- US/CD findings in form of hypoechoic areas in the ventral part of the tendon and hypervascularity entering the tendon from the ventral side corresponding to the tender area

Study III-V, inclusion criteria, patellar tendinopathy
- Pain during activity at the apex patella during activity for more than three months, no acute onset
- Clinically tenderness at the most proximal part of the patellar tendon, with the knee in full extension and quadriceps relaxed, and no other findings suggesting intra articular pathology
- US/CD findings in form of hypoechoic areas in the dorsal part of the tendon and hypervascularity entering the tendon from the dorsal side corresponding to the tender area in the proximal part of the tendon

Exclusion criteria
- Previous surgery or injection treatment
- Chronic inflammatory disease
- Medication with warfarine, an antithrombotic medicament
- Allergy to localanestetic
- Neurological disorders causing pain in the affected limb

Diagnostics in this thesis

Patient history
All patients were interviewed and the following parameters were recorded;
- Duration of pain during activity (>3 months)
- Onset of symptoms, acute or gradual?
- The character of pain; sharp and intolerable? Impairing?
- Medication
• Earlier treatments
• Height and weight
• Allergies or systemic diseases or medical issues
• Previous injuries

Clinical findings
Achilles tendon – examined in a prone position with gastrocnemius relaxed and feet hanging outside the bench. Swelling (0-3), tenderness (0-3), location of swelling and tenderness; midportion or distal tendon, tonus, range of motion (ROM) and Thompson’s sign was noted.

Patellar tendon and knee joint – examined in a supine position with quadriceps relaxed and the knee extended. We always started with an inspection in order to note muscular tonus and to see if there is any atrophy or any intra articular swelling. Then we continued with a standard examination to rule out other signs of intra articular pathology. Concerning the tendon we palpated the patellar tendon and note if there is any tenderness (0-3) in the proximal part at the apex patellae.

Ultrasound and colourDoppler
In all studies in this thesis the diagnosis at baseline was confirmed with US/CD. All tendons were examined with high resolution GS/US/CD using a WSX 13-5 linear multifrequency probe (Siemens-Acuson Antares Sonoline), at a greyscale frequency of 11.4 MHz and a CD frequency of 8.9 MHz. The same equipment was used for all examinations, and the same experienced sonographer performed all US/CD evaluations at baseline, at short term follow-ups and at endpoint. Intra-observer reliability for evaluation of the tendon structure and neovascularization (localized high blood flow) had been tested, as well as reproducibility for measures of thickness (for values please, see Study V).

Treatment methods in this thesis
Sclerosing injections
Before the injection treatment, the skin was disinfected with a solution of chlorhexidine. The skin was draped with a sterile paper-cover exposing only the area for injection. The injection was performed with a ø 0.7 x 50 mm needle connected to a 2 ml syringe. The decision to treat was made by the orthopedic specialist and the same experienced ultrasonographer performed all US/CD examinations. The injection was performed dynamically, with the aid of real-time GS/US/CD technique. Two different concentrations of polidocanol were used for treatment, 5 mg/ml and 10 mg/ml. Very small volumes 0.1–0.2 ml a maximum of 2 ml/treatment session of polidocanol was injected into the areas
of local increased blood flow. Needle tip was aimed at the entrance of the vessels into the tendon. Polidocanol was injected until the vessels were no longer visible at all with US/CD. The vessels approached had to correspond with the palpable pre-injection tenderness. A pressure bandage was then applied for 24 hours and the patients were informed about the regimen after the injection treatment. The patients were allowed careful walking right after the treatment and full tendon loading-activity was allowed 14 days after the treatment. A maximum of three treatments with at least 6–8 weeks in between were given before evaluation. US/CD images were taken before and after the procedure.

**Injecting midportion tendinotic Achilles tendinopathy**
All patients lay in a prone position, the US probe was held on the dorsal side of the Achilles tendon, parallel with the fibers, longitudinal plane. The injection was always done from the medial side of the tendon to minimize the risk of contact with the sural nerve. Injections were made only where the vessels entered the ventral part of the tendon and only the vessels that ran in a transverse direction were approached. Images showing US/CD findings before and after injections.

**Injecting tendinotic patellar-tendinopathy/jumper’s knee**
All patients lay in supine position with their knee joint in extension, quadriceps totally relaxed. The US probe was held on the ventral side of the patellar tendon, parallel with the fibers in a longitudinal plane. To confirm the position of the needle the probe was sometimes also held transverse to the fibers. Injections were made only where the vessels entered the dorsal part of the tendon and only the vessels that ran in a transverse direction were approached.
US-guided arthroscopy – patellar tendinopathy

Arthroscopy was performed in local anaesthesia. Local anaesthesia lidocain was infiltrated into the anteromedial, anterolateral portals and also injected the joint. The patients were in supine position with straight knee and quadriceps relaxed. The standard anteromedial and anterolateral portals were used. We had a pressure-controlled pump. US/CD was used per-operatively.

Sterile US gel was used and the US probe was draped. When surgery is performed in general anaesthesia, or when using local anaesthesia without adrenalin, the increased blood flow (neovessels) can be seen per-operatively using CD-technique (if the joint pressure is kept low). GS/US clearly visualizes the tendon structure pre- and per-operatively.

First, a standard arthroscopical evaluation of the whole knee joint was performed. Then the patellar tendon insertion into the patella was identified. For shaving, we used a 4.5 mm full radius blade. Simultaneous US guided the procedure. It is important that the shaverblade and the tube of the arthroscope is inserted into the joint as perpendicular as possible to the proximal part of the tendon, allowing for a better ultrasound view.

Careful shaving was performed in order to diminish the increased blood flow (neo-vessels) corresponding to the tendinotic area on the dorsal side of the tendon. We used the US monitor, preferably with the transducer showing the cross sectional view of the tendon. We carefully avoided from resecting tendon tissue and we only loosened the Hoffa’s fat pad (IFP) from the central part of its attachment to the patella. We tried to avoid resection of the IFP
as much as possible. The precision of the procedure was increased compared to when only using the arthroscopy monitor. The whole procedure of shaving was clearly visualized and we had the impression that there was less tissue trauma this way with simultaneous US/CD-guidance. The portals were closed with a tape. A bandage was used for 24 h. US/CD images were taken before and after the procedure. Since evaluating and comparing new treatment methods, no specific rehabilitation protocol was given.

US/CD findings before surgery in a tendinotic patellar tendon with increased blood flow.

GS/US showing the tip of the shaver during arthroscopy, longitudinal plane and cross sectional plane.

GS/US images showing US findings when finishing the procedure, still pressure and fluid in the joint. Hoffa’s fat pad separated in its central attachment from the patellar tendon.

US/CD findings directly after surgery with no pressure in the joint, no remaining high blood flow in the tendinotic area of the tendon.
Outcome measures

Visual analogue scale for pain rating
The visual analogue scale (VAS) was used and the patients rated the amount of pain in the tendon. VAS is a 100 mm long scale, where the patients estimate their pain. 0- equals “painless” and 100 equals “worst imaginable pain”. They estimated both pain during their own chosen tendon loading activity and pain at rest. This estimation was carried out at baseline and at all follow-ups. All VAS ratings were recorded by the same and independent person and saved in a database. VAS is a valid, reliable and precise scale (Williamson et al. 2005). The test-retest reliability is very high (intraclass correlation coefficient 0,97) for acute pain (Bijur et al. 2001). A 30-35% reduction in pain intensity was considered to represent clinical relevance (Rowbothham 2001).

Satisfaction with treatment
On a similar scale as VAS, 0-100 mm long the patients recorded if they were “satisfied” or “not satisfied” with their treatment at every follow-up. “Satisfied” meant painless return to their, at baseline, chosen tendon loading activity equaled 100, and “not satisfied at all” equaled 0 on the scale. If “not satisfied” there was no return to previous tendon loading activity or still pain in the tendon during tendon loading activity in different degrees.

US/CD findings
In all studies in this thesis the diagnosis at baseline was confirmed with greyscale US and CD. In study V, the US/CD findings were one of the primary outcomes. The US investigations were performed according to a routine protocol. Tendon thickness (anteroposterior distance) was measured in the longitudinal plane at the most proximal part of the tendon in the centre of the most tendinotic region, representing the widest/thickest part. Tendon structure and neovascularisation (localized high blood flow) were evaluated with the same criteria that were used at baseline and at short term follow-ups, according to a modified Öhberg model (Öhberg et al. 2002; Abate et al. 2012).

Ethical considerations
All studies in the present thesis were conducted with the approval of the Ethical Committee at the Medical Faculty of the Karolinska Institutet, Stockholm, Sweden, No 2005/1246-31/2 (study I-IV) and No 2011-929-32 (study V). All patients were informed both verbally and in writing prior to consent.
Statistics

Power analysis
A power analysis was based on the results from two previous pilot studies (Alfredson et al. 2005; Hoksrud et al. 2006). The analysis showed that 20 individuals in each group were needed to give a power of 80% to find a difference of 50 mm in VAS between the groups, on a 5% significance level. We estimated a higher difference (50 mm before and after treatment) than normally satisfactory, a difference in VAS of 30-35 mm, (Rowbothham 2001), to make sure that the groups would not become too small.

Calculations

In study I, the SPSS package (version 11.5, SPSS Inc., Chicago, Illinois, USA) was used for all statistical calculations. Mean and standard deviations were used to describe data. Differences between groups were calculated using a nonparametric test for independent samples (Mann Whitney U-test). When data were categorical, Chi-square test and Fisher’s exact test were used to evaluate differences between the groups. Differences before and after treatment were calculated with Wilcoxon signed rank test. P<0.05 was considered significant.

In study III, the pilot study concerning ultrasound guided arthroscopic shaving, the SPSS package (version 11.5) was used for all statistical calculations. The Wilcoxon signed rank test was used to study differences in patellar tendon pain during activity, recorded by the patients on a VAS, before and after treatment. P<0.05 was considered significant.

In study IV, the SPSS package (version 18.0) was used for all statistical calculations. Mean and SD were used to describe data. Differences between the groups were calculated using a non-parametric test for independent samples (Mann Whitney U-test). P<0.05 was considered significant.

In study V, the long term follow up, SPSS package (version 21) was used for all statistical calculations. Patient characteristics as well as descriptive frequencies are presented as mean and range. The statistical analysis for paired tests of both continuous and ordinal variables was calculated with the non-parametric Wilcoxon signed-rank test. Differences between groups were calculated using a non-parametric test for independent samples, Mann Whitney U-test. Spearman correlation was used for correlation analysis. P<0.05 was considered significant.
**Paper I**

**Sclerosing injections to treat midportion Achilles tendinosis: a randomized controlled study evaluating two different concentrations of Polidocanol**

Two to three ultrasound (US) and colour Doppler (CD)-guided injections of the sclerosing substance polidocanol (5 mg/ml) had been demonstrated to give good clinical results in patients with chronic midportion Achilles tendinopathy. This study aimed to investigate if a higher concentration of polidocanol (10 mg/ml) would lead to a less number of treatments, and lower volumes, needed for good clinical results. Fifty-two consecutive Achilles tendons (48 patients) with chronic painful tendinotic midportion Achilles tendinopathy, were randomized to treatment with polidocanol 5 mg/ml (group A) or 10 mg/ml (group B).

For basic data see **table 1** below (5 mg/ml group A, 10 mg/ml group B)

<table>
<thead>
<tr>
<th>Number of tendons</th>
<th>Male</th>
<th>Female</th>
<th>Age</th>
<th>BMI</th>
<th>Duration of symptoms in months</th>
<th>VAS pain activity at start</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>26</td>
<td>15</td>
<td>11</td>
<td>47.4 ± 7.8</td>
<td>25.1 ± 3.4</td>
<td>25.5 ± 17.1</td>
</tr>
<tr>
<td>B</td>
<td>26</td>
<td>20</td>
<td>6</td>
<td>51.8 ± 12.4</td>
<td>26.8 ± 4.2</td>
<td>28.0 ± 31.6</td>
</tr>
</tbody>
</table>

All patients had structural tendon changes and neovascularisation corresponding to the tender area in the Achilles midportion. US/CD-guided sclerosing injections were given, a maximum of three treatments with 6–8 weeks between treatment sessions before final evaluation. Patients who were not satisfied after three treatments were given additional treatments with polidocanol 10 mg/ml, up to five injections in total with 6-8 weeks in between. For evaluation, the patients recorded the severity of Achilles tendon pain during activity on a visual analogue scale (VAS for pain) and satisfaction with the result of treatment was also assessed.

**Clinical outcomes**

**Group A,** polidocanol (5 mg/ml), mean VAS pain after one to three treatments decreased significantly from 66 ± 14 to 25 ± 28 (P<0.05).

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50  Lotta Willberg | *Patellar and Achilles tendinopathy*
Group B, polidocanol 10 mg/ml, mean VAS pain after one to three treatments decreased significantly from 66 ± 21 to 24 ± 31 (P<0.05).

At follow-up, mean 14 months (range 2-35 months) after three treatments, 18/26 patients in group A (5 mg/ml) and 19/26 patients in group B (10 mg/ml) were satisfied with the treatment and had a significantly reduced level of tendon pain (P<0.05).

There was no significant difference between the two groups in VAS pain during activity after treatment. Nor were any significant differences shown between the groups concerning the number of treatments given; group A, 2.6 treatments and group B, 2.5 treatments or concerning the total volume injected; group A, mean 3.2 ± 1.6 ml and group B mean 3.1 ± 1.3 ml before a good clinical result was achieved — satisfied patient.

**Additional outcome**

**after a maximum of five sclerosing injections**

Group A; six patients were not satisfied after three treatments. They were offered and accepted treatment with additional injections of polidocanol (10 mg/ml). After one additional injection there were two patients who were not satisfied. These two patients were satisfied after a fifth injection.

Group B; seven patients were not satisfied after three treatments. They were offered and accepted treatment with additional injections of polidocanol (10 mg/ml). After one additional treatment, three patients were not satisfied. These three patients were satisfied after a fifth injection.

After five injections all patients (group A and group B) were satisfied with the result of treatment and there were no significant differences between the groups.

**Conclusion**

The results indicate that the effects by injecting polidocanol when aiming at the entrance of the vessels on the ventral side of the Achilles tendon midportion, are not related to the concentration 5 mg/ml or 10 mg/ml of polidocanol.

It seems that small volumes of a low concentration of polidocanol (5 mg/ml), injected under US/CD guidance are enough to cure the tendon pain in a high proportion of patients with midportion Achilles tendinopathy.

For clinical use, we recommend the use of polidocanol 5 mg/ml when treating chronic painful midportion Achilles tendinopathy. Furthermore, it appears that small volumes of polidocanol could be used for a good clinical result when treating midportion Achilles tendinopathy with US/CD guided sclerosing injections.
**Paper II**  
**Ultrasound – and Doppler-guided arthroscopic shaving to treat Jumper’s knee: a technical note**

In this technical note we present a new technique for arthroscopic treatment of chronic painful patellar tendinopathy – jumper’s knee. Arthroscopic shaving is performed with the simultaneous guidance of US/CD. Using this technique, the tendon and the areas with structural tendon changes and high blood flow are continuously demonstrated in the operating field. By this, the shaving procedure can be more exactly addressed to the area of interest on the dorsal surface of the patellar tendon and the trauma to the Hoffa’s fat pad and the tendon is minimized. We wanted to find a procedure that permitted the same postoperative regimen as permitted after US/CD-guided treatment with sclerosing injections.

During development of this technique, standard knee arthroscopy was performed except for that we worked with two monitors and US/CD- guidance simultaneously. We operated on altogether 39 patients with the diagnosis jumper’s knee – patellar tendinosis (37 males and 2 females) with a mean age of 27 years range 17–51). There were no side effects or complications using this procedure, and the short-term clinical results were promising. No outcome data is presented in this note. The exact procedure is described in “treatment methods in this thesis”.

In conclusion, we found the combined method, using simultaneous US/CD-guidance during the arthroscopic shaving to be practical and reliable. It renders high precision and less tissue trauma, compared to performing arthroscopic shaving alone.

**Paper III**  
**Treatment of Jumper’s knee: promising short-term results in a pilot study using a new arthroscopic approach based on imaging findings**

Sclerosing injections targeting the area with neovessels and nerves on the dorsal side of the patellar tendon has been demonstrated show promising clinical results in patients with chronic painful jumper’s knee – patellar tendinopathy (PT). However, a time consuming and painful treatment method with a mean number of three treatments with 6–8 weeks in between were needed for a good clinical result. This study aimed to evaluate a more radical approach to the area with neovessels and nerves by using US/CD-guided arthroscopic shaving. We wanted to see if we could use the same regimen after surgery as we use after sclerosing injection treatment. Two weeks after treatment allowing maximum patellar tendon loading activity. Fifteen elite and recreational athletes, 12 males and three
females with a long duration of pain symptoms from their patellar tendons were included. All patients had tried rest as treatment without any effect on the painful condition. For further basic data see table 2 below.

<table>
<thead>
<tr>
<th>Basic data</th>
<th>Mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30 (18-49)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>184 (172-200)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>81 (62-96)</td>
</tr>
<tr>
<td>Duration of symptoms (months)</td>
<td>27 (9-78)</td>
</tr>
<tr>
<td>VAS pain activity at start</td>
<td>81 (62-96)</td>
</tr>
</tbody>
</table>

In all patients US/CD examinations showed structural tendon changes with hypoechoic areas and a neovascularization on the dorsal side of the tendon with vessels entering the tendon transversally. The increased blood flow was corresponding to the painful and tender area. All patients were treated with US/CD-guided arthroscopic shaving. Postoperative regimen instructed to the patients was as follows.

Day 1: Partial weight bearing with crutches if needed. Start full non-weight bearing range of motion exercises. Days 2–7: Start walking and light bicycling activity. Light concentric and eccentric strength training for the quadriceps muscles was instituted. Days 8–14: During the second week after treatment, the patients were told to gradually increase their tendon loading activity with more sport specific training. No maximum jumping-, running-, or weight training activity was allowed during the first two weeks. Two weeks postoperatively: Maximum patellar tendon loading activity could be started if there was no marked muscle atrophy.

Outcomes
At the follow-up (mean 6 months) after treatment, there was a good clinical result in 13/15 tendons (6/8 elite athletes). The satisfied patients were back to previous (before onset of symptoms) sport activity level, and the amount of pain recorded on a visual analogue scale (VAS for pain) had decreased significantly. VAS for pain had decreased from before surgery; mean 79 (range 35-100) to after surgery; mean 12 (range 0-50), P < 0.05.

An additional telephone follow-up 13 months (mean) postoperatively showed that the same 13/15 were still satisfied and active in their sports, and that the 2/15 poor cases were still not satisfied with the treatment.
Conclusion
In the short-term perspective, it seems that US/CD-guided arthroscopic shaving of the area with neovessels and nerves on the dorsal side of the tendon in patients with PT/JK can reduce the tendon pain during tendon loading activity and allow for the majority of patients to relatively quickly return to patellar tendon loading sports activity at competing level. In this study the patients were allowed maximum patellar tendon loading activity after two weeks, if they wanted. There were no patients with severe quadriceps atrophy pre-operatively, but of course, such patients most likely need a longer rehabilitation period before returning to their sport. The results motivate further studies with larger materials and long term follow-up.

Paper IV
Sclerosing polidocanol injections or arthroscopic shaving to treat patellar tendinopathy/jumper’s knee? A randomised controlled study

We wanted to compare the clinical effects after treatment with US/CD-guided sclerosing polidocanol injections and US/CD-guided arthroscopic shaving proximal patellar tendinopathy/jumper’s knee (PT/JK).

Forty-five patients (52 tendons in 43 males and two females) with US/CD verified diagnosis of PT/JK were randomly assigned to treatment with US/CD-guided sclerosing polidocanol (10 mg/ml) injections (group A) or US/CD-guided arthroscopic shaving (group B). All patients were involved in patellar tendon loading sports or recreational activities, and had a long duration of pain symptoms from the proximal patellar tendon and seven patients had bilateral PT/JK.

No patient had an acute onset of pain. The patients had tried different types of treatment before referral, such as; rest for more than 3 months (n=45), eccentric training (n=33) and NSAIDs (n=11). All patients were active, ranging from recreational (n=19) to competition level (n=26). All patients were diagnosed (clinically and by US/CD examination) before inclusion to have chronic painful PT/JK in the proximal patellar tendon. In both groups the patients were allowed full weight bearing walking immediately after the treatment. Two weeks after treatment the patients were told to gradually increase the patellar tendon load up to full loading. In this study two fairly new treatment methods were compared why there was no specific rehabilitation protocol, or set time frames, preceding full tendon loading activity. Follow-ups were done at two weeks (Group B), every 6-8 weeks (Group A and B) and further follow-ups in both groups were also done at 6 and 12 months. If there was remaining tendon pain during sport activity and a remaining high blood flow in a transversal direction in the region with structural
tendon changes at follow-up in the tendons treated with sclerosing polidocanol injections, another injection was given. If the patient was not satisfied 6-8 weeks after completing three injection sessions it was considered as a failure.

**Table 3** Basic data for group A and group B (mean and SD).

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of tendons</th>
<th>Age</th>
<th>Follow-up time in months</th>
<th>Duration of symptoms in months</th>
<th>VAS pain activity at start</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>26</td>
<td>27 (7,6)</td>
<td>13,7 (6,9)</td>
<td>20 (10,4)</td>
<td>69 (17,3)</td>
</tr>
<tr>
<td>B</td>
<td>26</td>
<td>26,6 (7,6)</td>
<td>12,9 (7,8)</td>
<td>23,8 (15,5)</td>
<td>76 (13,6)</td>
</tr>
</tbody>
</table>

**Outcomes**

In group A, one patient did not continue the study because of pregnancy. In group B, all but one patient received the intended treatment. Before treatment, there were no significant differences between the groups regarding age, duration of symptoms or pain at rest or during patellar tendon loading activity. At the final follow-up, the patients in Group A, mean follow-up time 13,7 months (SD 6,9) had significantly lower VAS scores for pain at rest and during patellar tendon loading activity, and were significantly more satisfied with the treatment result, compared to the patients in, Group B, mean follow-up time in months 12,9 (SD 7,8). There were no significant differences in the follow-up time between the groups.

**Table 4**, results at endpoint, mean and SD, significance p-value.

<table>
<thead>
<tr>
<th>Group</th>
<th>VAS pain rest at follow-up</th>
<th>VAS pain activity at follow-up</th>
<th>Satisfaction with result of treatment (0-100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>19.2 (23.2)</td>
<td>41.1 (28.5)</td>
<td>52.9 (32.6)</td>
</tr>
<tr>
<td>B</td>
<td>5.0 (8.3)</td>
<td>12.8 (19.3)</td>
<td>86.8 (20.8)</td>
</tr>
<tr>
<td></td>
<td>p/ 0.004</td>
<td>p/0.001</td>
<td>p/0.000</td>
</tr>
</tbody>
</table>
Conclusion
Treatment outside the dorsal tendon alone is in strong contrast to the invasive methods used worldwide in which there is intratendinous excision of macroscopically abnormal tendon tissue through a longitudinal tenotomy. It is interesting that US-guided treatment outside the dorsal tendon seems to produce markedly better clinical results than have been reported from intratendinous surgery. Also, considering the rehabilitation after treatment, extratendinous procedures are associated with a possibility of a very quick (6–8 weeks) return to full tendon loading activity, whereas intratendinous procedures often require a very long (4–12 months) rehabilitation period. The current study only presents short-term results, but it seems promising. However, there is a need for further studies.

In conclusion, both treatment with US/CD-guided sclerosing polidocanol injections and US/CD-guided arthroscopic shaving showed good clinical results in patients with chronic painful patellar tendinopathy. Patients treated with the new surgical procedure US/CD-guided arthroscopic shaving had significantly less pain and they were more satisfied with the treatment results. Since the arthroscopic procedure is a one-stage treatment, return to sports was faster in this group.

Paper V – manuscript
Treatment of patellar tendinopathy with sclerosing injections or ultrasound-guided arthroscopic shaving – a long term follow-up of ultrasound findings and clinical results

Treatment of PT/JK knee with US-guided sclerosing injections or US-guided arthroscopic shaving has shown good clinical short-term results. Former studies indicate that the tendon stays sonographically abnormal after successful treatment.

In this follow-up study a total of 43 patients (41 males/2 females) with 57 treated tendons chose to participate. They were former participants in a prospective randomized trial evaluating treatment with US/CD-guided sclerosing injections (Group A) and US/CD-guided arthroscopic shaving (group B), and an additional nine patients from a previous pilot study evaluating the US/CD-guided arthroscopic shaving method (Group B), for chronic painful PT/JK. All patients included in this study came for an evaluation with US/CD. They also scored their level of patellar tendon pain during their specific sport or recreational activity, and at rest, on a 100 mm VAS-scale. Self-reported satisfaction with the result of treatment was also scored (0-100). All scores were compared with the
corresponding scores at baseline, before treatment and at the short term follow-up (mean 12 months).

**Table 5** Basic data Group A – sclerosing injections, Group B – arthroscopic procedure. Duration and time presented in months.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27.6 (9.7)</td>
<td>27.3 (7.8)</td>
<td>0.456</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>182 (6.3)</td>
<td>182 (5.1)</td>
<td>0.252</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77.5 (8.1)</td>
<td>79.6 (8.5)</td>
<td>0.213</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>21.1 (11.8)</td>
<td>22.7 (17.4)</td>
<td>0.37</td>
</tr>
<tr>
<td>Time to follow-up</td>
<td>14.2 (7.5)</td>
<td>10.7 (6.4)</td>
<td>0.111</td>
</tr>
<tr>
<td>Time to endpoint</td>
<td>43.7 (8.3)</td>
<td>48.8 (9.9)</td>
<td>0.065</td>
</tr>
</tbody>
</table>

mean (SD) mean (SD) significance

The same equipment was used for all examinations, and the same experienced sonographer performed all US/CD evaluations at baseline, at short term follow-up and at final follow-up. Intra observer reliability for evaluation of tendon structure and neovascularization (localized high blood flow) had been tested, as well as reproducibility for measures of thickness. US investigations were performed according to a routine protocol for investigation of the patellar tendon. Patients were in a supine position with knees stretched and fully relaxed. US/CD registrations were taken in both longitudinal and transversal plane. Tendon thickness (AP distance) was measured at the widest part of the proximal patellar tendon; in the centre of the most tendinotic region, in the longitudinal plane. Tendon structure and neovascularisation (localized high blood flow) were evaluated with the same criteria that were used at baseline and at short term follow-up, according to a modified Öhberg model.

Tendon structure; 0 – normal structure (homogenous echogenicity), 1 – light structural changes (discrete hypo-echogenic areas), 2 – moderate structural changes (some well defined hypo-echogenic areas), 3 – severe structural changes (extended hypo-echogenic areas).

Neovascularisation (high blood flow); 0 – no visible vessels, 1 – mild neovascularisation (solitary transversal vessels in the proximal/ventral part), 2 – moderate neovascularisation (moderate quantity, mostly transversal in the proximal part), 3 – severe neovascularization (several, mostly horizontal, vessels spread in the whole depth and more distally in the tendon).
Outcomes
At final follow-up (endpoint), in both groups there was a significant decrease in VAS during activity, among patients treated with sclerosing injections, from 64 to 17 and 74% were satisfied, and among patients treated with arthroscopic shaving from 77 to 13 and 80% were satisfied. There were no longer any significant differences in pain according to VAS between the groups.

A significant correlation, both at follow-up and at endpoint, between low local blood flow and low pain measured with VAS during activity (FU 0,40 p= 0,01; EP 0,48 p<0,01) and high patient-satisfaction (FU 0,45 p<0,01; EP 0,56 p<0,001) was found. In group B, a correlation was found at follow-up between large tendon thickness and high VAS for pain at rest (0,66 p<0,01).

At endpoint tendon structure had improved and CD detectable local blood flow had diminished significantly in both groups. There was also a significant decrease in AP thickness of the proximal patellar tendon in group B but not in group A. Sonographically, a more normal tendon structure, was seen earlier in group B. Interestingly, initially a significant increase in proximal patellar tendon AP thickness was seen in Group A, but at the final follow-up AP thickness was similar as before treatment.

Conclusions
There were good, and similar, clinical results with both methods at endpoint. Both treatments showed good results concerning pain reduction during activity. However, the US/CD-guided arthroscopic procedure rendered a quicker return to full activity and sports. The long term results in Group B were the same as in the short term follow-up study. In Group A clinical results had improved compared with the results presented in the short term follow-up study, to the same level as the results of Group B. At the endpoint the only factor with remaining difference between the two methods was the AP thickness in the tendon, where the tendon was significantly thinner and sonographically “more normalised” in the surgical group.

An interesting observation was the fact that the amount of increased blood flow was the first and quickest parameter to change in the surgical group who returned to full and painless activity fastest of the two groups. This fact among others in this study leaves a lot of questions unsolved, but there are some indications that the structural changes and the amount of neovascularization within the tendon tissue might correlate with clinical outcome and opens for further investigations in this direction.
DISCUSSION

VII
General discussion and clinical considerations

It has been said that “treatment effectiveness is inversely proportional to the number of available treatment choices”. In my opinion this is very true for chronic painful tendinopathy. The present thesis has focused on two different new treatment methods for chronic painful tendinotic midportion Achilles tendinopathy and chronic painful tendinotic proximal patellar tendinopathy with a special interest in the later of the two.

Tendinopathies are a major problem in sports medicine. The prevalence of Achilles tendinopathy in runners has been estimated to be 11% (James et al. 1978) and 20% of knee injuries presenting at a sports clinic have been diagnosed as patellar tendinopathy (Kannus et al. 1987). Fifty percent of patients with patellar tendinopathy have been reported to give up their sports career due to their knee problem (Kettunen et al. 2002). In a retrospective study by Cook et al. (1997) they showed that one out of three athletes visiting sports medicine clinics with this diagnosis was unable to return to their sports within six months.

In general, it is very important to establish the underlying pathology of a disease. Lack of scientific information makes the development of evidence-based treatment more or less impossible.

The pathology of tendinopathy is still relatively poorly understood. It is generally accepted though that in the chronically injured tendon the repair capacity of the tendon is exceeded. Chronic painful tendinopathy is considered to be a degenerative condition, or at least one with a failed healing response with a lack of a true inflammatory infiltrate and response. Consequently it has become increasingly recognised that anti-inflammatory strategies are largely ineffective in the management of chronic tendon conditions. Supporting the hypothesis that tendinopathy develops due to a failed chemical healing response could inducing a new chemical reaction be sufficient to induce a healing? An increased interest in the development and results of basic science of tendinopathies has been seen amongst clinicians. However, there is still a need for further research.

Radiologically, both US and MRI are being reported to correspond well to histopathological findings (Khan et al. 1998; Alfredson 2005b; Peers et al. 2005). In close relation to the high blood flow outside the tendinotic chronic painful Achilles and patellar tendons, sensory and sympathetic nerves have been found in immunohistochemical analyses of biopsies (Danielsson 2007).

Regions with localized high blood flow, shown with CD, corresponding to the painful and tender area in the chronic painful tendon may be of importance or at least to some extent explain the reason for pain and impaired function. However, the total diagnostic picture is even more complicated, especially concerning the patellar tendon. For example, in a study based on 320 patellar tendons in asymptomatic elite athletes representing different sports US hypoechoic areas
were present in 22 % of these pain less tendons. In a control group of non-athletic individuals, only 4 % of asymptomatic tendons showed these changes (Cook et al. 1998). Concerning the Achilles tendon there are also some reports on intratendinous changes verified with US and MRI in patients without complaints (Haims et al. 2000; Emerson et al. 2010). However, in one study by Peers et al. (2003) they discuss and evaluate the correlation between PD findings and the clinical severity in Achilles tendinopathy. The pathological findings are not always clearly described though. For example in cadaveric studies it is impossible to evaluate the existence of high blood flow and CD is not used in all studies. When reviewing the literature one problem is the lack of consistent terminology relating to the chronic painful conditions in tendons. The terminology can be confusing leading to difficulties when comparing different scientific studies.

**Midportion Achilles tendinopathy**

An abundant amount of different treatment modalities has been developed for treatment of chronic midportion Achilles tendinopathy. Concerning injection treatments different substances and techniques are in use. The rationale behind these treatments most often lack scientific evidence, and the exact location of the injection is not always clearly described. In general, the goal of treatment is to relieve symptoms.

In this thesis we evaluated the injection treatment with the sclerosing substance polidocanol for chronic painful tendinotic midportion Achilles tendinopathy (study I). A pilot study had shown promising results (Öhberg et al. 2002). Two to three US/CD-guided injections of polidocanol (5 mg/ml) was demonstrated to give good clinical results in a high proportion of the patients. The treatment is painful and in many cases it takes a relatively long time to recover, since there was 6-8 weeks between the treatment sessions. It seemed logical to question whether treatment with a higher concentration of polidocanol, 10 mg/ml than the previously used 5 mg/ml could lead to a less number of treatments needed for good clinical results.

We very strictly followed the initial method description and we were very strict with our inclusion criteria. We injected at the most 2 ml of polidocanol per treatment session aiming at the entrance of the vessels on the ventral side of the tendon. Patients were not considered for treatment, if any of the former described criteria was missing, which means that a tendon could show US/CD findings but if the patient did not experience any remaining pain or tenderness we refrained from further injections and just prospectively followed the patient. The good results in our study indicate that small volumes of a low concentration of polidocanol (5 mg/ml) injected under US/CD-guidance seem to be an alternative to cure the tendon pain in a many patients with chronic painful tendinotic midportion...
Achilles tendinopathy. No adverse effects were found. The design of the study has a few limitations that will be discussed later on.

During the years the injection of polidocanol has been a subject for debate in many contexts. Unfortunately, there is a lack of prospective randomized controlled studies. However, in one retrospective follow-up study using the initially described treatment method the authors reported sclerosing injections to be a promising alternative for treating patients with chronic painful tendinotic midportion Achilles tendinopathy (Clementson et al. 2008). In another retrospective study relatively poor results were demonstrated after sclerosing polidocanol injections. Unfortunately, these authors did not follow the initial treatment method described for US-guided sclerosing polidocanol injections. Based on their results they debate “the beneficial value of sclerosing the neovascularization in patients with midportion Achilles tendinopathy” (van Sterkenburg et al. 2010).

Concerning the sclerosing polidocanol injection treatment method, it is of utmost importance to make sure that the original method description is properly followed. It is not easy to perform. Another drawback of the method is that you need to be two persons to perform the injections and evaluations. Preferably one with orthopedic expertise and one US technician or radiologist to enable a correct interpretation of the US/CD findings and to accurately managing to position the injection needle with US/CD-guidance. The learning curve is not very long from a technical point of view. How to judge and handle the clinical aspects though takes fairly long time and a large number of patients are needed.

It also seems to be of utmost importance to have strict indications for treatment. We have seen patients where “to get rid of the vessels” was the indication, patients where large volumes were injected (5–10 ml per treatment), and patients who were injected every second week. Under these circumstances it is not possible to compare the results with those of the original method. Moreover, this may give the technique “bad reputation”, since the results have been unsatisfactory due to not following the original description of how to perform sclerosing polidocanol injections. It is important to be aware of that polidocanol can spread into the soft tissue and communicant veins in the lower leg might be at injury risk.

There has to be a focus on future randomized controlled trials to further evaluate this method. Preferably using eccentric training in a control group since eccentric training today has the most evidence concerning non-operative treatments of Achilles tendinopathy (Wasielewski 2007). We find the injection treatment method of polidocanol very good, though, if performed correctly.

**Patellar tendinopathy**

Patellar tendinopathy/Jumper’s knee is the main focus of this thesis. Hitherto, there is no golden standard in the treatment of patients with jumper’s knee.
Surgical methods vary considerably between different clinics and scientific evidence is lacking for both non-operative and operative treatments (Khan et al. 1998; Cook et al. 2001a). During recent years a number of review articles concerning the injection treatment (van Ark et al. 2011; Wiley et al. 2013) and a critical review of treatment options (Gaida et al. 2011) as well as a review of randomized controlled trials (Nilsson-Helander et al. 2012) have been published, though. All these publications conclude that eccentric training still appears to be the treatment of choice for patients suffering from patellar tendinopathy. However, the type of exercise, the frequency, load and dosage still need to be further analyzed. Other treatment methods, such as surgical treatment, sclerosing injections and shockwave therapy also need to be further investigated before optimal recommendations can be made about the treatment of choice. This means that the situation today is almost the same as some ten years ago despite more knowledge about the basics in the painful tendon.

All existing treatment models are time consuming, often painful and leads to varying clinical results. Our focus was to find a treatment method addressing the new knowledge about the pathology in the proximal dorsal part of the chronic painful impairing tendinotic patellar tendon. A one stage procedure with a fast return to patellar loading activity was our goal.

We invented a new method, US/CD-guided arthroscopic shaving, and believed that with simultaneous US/CD there could be a more exact localization of the pain producing tissue. We believed that this new arthroscopic shaving with simultaneous guidance of US/CD could be an alternative to treat patellar tendinopathy (study II). The trauma to the Hoffa´s fat pad and the tendon would be minimized. Arthroscopy itself leads to great advantages. It is cost effective and easy to perform in local anesthesia. It permits an evaluation of the knee joint in an outstanding way. Another advantage of the intraarticular evaluation is the fact that MRI, which is costly and inferior to arthroscopy in diagnostic aspects concerning for example plicaes, cartilage injuries etc, might not be needed. Technically, our new surgical method was fairly easy to perform and the visibility was really good in the US monitor. The Doppler function could, of course, only be used intermittently, since it detects all movements – like the oscillation of the shaver. During the evaluation of the method we found good results in the pilot study and no adverse effects of the US/CD-guided arthroscopy (study III). We could let the patients go back to full tendon loading activity approximately 6-8 weeks after the procedure. On the negative side, you have to be prepared to be guided solely by the US once starting the shaving procedure, since there will be a bleeding in the joint obstructing the arthroscopic visibility. There is a need for an extra pair of hands, an assistant, handling the US probe.

Pilot studies has shown promising results of sclerosing injections (Alfredson
et al. 2005a; Hoksrud et al. 2006). In our study IV and V we wanted to compare the results of these two fairly new treatment methods. In study IV, as in study III, we were very strict about the clinical findings and symptoms as with the US/CD findings for inclusion. One big problem in research on PT/JK is the different nomenclature that is used in the literature. When giving the sclerosing injections we were as strict in indications as with the Achilles tendons. Only small volumes, a maximum of 2 ml per treatment session addressing the entrance of the transversal vessels into the tendon on the dorsal proximal part of the tendon were injected. In the pilot study mentioned above (Hoksrud et al. 2006), there was only 3-5 weeks between the treatments, which is not in accordance with the initial method described. We choose to follow the initial description with 6-8 weeks between treatment sessions. When using this treatment for patellar tendinosis, high volumes might lead to intraarticular deposition, causing synovitis and fibrosis. It also seems to be crucial to be very specific when it comes to the injection technique, while depositing injections into the IFP can cause intolerable accentuated pain (Bennell et al. 2004; Hodges et al. 2009). US/CD-guidance is a necessity. In study IV we found that both treatment with US/CD-guided sclerosing polidocanol injections and arthroscopic shaving showed good clinical results. Interestingly enough, in study V, the long-term follow-up, showed similarly good clinical results with both methods at endpoint. The only remaining difference between the two methods was the AP thickness of the tendon. The tendon was significantly thinner and sonographically “more normalised” in the surgical group.

Another interesting observation is the fact that the amount of increased blood flow was the first parameter to change in the surgical group. They also returned to full and painless activity fastest of the two groups. This fact among others in study V leaves a lot of questions unsolved. There are some indications that the structural changes and amount of neovascularization within the tendon tissue might correlate with clinical outcome of treatment. These findings, being contradictory to those of former research opens for a new thinking and a need for further investigations in this direction.

A recent study from Hoksrud et al. evaluating sclerosing treatment with polidocanol in 101 patients with patellar tendinopathy showed that only a few patients were cured, and the majority of patients still reported substantial pain and showed reduced function after a 24 month follow-up (Hoksrud et al. 2012). In our studies we did not objectively measure function though, but we measured return to painless activity. In their study, they treated the patients with intervals of 4-6 weeks and injected the vessels entering from the ventral side. One can speculate whether their result really is comparable with sclerosing injections targeting the vessels and pathology on the dorsal side of the tendon. They also state that about two thirds of the patients with jumper's knee can be expected
to have structural tendon changes with neovascularization, and that there was no relationship between changes in US characteristics and knee function after sclerosing treatment (Hoksrud et al. 2008). This enhances the importance of using the same nomenclature. The authors recruited patients among elite athletes with a clinical diagnosis of jumper's knee for this study, which may explain that one third of the patients did not have any detectable US changes in the patellar tendon. Patients were examined with US/CD at baseline. Patients with structural changes and neovascularization received sclerosing injections, the US/CD examinations were performed 12-15 months after the sclerosing treatment, which may be too early to detect the possible changes that we found in study V.

For chronic painful tendinotic patellar tendinopathy the one stage US-guided arthroscopic procedure seems to be a good alternative. It needs further studies for evaluation, of course. The arthroscopic procedure is a valuable option, despite the effectiveness shown with sclerosing injections in the study by Hoksrud et al (2011). One third of their patients chose to seek additional treatment, arthroscopic surgery during the 44-month follow-up period, though.

Sclerosing injection treatment might be an option, but it is important to keep in mind that it is a painful treatment method often taking a long time before satisfactory results are achieved. For chronic painful tendinotic patellar tendinopathy the one stage US-guided arthroscopic procedure therefore may be a better option.

**Gender and tendons**

In females the collagen synthesis rate is reported to be lower than in males (Miller et al. 2007). The synthesis of collagen type I also seems to be affected by meno-pausal hormone alterations with a decrease in collagen type I leading to less tensile strength (Moalli et al. 2004). After surgery females generally have a prolonged period of complications and recovery, compared to males undergoing the same surgical treatment (Maffulli et al. 2008). Interestingly in one study evaluating eccentric training in patients with midportion Achilles tendinosis, the females showed poorer results than the males (Fahlström et al. 2003). For the midportion Achilles tendinopathy it is nowadays discussed whether it is a part of some metabolic syndrome instead of being primarily an overuse injury. In patients with asymptomatic Achilles tendon pathology a difference in fat distribution was found between males and females. This recent cohort study reported that males had predominantly a central fat distribution and females a peripheral distribution of fat. These findings might point in a direction to a relation between tendon pathology and fat metabolism, or insulin resistance in males (Gaida et al. 2010).
US and Doppler changes in the tendon correlating to clinical findings and symptoms

Tendinotic tendons show a degeneration of the extracellular matrix (Riley 2005) with disordered arrangement of collagen fibers, increased vascularity (Khan et al. 1999). Changes in vascularity have been suggested to be involved in the development of patellar tendinosis (Khan et al. 1998). Structural abnormalities in patellar tendons seen in US can be detected in painless individuals in high risk populations. The presence of US changes can be three times higher than the presence of clinical symptoms. Even in athletes, not regularly physically active, asymptomatic controls, such structural changes were shown in 10% of all painless patellar tendons (Gisslen et al. 2005). In these controls, Doppler technique did not show an increase in vascularity (Gisslen et al. 2005). However, an increase in vascularity can be detected in asymptomatic individuals in high risk sports (Cook et al. 2005). Studies on patellar tendons using US/CD/PD have demonstrated an increased vascularity, interpreted as neovascularization, within and dorsal to the area with structural tendinotic changes (Cook et al. 2004b; Alfredson et al. 2005; Gisslen et al. 2005). An association has been noted between the degree of such pathological vascularity and the level of pain in patellar tendinosis (Cook et al. 2005). In cases of clinically diagnosed “Jumper’s knee” it seems that this increased vascularity in CD is found in the majority of individuals (Gisslen et al. 2005; Hoksrud et al. 2008). The link between pain symptoms and increased blood flow has not yet been found. The vessels, which are considered neovessels, are by some authors described to be randomly oriented (Khan et al. 1999), while others have noted an increase also in the number of vessels aligned in parallel with the tendon fibers (Maffulli et al. 2000). These contradictory findings concerning the blood vessels are highly discussable. Based on clinical experience I would like to suggest that the transverse vessels could have a correlation to the severity of pain, function and the neurogenic component, whilst the vessels parallel to the tendon fibers are correlated with stiffness being a component of a healing process.

The importance of blood flow in terms of pain is puzzling. However, the treatment methods in this thesis only target the area with increased blood flow. The sclerosing injections and the US-guided arthroscopic shaving immediately reduce the increased blood flow (Alfredson et al. 2005a; Hoksrud et al. 2006) and the effect of treatment is immediate concerning the CD findings. When you study the treated tendon, directly after treatment, after some time you can often visualize formerly not detectable vessels with CD, intratendinously in a longitudinal direction in the full thickness of the tendon. There is sparse information in all studies concerning tendon pathology and about the actual CD findings, mostly only the existence of blood flow or not, is discussed. It could be proposed that there is a need for the quality of blood flow (in terms of direction,
extent, severity and entrance site of the vessels) to be described in studies when treating tendinotic tendinopathy.

To our knowledge there is only one study suggesting that increased blood flow after treatment could indicate a healing response (Alfredson et al. 2006) and. Furthermore, there is a pilot study on patients with chronic midportion Achilles tendinopathy. It shows that patients with good clinical results after 12 weeks of eccentric training show a more normalized tendon and decreased blood flow in US/CD than before treatment (Öhberg at al.2004). The results in study V in this thesis suggest that further research in this direction could lead us forward to a better understanding of the treatment responses from a clinical point of view.

The patients often complain about postfunctional and morning stiffness, also sharp intolerable impairing pain during activity, and sometimes also sharp pain at rest. This is a characteristic sign of chronic Achilles tendinopathy and “Jumper’s knee”. It is suggested, the more pain during activity and stiffness, the poorer stage of the tendon condition (Cook et al. 2002, Peers et al. 2003). This is also discussable, since sometimes increased stiffness is seen when the sharp pain is decreased. When sharp pain lessens in frequency and stiffness increases one could speculate whether this could be a sign of a healing process. I would like to separate sharp pain from stiffness in future studies, since in my experience the stiffness appears when the tendon is filled with longitudinal vessels in its whole depth and the tendon is wider in its whole length.

Sonographically, the structure normally looks less pathological at this stage of symptoms. If the treatment of “tendon pain” in the tendinotic tendon is successful, the tendon seems to normalize in both width and structure if the treatment is strictly extratendinous. If the treatment is intratendinous, maybe the tendon never normalizes. A long-term follow-up study revealed persistent structural
Some final clinical reflections

In midportion Achilles tendinopathy US/CD-guided sclerosing injections with polidocanol seems to be an option if non-operative treatment fails. Performing sclerosing injections according to the initial method described is, however, crucial. “Too much too soon” is not the idea. Still, eccentric training should be tried as a primary intervention according to the literature. If failure after 3-4 months and US/CD findings indicate a picture of ventral hypoechic areas and transversal vessels corresponding with the tenderness in the Achilles tendon, and if the patient still experience sharp pain during activity or at rest sclerosing injections could be tried. However, let the tendon get 3-4 months between the treatment sessions. If there is a lack of sharp pain, though, and an increase in stiffness, despite pathological US/CD findings, be patient, the tendon will probably heal. We suggest not to mix different treatments.

In chronic painful tendinotic patellar tendinopathy I would suggest an US/CD examination in order to confirm the diagnosis. Start the treatment with eccentric training including a decline board, and take the patient away from their sport for 6-8 weeks. Make a follow-up with an US/CD examination after 8-10 weeks. If non-operative treatment fails, if there is a lack of a “healing response” according to US/CD, and if there is still a sharp pain during activity I would suggest the new US-guided arthroscopic shaving approach.

In our larger material it is shown that two thirds of the patients have associated pathology intra articularly not visible on MRI (unpublished data), which makes the arthroscopy even more appealing. Not only can you treat the tendon, you can also get a proper view of the intra articular state.

Both treatment with US/CD-guided sclerosing polidocanol injections and US/CD-guided arthroscopic shaving have shown good clinical results in patients with chronic painful patellar tendinopathy. In athletes that are during their competitive season injection treatment could be an option to reduce pain.

If proceeding with surgical treatment, be aware not to resect too much of the Hoffa’s fat pad, since ventral impingement should be avoided. The IFP is a very potent structure. For example, IFP pain has been experimentally modelled with injection of hypertonic saline into the fat pad. The induced pain peaked 2–3 minutes after injection at an average intensity between 5.5 and 5.8 out of 10, and gradually declined over 15 minutes (Bennell et al. 2004; Hodges et al. 2009). Reported pain was not only inferior patella but also deep and retropatellar with
some reporting medial thigh pain. During the period of pain, the coordination of the quadriceps was altered with a delayed onset of vastus medialis obliquus (VMO) activity (Hodges et al. 2009). The EMG activity of both the VMO and the vastus lateralis muscles decreased in magnitude. This may support the fact that patients experiencing long-term anterior knee pain are weak and slow in their quadriceps muscle, especially VMO. Even if we did not have a specific rehabilitation protocol after surgery this is recommendable and should be mandatory when treating patients and not performing comparing studies. Most of the patients are very weak in their quadriceps and show impaired knee joint control. Full patellar tendon loading seems to be alright 6-8 weeks after surgical intervention concerning the patellar tendon. In order to perform in their sports, though, muscular strength and muscular control have to be in focus after surgery, which can be time consuming.

Studies concerning rehabilitation protocols, as a complement to the US-guided shaving procedure, have to be performed.

**Strengths and limitations**

One major strength in these studies is the fact that the same US technician has conducted all US/CD examinations. Studies using US, in the field of tendon research, often refers to tendon thickness, structural changes and amount of visible blood flow. However, the reliability of these measurements and the quality of the evaluations are not always reported. Intraobserver reliability have been addressed in our studies. We consistently have used the Öhberg score to describe the US/CD findings and also all images have been documented in the patients regular chart in our journal system. Furthermore, the same orthopaedic surgeon (LW) has seen all the patients at inclusion, operated on and injected all the patients together with the same US technician. The follow-ups have been carried out independently of the orthopaedic surgeon.

Another strength is the fact that we were very strict to follow our inclusion criterias and definitions of pathological findings. We also followed the initial description of how to perform the sclerosing injections to the point.

Developing a totally new treatment method, US/CD guided knee arthroscopy I believe also can be considered as a strength in this thesis.

The “cross-over design” in study I and IV may be seen as study limitations. If these studies should be repeated today I would probably avoid the “cross-over design”. However, from an ethical point of view it may be doubtful if it would be fair to the patients, especially when it comes to study IV, where one treatment seemed much more superior in time and pain during treatment. Therefore, it may be more appropriate to have the patients in focus. In other studies, patients with patellar tendinopathy receiving sclerosing injections have sought other clinics for
an arthroscopic intervention themselves before a final follow-up if the injection treatment fails. By the “cross-over design” in study IV we were able to “keep the patients under our wings” and prospectively follow them over a longer period of time.

Another study limitation could be that we did not use a specific activity or functional score such as the VISA-A or VISA-P score (Victorian Institute of Sport Assessment), for instance. For the Achilles tendons in study I our intention was to use the VISA-A score, but the function of the patients were so poor that they did not understand the questionnaire and most of them refrained from filling it in. This was the reason for not using the VISA-A score. Instead, we focused on evaluating Achilles tendon pain during each patient’s specific recreational or sport activity as well as at rest. It is likely to believe that the use of VAS for pain ratings and patient reports about how satisfied they are with their treatment may be appropriate tools for evaluating clinical outcome of the injection treatment with polidocanol in study I.

In terms of the patients with PT/JK, it was a mistake not to use the VISA-P score. It would have been good to be able to easier compare the results of the treatments to other studies. However, also for this group of patients we believe that evaluating patellar tendon pain during their chosen specific recreational or sport activity together with satisfaction with the treatment results may be appropriate tools when evaluating the clinical outcome of the treatments.

A possible limitation may be that the sample sizes of our groups are fairly small. However, when calculating the power of the studies we found 20 patients to be enough in each treatment group (study I and IV). In the pilot study, where our new treatment method, US/CD-guided arthroscopy, was evaluated we limited the number of patients, since we did not find it ethically defendable to operate on too many cases. We did not know if the tendon or the operated knee would react negatively on the load that we allowed very soon after the surgical procedure.

In study I, the follow-up time differs a lot in terms of range, mean 14 months (range 2-35 months). Some of the patients, who only needed one injection treatment, were very early back to full tendon loading activity without pain. They did not show up for the follow-ups, since they were satisfied. They were all offered visit times, but when calling to decline a visit they reported via telephone that they were painless.
CONCLUSIONS

VIII
Conclusions

For clinical use, we recommend polidocanol 5 mg/ml for US-guided injection treatment of chronic painful midportion Achilles tendinopathy, since there was no difference in results when using polidocanol 10 mg/ml. It is important to strictly follow the initial method description. Small volumes can be used.

We find the newly invented surgical method, US/CD-guided arthroscopic shaving, practical and reliable for treatment of proximal patellar tendinopathy (PT)/jumper´s knee (JK). There is a better precision and less tissue trauma compared to using arthroscopic shaving alone.

It seems that US-guided arthroscopic shaving of the region with high blood flow and nerves on the dorsal side of the tendon, can reduce the tendon pain during tendon loading activity and allow for a majority of patients with PT/JK a relatively quick (6-8 weeks) return to patellar tendon loading activity.

Treatment with US/CD-guided sclerosing polidocanol injections and US/CD-guided arthroscopic shaving show good clinical results for treatment of patients with PT/JK. Patients treated with arthroscopic shaving had a faster return to activity, significantly less pain and they were more satisfied with the treatment result.

In a long term follow-up both methods showed an improvement of the tendon structure in greyscale US. A decreased blood flow was seen with CD, in the region with tendon changes. There was a significant pain reduction during activity with both treatments. In the group treated with US/CD-guided sclerosing injections the clinical results had improved to the same level as the early results in the arthroscopic shaving group. The only remaining difference between the two methods concerned the anteroposterior (AP) thickness of the tendon. The AP thickness was significantly reduced and the tendon structure was improved in the US-guided arthroscopic shaving group, but not in the group treated with US/CD-guided sclerosing injections.

We recommend the newly invented method, US/CD-guided arthroscopic shaving method for patients with PT/JK because it allows for a fast return to sports, and it’s positive effects on tendon thickness and structure in the longer perspective.
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References


Emerson C, Morrissey D, Perry M et al. (2010). Ultrasonographically detected changes in Achilles tendons and self reported symptoms in elite gymnasts compared with controls–An observational study. Man Ther 15:37-42


Moore KL, Dalley AF (1999). Clinically oriented anatomy. 4th ed. Lippincott Williams & Wilkins, Baltimore, MD, USA


